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Outcomes of care during the last month of life: a systematic review to inform the development of a core outcome set

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Background: To date, there is a lack of standardization and consensus on which outcomes are central to assess the care provided to patients in the last month of life. Therefore, we aimed to conduct a systematic review to identify relevant outcomes to inform the development of a core outcome set for the best care for the dying person.

Methods: We conducted a systematic review of outcomes reported in the scientific literature about the care for the dying person in the last month of life. We searched for peer-reviewed studies published before February 2022 in four electronic databases. To categorise the outcomes, we employed the taxonomy developed by the "Core Outcome Measures in Effectiveness Trials" collaboration.

Results: Out of the 2,933 articles retrieved, 619 were included for analyses. The majority of studies (71%) were retrospective and with data extracted from chart reviews (71%) . We extracted 1,951 outcomes in total, from which, after deletion of repeated outcomes, we identified 256 unique ones. The most frequently assessed outcomes were those related to medication or therapeutic interventions and those to hospital/healthcare use. Outcomes related to psychosocial wellbeing were rarely assessed. The closer to death, the less frequently the outcomes were studied.

Conclusions: Most outcomes were related to medical interventions or to hospital use. Only a few studies focused on other components of integrated care such as psychosocial aspects. It remains to be defined which of these outcomes are fundamental to achieve the best care for the dying.

Keywords: Terminal care; core outcome set (COS); review; systematic

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Introduction

For study results to be applicable to health policy and clinical practice, the results must be relevant and important to key stakeholders, including patients, the public, health professionals, and policy makers (1). Therefore, in order to reduce outcome inconsistency and heterogeneity and to be able to compare the effects of different interventions between studies, a critical part of study design is the selection of commonly agreed outcomes (2). In the context of the care delivered in the last month of life, outcomes serve to develop interventions or therapeutic approaches to ensure that standards are met and that care and quality of life in this phase of life are improved for patients, caregivers, and families.

This systematic literature review represents the first step within the methodological approach of the Core Outcome Measures in Effectiveness Trials (COMET) initiative for outcome standardization through the development of core outcome sets (COSs) (2,3). A COS is the minimum of agreed outcomes that should be measured and reported in clinical studies for a certain clinical area and which can also be collected in routine care to guide patient care and decision making (4). Following the COMET approach, four stages are recommended for the development of COS (5). The first one is a systematic review of the literature to identify outcomes that have already been assessed in the literature. The second step aims to collect information to identify outcomes from the patient and family point of view. The third step consists of a Delphi process in which key experts score the importance of each of the outcomes identified in the first and second steps. The fourth and final step consists of a face-to-face consensus meeting of international experts, including patient and family representatives to propose and agree on the final COS. Throughout all the steps, the outcomes are classified according to a taxonomy developed by COMET, which includes five core areas: *Death*, *Physiological/clinical*, *Life impact*, *Resource use*, and *Adverse events*, *and covers* 38 outcome domains (6).

Therefore, the goal of this review was to identify outcomes that have been assessed in scientific literature in the last month of life, as a first step for the development of the COS for the best care for the dying person. We chose the last month of life, since is when the majority of the transitions to comfort care occur (7-9). We present this article in accordance with the PRISMA reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-23-435/rc) (10).

Highlight box

Key findings

- The results show that a minority of the outcomes that have been assessed in the last month of life assess psychosocial wellbeing or are reported by patients or caregivers.

What is known and what is new?

- To date, there is a lack of standardization and consensus on which outcomes are central to assess the care provided to patients in the last month of life.
- This study describes the outcomes that have been reported in the last month of life and highlights the main limitations of such outcomes.

What is the implication, and what should change now?

- This systematic review provides the basis for the development of a core outcome set (COS).
- Once we have the COS, we need to start designing studies based on the outcomes identified as fundamental to ensure that they are relevant outcomes for patients, families, caregivers, healthcare workers, and policy makers.

Methods

Design

We conducted a systematic review of outcomes reported in the scientific literature about the care for the dying person in the last month of life following the methods as recommended by COMET (2) The protocol for this systematic review and for the development of the COS has been previously published (11) and the systematic review was registered prospectively in PROSPERO- International prospective register of systematic reviews (CRD42020155875) (12) (Supplementary material 1 available at https://cdn.amegroups.cn/static/public/10.21037apm-23-435-1.pdf). Adjustments to the initial design for logistical reasons are described in an annex (Supplementary material 2 available at https://cdn.amegroups.cn/static/public/10.21037apm-23-435-1.pdf).

Patient and public involvement

Patient involvement is essential in the development of COSs as it ensures that the final outcomes reflect the priorities and experiences of patients and their caregivers. In this systematic review, the perspective of patients was incorporated by including both quantitative and qualitative studies, as qualitative studies offer a more comprehensive

view of patient perspectives and experiences.

In addition, in the subsequent phases of COS development, patient and public involvement continues through direct data collection from patient and family members, allowing their voices to be heard and their perspectives to be incorporated into the final outcome sets. For example, patients and families will be equal participants in the Delphi study and in the consensus meeting alongside clinicians and researchers, ensuring that their perspectives are fully integrated into the final COS.

Literature search

We searched for peer-reviewed scientific literature on studies published before February 24, 2022 (date of last search), in four electronic databases: Embase, MEDLINE (Ovid), PsychInfo, and CINAHL. We built our search construct for Embase and then translated it to the other three databases in consultation with an experienced medical information specialist. We combined terms related to the care (health care quality, patient satisfaction) of the dying (terminally ill, end of life) in the chosen timeframe (last/final month/weeks/days) (Supplementary material 3 available at https://cdn.amegroups.cn/static/public/10.21037apm-23-435-1.pdf). We searched only for papers with full text available in English and we did not apply date restrictions.

In selecting search terms for "end of life", we relied on a combination of those used by the National Institute for Health and Care Excellence in their development of the National Guidelines for the Care of Dying Adults in the Last Days of Life (13). Additionally, we applied a validated search filter for the field of palliative care, which showed in its validation study a sensitivity of 93.7% and a specificity of 97.4% (14).

Study selection and inclusion criteria

We included observational studies (case-control, cohort, cross-sectional and survey), qualitative studies, and interventional studies in adults (≥18 years old) if the study reported an outcome of care in the last month of life of people living with a chronic and progressive disease or condition. Studies were only included if they specifically mentioned the time frame in which the outcomes were assessed and if it was equal to or shorter than the last 30 days of life. If a study assessed an outcome over a longer period of time, even if the average time in which the outcome was reported for the participants was <30 days of life, it was excluded. For a study to be included, the outcome should have been assessed in all the participants within the last 30 days of life. Since support and wellbeing of families and caregivers are also important in the care provided to dying persons, we included studies reporting outcomes focused on the family, caregiver, or the healthcare providers if they were outcomes referring to caring or accompanying a person with a chronic condition in the last month of life. As the focus was on the last month and days of life, we excluded studies assessing only outcomes relevant to the family, caregiver, or healthcare provider after the patient's death. We also excluded studies reporting only costs or survival. Since euthanasia and physician assisted suicide are legal or regulated only in a few countries, we also excluded these studies, as well as studies in which the cause of death was suicide.

After pilot-testing the screening process, all titles and abstracts were independently screened by two investigators for potentially relevant articles. V.G.J. was the first screener for all the hits and S.C.Z., M.E., N.L., Z.M.R.D., N.G.J., and C.D.R. were the second screeners. Then, full-text review of potentially relevant articles was conducted following the same procedure. Each pair of reviewers resolved discrepancies through discussion and if no consensus was reached, a third independent reviewer was available to solve discrepancies. We used The Rayyan - Intelligent Systematic Reviews website (https://www.rayyan.ai/) for citation management during the screening process.

Data extraction

We extracted the data using a predesigned data collection form that included information on: country of data collection, population group, study design, outcome reported, time in which the outcome was reported, and source of information for the outcome. In accordance with the taxonomy developed by COMET for outcomes in medical research (6), we assigned each outcome one main category and subcategory. The taxonomy covers 38 outcome domains distributed within 5 core areas. The core area "death" includes outcomes such as survival and mortality rates. "Physiological/clinical" includes signs, symptoms, and laboratory tests. "Life impact" includes outcomes assessing the impact of the disease on physical daily life activities, on social functioning, role functioning (e.g., ability to care for children or work status), emotional functioning, or cognitive functioning. "Life impact" also includes outcomes assessing the quality of life, the perceived health status, and

the delivery of care (patient preferences, withdrawal from interventions, patient/care satisfaction, among others). "Resource use" includes economic outcomes, hospital use, medications and procedures, and the financial or time burden on carer or the society (e.g., need for home help or institutional care). Finally, the category "Adverse events" includes outcomes measuring unintended consequences of interventions.

Because of the heterogeneity in the time points at which outcomes were measured, we created four categories: "at the time of death", "last three days of life", "last two weeks of life", and "last month of life". Only outcomes that were assessed at the time of death were part of the "time of death" category. Outcomes that were assessed in the last 3 days, 2 days, last day or last hours were part of the "last three days" category. Outcomes that were evaluated within the last two weeks, the last 10 days, and the last week, were part of the "last two weeks" category. Finally, outcomes that were evaluated within the last 4 to 3 weeks of life were part of the "last month" category.

We grouped providers or sources of outcome information to create four final categories: "chart review", "caregivers", "healthcare personnel", and "patients". In the category "chart review", we included outcomes that were extracted from the clinical charts or from other medical data sources such as administrative registries. In the category "healthcare personnel", we included outcomes that were reported by nurses, general practitioners, or treating physicians. In the category "caregivers" we included outcomes that had been reported by the informal caregiver, health care proxy, surrogate, family, or friend. Finally, the category "patients" included only outcomes that were reported by the patient him or herself.

Following the recommendations from COMET (6), in case a study reported a composite outcome, we broke it down into its different components so that each one was an independent outcome. However, in some studies, this was not possible because they did not evaluate a predefined list of symptoms but instead inquired among the symptoms most frequently reported by the family. In these cases, we referred to these outcomes as "non-further described symptoms". Similarly, we broke down outcomes that contained multiple medications to report each one individually. However, some studies assessed, not a predefined list of medications, but the most used medications at certain stage. In these cases, we referred to these outcomes as "non-further described medication". Finally, we broke down outcomes containing multiple types of anticancer treatment, but in some cases, studies only assessed anticancer treatment as a whole. Therefore, besides "chemotherapy use", "radiotherapy use", "targeted oral therapy", and "immunotherapy use", we employed "non-further described anticancer treatment".

Due to the large number of outcomes found, we present the outcomes that were part of the highest decile (top 10%) both for the total outcomes and for the outcomes at each time point ("at the time of death", "last three days of life", "last two weeks of life", and "last month of life"). The complete list of outcomes can be found in the Supplementary material 4 (available at https://cdn.amegroups.cn/static/public/10.21037apm-23-435-1.pdf).

Results

General characteristics of the included papers

Out of the 2,933 articles, 619 (21%) were included in the final analysis (*Figure 1*). Of them, 71% were retrospective studies, 21% were prospective studies, and 4% were trials. The remaining studies were quasi-experimental, cross-sectional, qualitative or mixed methods. The majority (98%) were quantitative studies, but we also found 2% that were qualitative or mixed methods studies (*Table 1*). The data came from 43 different countries, mostly from the United States (US) (36% of the studies), followed by Canada (9% of the studies). Therefore, 46% of the studies contained data from the US. In second place, was Europe, with 32% of the data, followed by Asia with 13%, Oceania with 6%, and lastly, Africa with less than 1% of the data. The remaining 3% came from multiple countries.

Most of the studies (n=476, 77%) included only patients with one disease category. The other studies (n=143, 23%) included patients combining varying life-limiting diseases. Among the 77% studies that included only patients with one disease category, the most predominant disease category was patients with malignancies.

General characteristics of the outcomes

In total, we extracted 1,951 outcomes out of the 619 articles, with an average of 3.2 outcomes reported in each paper. Of those 1,951 outcomes, 256 were unique (Supplementary material 4 available at https://cdn.amegroups.cn/static/public/10.21037apm-23-435-1.pdf).

The time at which outcomes were evaluated varied between articles: 1,171 (60%) of the outcomes were assessed during the last month of life; 584 (30%) in the last

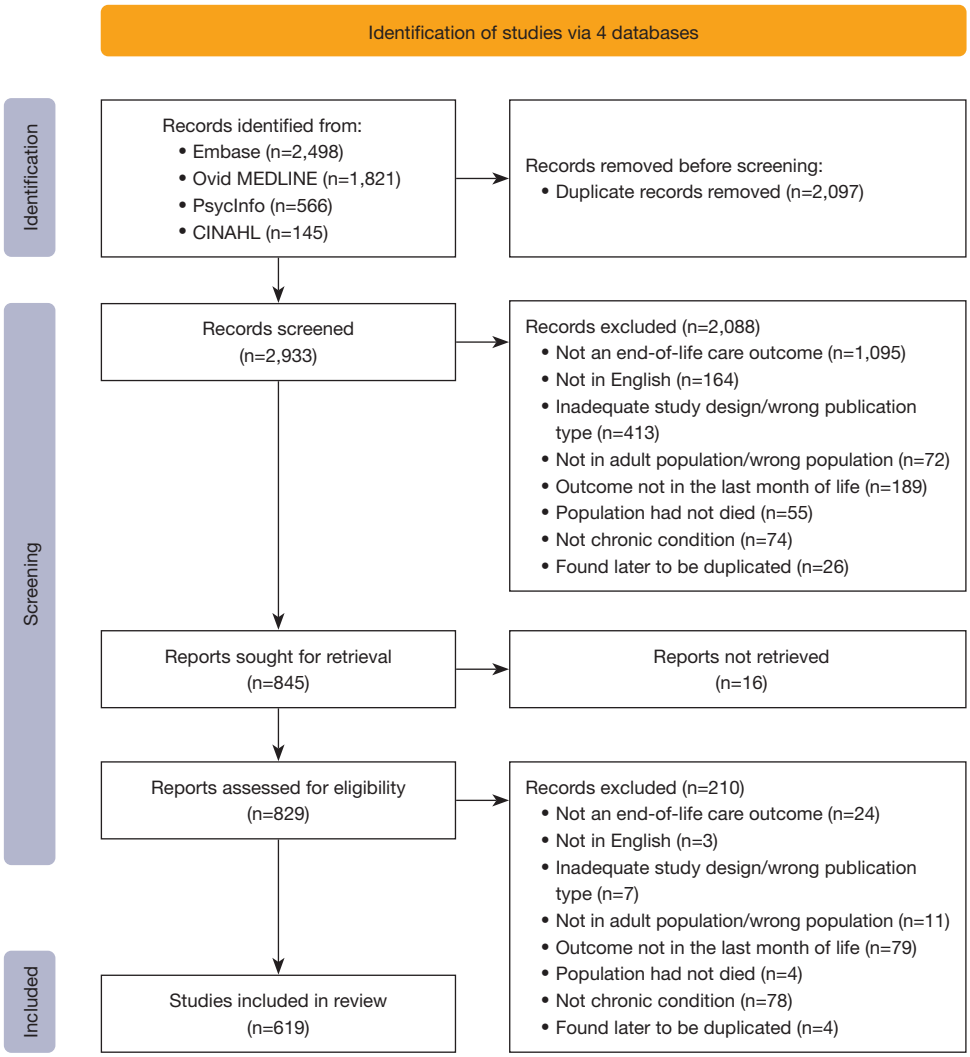

Figure 1 Flowchart of the studies included in the systematic review.

two weeks; 227 (12%) in the last three days, and 156 (8%), at the time of death. Even though most of the outcomes were assessed only at one time point, some of the outcomes (n=187, 10%) were assessed several times (*Table 2*).

The most common information source of the outcomes was chart review (71%), followed by caregivers (15%). Patients and healthcare personnel were investigated in equal proportions (11%). A minority of the outcomes were assessed using multiple sources (8%).

The subcategories that included the largest number of outcomes were: *Need for further intervention* (e.g., ventilation, artificial nutrition, blood transfusion, chemotherapy use), *Hospital* [e.g., emergency room (ER) visit, hospital admission, hospitalization length], *Delivery of care* (e.g., quality of care, quality of dying), *Personal circumstances* (e.g., place of death), and *General outcomes* (e.g., pain and non-further described symptoms) (*Table 3*).

Most often reported study outcomes

Out of the 256 unique outcomes, 31 were part of the top 10% most assessed (*Table 4*, *Figure 2*). About a third of them (n=10) belonged to the category *Resource use*, subcategory *Need for further intervention*: chemotherapy use, radiotherapy use, immunotherapy use, non-further described anticancer treatment, blood transfusion, antibiotic use, artificial nutrition, ventilation use, cardiopulmonary resuscitation (CPR), and symptom management. The studies that

Table 1 General characteristics of the studies

Characteristics	N (%)
Population included[†]	
Cancer	444 (71.7)
Dementia	57 (9.2)
Nursing homes	37 (6.0)
Under palliative care	28 (4.5)
Heart failure	25 (4.0)
Chronic kidney disease	23 (3.7)
COPD	22 (3.6)
Hospices	17 (2.7)
Frailty	5 (0.8)
ALS	2 (0.3)
Study design	
Observational	
Prospective	132 (21.3)
Retrospective	438 (70.8)
Quasi-experimental	4 (0.6)
Cross-sectional	10 (1.6)
Qualitative	6 (1.0)
Mixed-methods	5 (0.8)
Experimental	
Clinical trial	24 (3.9)

[†], more than one option is possible. COPD, chronic obstructive pulmonary disease; ALS, amyotrophic lateral sclerosis.

Table 2 General characteristics of the outcomes (n=1,951)

Characteristics	N [%]
Time frame[†]	
Last month	1,171 [60]
Last 2 weeks	584 [30]
Last 3 days	227 [12]
Time of death	156 [8]
Information source[‡]	
Clinical chart	1,387 [71]
Caregivers	290 [15]
Healthcare personnel	211 [11]
Patients	213 [11]

[†], multiple options are possible for one outcome; [‡], multiple options are possible for one outcome.

evaluated these outcomes assessed the frequency with which these interventions had been performed at the end of patients' lives, for example, the proportion of patients who had chemotherapy in the last month of life, or of patients who received CPR in the last week of life.

Within the same *Resource use* category, some other outcomes (n=5) belonged to the subcategory *Hospital*: ER visits, hospital admission, intensive care unit (ICU) admission, hospitalization length, and palliative care use. Studies that assessed those outcomes, evaluated the proportion of patients who used such hospital services. Also, within the *Resource use* category, other outcomes (n=3) belonged to the subcategory *Societal/carer burden*: hospice utilization, late hospice enrolment, and care setting transition (which assessed if there was a change in which clinical service provided care).

In the category *Physiological/clinical*, the frequency with which the following symptoms (n=7) were present at any time point within the last month was evaluated: pain, dyspnea, nausea or vomiting, anxiety, depression, appetite-related, and non-further described symptoms.

In the category *Life impact*, the following outcomes (n=6) were found: place of death, functional status, quality of life, quality of care, comfort, and quality of dying. Those studies assessing place of death reported, for example, the proportion of patients dying at home, in the hospital, or in a hospice.

Most often reported study outcomes per assessment time

From the top 10% of most assessed outcomes, ICU admission, and emergency room (ER) visits, were only part of the 10% in the last month of life. Non-further described symptoms and antibiotic use were only part of the top 10% in the last two weeks of life. Late hospice enrolment, hospice utilization, non-further described medications, and confusion were only part of the top 10% in the last three days of life.

Last month of life

Out of the 165 unique outcomes that were assessed in the last month of life, 16 made part of the top 10% most assessed (*Table 4*). Of them, the majority (n=9) belonged to the category *Resource use* (e.g., ER visit, hospital admission,

Table 3 COMET outcomes categories

Outcomes	Total, n (%)	Unique, n (%)
Total	1,951 (100.0)	257 (100.0)
COMET taxonomy		
Death		
1. Mortality/survival	–	–
Physiological/clinical	337 (17.3)	66 (25.7)
2. Blood and lymphatic system outcomes	–	–
3. Cardiac outcomes	1 (0.1)	1 (0.4)
4. Congenital or genetic outcomes	–	–
5. Endocrine outcomes	–	–
6. Ear outcomes	–	–
7. Eye outcomes	1 (0.1)	1 (0.4)
8. Gastrointestinal outcomes	67 (3.4)	10 (3.9)
9. General outcomes	132 (6.8)	21 (8.2)
10. Hepatobiliary outcomes	–	–
11. Immune system outcomes	–	–
12. Infection outcomes	–	–
13. Injury and poisoning outcomes	1 (0.1)	1 (0.4)
14. Metabolism and nutrition outcomes	–	–
15. Musculoskeletal and connective tissue outcomes	3 (0.2)	2 (0.8)
16. Outcomes relating to neoplasms: benign, malignant and unspecified (including cysts and polyps)	–	–
17. Nervous system	20 (1.0)	7 (2.7)
18. Pregnancy and perinatal outcomes	–	–
19. Renal and urinary outcomes	8 (0.4)	5 (1.9)
20. Reproductive system and breast outcomes	2 (0.1)	2 (0.8)
21. Psychiatric outcomes	46 (2.4)	3 (1.2)
22. Respiratory, thoracic and mediastinal outcomes	48 (2.5)	8 (3.1)
23. Skin and subcutaneous tissue	5 (0.3)	2 (0.8)
24. Vascular outcomes	3 (0.2)	3 (1.2)
Life impact	428 (21.9)	78 (30.4)
25. Physical functioning	19 (1.0)	1 (0.4)
26. Social functioning	2 (0.1)	2 (0.8)
27. Role functioning	–	–
28. Emotional functioning/wellbeing	25 (1.3)	12 (4.7)
29. Cognitive functioning	20 (1.0)	9 (3.5)

Table 3 *(continued)*

Table 3 *(continued)*

Outcomes	Total, n (%)	Unique, n (%)
30. Global quality of life	30 (1.5)	1 (0.4)
31. Perceived health status	–	–
32. Delivery of care	176 (9.0)	44 (17.1)
33. Personal circumstances	156 (8.0)	9 (3.5)
Resource use	1,180 (60.5)	107 (41.6)
34. Economic	–	–
35. Hospital	511 (26.2)	18 (7.0)
36. Need for further intervention	556 (28.5)	58 (22.5)
37. Societal/carer burden	113 (5.8)	31 (12.1)
Adverse event	6 (0.3)	6 (2.3)
38. Adverse events/effects	6 (0.3)	6 (2.3)

COMET, Core Outcome Measures in Effectiveness Trials.

and ICU admission), four to the category *Physiological/clinical* outcomes (e.g., pain, dyspnea, and anxiety), and three to the category *Life impact* (e.g., quality of life and quality of care).

Last two weeks of life

Out of the 156 unique outcomes that were assessed in the last two weeks of life, 15 made part of the top 10% most assessed (*Table 4*). Of them, the majority (n=8) were part of the category *Resource use* (e.g., chemotherapy use, ventilation use, CPR), five of the category *Physiological/clinical* (e.g., pain and nausea or vomiting), and two of the category *Life impact* (e.g., quality of life and quality of care).

Last three days of life

Out of the 91 unique outcomes that were assessed in the last three days of life, 10 made part of the top 10% most assessed (*Table 4*). Half of them (n=5) were part of the *Physiological/clinical* category (e.g., dyspnea and pain), three were part of *Resource use* category (hospice utilization, late hospice enrolment, and non-further described medication), and two were part of *Life impact* category (confusion and functional status).

Time of death

Out of the seven outcomes that were assessed at the time of death, two made part of the top 10% most assessed: place of death and death at the preferred place of death, both, from the category *Life impact* (*Table 4*).

Most often reported study outcomes per information source

From the top 10% most assessed outcomes, satisfaction with care was only in the top 10% reported by the caregivers. Non-further described symptoms, symptom management, and comfort were only in the top 10% reported by the healthcare personnel. Cancer treatment (i.e., chemotherapy, radiotherapy, immunotherapy, and non-further described anticancer treatment), antibiotic use, and hospital use (hospital admission, hospitalization length, ICU admission, and ER visits), palliative care use, artificial nutrition, hospice utilization, and late hospice enrolment were only in the top 10% extracted from clinical charts.

Clinical chart

Out of the 147 unique outcomes that were extracted from clinical charts, 16 made part of the top 10% most assessed (*Table 5*). The majority (n=15) of them belonged to the category *Resource use* (e.g., chemotherapy use, hospital admission, and hospice utilization). The remaining outcome belonged to the category *Life impact*: place of death.

Caregivers

Out of the 105 unique outcomes that were reported by the caregivers, 12 made part of the top 10% most assessed (*Table 5*). Of them, six were part of the category *Life impact* (e.g., quality of care, and satisfaction with care), four of the

Table 4 Frequency in which each outcome was assessed per time frame

Outcome	All time frames	Last month	Last two weeks	Last three days	Time of death
Chemotherapy use	8.7%	8.9%	16.3%		
Hospital admission	7.7%	12.4%	1.9%		
Place of death	7.2%				89.1%
ICU admission	6.8%	10.9%			
ER visit	6.4%	10.1%	1.9%		
Ventilation use	2.8%	3.1%	3.3%		
Hospitalization length	2.6%	4.0%			
CPR	2.5%	2.9%	2.2%		
Pain	2.4%	1.9%	3.9%	5.7%	
Quality of care	2.1%	2.0%	2.9%		
Dyspnea	1.8%	1.3%	2.6%	6.2%	
Artificial nutrition	1.7%	1.9%	2.1%		
Radiotherapy use	1.6%	2.1%	2.1%		
Late hospice enrollment	1.6%			11.5%	
Quality of life	1.5%	1.5%	2.4%		
Nausea or vomiting	1.4%		2.9%	3.1%	
Hospice utilization	1.4%			3.1%	
Anxiety	1.3%	1.2%	1.9%	3.5%	
Non-further described symptoms	1.1%		1.9%		
Depression	1.0%	1.1%		2.6%	
Functional status	1.0%	1.3%		2.2%	
Symptoms management	0.8%				
Antibiotic use	0.7%		1.7%		
Care setting transitions	0.7%				
Blood transfusion	0.7%				
Non-further described anticancer treatment	0.7%				
Comfort	0.7%				
Quality of dying	0.7%				
Palliative care use	0.7%				
Appetite-related issues	0.7%				
Immunotherapy	0.7%				
Non-further described medication				2.2%	
Confusion				2.2%	
Death at preferred place of death					6.4%

ICU, intensive care unit; ER, emergency room; CPR, cardiopulmonary resuscitation.

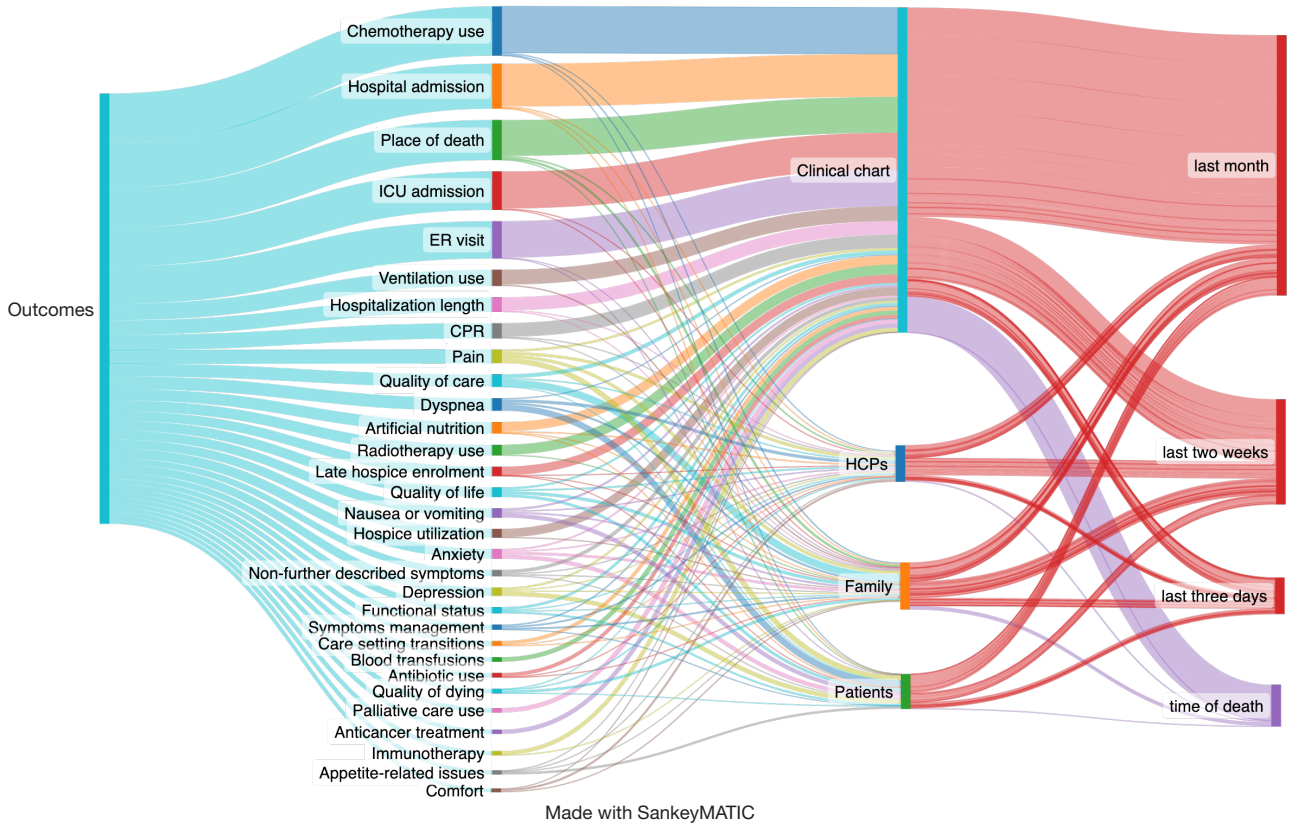

Figure 2 Top 10% outcomes (n=31) by the source of information and time frame. ICU, intensive care unit; ER, emergency room; CPR, cardiopulmonary resuscitation; HCP, healthcare personnel.

category *Physiological/clinical* (e.g., pain and dyspnea), and two of the category *Resource use* (CPR and ventilation use).

Health care personnel

Out of the 85 unique outcomes that were reported by healthcare personnel, nine made part of the top 10% most assessed (*Table 5*). Of them, four were part of the *Physiological/clinical* category (e.g., pain and dyspnea) and four were part of the *Life impact* category (e.g., comfort and quality of care). The remaining outcome was part of the *Resource use* category and it was symptom management.

Patients

Out of the 66 unique outcomes that were reported by patients, seven made part of the top 10% most assessed (*Table 5*). Of them, five were part of the *Physiological/clinical* category (e.g., pain and dyspnea) and two of the *Life impact* category (quality of life and functional status).

Discussion

Key findings

In this systematic review, we sought to identify the outcomes of care that were assessed in the last month of a person's life. We found most of these outcomes were related to medication and therapeutic interventions or to the use of hospital services and very few were related to psychosocial wellbeing. Also, most of the outcomes were extracted from clinical charts and few were gathered from information referred by the caregivers or the patients. Finally, the closer to death, the less frequently the different outcomes were studied.

Very few outcomes were related to psychosocial wellbeing. In fact, in the top 10% of the most evaluated outcomes, none were in the subcategories *Social functioning* or *Emotional functioning*, and the only outcome that was related to the impact on society or the caregiver was the use of hospice and its late entry. Dying is not a medical

Table 5 Frequency in which each outcome was assessed per information source

Outcome	Clinical chart	Caregivers	Healthcare personnel	Patients
Chemotherapy use	12.2%			
Hospital admission	10.6%			
Place of death	9.5%	2.4%		
ICU admission	9.4%			
ER visit	8.9%			
Ventilation use	3.9%	2.4%		
Hospitalization length	3.5%			
CPR	3.2%	2.8%		
Pain		5.9%	7.6%	9.4%
Quality of care		9.3%	4.3%	
Dyspnea		4.1%	7.1%	8.0%
Artificial nutrition	1.9%			
Radiotherapy use	2.3%			
Late hospice enrollment	2.2%			
Quality of life		5.2%	3.3%	7.0%
Nausea or vomiting			3.3%	5.6%
Hospice utilization	1.9%			
Anxiety		3.4%		7.5%
Non-further described symptoms			3.3%	
Depression		2.8%		6.6%
Functional status		3.1%		4.7%
Symptoms management			2.8%	
Blood transfusion				
Antibiotic use	0.9%			
Care setting transitions				
Immunotherapy	0.9%			
Appetite-related issues				
Comfort			4.3%	
Quality of dying		2.8%	2.8%	
Palliative care use	0.9%			
Anticancer treatment	0.9%			
Satisfaction with care		3.4%		

ICU, intensive care unit; ER, emergency room; CPR, cardiopulmonary resuscitation.

process but a process of the human condition (15). In this review we found that most of the outcomes were related to the clinical setting, therefore, in most of the studies, a medicalized death was studied, reporting medicalized outcomes. Consequently, it remains to be evaluated which of the outcomes identified in this systematic review serve to give recommendations on what to evaluate in studies focused on providing the best care for the dying and to give clinical recommendations to care for these patients.

For decades, it has been known that the outcomes chosen by health personnel differ from those that would be chosen by the patients themselves, due to the difference in the perception that both have about the disease (16,17). Patients' vision of their own disease and its consequences is much broader. Because of this, the outcomes chosen and reported by health personnel may have limited relevance to patients during their last month of life (18). Despite this, we found that a minority of the outcomes were reported by the caregivers or the patients themselves. Although it is complicated to evaluate patient-reported outcomes or care in the days near death because of patient frailty and family stress, strategies for doing so have been studied and reported. For example, researcher flexibility in terms of time, location, and manner of data collection are essential to allow the family to respond in a way that suits their conditions (19). Interviewing family members retrospectively to inquire about the last days of the patient's life has also been employed as a strategy (20).

Recognising the importance of patient and family views, the final COS will be developed by integrating not only the outcomes from this systematic review, but also data from an international cohort study incorporating the perspectives of patients, caregivers and health professionals about important aspects to be taken into account in the care of the dying (11). We will also conduct a Delphi survey with experts (including caregivers and patients) and will undertake a consensus meeting of the stakeholders to identify the most relevant outcomes.

In addition, the lack of a standard temporal definition of 'end-of-life' is one of the dilemmas that arise in defining which specific outcomes of care are most important when caring for the dying (21); however, attempts have been made to define some terms, such as "actively dying" being defined as the hours or days before death (21,22). According to this definition, it is in this phase where we found the lowest number of evaluated outcomes.

Clinical and scientific implications

For many outcomes, it is still controversial or even unknown whether the outcome is something that should be achieved or avoided to provide the best care for the dying. For example, with the outcome "antibiotic use", it is known that there are adverse effects of antibiotic use in patients whose goal of treatment is to palliate symptoms, such as drug interactions, antibiotic-associated diarrhea, intravenous line discomfort, and of worldwide concern, bacterial resistance (23,24). However, there is also evidence of beneficial effects, such as symptoms' improvement, which may outweigh the potentially adverse effects (25) and that even at present, palliative care physicians prefer to use antibiotics in the majority of cases in which the treatment goal is to palliate symptoms (88–100%) (26). Therefore, although this review presents the outcomes assessed in the last month of patients' lives, for the majority of the outcomes, it is not a simple task to reframe it into an outcome for the best care of the dying. Therefore, it is also important for future research to better define outcomes focused not only on assessing the care of the dying but more importantly the best care of the dying and from the patient's perspective. For example, not only assessing frequency of hospital use in the last month but also access to hospitals, or instead of the frequency of patients who received chemotherapy in the last month, report those who continued or discontinued the therapy according to their preferences after discussions with health personnel.

It also remains for future research to evaluate for whom each of the outcomes is important, whether for the family, the patient, or the health personnel. In the same way, although this review provides the basis for building a COS for the best care of the dying, as part of the holistic approach of palliative care, there is still a need to evaluate and define outcomes for the best care of the health care provider caring for the dying (for example, burnout avoidance, or having the chance of discussing a difficult case with colleagues).

Strengths and limitations

This review includes a large volume of data collected from different countries, which is a reliable representation of the outcomes that have been studied in the care during the last month of life over the years, across countries. The fact that this review follows a predefined methodology makes its findings robust and sound. Moreover, being part of an initiative of homogenization and comparison of outcomes, it allows comparison of the type of outcomes found in this review and their categories with the outcomes reported in other reviews following the same methodology. Another

strength of our study is that, in order to limit heterogeneity in the times in which the outcomes were evaluated, we limited the search and extraction of outcomes to the last month of life instead of using ambiguous terms such as "the end of life". Furthermore, instead of only including quantitative studies reporting outcomes of interest for the researchers, we included qualitative and mixed methods studies to capture the perspective of lay people such as patients, caregivers, and families (27). However, only 2% of the studies had a qualitative or mixed methods design, suggesting that most of the outcomes were not defined by the patients, but by the researchers.

However, our study has certain limitations. The taxonomy developed by COMET was developed following a systematic review to identify ways of classifying outcomes used in clinical trials (6). Although it was designed for that type of study, it can be extrapolated to observational studies such as the majority that are included in this systematic review. For our specific topic, which is palliative care, and the specific question of outcomes for the best care of the dying, the addition of other levels to the taxonomy (as encouraged by the taxonomy authors (6), such as one that classifies according to the objective of the outcome (e.g., prolong life, treat acute crisis, withdrawal of therapy, symptomatic management, or psychosocial support) or the target group (e.g., patient or caregiver) could have added more clarity. However, since we were limited by the incomplete definitions of the outcomes presented in the source literature itself, such a granular distinction could not have been achieved for all outcomes. However, in the final COS, comprehensive definitions about the outcomes will be established with the stakeholders taking part in the Delphi and Consensus meeting (11).

Conclusions

A minority of the outcomes assessed psychosocial wellbeing, were reported by patients or caregivers, or assessed closer to death. Thus, the majority of the results are related to medication and therapeutic interventions or hospital use. Consequently, it remains to be defined which of these outcomes of the care of the dying are fundamental to achieve the best care of the dying from the perspective of all involved, including the patients and the caregivers.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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