HPR113

Patient-Reported Outcomes in the Labeling of New Oncology Drugs: A Comparative Analysis of the FDA, EMA, and NMPA

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Background and Objective

- While there is global consensus on Patient-Focused Drug Development (PFDD), translating Patient-Reported Outcomes (PROs) into clinical practice relies heavily on their inclusion in drug labeling.
- Despite encouragement from regulatory agencies, few approved oncology drug labels currently incorporate PRO data. Agencies maintain a cautious approach with significant disparities in approval standards; historically, the European Medicines Agency (EMA) is more receptive to Health-Related Quality of Life (HRQOL) claims, whereas the US Food and Drug Administration (FDA) strictly favors specific symptom improvement.
- Current research predominantly compares the FDA and EMA (often limited to pre-2022 data).Although China's National Medical Products Administration (NMPA) has emerged as a critical player in global oncology R&D, systematic evaluations integrating all three agencies remain scarce.
- This study aims to systematically assess longitudinal trends, characteristics, and regional differences of PRO inclusion in novel oncology drug labeling across the FDA, EMA, and NMPA .

Methods

- **Data Sources & Timeframes**
  - ✓ **Data Sources：** Official drug labels from FDA (USPI), EMA (SmPC), NMPA (PI), and trial designs from ClinicalTrials.gov.
  - ✓ **Study Period:** Commenced from the publication year of pivotal PRO guidelines for each agency (FDA: 2009–2025; EMA: 2005–2025; NMPA: 2021–2025).
- **Inclusion and Exclusion Criteria**
  - ✓ **Inclusion:** (1) New molecular entities (NMEs) or original therapeutic biologics for oncology indications that received their first approval during the specified timeframes; (2) Indications clearly defined as solid tumors or hematological malignancies.
  - ✓ **Exclusion:** (1) Generic drugs, biosimilars, or previously approved active substances with only modifications in dosage form or route of administration; (2) Drugs indicated strictly for non-therapeutic purposes, such as cancer prevention, diagnosis, or supportive care; (3) Drugs for which the official label was not publicly available or the full text could not be obtained by the data extraction cutoff date.
- **Data Extraction**
  - ✓ **Key Variables:** Drug characteristics, pivotal trial designs (randomization, blinding, endpoint hierarchy), PRO measurement tools (PROMs), statistical presentation, claim types and the concepts assessed .
  - ✓ **Analysis:** Descriptive statistics to evaluate regional differences.

Results

- **Inclusion Rates and Annual Distribution of PRO Labeling:**
  - **FDA (6.99%):** Maintains an extremely strict evidentiary threshold.
  - **EMA (33.67%):** Demonstrates the highest receptivity to PRO inclusion.
  - **NMPA (12.23%):** Shows steady growth and moderate acceptance since 2021.

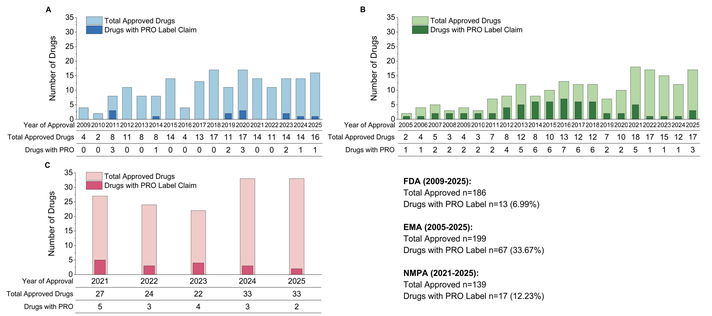

Fig. 1 Annual number of novel oncology drug approvals and PRO labeling inclusions. (A) Annual approvals by the FDA (2009–2025). (B) Annual approvals by the EMA (2005–2025). (C) Annual approvals by the NMPA (2021–2025).

- **Characteristics & Divergent Regulatory Thresholds for PRO Labeling:**
  - **FDA- Stringent & Symptom-Driven:**Prefers blinded trials and inferential statistics for symptom claims, omitting broad HRQOL.
  - **EMA- Flexible & HRQOL-Receptive:**Tolerates open-label designs and broadly accommodates multidimensional HRQOL claims.
  - **NMPA- Evolving but Qualitatively Driven**:Balances symptoms and HRQOL, yet 36.4% of labels lack quantitative outcome data.

Table 1. Comparative Profile of PRO Evidence and Labeling Claims among FDA, EMA, and NMPA

Domain & Key Characteristics	FDA	EMA	NMPA
I. Approval & Trial Baselines	(N = 13 Drugs / 18 Trials)	(N = 67 Drugs / 104 Trials)	(N = 17 Drugs / 20 Trials)
Regular Approval Pathway	69.2%	**97.0%**	64.7%
Blinded Trial Design	**72.2%**	55.8%	60.0%
Pre-specified as Secondary Endpoint	61.1%	78.9%	**85.0%**
II. Statistical Presentation	(N = 21 Claims)	(N = 117 Claims)	(N = 22 Claims)
Inferential Statistics (e.g., explicit p-values)	**47.6%**	33.3%	13.6%
No Specific Outcome Data Provided	9.5%	21.4%	**36.4%**
III. Evaluation Dimensions	(N = 21 Claims)	(N = 117 Claims)	(N = 22 Claims)
Symptoms Burden / Relief	**71.4%**	51.3%	40.9%
Health-Related Quality of Life (HRQOL)	**0.0%**	**53.0%**	36.4%
Safety / Tolerability	23.8%	4.3%	**0.0%**

- **PROM Instrument Preferences:**
  - **FDA** strongly favors specific symptom tools (e.g., BPI-SF) and toxicity assessments (PRO-CTCAE).
  - **EMA** prefers broad HRQOL instruments (EORTC QLQ-C30) and EQ-5D.
  - **NMPA** demonstrates a balanced distribution across disease-specific tools, general HRQOL instruments, and general symptom measures.

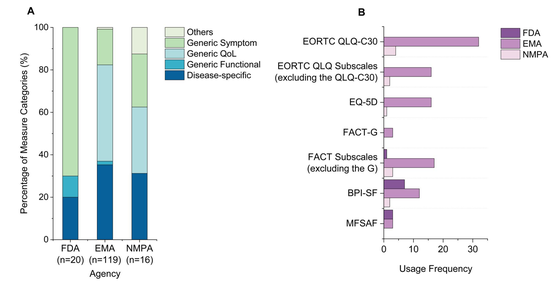

Fig. 2 Distribution and categorization of Patient-Reported Outcome Measurement (PROM) instruments in approved labels. (A) Categorization of PROMs utilized across the FDA, EMA, and NMPA based on measurement concepts. (B) Frequency of the most commonly used PROM instruments across the three regulatory agencies.

- **Cross-Regional Comparison of Multi-Agency Approved Drugs**
  - Among 55 oncology drugs concurrently approved across all three agencies, only **ONE drug** (Darolutamide/Nubeqa) successfully secured PRO claims across all three regions.
  - It evaluated a proximal core symptom ("time to pain progression" via BPI-SF) as a secondary endpoint, backed by robust RCT design and strict inferential statistics.

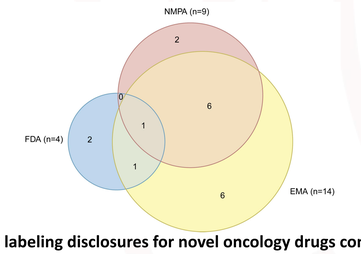

Fig. 3 Overlap in PRO labeling disclosures for novel oncology drugs concurrently approved by the FDA, EMA, and NMPA. This is an area-proportional diagram. Due to geometric rendering limitations, a slight visual overlap exists between the FDA and NMPA circles, although the actual intersection value for this specific overlap is 0.

Conclusion

PROs have not yet fully realized their potential in the regulatory review of new oncology drugs. We recommend the following:

- Adopt a mixed-measurement strategy integrating proximal core symptom evaluations with multidimensional HRQOL metrics to facilitate simultaneous cross-regional approvals.
- Incorporate PROs into strict pre-specified statistical testing hierarchies and utilize robust RCT designs to elevate them from supplementary references to confirmatory evidence.
- China's framework must transition from descriptive qualitative evaluation to quantitative confirmatory data, requiring explicit guidelines on MCID thresholds and missing data handling.
- Strictly adhere to international standards (e.g., SISAQOL-IMI, SPIRIT-PRO, CONSORT-PRO) and engage in early regulatory dialogues to tailor PROM selection to specific agency expectations.

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