

The Use of Patient-Reported Outcomes for New Drugs Approval in Europe: A Review of European Public Assessment Reports from 2017 to 2021

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BACKGROUND

- Health authorities and payers increasingly recognize the importance of the patient's perspective and patient-reported outcomes in the decision-making process regarding the introduction of new health technologies. However, the wide variety of outcome measures included in clinical trials and the differences in terms of data collection and specific needs for individual countries, is such that the role of **Patient-Reported Outcomes (PROs)** requires further characterization (1)
- The collection of **PROs** through **Patients-Reported Outcome Measures (PROMs)** can provide decision makers with important evidence on the condition and treatment received from the patient's perspective; this information, indeed, is not acquired from conventional efficacy and adverse event reporting data.
- The outcomes reported by the patients are not systematically analyzed by regulatory bodies at European level and beyond. In the European Medicines Agency (EMA) "Regulatory Science Strategy to 2025" (2), the Agency shows a growing interest in developing systematic ways to incorporate PROs and patient preferences into drug development, in order to get to a comprehensive evaluation of the benefits and risks of therapies.

RESEARCH OBJECTIVES

To investigate the consideration of patient-reported outcomes (PROs) and related measures (PROMs), together with characteristics associated to their use, in regulatory decision-making for new drugs approval in Europe between 2017 and 2021.

METHODS

- All drugs for human use authorized by EMA between January 2017 and December 2021 were identified and the corresponding European Public Assessment Reports (EPARs) downloaded for review. An ad hoc template was created to record systematically relevant information (e.g., therapeutic area, generic/biosimilar, orphan status, authorization date) and PROs/PROMs characteristics (e.g., primary/secondary endpoint, generic/specific measure, assessment time).
- The data extraction form was first piloted on a sample of 20 reports by three reviewers independently and then completed by at least two reviewers. Multivariate logistic regression was performed in Stata to identify the variables that impacted on the use of patient-reported evidence in EPARs.

RESULTS

A total of **403** EPARs were included in the analysis; 197 (**48.9%**) reported any use of PROs/PROMs. The use of PROMs was more common in some therapeutic areas than others (e.g., rheumatology: 94.4% vs. infectious diseases: 18.5%), and for orphan drugs (**66.7%**) [Figure 1]. The use of PROs/PROMs changed over time (from **51.8%** in 2017 to **54.3%** in 2021) [Figure 2]; however, in **over 70%** of cases PROs were secondary or exploratory endpoints [Figure 3]. The most common PRO was quality of life (**30.7%**) [Figure 4]. Among the PROMs, 167 (**25.3%**) were generic. EQ-5D (**9.5%**), SF-36/SF-12 (**6.1%**) and EORTC QLQ-C30 (**5.1%**) were the instruments most frequently used [Figure 5]. The average number of measures for each EPAR was 1.6 (range: 0-14). The likelihood of using PROs/PROMs was negatively affected by generic (OR=0.01, p<0.00) and biosimilar status (OR=0.44, p=0.02) [Table1].

Figure 1: Use of PROs/PROMs and drug characteristics

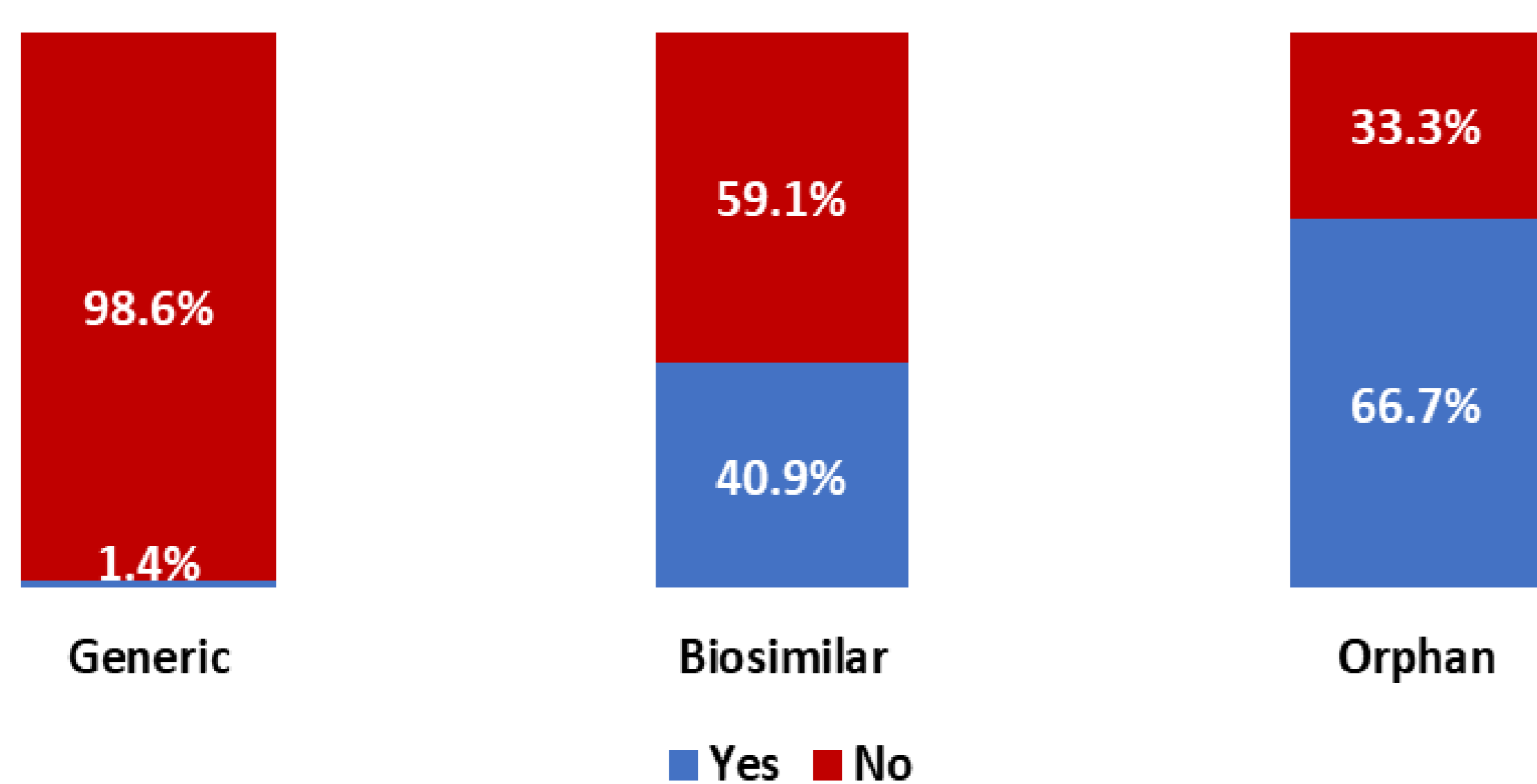


Figure 2: Use of PROs/PROM over time

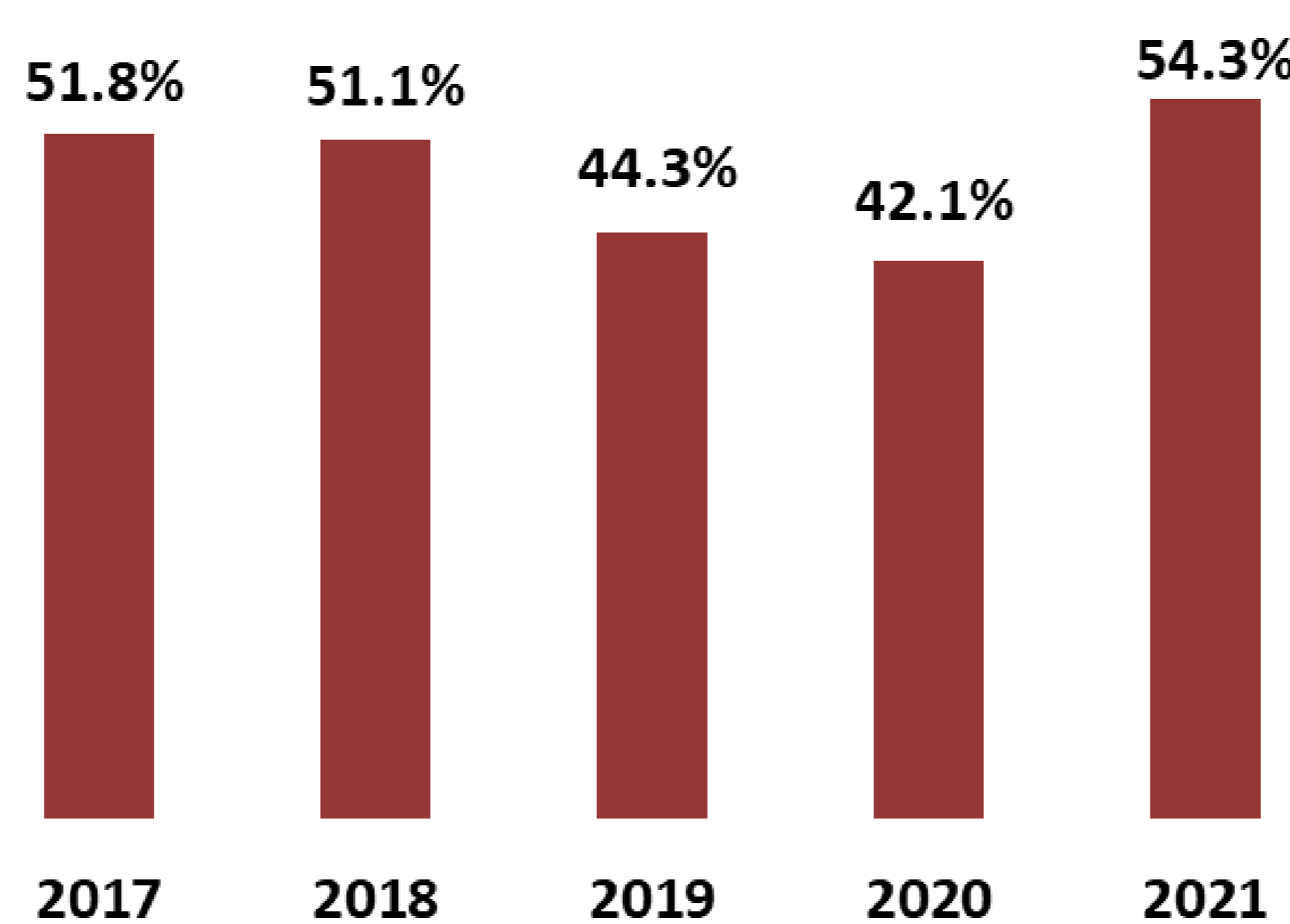


Figure 3: PRO study endpoint

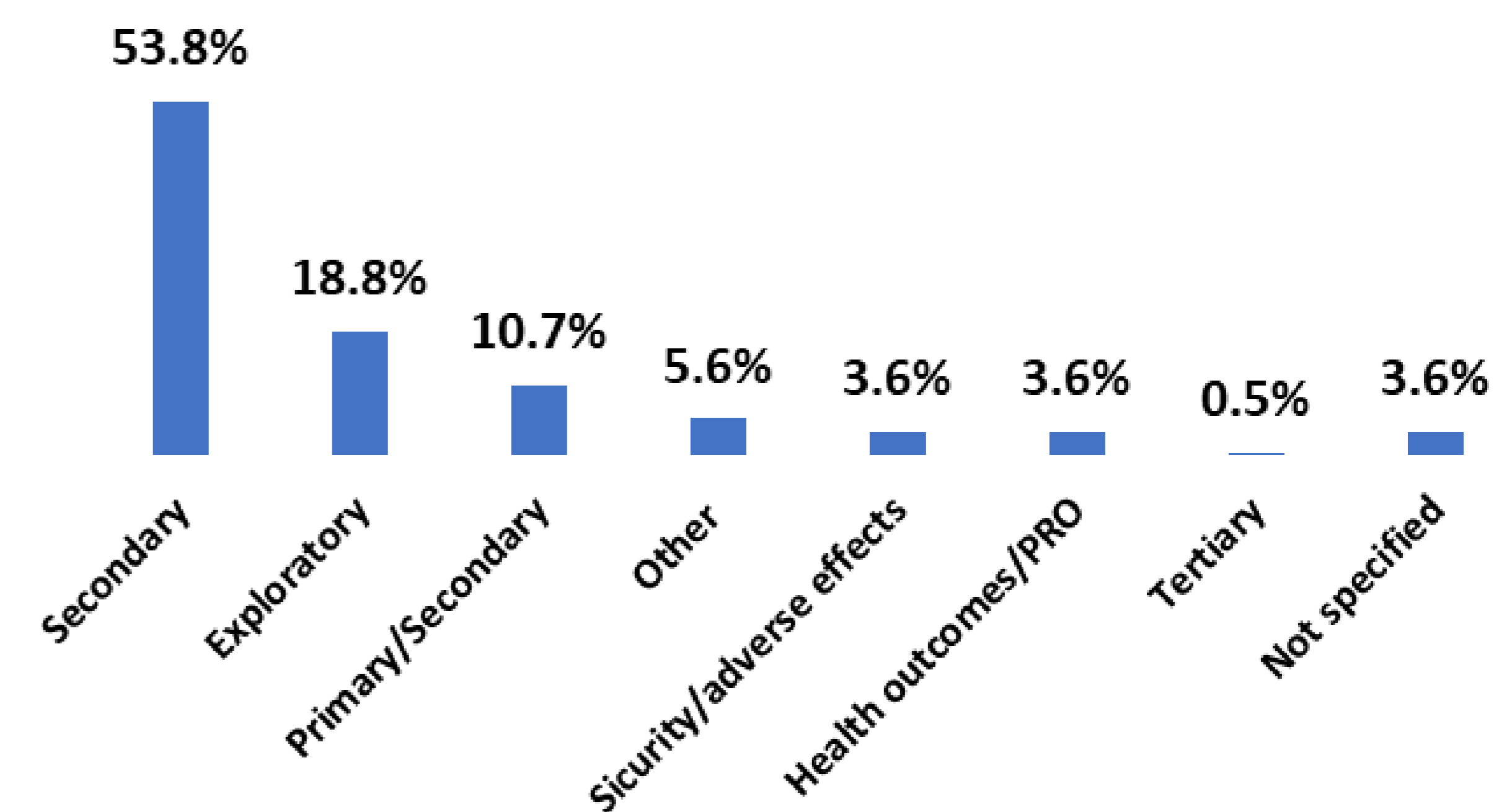


Figure 4: PRO Concept

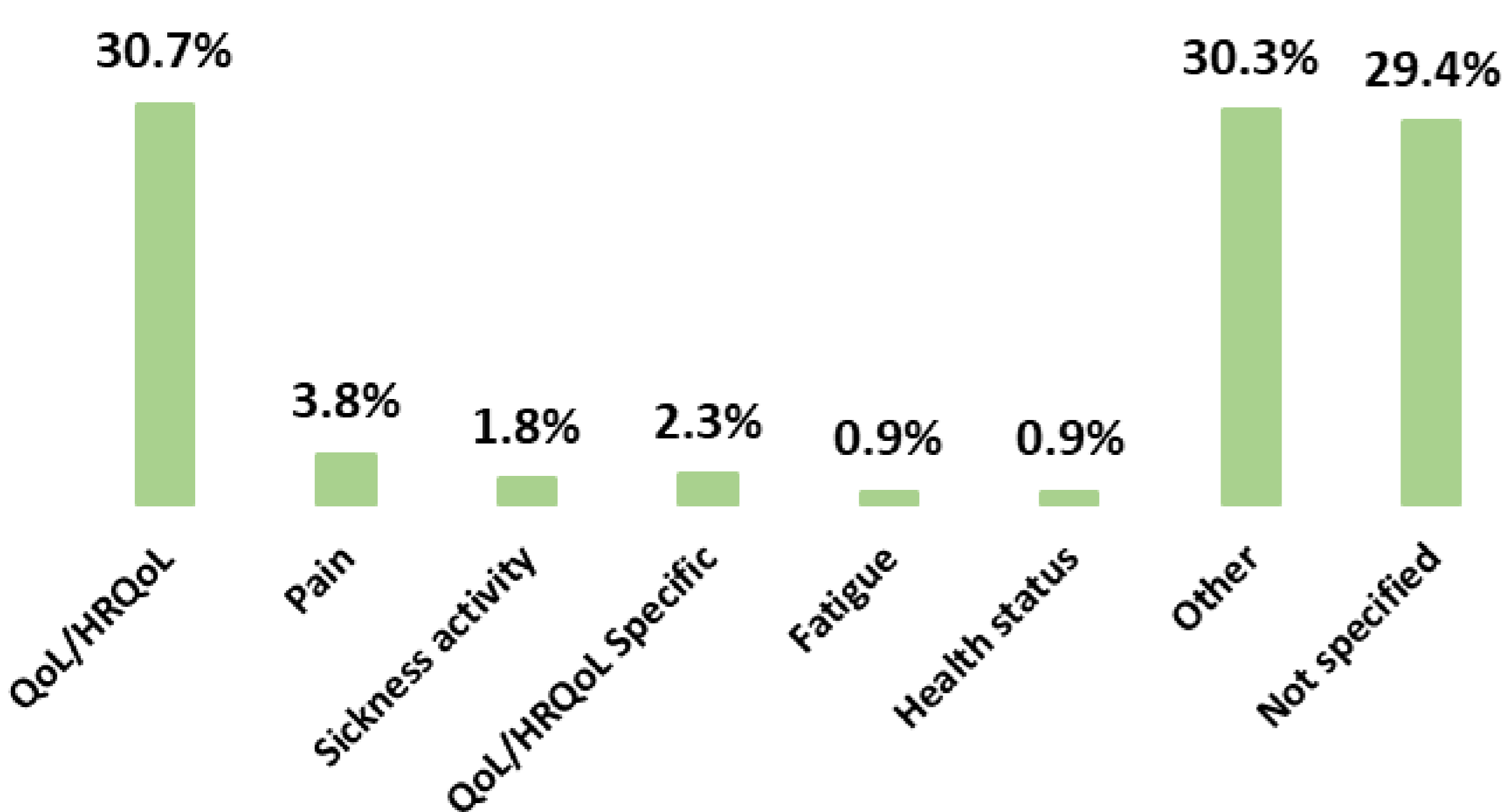


Figure 5: Type of PROMs

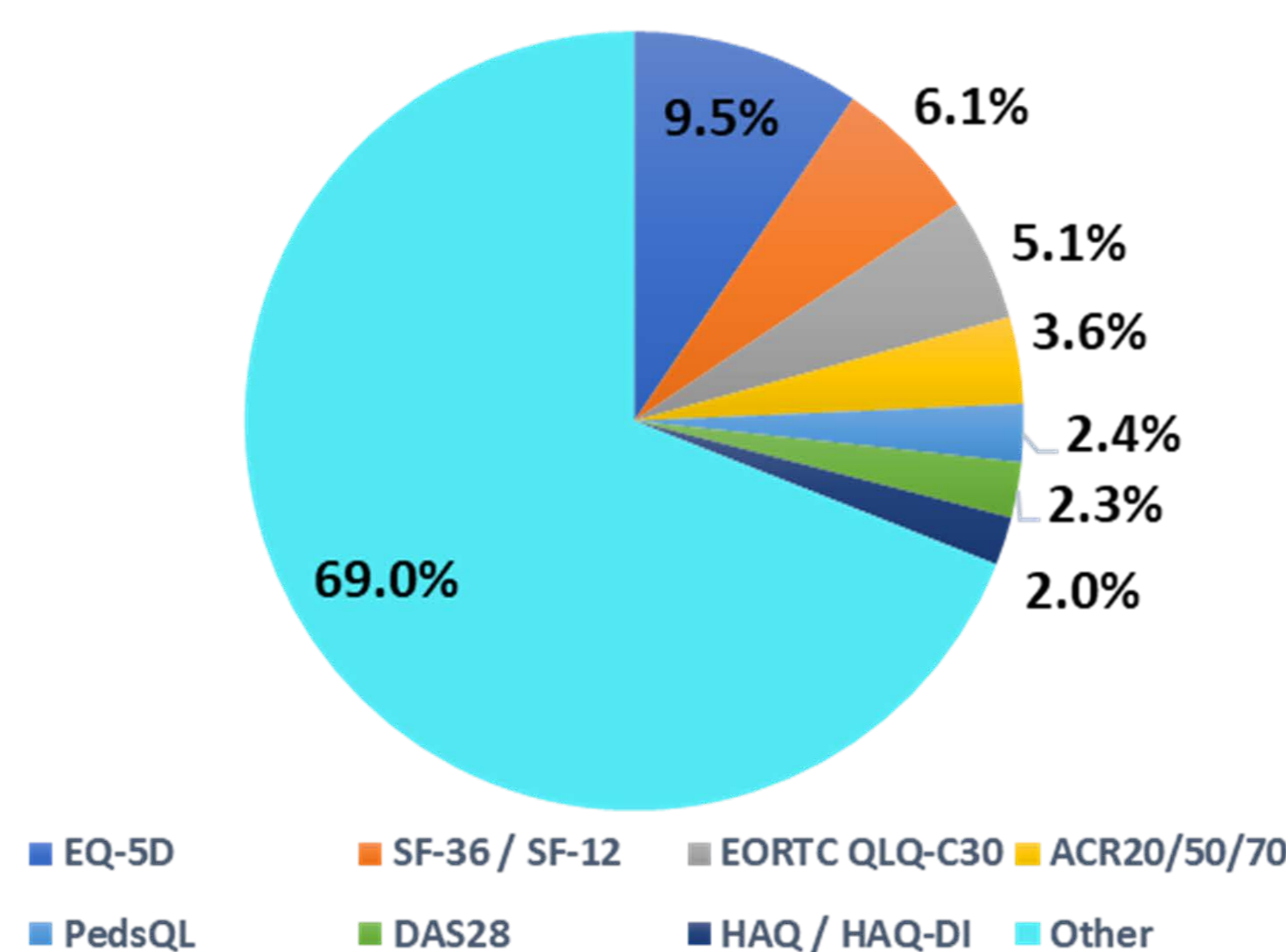


Table 1: Logistic regression

PROs/PROMs	OR	St.Err.	t-value	p-value	[95% Conf. Interval]	Sig.
Generic	0.01	0.01	-4.64	0.00	0.01 0.07	***
Biosimilar	0.44	0.15	-2.41	0.016	0.22 0.86	**
Orphan	1.34	0.39	1.02	0.307	0.76 2.36	
2017	1.00					
2018	0.76	0.27	-0.79	0.428	0.38 1.51	
2019	0.64	0.25	-1.15	0.251	0.30 1.37	
2020	0.51	0.18	-1.89	0.059	0.26 1.03	*
2021	0.91	0.33	-0.27	0.786	0.45 1.85	
Constant	2.06	0.56	2.64	0.008	1.20 3.51	***

Mean dependent var 0.489 SD dependent var 0.500
Pseudo r-squared 0.202 Number of obs 403
Chi-square 112.857 Prob > chi2 0.000
Akaike crit. (AIC) 461.618 Bayesian crit. (BIC) 493.610

***p<.01, **p<.05, *p<.1

DISCUSSION

- This study showed that still less than half of EPARs reported any use of PROMs, signaling probably a limited role of those outcomes in marketing authorization
- A progressive harmonization of the PROMs, through consensus generation among relevant stakeholders, across key target domains and indications, could favor the inclusion of PROs evidence in regulatory approvals
- Digital health solutions for continuous monitoring of electronic PROs may help once issues of interoperability, security, privacy, logistics and ethics have been addressed

REFERENCES

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- EMA (2020). Regulatory Science Strategy to 2025. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf.