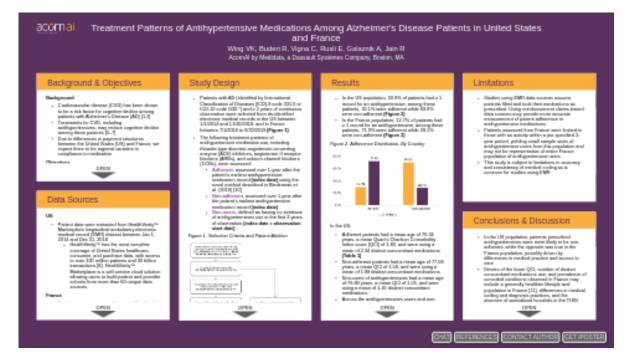# Treatment Patterns of Antihypertensive Medications Among Alzheimer's Disease Patients in United States and France

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PRESENTED AT:

BACKGROUND & OBJECTIVES

Background

- Cardiovascular disease (CVD) has been shown to be a risk factor for cognitive decline among patients with Alzheimer's Disease (AD) [1,2]

- Treatments for CVD, including antihypertensives, may reduce cognitive decline among these patients [3–7]

- Due to differences in payment structures between the United States (US) and France, we expect there to be regional variation in compliance to medication

Objectives

- The objective of this study was to examine treatment patterns of antihypertensive medication use and clinical characteristics among patients with AD in the US and France

DATA SOURCES

US

- Patient data were extracted from HealthVerity™ Marketplace longitudinal ambulatory electronic medical record (EMR) dataset between Jan 1, 2014 and Dec 31, 2018
  - HealthVerity™ has the most complete coverage of United States healthcare, consumer, and purchase data, with access to over 330 million patients and 30 billion transactions [8]. HealthVerity™ Marketplace is a self-service cloud solution allowing users to build patient and provider cohorts from more than 60 unique data sources.
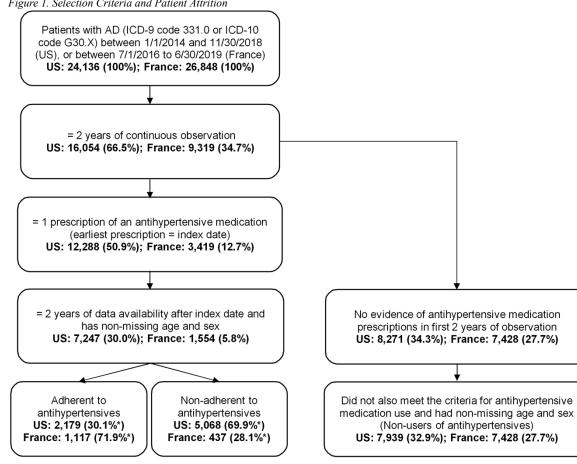
France

- Patient data was extracted from the The Health Improvement Network® (THIN®) France database between July 1, 2016 and June 30, 2019
  - THIN® is an anonymized EMR powered by Cegedim Health Data®–division. THIN® is a large European database, collecting data at the physicians' level.

All data were converted to the Observational Medical Outcomes Partnership (OMOP) Common Data Model, version 5 [9].

Analyses were conducted in Aginity Workbench for Redshift v4.9.3.2873 and R v1.1.456.

STUDY DESIGN

- Patients with AD (identified by International Classification of Diseases [ICD]-9 code 331.0 or ICD-10 code G30.*) and ≥ 2 years of continuous observation were selected from de-identified electronic medical records in the US between 1/1/2014 and 11/30/2018, and in France between 7/1/2016 to 6/30/2019 **(Figure 1)**

- The following treatment patterns of antihypertensive medication use, including thiazide-type diuretics angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and calcium channel blockers (CCBs), were assessed:
  - **Adherent**, assessed over 1-year after the patient's earliest antihypertensive medication record **(index date)** using the novel method described in Biederman et al. (2019) [10]
  - **Non-adherent**, assessed over 1-year after the patient's earliest antihypertensive medication record **(index date)**
  - **Non-users**, defined as having no evidence of antihypertensives use in the first 2 years of observation **(index date = observation start date)**
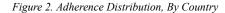
Figure 1. Selection Criteria and Patient Attrition

Patients with AD (ICD-9 code 331.0 or ICD-10 code G30.X) between 1/1/2014 and 11/30/2018 (US), or between 7/1/2016 to 6/30/2019 (France)
US: 24,136 (100%); France: 26,848 (100%)

= 2 years of continuous observation
US: 16,054 (66.5%); France: 9,319 (34.7%)

= 1 prescription of an antihypertensive medication (earliest prescription = index date)
US: 12,288 (50.9%); France: 3,419 (12.7%)

= 2 years of data availability after index date and has non-missing age and sex
US: 7,247 (30.0%); France: 1,554 (5.8%)

No evidence of antihypertensive medication prescriptions in first 2 years of observation
US: 8,271 (34.3%); France: 7,428 (27.7%)

Adherent to antihypertensives
US: 2,179 (30.1%*)
France: 1,117 (71.9%*)

Non-adherent to antihypertensives
US: 5,068 (69.9%*)
France: 437 (28.1%*)

Did not also meet the criteria for antihypertensive medication use and had non-missing age and sex (Non-users of antihypertensives)
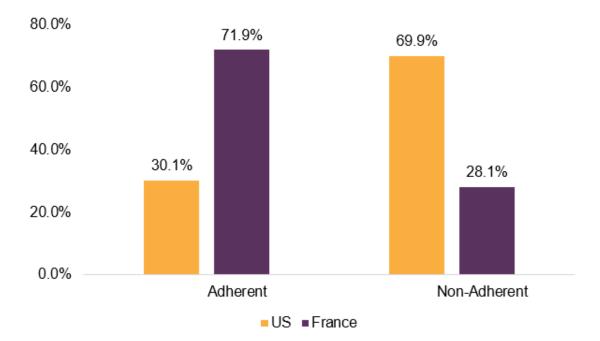**US: 7,939 (32.9%); France: 7,428 (27.7%)**

*Out of patients with a prescription, = 2 years of data availability after index date, and non-missing age and sex

- Demographic and clinical characteristics (listed in **Table 1**) were identified using ICD-9-CM, ICD-10-CM, Anatomical Therapeutic Chemical (ATC), and RxNorm codes for each antihypertensive use category and were assessed during the 1st year post-index date

- Patient characteristics of antihypertensive medication users were compared to non-users using chi-squared (for categorical variables) and Student's t tests (for continuous variables)

RESULTS

- In the US population, 50.9% of patients had ≥ 1 record for an antihypertensive; among these patients, 30.1% were adherent while 69.9% were non-adherent **(Figure 2)**

- In the France population, 12.7% of patients had ≥ 1 record for an antihypertensive; among these patients, 71.9% were adherent while 28.1% were non-adherent **(Figure 2)**

Figure 2. Adherence Distribution, By Country

In the US,

- Adherent patients had a mean age of 76.34 years, a mean Quan's Charlson Comorbidity Index score (QCI) of 1.83, and were using a mean of 2.34 distinct concomitant medications **(Table 1)**

- Non-adherent patients had a mean age of 77.08 years, a mean QCI of 1.58, and were using a mean of 1.99 distinct concomitant medications

- Non-users of antihypertensives had a mean age of 76.89 years, a mean QCI of 1.05, and were using a mean of 1.45 distinct concomitant medications

- Across the antihypertensives users and non-users,
  - The top three most common comorbid conditions assessed were depression (adherent: 23.9%; non-adherent: 19.1%; non-users: 19.3%), coronary artery disease (adherent: 18.5%; non-adherent: 15.1%; non-users: 9.6%), and hypothyroidism (adherent: 17.0%; non-adherent: 14.0%; non-users: 14.0%)
  - Approximately one-third of patients were male (adherent: 34.5%; non-adherent: 37.1%; non-users: 36.2%)

- Among antihypertensives users, in both adherent and non-adherent patients, ACE inhibitors were the most commonly prescribed antihypertensives, followed by thiazide diuretics, ARBs, and CCBs

In France,

- Adherent patients had a mean age of 76.05 years, a mean QCI of 1.12, and were using a mean of 1.84 distinct concomitant medications **(Table 1)**

- Non-adherent patients had a mean age of 75.89 years, a mean QCI of 1.03, and were using a mean of 1.54 distinct concomitant medications

- Non-users of antihypertensives had a mean age of 63.76 years, a mean QCI of 0.64, and were using a mean of 0.86 distinct concomitant medications

- Across the antihypertensives users and non-users,
  - The top three most common comorbid conditions assessed were mild cognitive impairment (100% of all patients), depression (adherent: 19.7%; non-adherent: 11.9%; non-users: 10.5%), and hypothyroidism (adherent: 9.7%; non-adherent: 8.9%; non-users: 5.9%)

- Approximately 40% of patients were male (adherent: 42.7%; non-adherent: 43.9%; non-users: 35.5%)

- Among antihypertensives users, in both adherent and non-adherent patients, ARBs were the most commonly prescribed antihypertensives, followed by ACE inhibitors, CCBs, and thiazide diuretics

Table 1. Demographic and Clinical Characteristics By Antihypertensive Use and Country

	US						France					
	Adherent		Non-Adherent		Non-Users		Adherent		Non-Adherent		Non-Users	
	N=	2,179	N=	5,068	N=	7,939	N=	1,117	N=	437	N=	7,428
Patient Characteristic	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD
Demographics												
Age (mean, SD)	76.34[4]	7.96	77.08	8.04	76.89	8.89	76.05[3]	10.64	75.89[3]	11.33	63.76	22.23
Male (n, %)	752	34.5%	1,878	37.1%	2,877	36.2%	477[3]	42.7%	192[3]	43.9%	2,635	35.5%
Clinical Characteristic												
Quan's Charlson Comorbidity												
Index score[1] (mean, SD)	1.83[3]	1.92	1.58[3]	1.86	1.05	1.61	1.12[3]	1.07	1.03[3]	1.02	0.64	0.78
Number of distinct concomitant												
medications[2] (mean, SD)	2.34[3]	1.69	1.99[3]	1.58	1.45	1.54	1.84[3]	1.35	1.54[3]	1.33	0.86	1.14
Atrial fibrillation (n, %)	349[3]	16.0%	546*	10.8%	665	8.4%	3	0.3%	0	0.0%	8	0.1%
Bipolar disorder (n, %)	19	0.9%	43	0.8%	93	1.2%	1	0.1%	1	0.2%	22	0.3%
Coronary artery disease (n, %)	403[3]	18.5%	764[3]	15.1%	762	9.6%	79[3]	7.1%	30[3]	6.9%	116	1.6%
Depression (n, %)	520[3]	23.9%	966	19.1%	1529	19.3%	220[3]	19.7%	52	11.9%	779	10.5%
Epilepsy (n, %)	105	4.8%	177[5]	3.5%	350	4.4%	12	1.1%	6	1.4%	91	1.2%
Glaucoma (n, %)	45[4]	2.1%	87[5]	1.7%	101	1.3%	7[5]	0.6%	4[4]	0.9%	13	0.2%
Hearing loss (n, %)	106	4.9%	252	5.0%	340	4.3%	14	1.3%	4	0.9%	51	0.7%
Hyperthyroidism (n, %)	17[5]	0.8%	27	0.5%	32	0.4%	6	0.5%	4	0.9%	55	0.7%
Hypothyroidism (n, %)	370[4]	17.0%	707	14.0%	1113	14.0%	108[3]	9.7%	39[5]	8.9%	435	5.9%
Mild cognitive impairment (n, %)	95	4.4%	223	4.4%	317	4.0%	1,117	100.0%	437	100.0%	7,428	100.0%
Osteoporosis (n, %)	154[5]	7.1%	326[3]	6.4%	690	8.7%	23[3]	2.1%	6	1.4%	43	0.6%
Parkinson's disease (n, %)	41	1.9%	102[5]	2.0%	205	2.6%	17	1.5%	8	1.8%	112	1.5%
Pneumonia (n, %)	56[4]	2.6%	101	2.0%	133	1.7%	19[5]	1.7%	4	0.9%	65	0.9%
Schizophrenia (n, %)	8	0.4%	22[5]	0.4%	61	0.8%	0	0.0%	0	0.0%	3	0.0%
Stroke/Transient ischemic attack												
(n, %)	156[3]	7.2%	311[3]	6.1%	292	3.7%	57[3]	5.1%	19[3]	4.3%	110	1.5%
Antihypertensive Medication Use												
Thiazide diuretics	965	44.3%	1694	33.4%			101	9.0%	26	6.0%		
ARBs	792	36.4%	1533	30.3%			525	47.0%	191	43.7%		
CCBs	363	16.7%	545	10.8%			187	16.7%	67	15.3%		
ACE Inhibitors	1,292	59.3%	2724	53.8%			471	42.2%	177	40.5%		

[1]Quan H, Sundararajan V, Halfon P, et al. Coding Algorithms for Defining Comorbidities in ICD-9-CM and ICD-10 Administrative Data: Medical Care. 2005;43(11):1130-1139.
[2]Included treatment agents from the following medication classes: Alzheimer's medications, antiplatelets, statins, antipsychotics, anxiolytics, and antidepressants
[3]p<0.001 when compared to no antihypertensive use
[4]p<0.01 when compared to no antihypertensive use
[5]p<0.05 when compared to no antihypertensive use

Comparing the US and France,

- Antihypertensives non-users were over 10 years younger in France compared to in the US

- QCI scores and number of distinct concomitant medications were lower across the antihypertensives users and non-users in France compared to in the US

- The prevalence of comorbidities were lower in France in all conditions (except mild cognitive impairment) and across the antihypertensives users and non-users compared to in the US
    - Notably, atrial fibrillation was observed in 8.4% to 16.0% of patients in the US while between 0.1% and 0.3% were observed in France
    - Mild cognitive impairment was observed in 100% of all patients in France, while it was observed in 4.0% to 4.4% of patients in the US

- Choice of antihypertensives prescribed by providers differed between the two countries; thiazide diuretics were the least prescribed in France (9.0% and 6.0%) while being the second most commonly prescribed in the US (44.3% and 33.4%), and ACE inhibitors were the most commonly prescribed in the US (59.3% and 53.8%) while ARBs were the most prescribed in France (47.0% and 43.7%)

LIMITATIONS

- Studies using EMR data sources assume patients filled and took their medications as prescribed. Using reimbursement claims-based data sources may provide more accurate measurement of patient adherence to antihypertensive medications

- Patients assessed from France were limited to those with an activity within a pre-specified 3-year period, yielding small sample sizes of antihypertensive users from this population and may not be representative of entire France population of antihypertensive users

- This study is subject to limitations in accuracy and consistency of medical coding as is common for studies using EMR

CONCLUSIONS & DISCUSSION

- In the US population, patients prescribed antihypertensives were more likely to be non-adherent, while the opposite was true in the France population, possibly driven by differences in medical practice and access to care

- Drivers of the lower QCI, number of distinct concomitant medications use, and prevalence of comorbid conditions observed in France may include a generally healthier lifestyle and population in France [11], differences in medical coding and diagnosis practices, and the absence of specialized hospitals in the THIN network; these may also explain the large differences observed in the prevalence of atrial fibrillation and mild cognitive impairment between the two countries

- Differences were observed in the choice of antihypertensive medications prescribed to patients, suggesting clinical guidelines for antihypertensive treatment may differ between the two countries

- Further research is needed to identify modifiable characteristics associated with non-adherence of antihypertensives in patients with AD in these countries

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