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Introduction

- A plant-derived highly purified pharmaceutical formulation of cannabidiol (CBD; Epidiolex®) is approved in the US for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients aged ≥1 year¹
 - The recommended maintenance dosage of CBD is up to 10-20 mg/kg/day for LGS and DS and 25 mg/kg/day for TSC. The label recommends a starting dose of 5 mg/kg/day, which can be increased to 10 mg/kg/day after 1 week and further increased to a maximum recommended maintenance dose as required and/or tolerated
- Prescriptions for CBD in the US are predominantly filled via large national specialty pharmacies (SPs). Real-world data gathered from SPs can reveal broader insights into persistence patterns^{2,3}
- While single-center observational studies demonstrated that 75%-77% of patients continued long-term CBD treatment,^{3,4} persistence and discontinuation patterns have not been assessed in larger samples

Objective

- To characterize real-world dosing patterns and persistence on CBD in the US

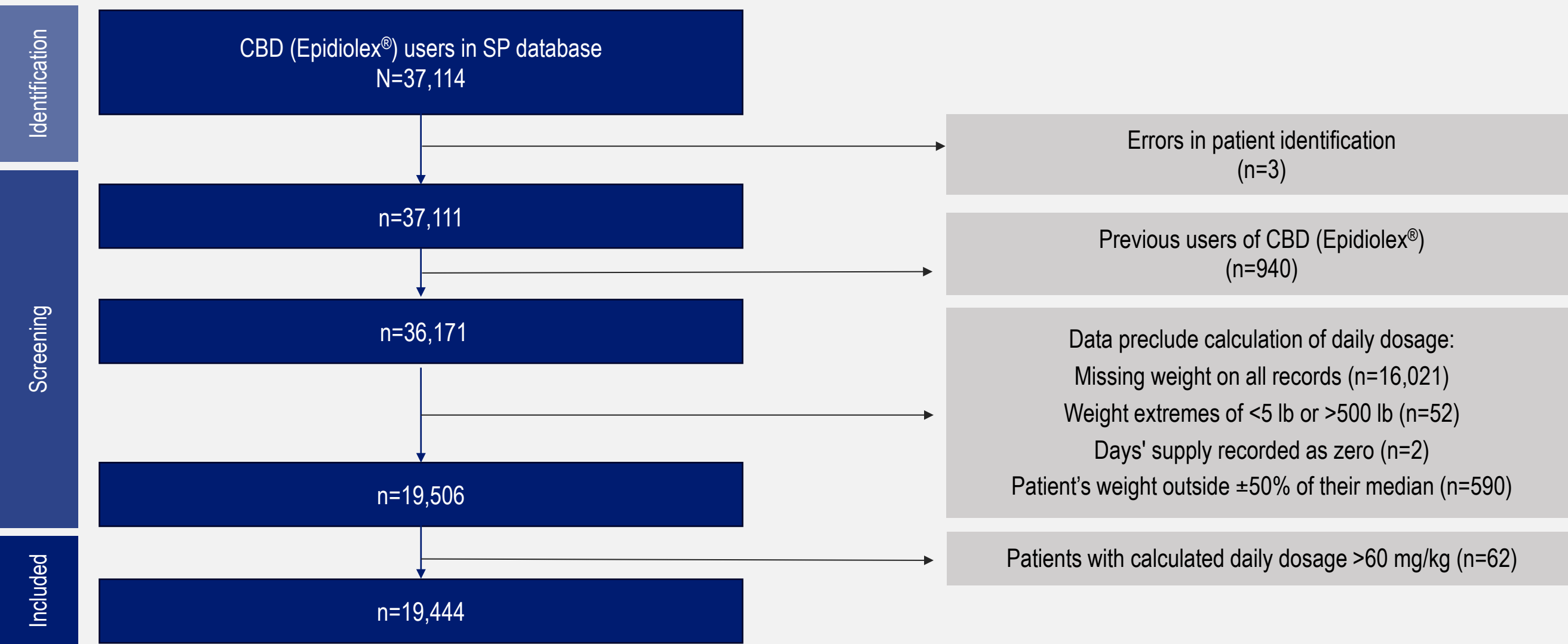
Methods

- A retrospective study of patient-level, deidentified US SP fill records for new CBD (Epidiolex®, 100 mg/mL oral solution) users from November 15, 2018, to July 12, 2023, was conducted
- Dosage was derived from patient weight, quantity dispensed and days of CBD supplied
- Overall probability of persistence, defined as initial CBD pharmacy fill through discontinuation or censoring, was analyzed via Kaplan-Meier methods
- Discontinuation was defined as a 60-day gap in supply on hand.^a Patients with continuous supply beyond July 12, 2023, were censored at their last recorded day of supply
- Monthly risk of discontinuation was defined as

=
$$\frac{\text{number of patients who discontinued in the month}}{\text{number of patients who had not yet discontinued or censored at the start of the month}}$$

- The average monthly dosage up to and including the current month was used as a time-dependent predictor in a Cox regression model of likelihood of discontinuation
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Figure 1. Patient selection process



CBD, cannabidiol; lb, pounds; SP, specialty pharmacy.

- Of the 37,114 CBD users, 19,444 new users were included in this analysis (Figure 1)

Results

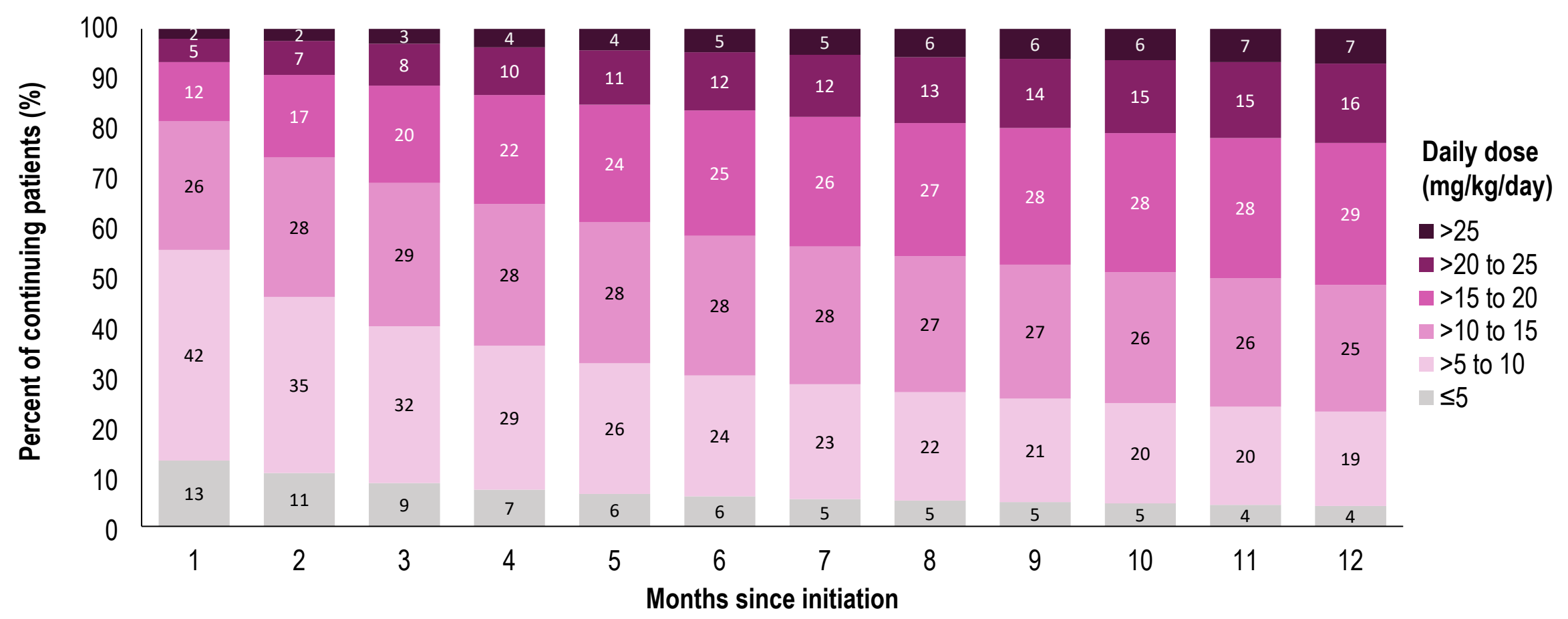
Table. Demographics, payer type, and fill patterns

	n (%)		n (%)
Age, years ^a		No. of days supplied initial fill ^b	
≤6	3108 (19.8)	≤15	158 (0.8)
>6 to 12	3387 (21.6)	>15 to 45	19,097 (98.2)
>12 to 18	3200 (20.4)	>45 to 75	95 (0.5)
>18	5989 (38.2)	>75 to 100	93 (0.5)
Sex ^a , n (%)		>100	1 (0.0)
Female	7095 (46.2)	No. of days supplied per fill from all fills ^b , n (%)	
Male	8259 (53.8)	≤15	2484 (0.5)
Payer type for initial fill ^a , n (%)		>15 to 45	484,784 (98.5)
Commercial	10,302 (53.3)	>45 to 75	1213 (0.2)
Medicaid/Medicare/government insurance	8581 (44.4)	>75 to 100	3477 (0.7)
Cash	96 (0.5)	>100	17 (0.0)
Other	346 (1.8)		

^aPercentages exclude unknown or missing/blank data; ^bMean number of days of CBD supply was 30 days. CBD, cannabidiol.

- Among patient records included in this analysis, 38% were aged >18 years, 53% had a commercial insurance plan for healthcare coverage, and 44% had Medicaid, Medicare, or other government insurance (Table)

Figure 2. Daily CBD dose over time among continuing patients



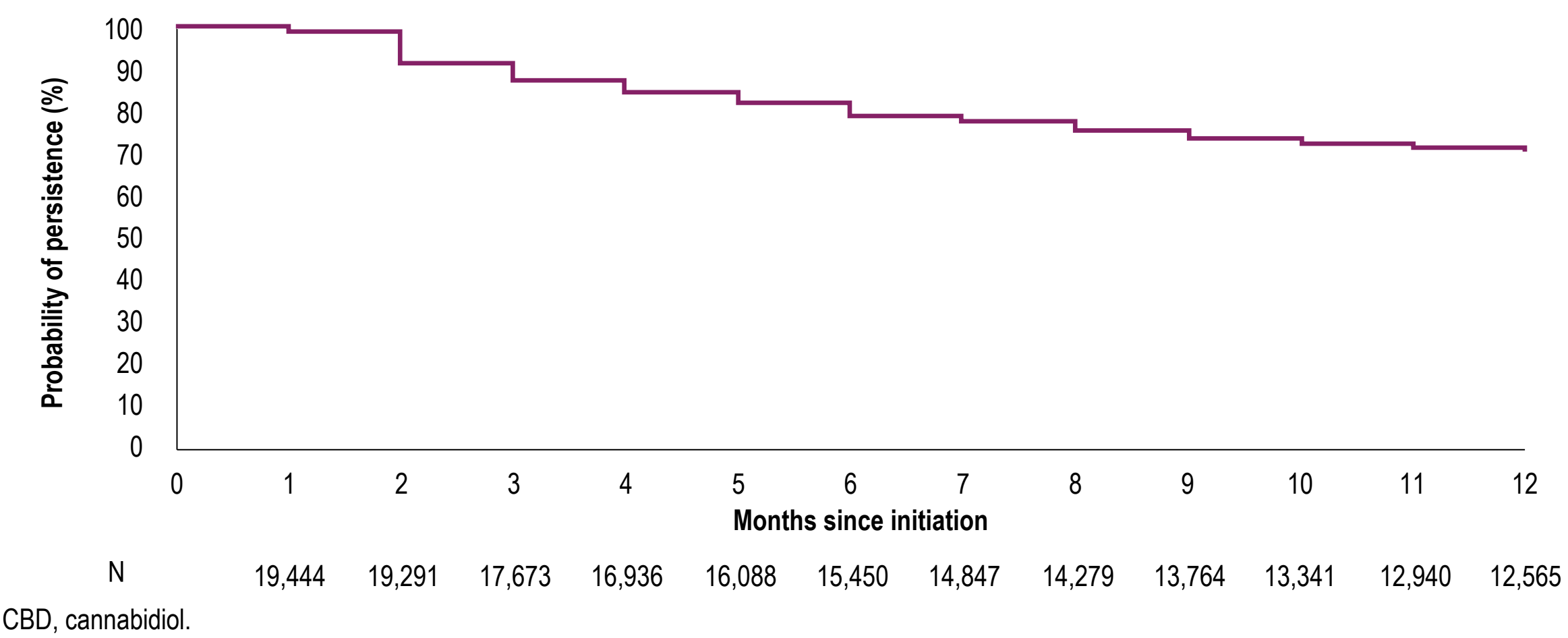
CBD, cannabidiol.

- In over half of the patients (~56%), CBD dose started at ≤10 mg/kg/day, and the proportion of patients with doses >15 mg/kg/day increased over time (Figure 2)
- Among patients continuing CBD, the proportion of those receiving higher doses increased over time; ie, 17% of patients at Month 2 were receiving >15-20 mg/kg/day, and the proportion increased to 29% at Month 12
- The predominant dose at 12 months was >15-20 mg/kg/day

Conclusions

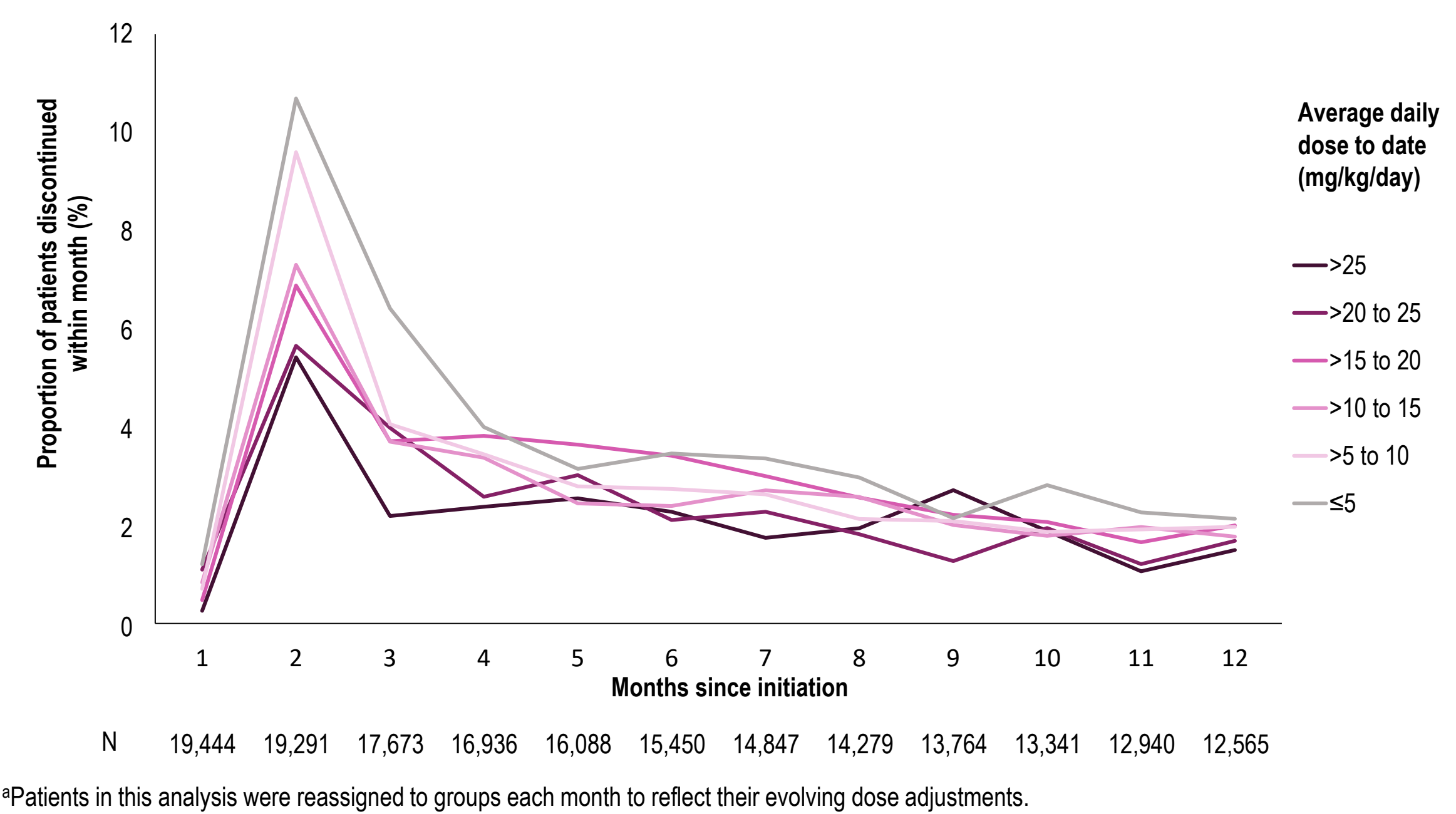
- At 12 months, the majority of patients (~70%) met the definition of persistence on CBD
- Over half of the SP patients (~56%) in this database initiated CBD at doses ≤10 mg/kg/day, consistent with the approved label; about half of patients (~51%) were receiving doses >15 mg/kg/day at 12 months
- The monthly risk of discontinuation stabilized to ≤4% after Month 3

Figure 3. Kaplan-Meier curve: 12-month persistence analysis over all dosages of CBD



- At 12 months, the probability of persistence on CBD was 69.9% (Figure 3)
 - Probability does not include patients who may have restarted treatment after discontinuation

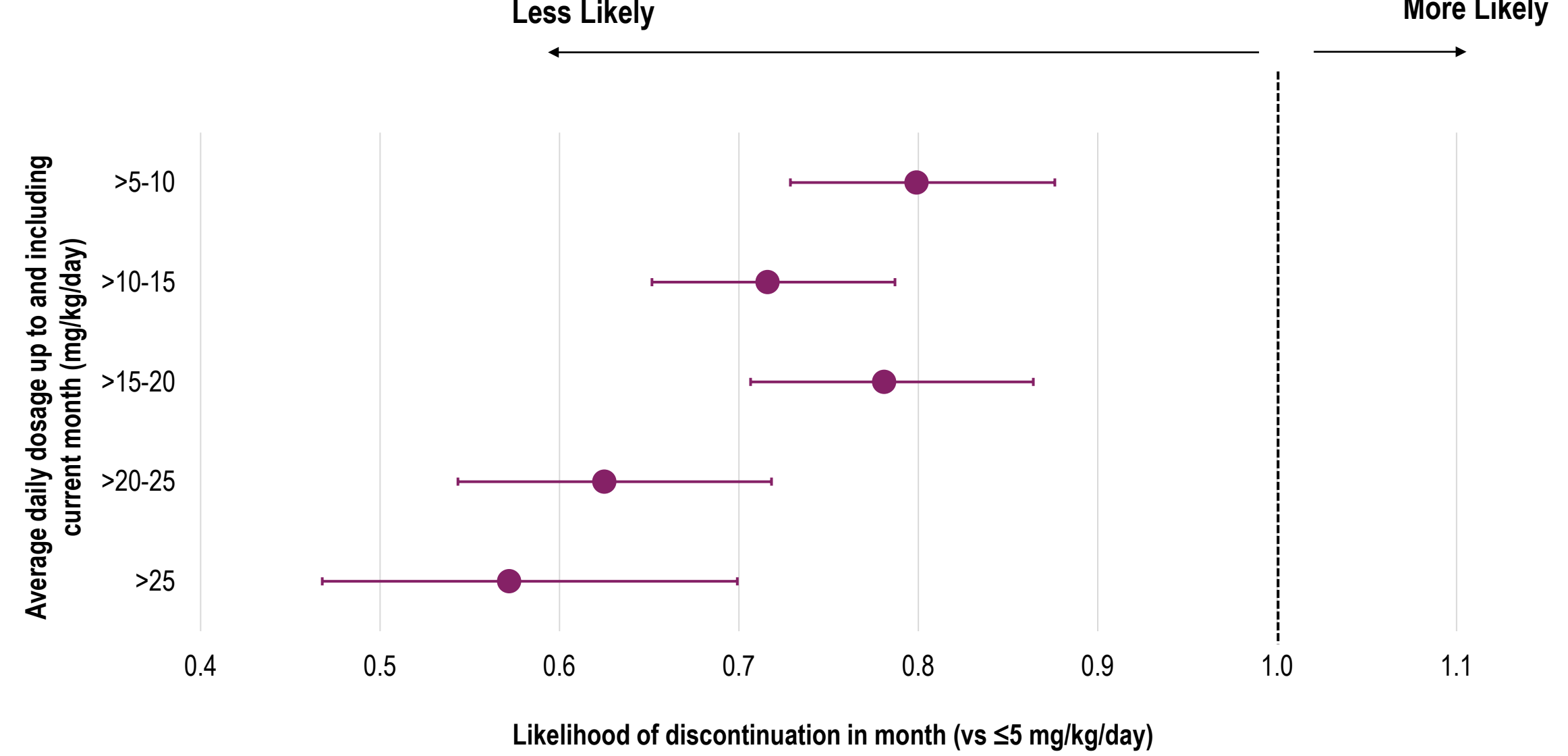
Figure 4. Likelihood of discontinuation by average dose through current month^a



^aPatients in this analysis were reassigned to groups each month to reflect their evolving dose adjustments.

- The likelihood of discontinuation was lowest among patients with an average CBD dosage of >20 mg/kg/day (Figure 4)
- After Month 3, the risk of discontinuation in any month was ≤4% across all dosing groups

Figure 5. Relative likelihood of discontinuation in any month by average of daily dose over prior months – Cox regression



- Average doses of ≤5 mg/kg/day were associated with the greatest likelihood of discontinuation, and average doses of >20 mg/kg/day were associated with the lowest likelihood of discontinuation (Figure 5)
- Compared with patients receiving an average dose of ≤5 mg/kg/day, patients with higher average doses of >10-15 mg/kg/day, >15-20 mg/kg/day, >20-25 mg/kg/day, and >25 mg/kg/day were at least 28%, 22%, 38%, and 43%, respectively, less likely to discontinue CBD at any given month

Limitations

- Diagnosis codes were not available for this analysis; therefore, the condition for which CBD was prescribed is unknown
- SP data represent only prescription fill patterns and do not directly measure efficacy, tolerability, or whether supplied drug was taken by the patient
- Not all sources for CBD prescriptions are captured. Patients who switched to an institutional or health system SP would have been counted as discontinued, underestimating the actual persistence
- Administration of CBD with food increases bioavailability and results in a more predictable pharmacokinetic profile¹; however, information regarding patients' fed state when dosing was not available

- An average dose of >20 mg/kg/day was associated with the lowest likelihood of discontinuation in any given month; risk of discontinuation at >20 mg/kg/day was at least 38% lower compared with ≤5 mg/kg/day
- Given the increased likelihood of persistence at higher daily dosage, dose adjustments should be considered when needed based on individual patient response and tolerability
- Healthcare professionals can support persistence on CBD by educating patients and caregivers on time to onset of effectiveness, dose adjustments, and managing adverse events³

^aSupply on hand is defined as a combination of any remaining days' supply (from previous fills) and the number of days in the new supply received.

First presented at the Academy of Managed Care Pharmacy (AMCP) Annual Meeting, 2025.

References: 1. Epidiolex® (cannabidiol) oral solution. Prescribing information. Jazz Pharmaceuticals, Inc.; 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/210365s021bl.pdf. 2. Dial H, et al. *Am J Health Syst Pharm*. 2022;79(18):1592-1598. 3. Barnes JP, et al. *Epilepsy Res*. 2024;200:107300. 4. Georgieva D, et al. *Epilepsy Behav*. 2023;141:109159

Acknowledgments: Medical writing assistance was provided by Bhargavi Ramesh of Syneos Health, and funded by Jazz Pharmaceuticals, Inc., in accordance with Good Publication Practice (GPP) 2022 guidelines.

Support: The study was sponsored by Jazz Pharmaceuticals, Inc.

Disclosures: GP, LB, WN, and TS are employees of Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in Jazz Pharmaceuticals, Inc. HNV and SC are former employees of Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in Jazz Pharmaceuticals, Inc.

