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Persistence and Adherence to Nucleos(t)ide Analog Treatment for Chronic Hepatitis B

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Introduction

- Antiviral drug resistance is a major barrier to success of nucleos(t)ide analog (NUC) treatment of chronic hepatitis B (CHB)
- Medication persistence and adherence are important in preventing drug resistance
- Pharmacy refill data are one of several methods to assess adherence to medications

Objective

- Determine the persistence rates and the adherence rates to NUC therapy among patients with CHB who were receiving lamivudine (LAM), adefovir dipivoxil (ADV), or entecavir (ETV)
- Determine the factors associated with persistence and adherence

Methods

- Analysis of pharmacy claims data of two cohorts of US CHB patients receiving LAM, ADV, or ETV in January 2007 and January 2008
  - Refill data of each cohort were collected monthly, from January-December of each year
  - Demographic and sample characteristics data only available for the 2008 cohort
  - Data were provided by Wolters Kluwer Pharma Solutions, a US pharmaceutical data provider
- Data were analyzed from 'new' and 'existing' patients
  - New patients: those who had no pharmacy claim for LAM, ADV, or ETV 18 months prior to enrollment
  - Existing patients: those who had pharmacy claims for at least one of these drugs within 18 months prior to enrollment
- Persistence was defined as continuing acquisition of the medication (by pharmacy refill data) during a 12-month period
- Adherence was defined as the percent of days in which patients had medication during the period in which the medication was prescribed
  - Good adherence was arbitrarily defined as an adherence rate ≥ 91%
- Statistical Analyses
  - Student t test to compare continuous variables and Chi square test to compare categorical variables
  - Univariate logistic regression to determine the factors associated with good adherence in 2008 cohort, variables analyzed included age, gender, type of medical insurance, type of medication, and new vs. existing patients
  - Variables with p value < 0.1 on univariate analysis were further analyzed by multivariate logistic regression to determine the independent predictors of good adherence

Results

- **Data were available for 7,784 CHB patients from US**
  - 2007: 3,695 patients
  - 2008: 4,089 patients
- **Persistence**
  - The persistence rate of patients in the combined 2007 and 2008 cohorts was 85.5 ± 3.1%
  - Existing patients had higher persistence rates than new patients
  - Persistence rates decreased during the course of the year, with the most rapid decrease between month 3 and 6
- **Adherence**
  - Overall adherence rate for the combined 2007 and 2008 cohorts was 86.7 ± 18.9%
  - Existing patients had higher adherence rate than new patients (86.9 ± 18.7% vs. 84.1 ± 21.8%, p=0.02)
  - Factors associated with good adherence (adherence rate ≥ 91%) for the 2008 cohort
    - Existing patients vs. new patients, p=0.02
    - Patients older than 45 years, p=0.001
   - Receipt of ADV or ETV (vs. LAM), p<0.001

Table 1. Characteristics of US Patients Receiving NUC Treatments in January 2007 and January 2008

	LAM	ADV	ETV	All	p value
2007 & 2008 Cohort					
Patients, n (%)	1649 (21.2)	3976 (51.1)	2159 (27.7)	7784	
New Patients	77 (4.7)	192 (4.8)	158 (7.3)	427 (5.5)	<0.001
Existing Patients	1572 (95.3)	3784 (95.2)	2001 (92.7)	7357 (94.5)	
2007 Cohort					
Patients, n (%)	858 (23.2)	1994 (54.0)	843 (22.8)	3695	
New Patients	42 (4.9)	100 (5.0)	63 (7.5)	205 (5.5)	0.02
Existing Patients	816 (95.1)	1894 (95.0)	780 (92.5)	3490 (94.5)	
2008 Cohort					
Patients, n (%)	791 (19.3)	1982 (48.5)	1316 (32.2)	4089	
New Patients	35 (4.4)	92 (4.6)	95 (7.2)	222 (5.4)	0.002
Existing Patients	756 (95.6)	1890 (95.4)	1221 (92.8)	3867 (94.6)	

Table 2. Characteristics of US Patients in the 2008 Cohort

	LAM	ADV	ETV	All	p value
Patients, n (%)	791 (19.3)	1982 (48.5)	1316 (32.2)	4,089	
New Patients	35 (4.4)	92 (4.6)	95 (7.2)	222 (5.4)	0.002
Existing Patients	756 (95.6)	1890 (95.4)	1221 (92.8)	3867 (94.6)	
Gender, n (%)					
Male	515 (65.1)	1223 (61.7)	842 (64.0)	2580 (63.1)	0.27
Female	263 (33.2)	710 (35.8)	449 (34.1)	1422 (34.8)	
Unknown	13 (1.7)	49 (2.5)	25 (1.9)	87 (2.1)	
Age Groups, n (%)					
<18 years	21 (2.7)	9 (0.5)	5 (0.4)	35 (0.9)	<0.001
18-45 years	183 (23.1)	632 (31.9)	453 (34.4)	1268 (31.0)	
>45 years	576 (72.8)	1298 (65.5)	837 (63.6)	2711 (66.3)	
Unknown	11 (1.4)	43 (2.2)	21 (1.6)	75 (1.8)	
Type of Insurance, n (%)					
Commercial	515 (65.1)	1463 (73.8)	984 (74.8)	2962 (72.4)	<0.001
Medicare	173 (21.9)	326 (16.4)	210 (16.0)	709 (17.3)	
Medicaid	91 (11.5)	168 (8.5)	102 (7.8)	361 (8.8)	
All Other Payors	12 (1.5)	25 (1.3)	20 (1.5)	57 (1.4)	

Figure 1. Persistence to HBV Medications in The Combined 2007 and 2008 US Cohorts
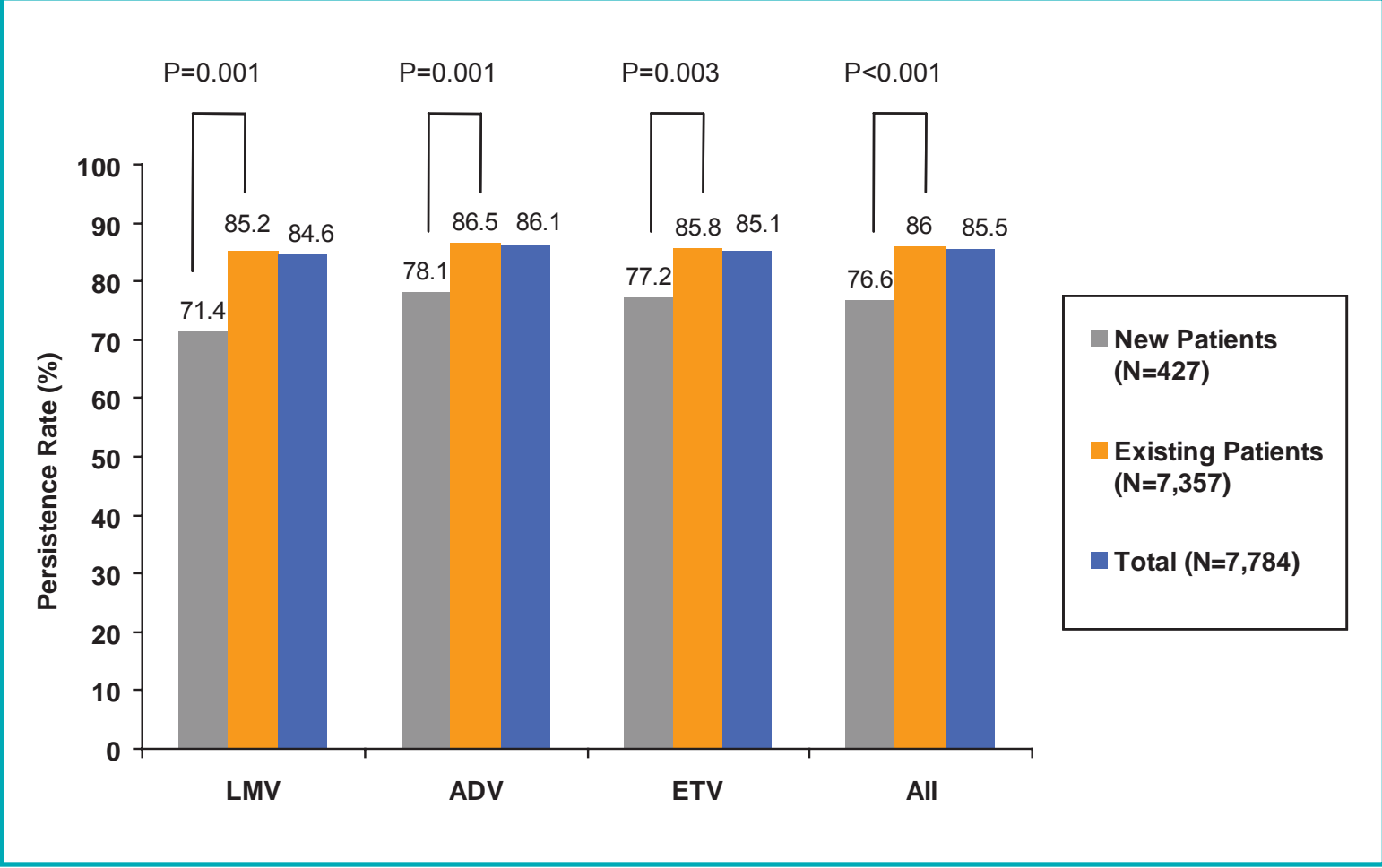
Results (cont'd)

Figure 2. Persistence to HBV Medications in The Combined 2007 and 2008 US Cohorts
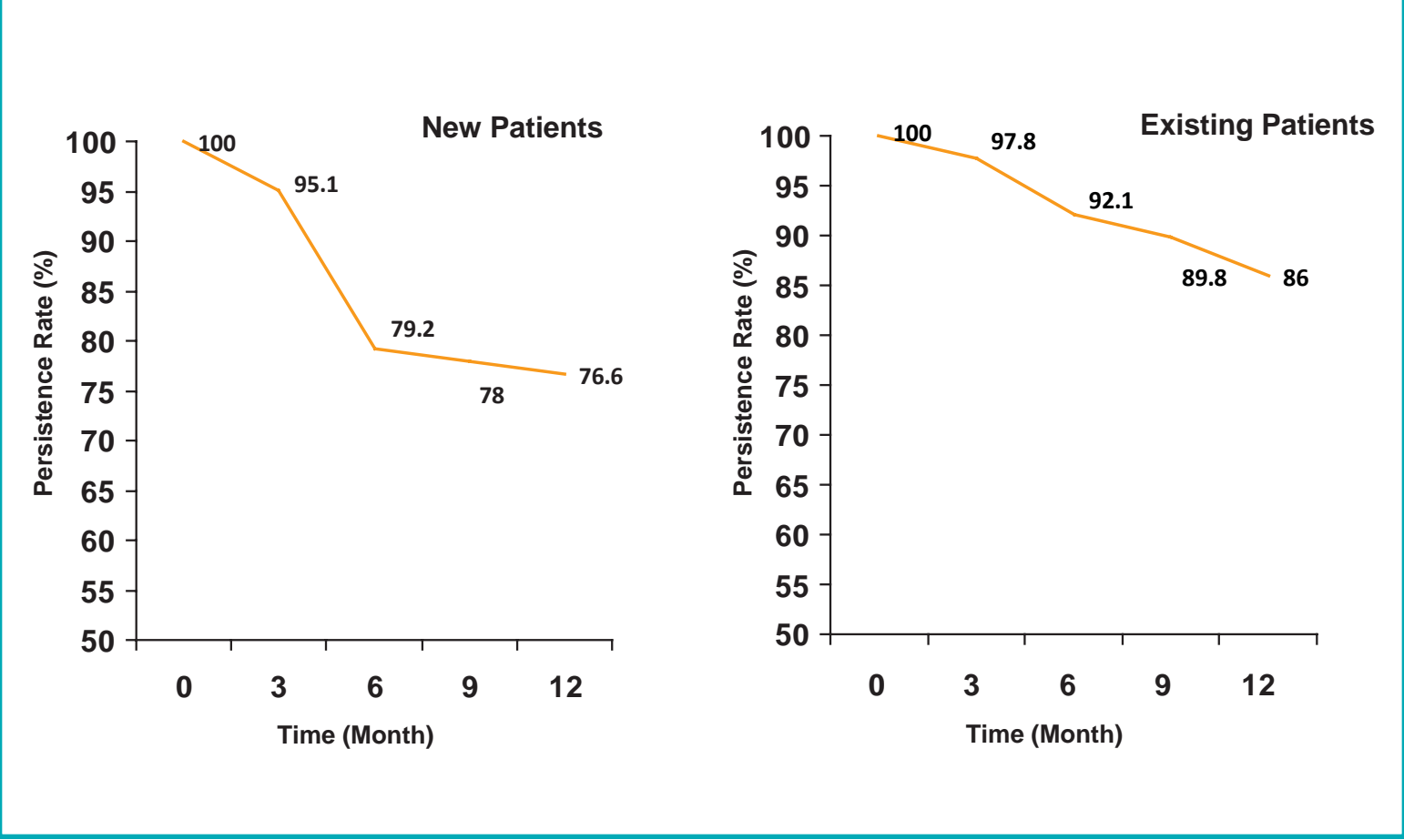

Figure 3. Adherence to HBV Medications in The Combined 2007 and 2008 US Cohorts
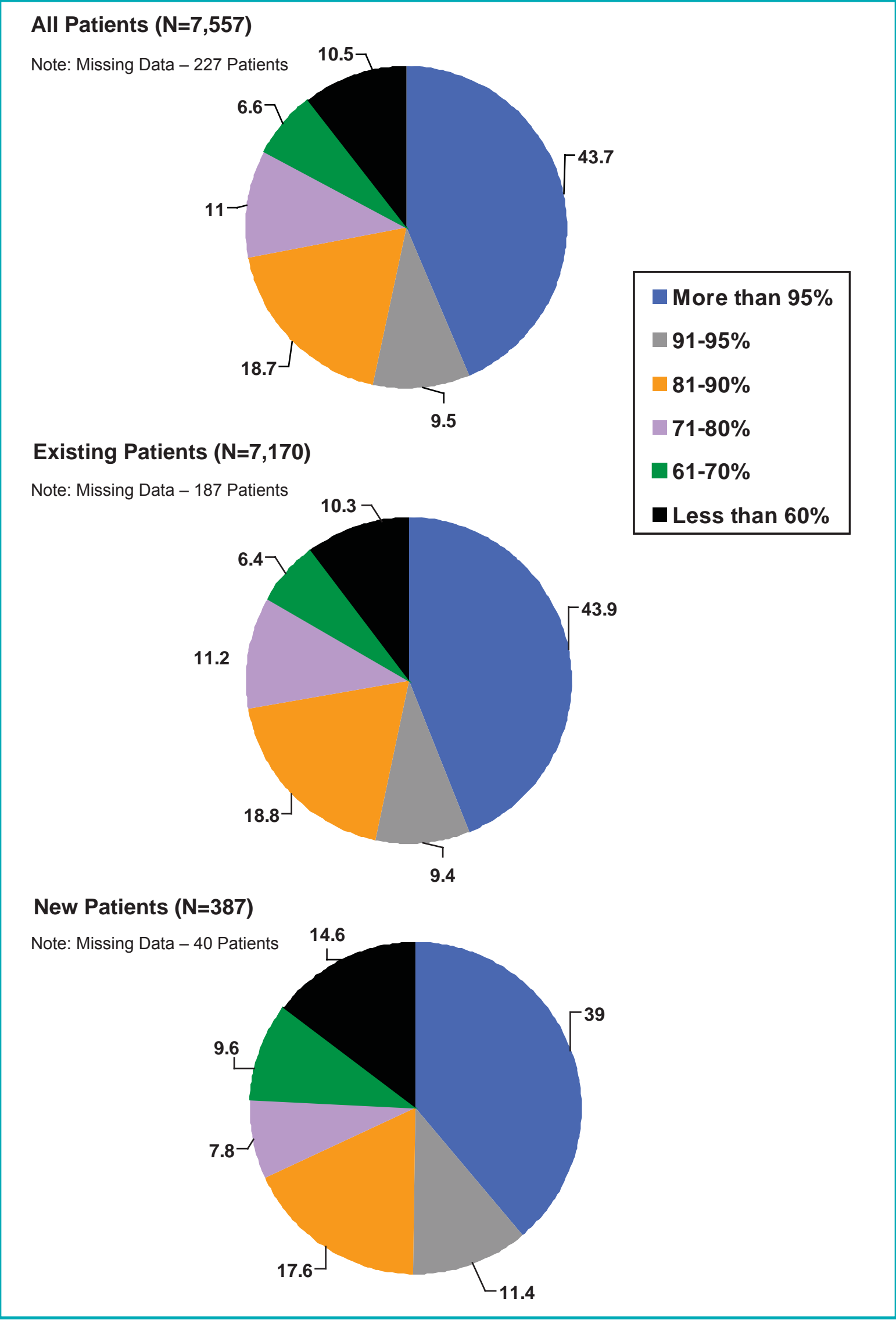

All Patients (N=7,557)
Note: Missing Data – 227 Patients

Existing Patients (N=7,170)
Note: Missing Data – 187 Patients

New Patients (N=387)
Note: Missing Data – 40 Patients

Legend: More than 95%, 91-95%, 81-90%, 71-80%, 61-70%, Less than 60%

Table 3. Factors Associated with Adherence Rate More than 91% in the US Cohort

		Univariate Analysis	Multivariate Analysis	
		p value	Odds Ratio (95%CI)	p value
Age	Age <45 years	0.002	0.78 (0.68-0.90)	0.001
	Age >45 years		reference	
Type of Medication	LAM	<0.001	0.61 (0.51-0.73)	<0.001
	ADV		reference	
	ETV		1.01 (0.87-1.16)	
New/Existing Patients	New Patients	0.04	0.71 (0.53-0.94)	0.02
	Existing Patients		reference	

Conclusions

- **Persistence rate of all US patients to nucleos(t)ide analog therapy for CHB was high (85.5%) particularly in existing patients**
- **Persistence rates decreased rapidly during the first 6 months especially for new patients**
- **Adherence rate was high (86.7 ± 18.9%) particularly in existing patients**
- **New patients, those receiving LAM, and adults less than 45 years were less likely to maintain good adherence**
- **Health education for new patients and young patients (age less than 45 years) may improve persistence and adherence to HBV medications**
- **The impact of persistence and adherence on virologic response and antiviral resistance should be studied**

Acknowledgement