



Unmet Treatment Need in a Real-World US Population of Patients with Hereditary Angioedema Treated for Over a Year with Long-Term Prophylaxis

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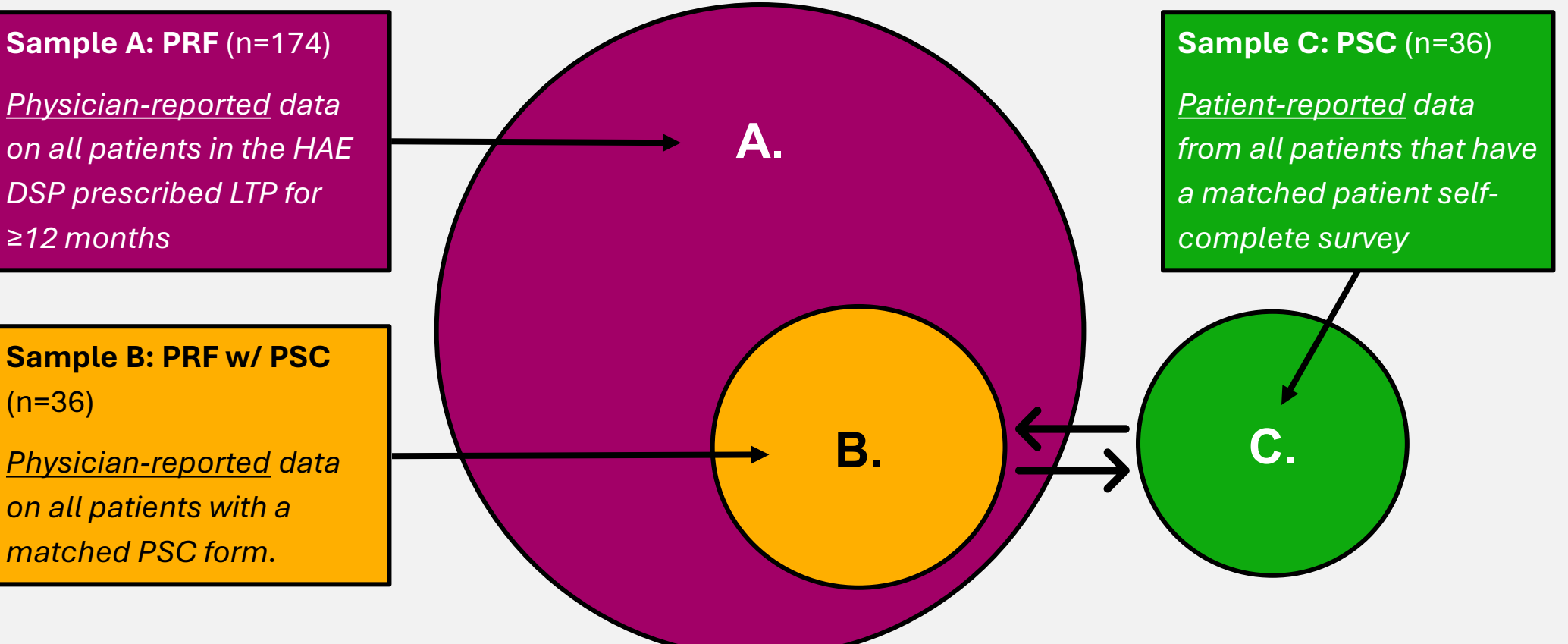
RATIONALE

- Hereditary angioedema (HAE) is a rare genetic disorder that results in recurrent episodes of localized tissue swelling often affecting extremities, abdomen and airways¹.
- Numerous long-term prophylaxis (LTP) therapies have been approved for hereditary angioedema (HAE) in recent years².
- Understanding the remaining unmet need is critical to improve HAE patient management and outcomes.

STUDY DESIGN

- US data were drawn from the Adelphi HAE II Disease Specific Programme (DSP) collected January 2023–January 2024. The DSP methodology has been previously published and validated³⁻⁶.
- Physicians provided data for patients with HAE including patient demographics, clinical characteristics, HAE attacks, treatment history, satisfaction and unmet need with current LTP treatment. Patients of the participating physicians were invited to voluntarily complete a pen-and-paper questionnaire covering similar topics.
- Figure 1**, describes how the physician-reported, patient record form (PRF) and patient self-completion (PSC) forms are utilized for this study.
- All patients prescribed long-term prophylaxis (LTP) for at least 12 months at the time of survey were included in this analysis. All analyses included were descriptive in nature.

Figure 1. Diagram showing the relationship between the PRF, PRF w/ PSC and PSC samples collected as part of the HAE DSP.



HAE: Hereditary angioedema, DSP: Disease Specific Programme, PRF: Patient Record Form (Physician Completed), PSC: Patient self-completed form

RESULTS

- Overall, 53 physicians reported on 174 patients (PRF) with a mean (standard deviation; SD) age of 35 (13) years, 51% were male and 72% were white. A subset of 36 patients completed matched surveys (PSC). This subset is reported here and was similar in demographics (mean (SD) age 35 (13) years, 61% male and 77% white), **Table 1**.

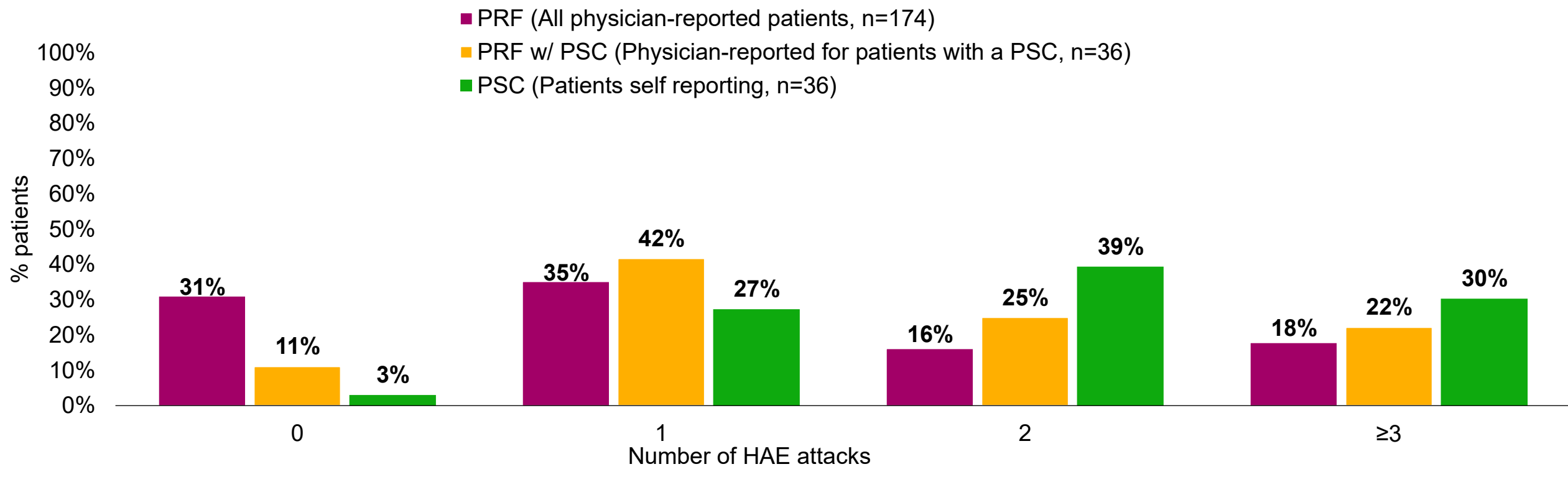
Table 1: Physician-reported HAE patient demographics and clinical characteristics

| | PRF (n=174) | PRF w/ PSC (n=36) |
|---|-------------|-------------------|
| Age; years, mean (SD) | 35 (13) | 35 (13) |
| Sex; male, n (%) | 89 (51) | 22 (61) |
| Ethnicity; White, n (%) | 126 (72) | 28 (78) |
| Employment; | | |
| Working full time, n (%) | 115 (66) | 17 (47) |
| Working part-time, n (%) | 13 (7) | 8 (22) |
| *Other, n (%) | 46 (26) | 11 (31) |
| HAE Type; | | |
| Type I, n (%) | 133 (76) | 26 (72) |
| Type II, n (%) | 33 (19) | 7 (19) |
| Normal C1-INH, n (%) | 3 (2) | 1 (3) |
| Unknown/undetermined, n (%) | 5 (3) | 2 (6) |
| Top 3 concomitant conditions; | | |
| Anxiety, n (%) | 40 (23) | 7 (19) |
| Depression, n (%) | 36 (21) | 8 (22) |
| Hypothyroidism, n (%) | 12 (7) | 3 (8) |
| Time from diagnosis to survey; years, n | 150 | 33 |
| Time from diagnosis to survey; mean (SD) | 8 (10) | 8 (12) |

HAE: Hereditary angioedema; SD: Standard deviation; C1-INH: C1 esterase inhibitor *Other includes student, homemaker, retired and long-term sick leave

- Amongst the subset of patients with self-reported data, 30% (PSC) reported experiencing ≥3 HAE attacks in the past 12 months whilst their physicians reported 22% had ≥3 HAE attacks (PRF w/PSC, **Figure 2**).

Figure 2: Physician- and Patient-reported HAE attacks experienced in the 12 months prior to survey



HAE: Hereditary angioedema; PRF: Patient-record form; PSC: Patient self-complete

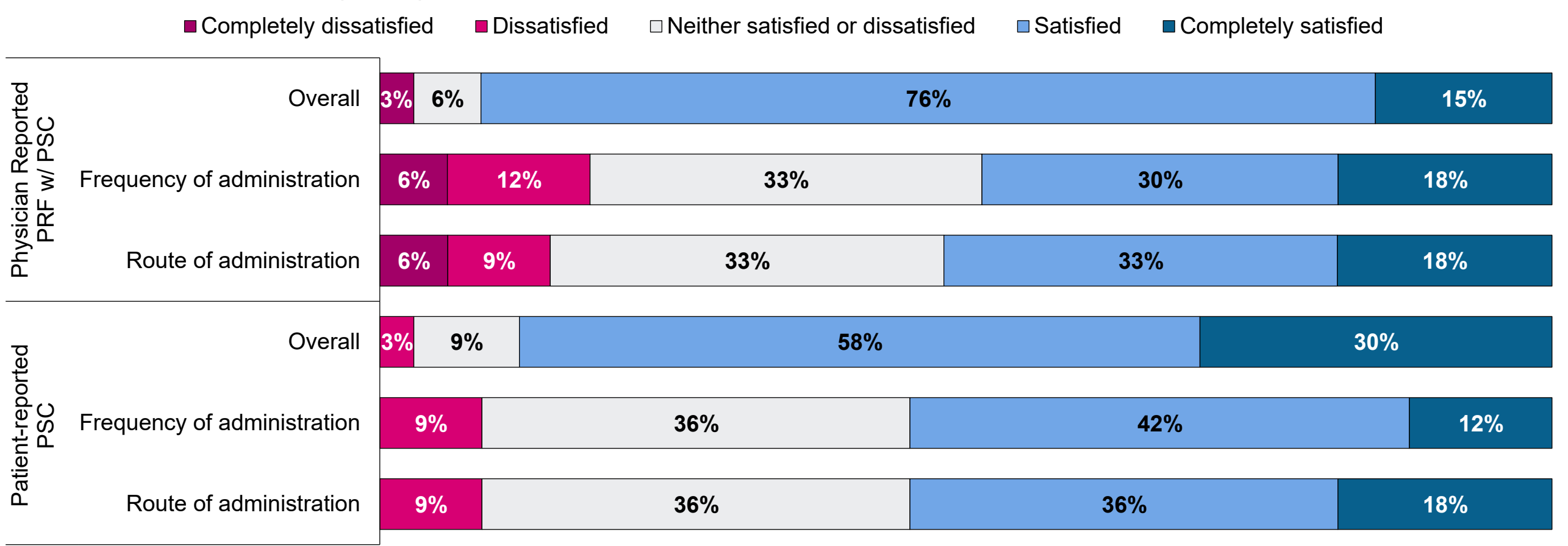
- Lanadelumab was the most frequently reported prescribed LTP treatment at the time of survey (**Table 2**) in both the overall PRF (38%) and PRF w/ PSC samples (28%, joint with subcutaneous C1-INH). Berotralstat was prescribed to 23% of PRF and 25% of PRF w/ PSC samples respectively
- Among the matched PRF w/ PSC sample, 53% of physicians reported satisfaction with the frequency and 56% with the route of administration respectively. Similarly, 55% of patients reported satisfaction with the frequency and 55% with the route of administration (PSC), **Figure 3**.

Table 2: Physician-reported HAE patient treatment history

| | PRF (n=174) | PRF w/ PSC (n=36) |
|--|-------------|-------------------|
| Treatment prescribed at time of survey | | |
| LTP and ODT, n (%) | 125 (72) | 27 (75) |
| LTP only, n (%) | 49 (28) | 9 (25) |
| Current LTP treatment prescribed | | |
| Lanadelumab, n (%) | 66 (38) | 10 (28) |
| Berotralstat, n (%) | 40 (23) | 9 (25) |
| Subcutaneous C1-INH, n (%) | 33 (19) | 10 (28) |
| Intravenous C1-INH, n (%) | 16 (9) | 3 (8) |
| Danazol, n (%) | 16 (9) | 4 (11) |
| Tranexamic acid, n (%) | 6 (3) | 0 (0) |
| Time since current LTP treatment initiation; years, mean (SD) | 3 (3) | 3 (4) |

HAE: Hereditary angioedema; LTP: long-term prophylaxis; ODT: On-demand therapy; SD: Standard deviation; C1-INH: C1 esterase inhibitor

Figure 3: Physician- and patient-reported treatment satisfaction with aspects of LTP treatment for patients with self-reported data (n=33)



PRF: Patient record form; PSC: Patient self-complete. N=3 missing responses excluded

- At least one unmet need was reported by 89% of physicians (PRF+PSC) and 53% of patients (PSC) regarding the current LTP, **Figure 4a and 4b**. Physicians reporting on patients with a PSC, most commonly reported ‘gastrointestinal side effects’ (36%) as an unmet need (**Figure 4a**), whilst patients self-reported most frequently experiencing pain/bruising/burning with their LTP as an unmet need (**Figure 4b**).

Figure 4a: Physician-reported unmet needs of current prophylaxis treatment (top 5)

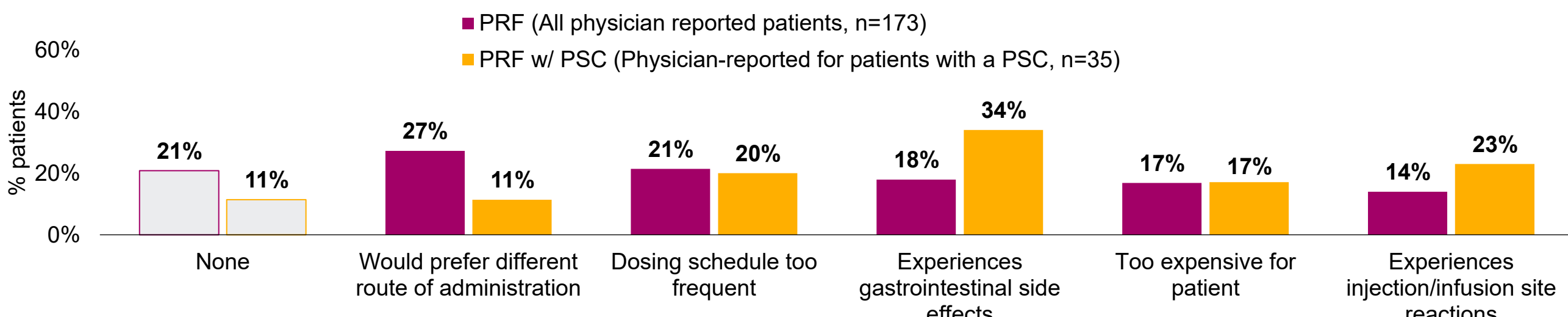
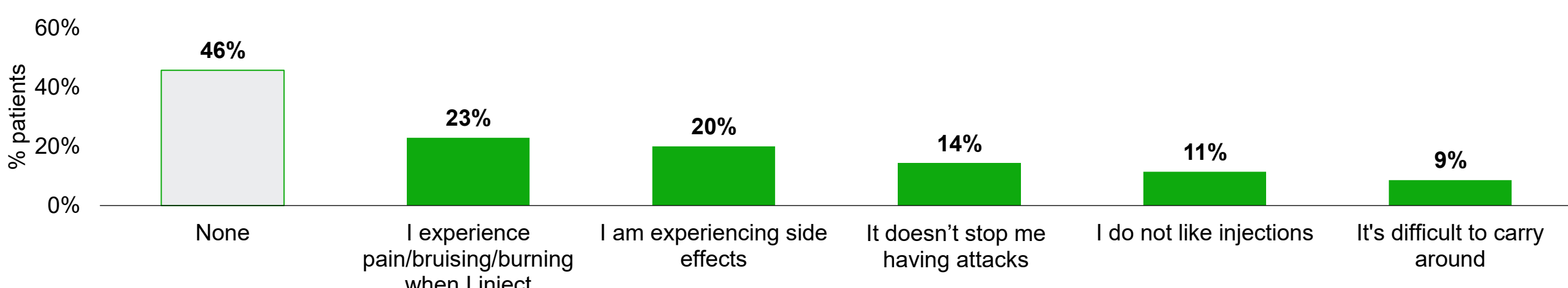


Figure 4b: Patient-reported unmet needs of current prophylaxis treatment (PSC, top 5, n=35)



PRF: Patient record form; PSC: Patient self-complete. N=1 don't know response excluded as the physician-reported treatment, but the patient did not report any treatment

CONCLUSION

- Although limited by sample size, almost one-third of patients and almost a quarter of physicians reported breakthrough HAE attacks in the 12 months prior to survey.
- Almost half of both physicians and patients reported a lack of satisfaction with the route or frequency of administration and unmet needs with current LTP.

LIMITATIONS

- The DSP is not based on a true random sample of physicians or patients. Whilst minimal inclusion criteria governed the selection of participating physicians and patients, participation was influenced by willingness to complete the survey.
- These data were collected prior to January 2024 and therefore more recently approved LTP options, including donidalorsen and garadacimab, were not included in this analysis.
- The quality of data obtained relies on how accurately physicians and patients were able to recall and report information (recall bias) and inclusion was dependent on visiting a physician during the survey period, those that consult more frequently are more likely to be included (consultation bias).

DISCLOSURES

- EDF and KFV are employees and shareholders of Ionis Pharmaceuticals.
- AZ is an employee of Ionis Pharmaceutical.
- MT is an employee of Otsuka Pharmaceutical Europe Ltd.
- GG is an employee of Adelphi Real World

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