

Refill patterns, dispensing adherence and potential waste in medical cannabis: a retrospective observational study at an Italian Regional Centre

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Abstract

Background

Medical cannabis therapy is embedded in complex regulatory and compounding pathways, in which traceability is high up to the point of dispensing but more limited during home use. Compounded preparations, often supplied in standardised volumes and characterised by limited beyond-use dates, may generate discrepancies between the amount dispensed, the prescribed dosage and the patient's actual therapeutic need. This study evaluated refill patterns as an indirect indicator of dispensing adherence and estimated the potential waste associated with compounded cannabis-based preparations.

Methods

A retrospective, single-centre, longitudinal observational study was conducted at the Regional Cannabis Compounding Centre of the Marche Region, Italy. Dispensations performed between 1 January and 31 December 2025 were included. Dispensing adherence was estimated using the gap between the expected refill date and the actual dispensing date; potential waste was defined as the amount dispensed that was not justified by the theoretical need within the 60-day validity period of the preparation. The analysis was descriptive.

Results

Overall, 1233 dispensations relating to 372 patients were analysed; 845 evaluable dispensations subsequent to the first were used to evaluate refill patterns. Among patients with known sex, 76.1% were female, and the most frequent therapeutic indication was chronic pain. A total of 67.3% of dispensations showed no estimated potential waste. Total potential economic waste was €10545.20. The highest mean waste by preparation was observed for Bedrocan, whereas the greatest aggregate economic impact was attributable to FM2. The highest mean waste by refill pattern was observed among patients classified as adherent.

Conclusions

These findings suggest that potential waste in medical cannabis therapy does not depend exclusively on patients' refill behaviour, but also on structural factors of the dispensing model, including prepared volumes, low daily dosages, limited validity periods and progressive titration.

Trial registration

Not applicable.

Background

Medical cannabis is used in several clinical contexts as symptomatic or supportive treatment, particularly when conventional therapies are ineffective or not tolerated. The main indications discussed in the literature include chronic pain, especially neuropathic pain, spasticity associated with multiple sclerosis, chemotherapy-induced nausea and vomiting, appetite stimulation in cachexia, and some forms of drug-resistant epilepsy [1–6]. Its clinical interest derives from the interaction of phytocannabinoids, particularly delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), with the endocannabinoid system and additional molecular targets [2, 3].

The clinical use of cannabis, however, presents specific challenges. Unlike many industrially manufactured medicines, compounded cannabis preparations require personalisation of formulation, concentration, dosage form and dosing regimen. The heterogeneity of compounded preparations and the variability of clinical response make it difficult to standardise therapeutic pathways, requiring individual titration according to the practical “start low, go slow” approach [7, 8]. This process may lead to dose changes over time and make it difficult to estimate the actual consumption of the preparation with precision.

In the Italian context, medical cannabis is regulated by a strict framework governing production, procurement, prescription, compounding, recording and dispensing [9–13]. The substance is managed within the healthcare system through traceability procedures similar to those applied to controlled substances. However, control is particularly robust up to the point of delivery to the patient and becomes more limited during home use. Once dispensed, the compounded preparation cannot be returned or reused within the healthcare circuit, even in the event of treatment discontinuation, dose modification or non-use.

This feature introduces an important organisational issue: the potential discrepancy between the quantity prescribed, compounded, dispensed and actually required for therapy. Oil-based preparations may be supplied in volumes that are not always fully adaptable to individual dosing needs and are characterised by a limited period of validity. In patients receiving low doses or undergoing titration, the dispensed volume may therefore exceed the amount theoretically usable within the valid period, resulting in potential waste of raw material and an economic impact on the Regional Health Service.

In the absence of direct and systematic tools to measure home administration, the analysis of refill timing represents a possible indirect strategy for observing post-dispensing behaviour. Comparing the expected refill date, calculated on the basis of the prescribed daily dose, with the actual refill date makes it possible to describe patterns of continuity, early refill, delayed refill or discontinuity. This measure is not equivalent to actual therapeutic adherence, but it may represent a useful indicator for organisational surveillance and for identifying potential areas of quantitative inappropriateness.

The aim of the present study was to analyse dispensing patterns for medical cannabis in a real-world regional clinical practice setting, estimate dispensing adherence using refill timing, quantify potential waste and evaluate its economic impact. An additional objective was to explore whether waste was more closely associated with patients' refill behaviour or with structural features of the prescribing and dispensing model.

Methods

Study design and setting

A retrospective, single-centre, longitudinal observational study was conducted to analyse medical cannabis dispensing patterns (refills). The study was performed at the Regional Cannabis Compounding Centre (CRAC) of the Marche Region and included all dispensations performed between 1 January and 31 December 2025.

The CRAC operates within a structured regional model for managing compounded cannabis-based preparations. Within the regional pathway, the hospital pharmacist is responsible for prescription verification, procurement of raw materials, compounding, recording and dispensing. The management of cannabis as a controlled substance also requires documentary traceability and recording of movements, but does not allow direct monitoring of home use after delivery to the patient.

Population

All patients who received at least one medical cannabis dispensation at the Regional Centre during the observation period were included. For the analysis of refill patterns, each patient's first dispensation was excluded by definition, and subsequent dispensations were considered only when the interval between consecutive refills and the prescribed daily dose could be evaluated from complete and interpretable records.

Patients with only one dispensation during the study period could contribute to the descriptive population analysis but not to the refill-specific analysis, because refill behaviour over time could not be assessed. Subsequent dispensations with incomplete or non-interpretable prescription data were also excluded from the refill analysis. Patients were identified using a unique anonymous alphanumeric code.

Data sources and variables

Data were collected from therapeutic plans, non-repeatable medical prescriptions and electronic records used by the hospital pharmacy. For each patient, demographic information, clinical and prescription-related variables, and dispensing data were extracted.

The variables considered included age, sex, therapeutic indication, type of preparation, dispensing date, quantity dispensed in mL and daily dose expressed in mL/day. Age was available in grouped classes (< 40, 40–60, 60–80 and > 80 years) in the analytic extract and was summarised as recorded. Therapeutic indications were coded according to the categories used in the regional pathway: pain associated with spasticity, chronic pain, nausea and vomiting associated with chemotherapy/radiotherapy/HIV, cachexia/anorexia, resistant glaucoma, Gilles de la Tourette syndrome and other indications.

Based on the collected variables, several derived variables were calculated: theoretical treatment duration, expected refill date, interval between consecutive dispensations, refill gap, theoretical need within the validity period and potential waste.

Definition of refill adherence

Adherence was assessed indirectly by analysing refill timing. The theoretical duration of therapy was calculated as the ratio between the quantity dispensed and the prescribed daily dose. The expected refill date was obtained by adding the theoretical duration to the dispensing date. The refill gap was defined as the difference, in days, between the actual refill date and the expected refill date. Negative values indicated early refill, whereas positive values indicated delayed refill.

A tolerance interval of ± 10 days around the expected refill date was defined. Dispensations subsequent to the first were classified into four patterns: adherent, if the refill occurred between -10 and $+10$ days from the expected date; early, if the refill occurred more than 10 days earlier than expected; delayed, if the refill occurred more than 10 days later than expected but within 60 days; and discontinuous, if the refill occurred more than 60 days later than expected or the dispensing sequence was otherwise irregular in a manner compatible with possible treatment interruption. This definition describes dispensing adherence and does not directly measure actual home administration of the preparation.

Definition of potential waste and economic analysis

Potential waste was defined as the portion of the dispensed preparation that was not justified by the theoretical need within the preparation's validity period. Considering an average validity of oil-based extracts of 60 days, the quantity theoretically usable was calculated as the daily dose multiplied by 60 days. This 60-day validity period reflected the standard beyond-use dating applied to oil-based cannabis preparations within the regional compounding pathway. Potential waste was then estimated as the difference between the quantity dispensed and the theoretically usable quantity, setting negative values to zero.

The economic impact of potential waste was estimated by converting the potentially excess mL into cost, based on the unit cost associated with each specific type of preparation. Unit costs were derived from the regional pharmacy costing system used for cannabis-based compounded preparations during

the study period. Results were expressed as the mean economic value per dispensation and as the overall economic value by type of preparation during the observation period.

Statistical analysis and ethics

The statistical analysis was descriptive. Categorical variables were reported as absolute frequencies and percentages. Continuous variables were described using mean, median and standard deviation, when available. In some cases, as specified in the Results section, statistics were estimated from data grouped into frequency classes and should therefore be interpreted as descriptive values.

The tax identification code was used exclusively during the preliminary extraction phase to verify patient uniqueness and avoid duplicate records; it was then removed and replaced by an anonymous alphanumeric code. No direct or indirect personal identifiers were included in the analytical dataset. The study used retrospective dispensing data collected during routine clinical practice, with no direct intervention on patients. Data were anonymised before analysis in accordance with the Declaration of Helsinki, Regulation (EU) 2016/679 (GDPR), Italian Legislative Decree 196/2003 as amended by Legislative Decree 101/2018, and applicable national data-protection legislation. Individual informed consent was not required because the analytical dataset could not be traced back to identified or identifiable individuals.

Reporting standards

The study was reported in accordance with the STROBE reporting guideline for observational studies. A populated STROBE checklist is provided as Additional file 1. During manuscript preparation, ChatGPT (OpenAI), an artificial intelligence-based language model, was used for editorial drafting support and linguistic restructuring of the authors' Italian-language draft. The authors reviewed, verified and edited all content and take full responsibility for the final manuscript.

Results

Study population and dispensations

During the observation period, 1233 medical cannabis dispensations relating to 372 unique patients were analysed. Of these, 372 represented each patient's first dispensation, leaving 861 subsequent dispensations potentially eligible for refill analysis. The refill-pattern and dispensing-adherence analysis included 845 evaluable subsequent dispensations; therefore, 16 of the 861 subsequent dispensations were not included in that analysis under the study evaluability criteria described above.

Among the 368 patients with available sex data, 280 were female (76.1%) and 88 were male (23.9%); data were missing for 4 patients (Fig. 1). The age distribution, calculated for the 368 patients with available demographic data, showed a prevalence of the 60-80-year age class ($n = 153$) and the 40-60-

year age class (n = 134), followed by patients aged > 80 years (n = 56) and patients aged < 40 years (n = 25). Overall, the study population therefore consisted mainly of adults and older adults (Fig. 2).

Figure 1. Distribution of the study population by sex. Sex data were available for 368 of 372 patients.

Figure 2. Distribution of the study population by age class. Age data were available for 368 patients and were recorded in grouped classes.

The most frequent therapeutic indication was chronic pain, which affected 304 patients, corresponding to 84.0% of patients with available indication data. Ten patients had missing indication data. The other indications were much less represented overall (Fig. 3).

Figure 3. Distribution of the study population by therapeutic indication. Percentages are calculated among patients with available indication data (n = 362); 10 patients had missing indication data. A logarithmic x-axis is used to improve readability of less frequent categories.

Table 1
Characteristics of the study population

Characteristic	Value
Unique patients included	372
Patients with known sex	368
Female sex	280/368 (76.1%)
Male sex	88/368 (23.9%)
Age < 40 years	25/368 (6.8%)
Age 40–60 years	134/368 (36.4%)
Age 60–80 years	153/368 (41.6%)
Age > 80 years	56/368 (15.2%)
Most frequent indication	Chronic pain: 304 patients (84.0% of cases with available indication)
Indication not available	10 patients
<i>Note. Percentages are calculated for cases with available data.</i>	

Dispensed preparations

Personalised preparations represented the most frequently dispensed category, with 671 dispensations (54.4%), followed by FM2-based preparations, corresponding to 305 dispensations (24.7%). The remaining categories were Bedrolite (98 dispensations; 7.9%), CBD (84; 6.8%), Bediol (55; 4.5%) and Bedrocan (20; 1.6%).

Table 2
Distribution of dispensations by type of preparation

Preparation	Dispensations, n	Percentage
Personalised preparations	671	54.4%
FM2	305	24.7%
Bedrolite	98	7.9%
CBD	84	6.8%
Bediol	55	4.5%
Bedrocan	20	1.6%
Total	1233	100.0%

Refill patterns and theoretical treatment coverage

The refill gap, calculated for the 845 dispensations subsequent to the first, showed an estimated mean of -0.3 days, a median of -7.7 days and a standard deviation of 31.2 days. Although the mean value was close to zero, the high dispersion indicated marked variability in refill behaviour, with both early refills and prolonged delays.

The classification of refill patterns showed a predominance of early refills (49%), followed by delayed refills (23%), adherent refills (22%) and discontinuous patterns (7%). The theoretical treatment duration calculated on the basis of the prescribed daily dose was concentrated in the 30-60-day class, but a non-negligible proportion of dispensations had theoretical coverage exceeding 90 days. Descriptive statistics estimated from grouped data showed a mean theoretical duration of approximately 61.0 days, a median of 52.0 days and a standard deviation of 25.9 days.

Table 3
Main indicators of refill patterns and theoretical treatment coverage

Indicator	Value
Dispensations subsequent to the first included in the refill analysis	845
Mean refill gap	-0.3 days
Median refill gap	-7.7 days
Standard deviation of refill gap	31.2 days
Early refill pattern	49%
Delayed refill pattern	23%
Adherent refill pattern	22%
Discontinuous pattern	7%
Mean theoretical treatment duration	61.0 days
Median theoretical treatment duration	52.0 days
Standard deviation of theoretical treatment duration	25.9 days
<i>Note. Some statistics are descriptive estimates derived from data grouped into frequency classes.</i>	

Potential waste and economic impact

Most dispensations showed no estimated potential waste: 67.3% fell into the 0 mL class. The remaining dispensations showed variable levels of potential waste: 5.0% in the > 0–10 mL class, 8.6% in the > 10–30 mL class, 13.5% in the > 30–60 mL class and 5.6% in the > 60 mL class. The median potential waste was 0 mL.

The distribution was markedly right-skewed: potential waste did not affect all dispensations uniformly, but was concentrated in a subgroup of cases with more substantial excess volumes. During the observation period, the overall economic value of potential waste was estimated at €10545.20.

Table 4
Potential and economic waste by type of preparation

Preparation	Dispensations, n	Mean waste, mL	Mean economic waste	Total economic waste
Personalised preparations	671	1.46	€1.30	€848.90
FM2	305	29.77	€19.30	€5892.90
Bedrolite	98	33.65	€8.10	€794.20
CBD	84	16.67	€13.40	€1127.50
Bediol	55	13.53	€8.80	€482.90
Bedrocan	20	39.30	€69.90	€1398.80
Overall total	1233	-	-	€10545.20
<i>Note. Total economic value depends both on mean waste per dispensation and on the number of dispensations for each preparation type.</i>				

The comparison between preparation types showed higher mean potential waste values for Bedrocan (39.30 mL), Bedrolite (33.65 mL) and FM2 (29.77 mL), whereas personalised preparations showed the lowest mean value (1.46 mL). Considering the mean economic impact, Bedrocan was the category with the highest value (€69.90 per dispensation). However, the greatest overall economic impact was attributable to FM2 (€5892.90; 55.9% of the total), due to its higher dispensing frequency.

Relationship between refill pattern and potential waste

The analysis of mean potential waste in relation to refill adherence patterns showed descriptive differences between groups. The highest value was observed among patients classified as adherent, with a mean waste of 19.74 mL and a mean economic value of €13.77. This was followed by discontinuous, delayed and early refillers. The lowest mean value was observed among early refillers.

Within the 845 dispensations included in the refill-pattern analysis, the overall mean potential waste was 12.56 mL and the mean economic value was €8.20. The most relevant finding is that the highest mean levels were not associated with apparently less regular patterns, but with patients who refilled the preparation in a manner compatible with the expected date. This result suggests that potential waste does not depend exclusively on patient refill behaviour.

Table 5
Mean potential and economic waste by refill pattern

Refill pattern	Mean waste, mL	Mean economic waste
Adherent	19.74	€13.77
Discontinuous	14.98	€7.50
Delayed	12.20	€7.10
Early	9.21	€6.34
Overall mean	12.56	€8.20
Note. The 12.56 mL overall mean refers specifically to the 845 dispensations included in the refill-pattern analysis; Table 4 reports preparation-specific means across the full set of 1233 dispensations.		

Discussion

Principal findings

This study systematically describes refill patterns and potential waste associated with the dispensing of medical cannabis at an Italian Regional Centre. The main findings are fourfold. First, refill timing showed high variability despite an overall mean gap close to zero. Second, potential waste did not affect most dispensations, but was concentrated in a minority of cases with substantial excess volumes. Third, personalised preparations were associated with substantially lower mean waste values than some standardised formulations. Fourth, the highest mean waste was observed in patients classified as adherent, suggesting that the phenomenon cannot be explained solely by refill regularity.

These elements support the interpretation of potential waste as having a structural component. In other words, even a patient who refills the preparation within the expected timeframe may receive a quantity exceeding the amount theoretically usable within the validity period, especially when the daily dosage is low, when treatment is being titrated or when the compounded volume is not fully adaptable to the individual need.

Refill as an organisational indicator

The refill gap is a useful indicator for describing post-dispensing behaviour, but it should be interpreted with caution. Early refills may reflect a precautionary behaviour aimed at avoiding treatment interruption, logistical difficulties in accessing the Centre, the need to plan refills in advance, or home stockpiling. Conversely, delayed or discontinuous refills may be compatible with treatment discontinuation, underuse, dose changes, intercurrent clinical events or failure to continue follow-up.

The retrospective nature of the data does not allow these explanations to be distinguished. However, the high dispersion observed confirms that refill data may be used as an organisational surveillance tool.

The systematic integration of refill indicators into information systems could allow pharmacists and prescribing physicians to identify patients with irregular patterns and activate counselling, dosage reassessment or verification of treatment continuity.

Potential waste and preparation type

Estimated potential waste should be distinguished from actual waste. The calculated value does not necessarily document product that was actually unused or disposed of, but indicates the theoretically excess amount relative to the estimated need within 60 days. This indicator is nonetheless relevant because it identifies a potential area of quantitative inefficiency in a pathway characterised by costs, regulatory constraints and the impossibility of reusing preparations that have already been dispensed.

The differences observed between preparations are consistent with a role of compounding and dispensing methods. The low mean waste of personalised preparations suggests that greater adaptability of the compounded volume to the patient's dosage may reduce the discrepancy between quantity dispensed and theoretical need. Conversely, higher mean values in some standardised formulations indicate that concentration, dispensed volume and validity period may combine unfavourably, especially in patients receiving low doses.

From an economic perspective, the case of FM2 is particularly relevant. Although Bedrocan showed the highest mean waste value per dispensation, FM2 represented the main source of aggregate economic impact. This finding shows that optimisation strategies should consider not only the mean cost per individual dispensation, but also the frequency of use of each formulation within the regional system.

Structural waste and clinical interpretation

The observation of higher mean waste among adherent patients is the most meaningful interpretive finding. In theory, greater waste might have been expected among delayed or discontinuous patients, because treatment interruption or irregularity could promote accumulation and non-use. The data do not confirm this hypothesis: higher waste among regular refillers suggests that the problem may derive, at least in part, from the way in which therapy is quantified, compounded and dispensed.

This evidence suggests that potential waste should be considered not only as a consequence of patient adherence, but as the result of the interaction between clinical, prescribing and organisational factors. These include dosage variability, progressive titration, low daily doses, the availability of standardised formats or volumes, limited validity periods and the difficulty of monitoring home residues. The concept of structural waste therefore describes a portion of excess volume generated by the mismatch between the quantity compounded and the actual theoretical need, even in the presence of apparently appropriate refill behaviour.

Organisational and policy implications

The findings have direct implications for the role of the hospital pharmacist. Formal prescription verification should be complemented by an assessment of quantitative appropriateness, particularly in

patients receiving low doses or undergoing titration. Conversion tools between drops/day, mL/day, mg/day, mL/month and mg/month may support dialogue between the prescribing physician and the pharmacist, enabling a more accurate estimate of need and greater personalisation of compounded volumes.

An operational approach could include systematic calculation of theoretical coverage before compounding; alerts for dispensations with theoretical duration exceeding the validity period; reassessment of volume in patients receiving low doses; periodic monitoring of refills; verification of dose changes; and counselling on correct use, storage and disposal of the preparation. These interventions should not limit access to therapy, but should make it more appropriate and sustainable.

The study findings are consistent with a regional organisational review pathway oriented towards standardisation, digitalisation and greater appropriateness of care. Marche Regional Government Resolution No. 749 of 16 June 2026, concerning procedural and organisational guidelines for the dispensing and compounding of cannabis-based magistral preparations, provides a favourable framework for integrating refill indicators, dosage conversions and consumption monitoring into audit and planning processes [14].

Strengths and limitations

The main strength of this study is the analysis of a real-world clinical practice dataset covering a full year of activity at a Regional Centre. The availability of prescription and dispensing data makes it possible to describe a phase of the therapeutic pathway that is often poorly explored: the period after dispensing, during which issues related to continuity, home traceability and economic sustainability emerge.

The study also has limitations. Adherence was assessed indirectly through refills and not by measuring actual intake. Estimated waste represents potential waste and not necessarily a quantity actually unused or disposed of. Some statistics were estimated from grouped data rather than complete individual-level data, requiring caution in interpretation. Finally, the retrospective single-centre design limits the generalisability of the results to other regional or organisational contexts. Potential sources of bias include the retrospective nature of the analysis, the reliance on dispensing records as indirect indicators of use, incomplete or non-interpretable prescription data in some observations, and the absence of direct measurement of residual product at home.

Future studies should integrate refill data with longitudinal clinical information, dose changes, patient-reported outcomes, recording of residues actually present at home and comparison between different regional models. It would also be useful to evaluate the impact of digital tools and dosage conversion tables on the reduction of potential waste and the improvement of therapeutic continuity.

Conclusions

The analysis of refill patterns and potential waste of compounded cannabis-based preparations shows that post-dispensing management is a relevant component of the therapeutic pathway. In the Regional

Centre analysed, most dispensations showed no potential waste; however, a proportion of cases showed substantial theoretical excess volumes, with an estimated overall economic impact of €10545.20 in 2025.

The higher mean waste observed among patients classified as adherent indicates that the phenomenon cannot be attributed solely to refill irregularities, but may derive from structural elements of the dispensing model. The reduction of potential waste should therefore be pursued not by limiting access to therapy, but by improving the personalisation of compounded quantities, refill monitoring, integration between prescriber and pharmacist, and digitalisation of the pathway. These interventions may contribute to making medical cannabis therapy more appropriate, safe and sustainable.

Abbreviations

CBD
cannabidiol
CRAC
Regional Cannabis Compounding Centre
DGR
Regional Government Resolution
FM2
Italian nationally produced cannabis variety/preparation
mL
millilitre
SSR
Regional Health Service
THC
delta-9-tetrahydrocannabinol

Declarations

Ethics approval and consent to participate:

This retrospective observational study analysed anonymised dispensing data collected during routine clinical practice. No intervention, treatment modification, additional procedure or direct contact with patients was undertaken for research purposes. Identifiable personal data were used only during the preliminary extraction phase to verify patient uniqueness and were not included in the analytical dataset. According to the institutional assessment of IRCCS-INRCA, formal ethics committee approval was not required because the study was retrospective, involved no intervention on patients and was conducted on anonymised data that could not be traced back to identified or identifiable individuals. The study was conducted in accordance with the Declaration of Helsinki, Regulation (EU) 2016/679 (GDPR), Legislative

Decree 196/2003 as amended by Legislative Decree 101/2018, and applicable national data-protection legislation. Individual informed consent was not required for the same reasons.

Consent for publication:

Not applicable. The manuscript does not contain any individual person's data, images, videos or identifiable personal details.

Competing interests:

The authors declare that they have no competing interests.

Additional files

Additional file 1. File format: DOCX. Title: STROBE checklist. Description: Completed STROBE reporting checklist for this retrospective observational study.

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Author Contribution

EV, PC and MDM contributed to the conception and design of the study. EV, AF, FV, LM, DR and NM contributed to data collection and data organisation. EV, PC, PF and MDM contributed to data analysis and interpretation. LB contributed to methodology, ethical interpretation and supervision. EV drafted the first version of the manuscript. MN, PF, LB and MDM critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Availability of data and materials:

Aggregated data supporting the main findings are included in this article. The anonymised individual-level dataset used and/or analysed during the current study is not publicly available because of confidentiality and data-protection restrictions, but may be available from the corresponding author on reasonable request and subject to applicable institutional procedures.

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Figures

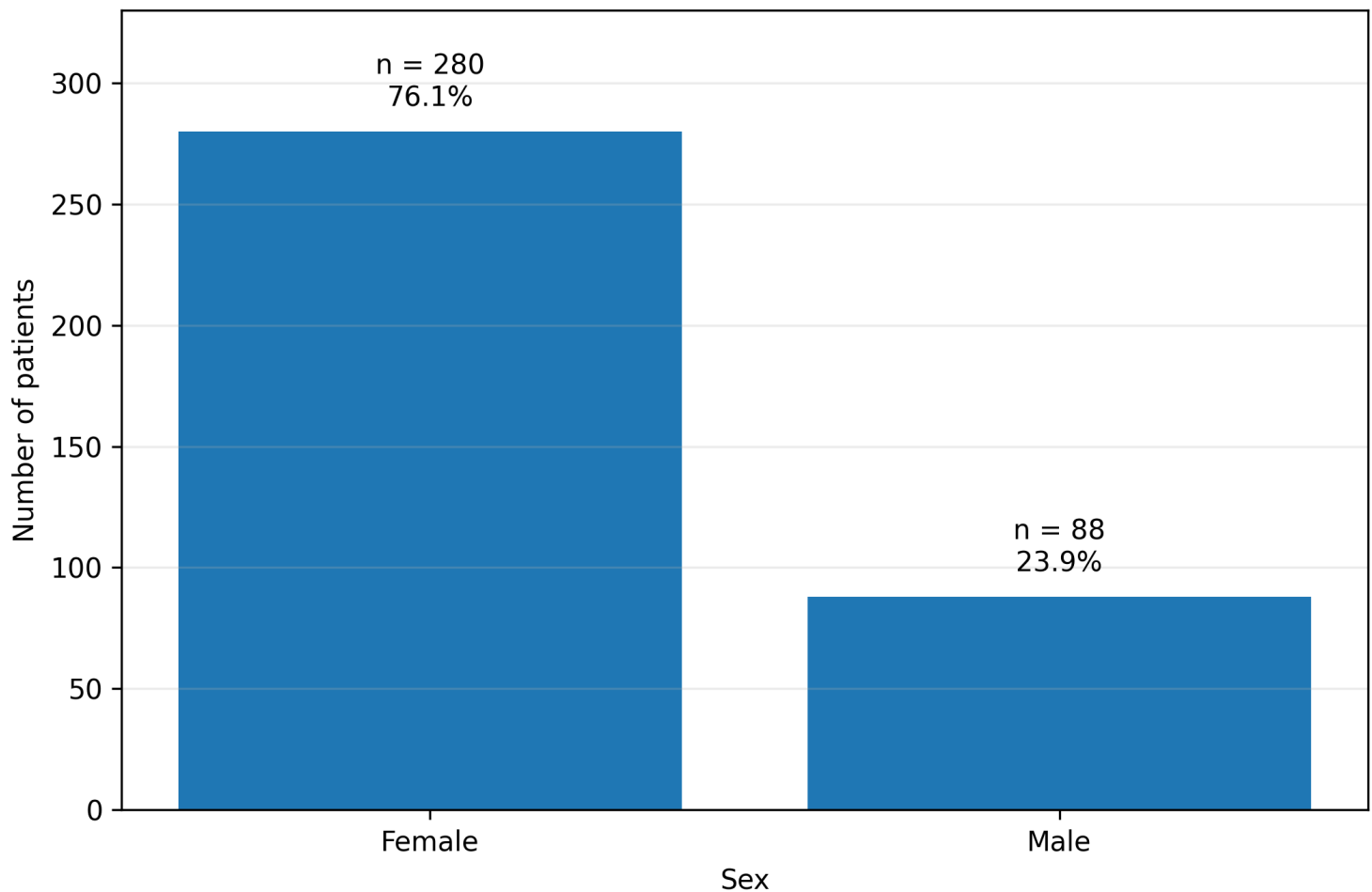


Figure 1

Distribution of the study population by sex. Sex data were available for 368 of 372 patients.

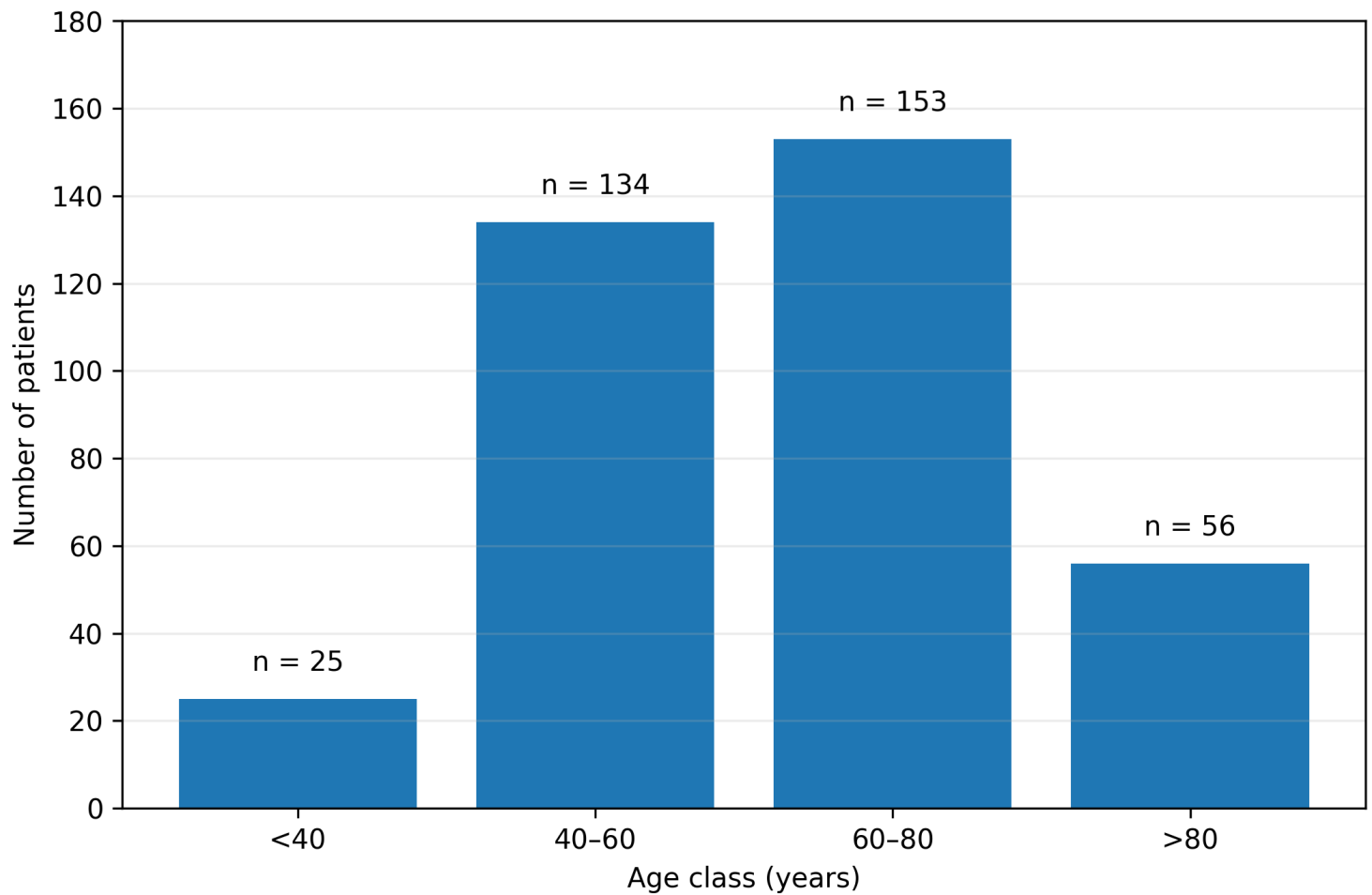


Figure 2

Distribution of the study population by age class. Age data were available for 368 patients and were recorded in grouped classes.

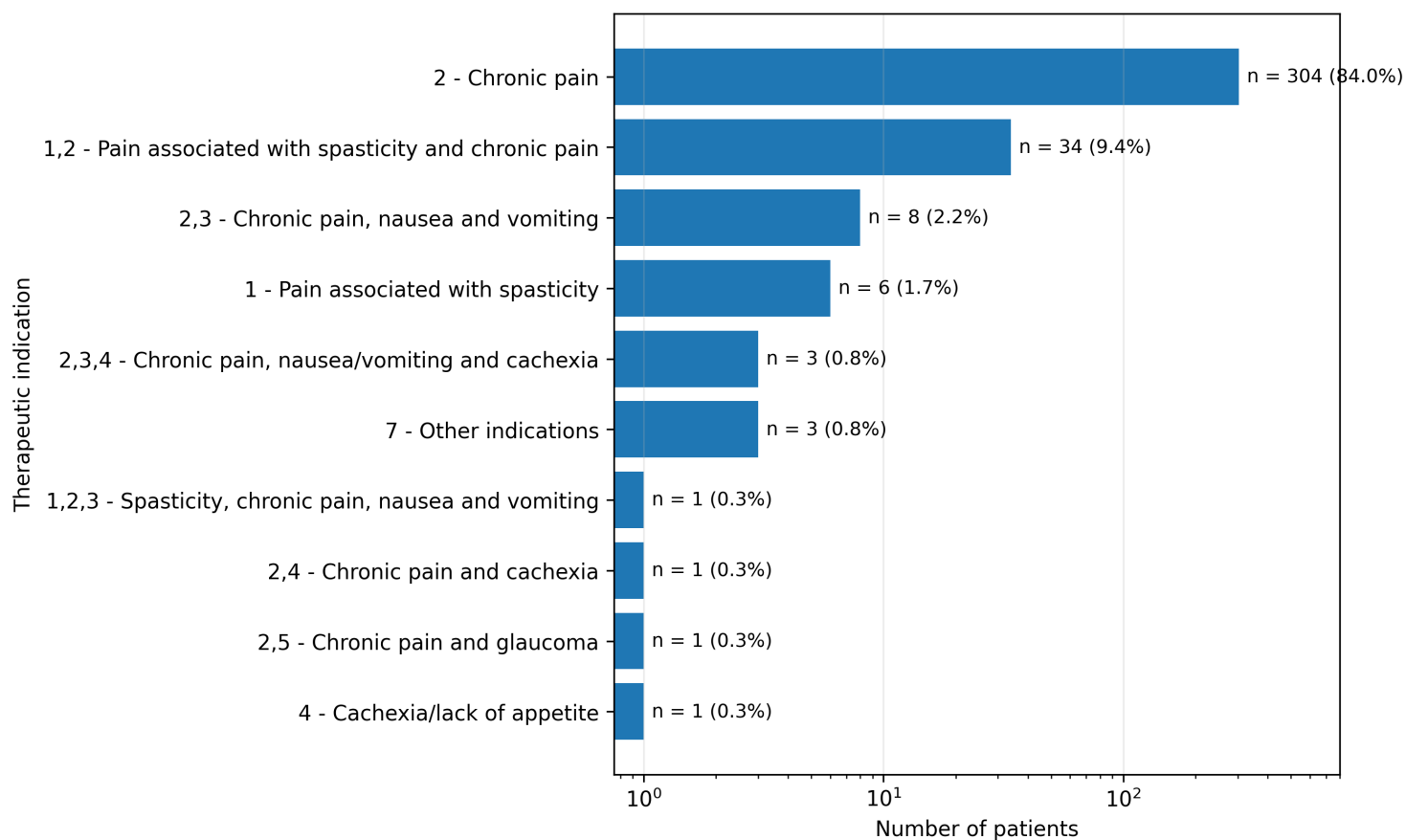


Figure 3

Distribution of the study population by therapeutic indication. Percentages are calculated among patients with available indication data (n = 362); 10 patients had missing indication data. A logarithmic x-axis is used to improve readability of less frequent categories.