

Standardizing an Annual Reference Comparator of Healthcare Utilization of Painful Diabetic Neuropathy (PDPN): A U.S. Claims Cohort Meta-Analysis for Modeling and Payer Benchmarking

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Background and Rationale

Diabetic peripheral neuropathy (DPN) remains a common complication of diabetes, with estimates reporting that up to 50%-66% of patients with diabetes will develop DPN during their lifetime¹ and approximately 20%-40% of these patients will experience pain associated with DPN, known as painful DPN (PDPN).²

PDPN is often undertreated, as many patients discontinue commonly used oral treatments within months of initiation due to intolerability or lack of efficacy.³ This can lead to increased healthcare utilization, including emergency room (ER) visits, inpatient hospital admissions, outpatient encounters, and office visits as patients continue to experience neuropathic pain.^{4,5}

However, no standardized annual reference comparator for PDPN healthcare utilization and costs currently exists to support economic modeling and payer cost benchmarking in the United States.

Objective

To develop a standardized annual reference comparator for PDPN using US claims studies to estimate background healthcare resource use, prevalence, and costs for payer decision-making, addressing variability across published PDPN claims analyses that limits their use in decision-analytic models.

Methods

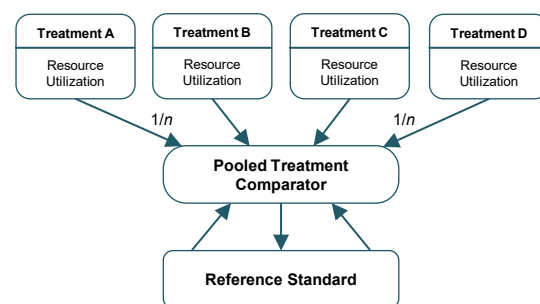
Overview

- We synthesized evidence from multiple US claims studies of PDPN to construct a standardized reference comparator of healthcare utilization.
- A pooled comparator approach was used in which resource utilization estimates from multiple PDPN cohorts were combined to generate a common reference standard (Figure 1).
- Diagnosis of painful DPN, non-painful DPN, and DM with no DPN were based on ICD codes.
- This approach enables consistent comparison of healthcare resource use when direct comparisons across studies are unavailable.

Reference Standard Construction

- Event rates and encounter probabilities were estimated using generalized linear mixed models (Poisson and binomial-logit links).
- Resource utilization estimates from each study cohort were standardized to a 12-month period.
- Results were pooled with equal weighting to create a composite reference standard that served as the common comparator.

Figure 1. Pooled Comparator Methodology for Resource Use Analysis

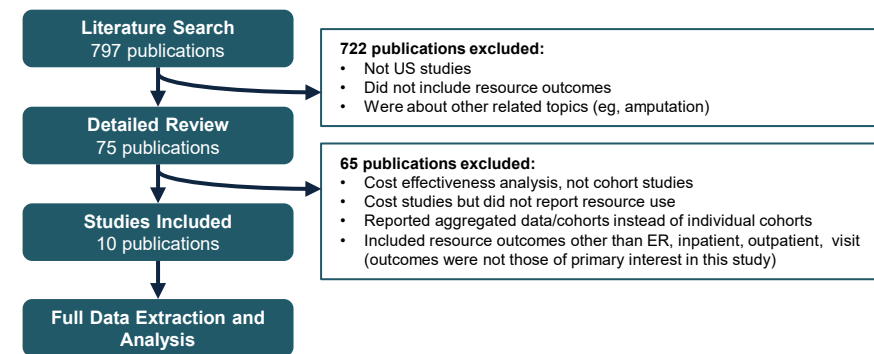


Key Advantages

- Maintains internal consistency across all comparisons
- Reduces bias from selecting arbitrary single-study or single-treatment comparators
- Enables transparent relative positioning of each intervention
- Accounts for heterogeneity across available PDPN claims studies and patient cohorts

Methods (cont.)

Figure 2. Literature Search and Data Extraction



- Targeted PubMed and Cochrane searches (1995-August 2025) identified US claims-based cohort studies reporting healthcare utilization in DPN.
- Ten eligible studies contributed data on ~401,202 adults with PDPN and ~202,000 comparator adults with type 2 diabetes mellitus (T2DM) without PDPN.

Analytic Methods

- Absolute values of utilization, cohort size, costs, and dates of costs were extracted; costs were CPI adjusted to 2025 USD.
- The expected healthcare utilization in PDPN includes reporting of the prevalence of ≥ 1 event per year across provider fees, outpatient visits, ER visits, and inpatient admissions. Expected events = $\lambda \times$ exposure time and $\lambda =$ total events \div total person-time.
- Using a binomial-logit mixed model (primary) with a Paule-Mandel/Knapp-Hartung cross-check, pooled logits were back-transformed to annual prevalence and results expressed per 1,000 patient-years (PY).

Results

- Results from a pooled sample of 10 US studies including ~400,000 PDPN patients are presented in Table 1.

Table 1. Primary Reference Comparator (All DPN): Annual Prevalence and Rates per 1,000 PY

Resource Type	Prevalence of ≥ 1 event/year, % (95% CI)	Per 1,000 PY (95% CI)
Provider Fees	93.6 (86.9–96.9)	936 (869–969)
Outpatient Visits ^a	85.4 (70.6–93.4)	854 (706–934)
ER	27.5 (21.2–34.8)	275 (212–348)
Inpatient Admissions	25.4 (20.2–31.4)	254 (202–314)

^aAll outpatient services including hospital. $\lambda =$ encounters per resource category \times cohort person-time (events per person-month). Estimates are from the primary binomial-logit mixed model. Rates per 1,000 patient-years are re-expressions of annual prevalence for payer benchmarking. These reflect occurrence (≥ 1 event) rather than visit counts.

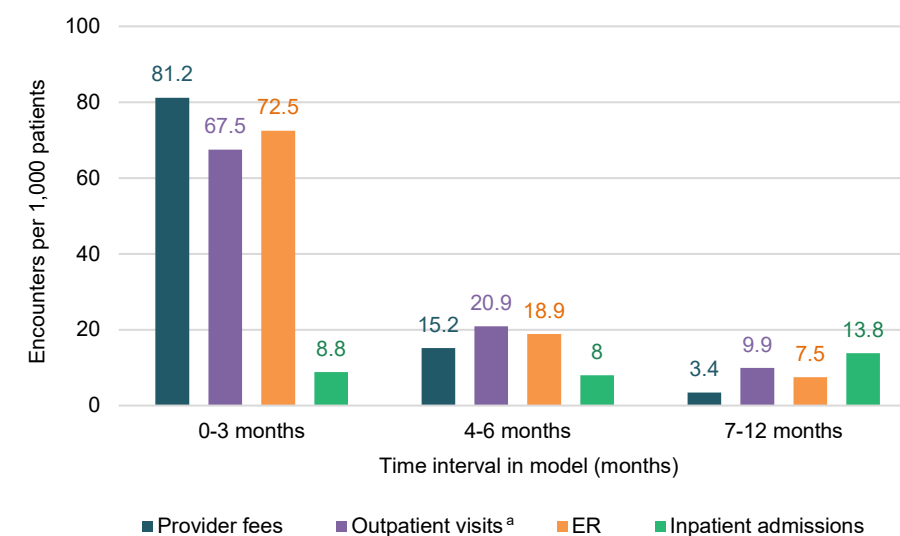
Table 2. Prevalence Comparison of Severe DPN, Non-Painful DPN, and No DPN Cohorts vs All DPN (Absolute Percentage-Point Differences)

Resource Type	Severe DPN, % (95% CI) [Δ vs All DPN]	Non-Painful DPN, % (95% CI) [Δ]	DM and No DPN, % (95% CI) [Δ]
Provider Fees	92.1 (88.3–94.8) [–1.5]	89.6 (84.8–93.1) [–4.0]	90.0 (76.2–96.2) [–3.6]
Outpatient Visits ^a	83.8 (59.3–94.8) [–1.6]	72.3 (38.7–91.5) [–13.1]	70.7 (42.9–88.6) [–14.7]
ER	29.7 (18.1–44.6) [+2.2]	22.7 (18.0–28.3) [–4.8]	27.3 (17.4–40.1) [–0.2]
Inpatient Admissions	24.9 (20.7–29.8) [–0.5]	20.6 (14.3–28.8) [–4.8]	18.2 (10.5–29.6) [–7.2]

^aAll outpatient services including hospital. Each cell shows subgroup prevalence (95% CI) for ≥ 1 event/year. Δ represents the absolute percentage-point difference from the All DPN reference in Table 1. These estimates provide plausible bounds for scenario analyses (e.g., greater acute-care use with increasing DPN severity).

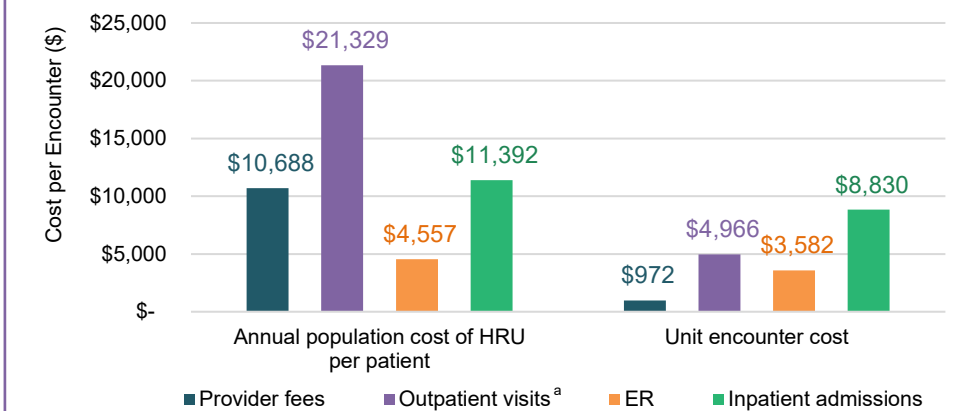
- Pre-specified cohorts (Severe DPN, Non-painful DPN, and DM and no DPN) behaved as expected, providing plausible bounds for scenario testing (Table 2).
- This analysis captures resource occurrence (≥ 1 event) rather than intensity/frequency, meaning modeled estimates using this reference comparator are conservative.
- Annual utilization rates were distributed across follow-up intervals assuming constant event intensity. Interval distribution was informed by Yang discontinuation hazards ($\approx 50\%$ discontinuation by 3 months). Resource utilization was highest within 3 months of PDPN treatment discontinuation and declined in subsequent periods (Figure 3).

Figure 3. Modeled Healthcare Costs Across Follow-Up Intervals Using Annual PDPN Utilization and Published Discontinuation Hazards



^aAll outpatient services including hospital. Utilization rates (λ) for each category represent encounters per person-month calculated from pooled cohort person-time. Annual utilization rates were distributed across intervals using treatment discontinuation hazards reported in the PDPN literature.

Figure 4. Healthcare Costs by Resource Type: Annual Patient Cost vs Unit Encounter Cost



^aAll outpatient services including hospital. Annual costs reflect population-level utilization rates, while encounter-level costs reflect the cost of a single event.

Conclusions

- A standardized reference of expected annual healthcare utilization in PDPN was developed for comparison modeling by pooling data from ~400,000 US PDPN patients across 10 claims-based cohort studies, establishing the first unified benchmark for payer use.
- Routine healthcare utilization, including provider fees and outpatient hospital visits, was nearly universal among patients with DPN, while acute-care services (ER visits and inpatient admissions) occurred in approximately one in four patients.
- Resource use was consistently higher among patients with painful DPN vs nonpainful DPN and patients with DM and no DPN, as well as in the first 3 months following treatment discontinuation, highlighting the additional clinical and economic challenges associated with neuropathic pain.
- This reference comparator provides payer-ready inputs for benchmarking and economic models, offering conservative, occurrence-based estimates for future economic evaluations.

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Disclosures

JF, LM, JL – employees of Averitas Pharma. NS – received research funding from the Migraine Research Foundation, the National Institute of Neurological Disorders and Stroke (NINDS), the National Center for Complementary and Integrative Health, the National Institutes of Health (NIH), UCSD Academic Senate, UCSD Department of Anesthesiology Research Advisory Group, and ShiraTronics; has served on advisory boards for Lundbeck, Rapport, and Vertex; and has consulted for Averitas, Delphian, Eli Lilly, Lohocla, Salvia, Syqe, and Vertex. HK – has served on a speaker bureau for Averitas Pharma and has consulted for Abbott, Nalu, SPR, Curonix, and Nervonic. Writing, creative, and editorial support were provided by Averitas Pharma, Inc., a subsidiary of Grünenthal GmbH.

Funding

The development of the annual reference comparator and preparation of this poster were supported by Averitas Pharma.

Abbreviations

CPI, consumer price index; DM, diabetes mellitus; DPN, diabetic peripheral neuropathy; ER, emergency room; ICD, international classification of diseases; PDPN, painful diabetic peripheral neuropathy; PY, patient-years.