

# Characteristics of FDA Letters Citing Regulatory Violations Involving Patient-Reported Outcomes (PRO), 1997-2025

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## Objectives

To assess warning and untitled letters issued by FDA CDER from 1997 to 2025 that cited regulatory violations involving patient-reported outcomes in marketing and advertising materials.

## Methods

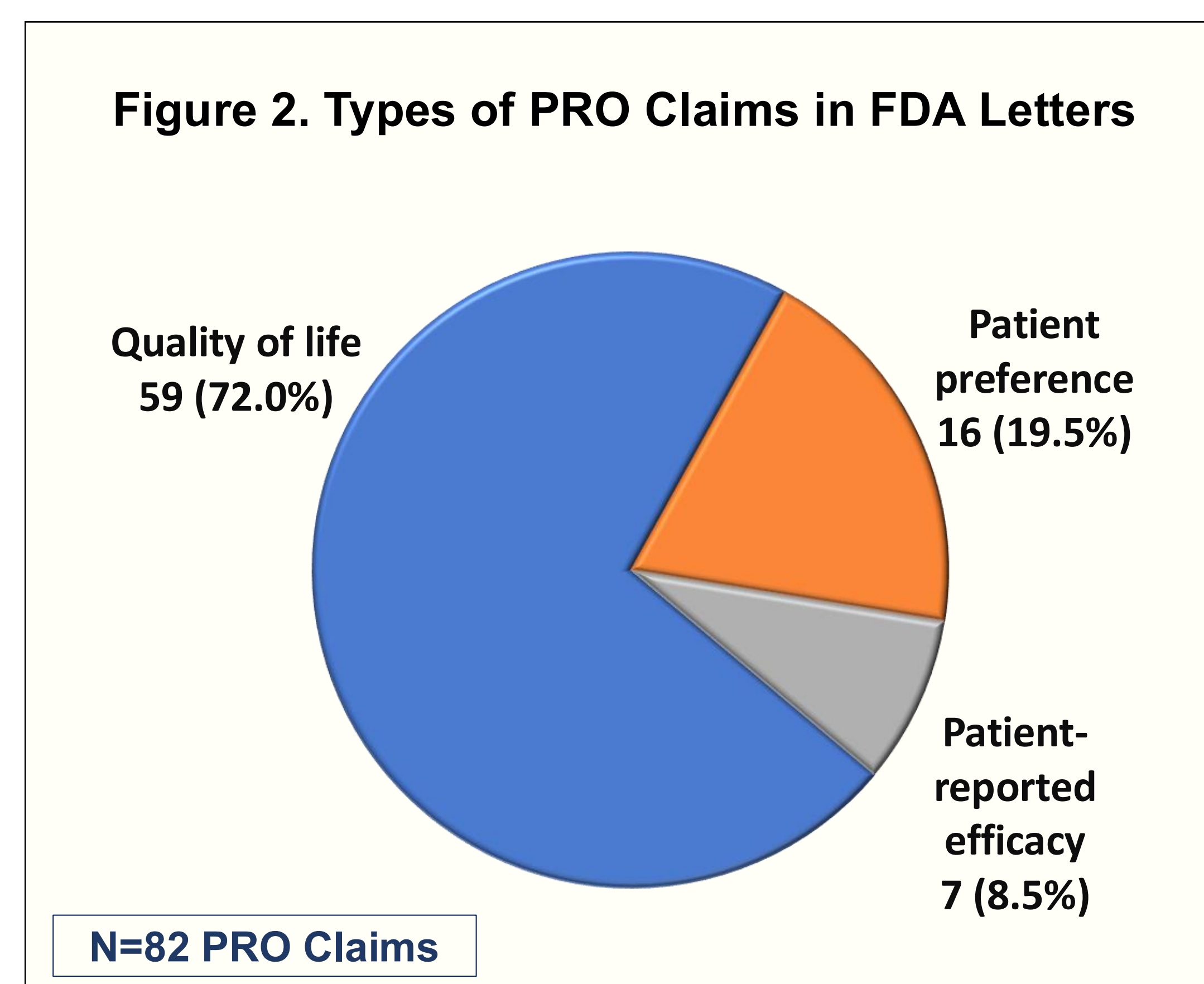
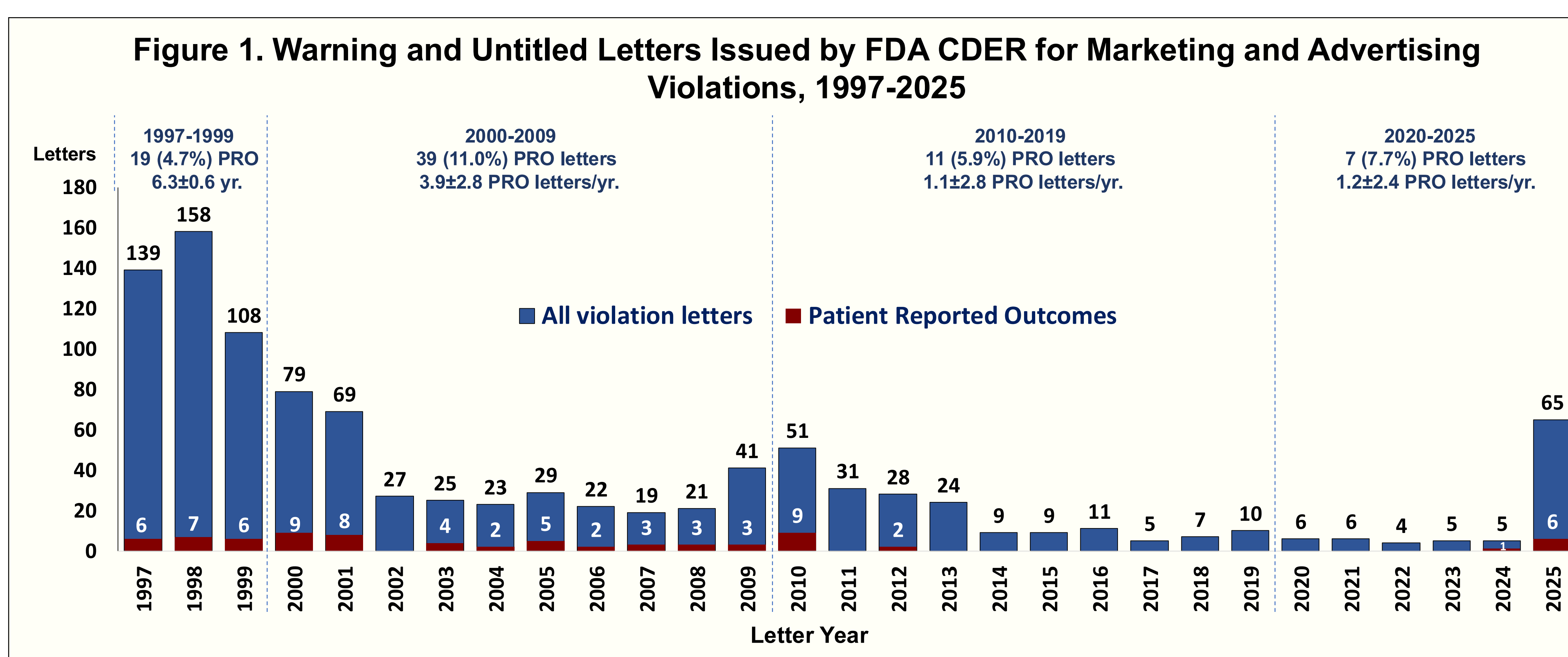
This retrospective descriptive analysis examined warning and untitled letters collected from the FDA website. Letters were classified by product class, media format, and type of violation. PRO claims were categorized by claim type and regulatory violation type.

## Results

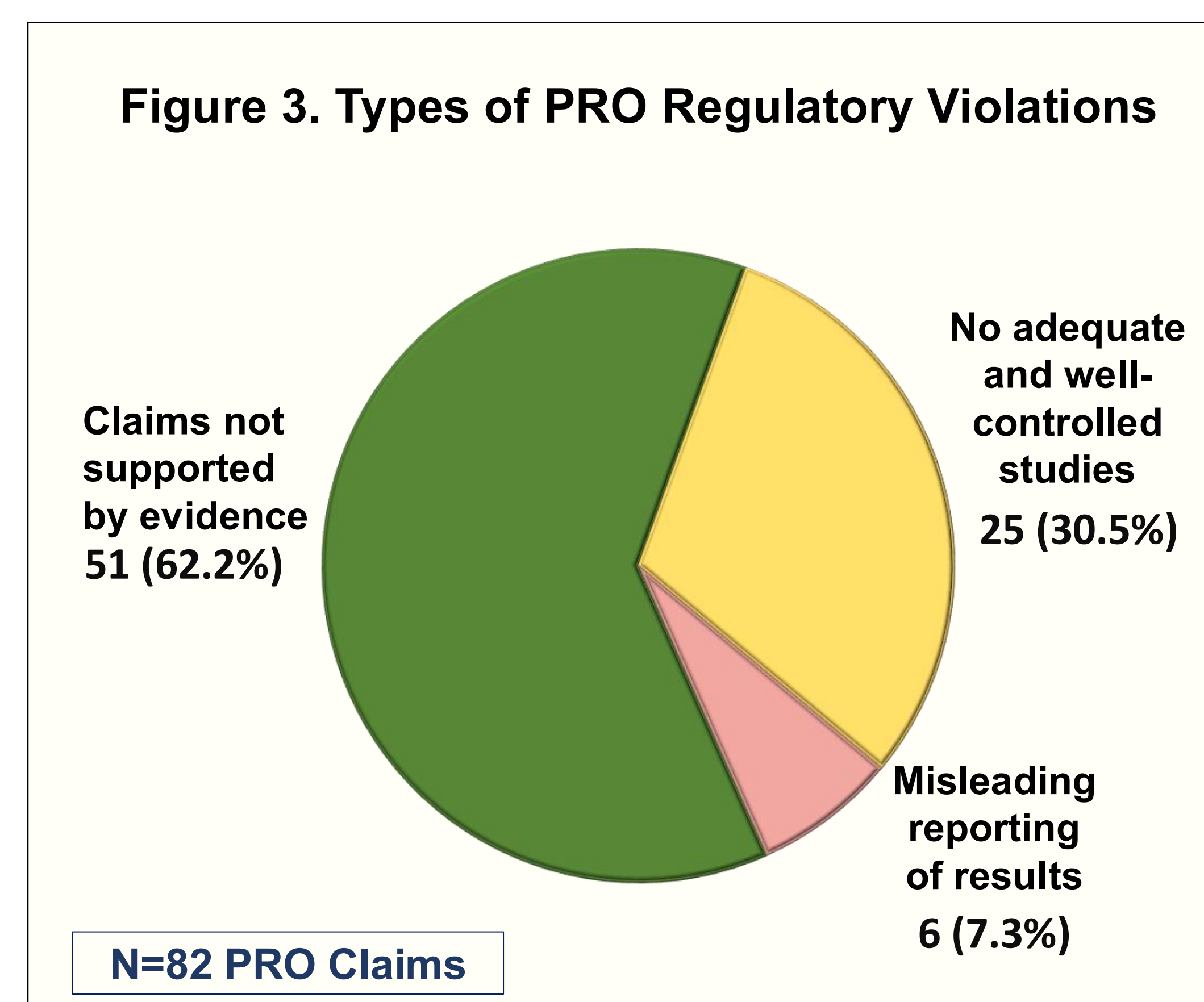
From 1997 to 2025, CDER issued 1,036 letters citing marketing and advertising regulation violations with an average±stdev. of 35.7±40.3 letters per year. The annual average number of marketing and advertising-related letters declined over time, from 135.0±25.2 letters in 1997-1999 to 15.2±24.4 letters in 2020-2025. CDER issued 65 letters in 2025.

Overall, the FDA issued 76 letters (7.3%) involving PROs with an average±stdev. of 2.6±3.1 letters per year. The annual average number of PRO-related warning and untitled letters declined over time, from 6.3±0.6 letters in 1997-1999 to 1.2±2.4 letters in 2020-2025. CDER issued 6 PRO-related letters in the year 2025.

## Results



The increase in PRO-related letters in 2025 coincided with a renewed HHS/FDA enforcement focus on misleading prescription drug promotion. FDA did not issue letters involving PROs in 13 years: 2002, 2011, and 2013-2023. The therapeutic class with the highest number of letters was antineoplastic and immunomodulating agents (23, 30.3%).



In addition, 16 letters (21.1%) involved unapproved or investigational drugs. Regarding communication media, 27 letters (35.5%) involved direct-to-consumer advertising (DTC), and 9 letters (11.8%) involved television broadcasting; 6 of the television-related letters were issued in 2025. The letters involving PROs contained a total of 82 PRO claims.

Quality-of-life claims were the most common claim type (59, 72.0%).

Patient-preference and patient-reported efficacy claims accounted for 16 (19.5%) and 7 (8.5%) of the claims with regulatory violations, respectively. The regulatory violations involved claims not supported by evidence for the promotional claims (51, 62.2%), lack of adequate and well-controlled studies (25, 30.5%), and misleading reporting of results (6, 7.3%).

## Conclusions

Despite the large number of marketing activities undertaken by companies and the growing use of PROs to support efficacy and safety claims for new drugs, the number of FDA violation letters involving PRO claims declined substantially after 2010.

In 2025, FDA issued 65 marketing and advertising warning and untitled letters, the highest annual total number since 2001. Most PRO-related letters issued in 2025 involved direct-to-consumer advertising, especially TV broadcasting, and coincided with a renewed FDA enforcement focus on misleading drug promotion.

Quality-of-life claims were the most cited PRO-related claims. Most claims mentioned in the letters lacked adequate evidentiary support or were not supported by adequate and well-controlled studies.