Review

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Corticosteroids for Anorexia-Cachexia and Asthenia Syndrome in Palliative Care: A Scoping Review

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Anorexia–cachexia–asthenia syndrome (ACAS) is a common, distressing problem in palliative care that impairs comfort, function and quality of life. Corticosteroids are frequently used in practice, but their efficacy, duration of benefit and safety—especially medium- and long-term—remain unclear. We conducted a scoping review following Joanna Briggs Institute guidance and reported per PRISMA-ScR. This study was not prospectively registered in an international database. We searched PubMed/MEDLINE, Scopus, Web of Science and the Cochrane Library for original articles published between 2001 and 2025 in English, Spanish or Portuguese. We included randomized trials and observational studies assessing corticosteroid use for anorexia, fatigue/asthenia or cachexia in adults receiving palliative care. Data were charted in a standardized template and synthesized narratively. After screening and full-text assessment, 18 studies (total N ≈ 6306) were included; most were observational, and populations and regimens were heterogeneous. 13/18 studies reported improved appetite, 10/18 reported improved fatigue/asthenia, and only 1/18 used objective cachexia measures. Dexamethasone and methylprednisolone were the most commonly evaluated agents. Corticosteroids produced rapid improvements in appetite and, to a lesser extent, fatigue—often within 48–72 hours—but benefits were generally short-lived, commonly waning after 2–4 weeks. Evidence for sustained effects on cachexia or objective muscle mass was limited; most studies reported weight or appetite changes without objective muscle-mass assessment. Reported harms included hyperglycemia/worsening glycemic control, fluid retention/edema, neuropsychiatric effects (insomnia, mood changes, agitation, delirium), steroid-induced muscle weakness and increased infection risk, particularly with prolonged use. We conclude that corticosteroids may offer useful, short-term symptomatic relief for anorexia and fatigue in palliative care but should be used judiciously, individualized, and for limited periods with close monitoring for metabolic, neuropsychiatric and infectious adverse effects. Future research should prioritize dose-finding randomized trials, objective cachexia measures, and multimodal interventions to extend benefit.

Keywords: cancer-related fatigue; palliative medicine; end-of-life care; anti-inflammatory therapy; supportive oncology; quality of life

Introduction

Anorexia-cachexia-asthenia syndrome (ACAS) is a complex and multifactorial clinical condition characterized by the coexistence of anorexia, involuntary weight loss, and persistent asthenia [1–3]. This is a frequent manifestation in patients with advanced chronic diseases (55% to 80%), particularly in oncological settings (20% to 80%, being more frequent in more advanced stages of the disease), and represents one of the most relevant clinical challenges in palliative care practice, due to its direct impact on the functionality, prognosis, and quality of life of patients [4–7].

From a pathophysiological point of view, ACAS results from a complex interaction between systemic inflammation (involving mediators like hormones (e.g., leptin), neuropeptides (e.g., neuropeptide Y, melanocortin, melanin-concentrating hormone and orexin) and cytokines (e.g., interleukin 1, interleukin 6, tumor necrosis factor alpha and interferon gamma)), metabolic alterations (in carbohydrate, lipid and protein metabolism), and neuroendocrine dysfunction (within the hypothalamus, the brain's central regulator of energy homeostasis, imbalance of orexigenic and anorexigenic peptides ghrelin resistance and leptin abnormalities), leading to decreased appetite, reduced caloric intake, and increased protein catabolism [6,8–10]. This process culminates in progressive muscle atrophy, weight loss, and functional deterioration, frequently accompanied by intense and refractory fatigue, with significant repercussions on physical performance and overall well-being [5,6].

Corticosteroids exert rapid symptom-modifying effects through both genomic and non-genomic mechanisms that suppress systemic inflammation. Glucocorticoids bind the intracellular glucocorticoid receptor, modulating gene transcription to up-regulate anti-inflammatory proteins and repress pro-inflammatory transcription factors such as NF-κB and AP-1. This leads to reduced synthesis and release of key cytokines implicated in ACAS (notably IL-1, IL-6 and TNF-α), decreased acute-phase reactants (e.g., CRP), and lowered peripheral and central inflammatory signaling that affects appetite regulation and fatigue. Non-genomic actions (membrane effects) can produce more immediate physiological changes, which help explain the rapid onset of symptomatic relief observed clinically, often within 48–72 hours of treatment initiation. However, these anti-inflammatory effects are typically transient and dose- and time-dependent, which may account for the short-lived clinical benefits described in the literature [11–14].

Despite advances in understanding the pathophysiological mechanisms of ACAS, the scientific evidence regarding the role of corticosteroids in its treatment remains understudied, fragmented, and marked by high heterogeneity. This observation is supported by previous syntheses and large observational reports, which have highlighted small trial sizes, heterogeneous outcomes, and limited objective assessments of cachexia [15–17].

Given its multifactorial nature, the therapeutic approach to ACAS should be integrated and multidisciplinary, combining nutritional interventions, adapted physical exercise and supervised rehabilitation, psychosocial support, and pharmacological strategies, according to care goals and disease stage [1,5,15,16,18].

However, despite this combined approach, effective symptom control often remains limited, particularly in advanced stages of the disease [1,5,15,16].

Among the current pharmacological options, corticosteroids, namely dexamethasone (DEX), prednisolone (PRE), and methylprednisolone (MPD), are widely prescribed in clinical practice, mainly for their ability to stimulate appetite, improve subjective well-being, and, in some cases, reduce fatigue associated with advanced disease [19–24].

Despite their frequent use, available evidence suggests that the beneficial effects of corticosteroids are generally rapid but short-lived, with loss of effectiveness after two to four weeks of treatment [21–24]. Furthermore, prolonged use is associated with a significant risk of adverse metabolic, infectious, and musculoskeletal effects, which limits its sustained application [25–27]. These limitations make a careful assessment of the benefit-risk ratio essential and justify the need to systematically clarify the true magnitude of the effect of corticosteroids in the treatment of ACAS [15,24].

Given the exploratory nature of the question and the expected heterogeneity of the literature, we conducted a scoping review following the Joanna Briggs Institute guidance to map and summarize available evidence on corticosteroid use in ACAS in palliative care.

Population-Concept-Context (PCC) framework (used to define the review question): Population—adults ($\geq$18 years) with advanced disease receiving palliative care; Concept—use of systemic corticosteroids to manage anorexia, cachexia, and/or asthenia/fatigue; Context—home-based palliative care.

The primary aim of this study is to systematically evaluate the available evidence on the effectiveness of corticosteroids in alleviating the core symptoms of anorexia–cachexia–asthenia syndrome (ACAS) in adults receiving palliative care. Secondary objectives include assessing the magnitude, duration, and consistency of the observed clinical benefits, as well as identifying potential risks and adverse effects associated with corticosteroid use. Ultimately, this review seeks to support safer and more targeted therapeutic decision-making, in line with best practices for the multidimensional management of anorexia-cachexia syndrome (ACAS) in palliative care (PC).

Methods

This study was conducted as a scoping review following Joanna Briggs Institute [28] methodology and reported in accordance with PRISMA-ScR (and PRISMA 2020 where applicable) [29]. A scoping review approach was adopted to map the extent, range and nature of available evidence, given anticipated heterogeneity in study designs, study populations and outcomes.

Based on this methodological framework, the following guiding question was formulated: "What is the impact of using corticosteroids for the treatment of ACAS in adults in PC?".

Registration

This scoping review was not prospectively registered.

Data Sources and Search Strategy

The bibliographic search was conducted between May and July 2025, using the PubMed/MEDLINE, Cochrane Library, Scopus (Elsevier) and Web of Science (WoS) databases. Studies published in English, Spanish and Portuguese were considered, and studies published between 2001 and 2025 were selected.

To ensure a comprehensive and consistent search across different platforms, MeSH descriptors and equivalent free terms were used, duly adapted to each database. The final search strategy integrated combinations of the following terms: (corticosteroids OR dexamethasone OR prednisone); AND (cachexia OR anorexia OR fatigue OR asthenia); AND ("symptomatic control" OR "symptom management"); AND ("palliative care" OR "terminal care" OR "end-of-life care").

Inclusion and Exclusion Criteria

Original studies available in full text were included, namely randomized clinical trials, prospective or retrospective observational studies, and formal systematic reviews that assessed the use of corticosteroids in the control of anorexia, cachexia, asthenia, or fatigue in adults in palliative care.

Opinion articles, editorials, narrative reviews, commentaries, and scientific correspondence were excluded, as were studies conducted in populations under 18 years of age, works without full-text access, and investigations undertaken in non-palliative populations, such as patients undergoing active cancer treatment or with non-advanced inflammatory pathologies. These criteria aimed to preserve the methodological robustness of the review and ensure the clinical relevance of the results obtained.

Study Selection Process

The selection of studies was conducted systematically and rigorously, in accordance with the PRISMA 2020 recommendations [30]. The process was conducted in two independent stages by two reviewers (CP and HR) to increase reliability and minimize potential selection bias.

In the first phase, the titles and abstracts identified in the initial search were screened, and 116 potentially relevant articles were selected. In the second phase, the full texts of the previously selected articles were evaluated against the defined inclusion and exclusion criteria; 43 articles were deemed eligible for detailed methodological assessment.

After full-text review, 22 studies initially met the inclusion criteria; however, 4 were excluded because they did not align with the context of PC, resulting in a final sample of 18 studies included in this scoping review.

Any disagreements between the reviewers were resolved by a third reviewer (JRN), who acted as an arbitrator in the consensus process, reinforcing the consistency and transparency of the study selection.

Data Extraction and Synthesis

Data extraction was performed using a standardized table created in Microsoft Excel®, in which information regarding authors and year of publication, country and context of care, study design, population characteristics, type, dose and duration of corticosteroid therapy, results achieved and evaluated (appetite, weight, fatigue, quality of life and survival), adverse effects described and main methodological limitations were recorded.

Adverse events were extracted descriptively from each included study; because reporting formats and denominators varied, we present a narrative synthesis of the most frequently reported harms rather than pooled incidence estimates.

For clarity, we distinguish between 'weight loss' (patient-/clinician-reported reduction in body weight or unintentional weight loss) and 'cachexia' (a clinical syndrome characterized by involuntary weight loss with loss of skeletal muscle mass and metabolic alterations, ideally assessed by objective measures such as lean body mass, CT-based muscle area, bioimpedance, or validated cachexia criteria). Where studies reported only self-reported or weight-recorded changes without objective muscle/mass assessment, we classified these outcomes as 'weight loss' rather than 'cachexia'.

Given the marked heterogeneity of the included studies, particularly in methodological design, drugs used, doses administered, and assessment scales employed, a descriptive synthesis of the results was chosen. This approach enabled a more realistic comparison of the individual contributions of each study, the identification of consistent patterns in efficacy and duration of effects, and clear evidence of existing gaps in the literature, thereby favoring a critical and integrated reading of the available evidence.

To facilitate readability and ensure a more structured presentation, the studies were organized into tables according to the main symptom analyzed (anorexia, fatigue, and

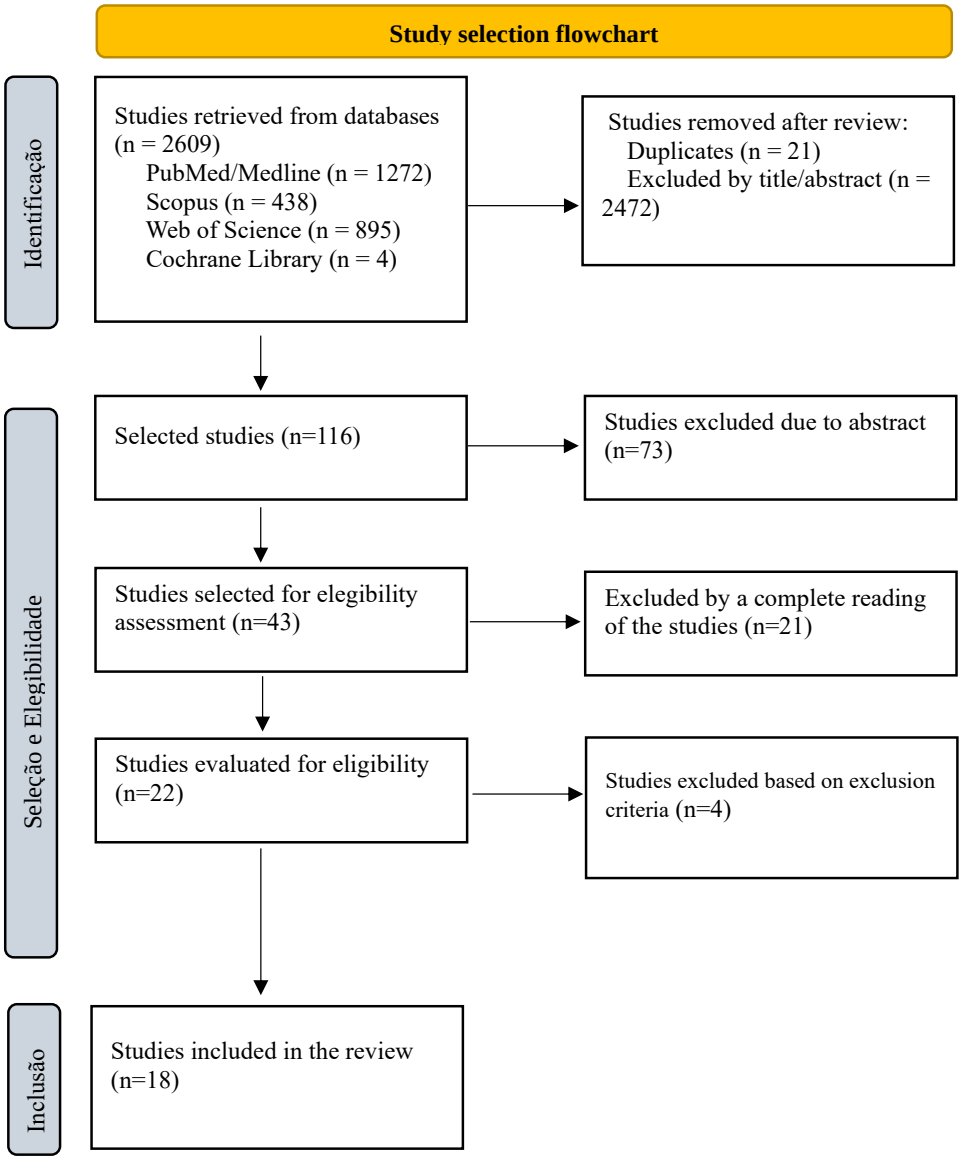

Fig. 1. Study selection flowchart, according to the PRISMA methodology.

asthenia). In cases where an article evaluated more than one symptom, this was included in all corresponding tables and, in addition, grouped in all corresponding tables, allowing integrated highlighting of studies that addressed multiple domains of ACAS.

Risk of Bias Assessment

A formal assessment of risk of bias using specific tools, such as RoB 2.0 for randomized clinical trials or the Newcastle-Ottawa Scale for observational studies, was not performed because the included studies exhibited marked methodological and conceptual heterogeneity.

Nevertheless, a narrative analysis of the main sources of bias identified was carried out, highlighting the small sample size of most studies, the frequent absence of control groups, the substantial variability in therapeutic regimens (including type, dose and duration of corticosteroids), and the limitations inherent in the predominance of observational studies, which are often vulnerable to selection bias and confounding factors. This analysis enabled a more rigorous contextualization of the quality of the available evidence and the interpretation of the results.

Evidence Grading (Strength of Recommendation Taxonomy)

We graded the strength of evidence for key clinical outcomes using the Strength of Recommendation Taxonomy (SORT) [31]. Using SORT, we assigned levels as follows: Level 1—consistent, patient-oriented evidence from high-quality randomized controlled trials or

systematic reviews/meta-analyses of such trials; Level 2—limited patient-oriented evidence from cohort studies, lower-quality RCTs, or systematic reviews of such studies; Level 3—expert opinion, case series, or disease-oriented evidence. Two reviewers (CP and HR) independently assigned SORT levels to outcome domains (appetite, fatigue/asthenia, cachexia, harms) based on study design, methodological quality, and consistency of findings; disagreements were resolved by discussion and, when needed, arbitration by a third reviewer (JRN). We report SORT levels alongside outcome summaries in the Results and Discussion to aid interpretation of the overall strength of the evidence.

Results

After applying the selection, eligibility, and inclusion criteria, 18 studies were included in the scoping review. The PRISMA flowchart (Fig. 1) illustrates in detail all the steps of study identification, screening, eligibility, and inclusion.

The 18 studies included in this review, published between 2001 and 2025, presented distinct approaches regarding the symptoms evaluated. Of the 18 included studies, 13/18 (72%) reported a clinically meaningful improvement in appetite following corticosteroid therapy, 10/18 (56%) reported improvement in fatigue/asthenia, and only 1/18 (6%) assessed cachexia using objective muscle-mass measures. Where responder proportions were reported, appetite response rates ranged approximately from 40% to 80% across studies, with observational cohorts commonly near 40–50%. Seven studies (7/18, 38.9%) analyzed the effectiveness of corticosteroids in fatigue; five (5/18, 27.8%) focused exclusively on anorexia; another five (5/18, 27.8%) evaluated anorexia and asthenia simultaneously; and only one study (1/18, 5.6%) addressed, in an integrated way, all three symptoms of the syndrome. Magnitude estimates varied by outcome measure and timepoint (different scales and follow-up intervals), so we report descriptive study-level counts and ranges rather than pooled effect sizes.

The study population comprised 6306 adults with advanced chronic diseases, primarily oncological, in palliative care settings. The average age ranged from 56 to 80 years. Overall, the pooled sample included both men and women, but sex distribution varied across studies (see Table 1, Ref. [21,24,32–42]); for example, Yennurajalingam *et al*. (2013) [32] enrolled 25 males and 42 females. Therefore, we report a generally mixed sex representation across the review but emphasize study-level heterogeneity in sex ratios when interpreting subgroup applicability. Among the clinical criteria most frequently used to characterize participants were significant loss of appetite, intense fatigue, weight loss greater than 5% in the previous six months, reduced functional status, hypoalbuminemia, guarded prognosis, and unplanned hospitalizations [21,22,33,34]. In several studies, these criteria appeared combined, reflecting a common profile of patients in a phase of marked functional decline [21,33,35,43,44].

Table 1 presents studies that evaluated the impact of corticosteroids on fatigue in patients with advanced cancer receiving palliative care. These studies include randomized clinical trials, observational studies, and systematic reviews, predominantly involving oncology populations, in which different corticosteroids, doses, and treatment durations were used. The main results analyzed relate to the intensity of fatigue, physical well-being, and, in some cases, quality of life.

The analyzed studies suggest that corticosteroids, particularly DEX, may have a beneficial effect in relieving fatigue in patients with advanced pulmonary carcinoma [21,32–35,37,39–41]. Most randomized clinical trials evaluated the administration of DEX orally, generally at doses between 4 and 8 mg/day, for short treatment periods (7 to 14 days).

Among randomized clinical trials, Yennurajalingam *et al.* (2013) [32] demonstrated that DEX 4 mg twice daily significantly improved fatigue and quality of life on days 8 and 15 (n = 84).

Paulsen *et al*. (2014) [21] reported similar results with MPD, reinforcing the rapid yet transient nature of its effect. Miyazaki *et al*. (2024) [37] evaluated betamethasone and highlighted variations in results across scales, revealing the complexity of measuring fatigue.

Other studies, such as the pilot study by Eguchi *et al*. (2015) [35], demonstrated only positive trends without statistical significance. However, Yennurajalingam *et al*. (2025) [33] suggested that combining corticosteroids with physical activity may prolong the benefits, highlighting multimodal strategies as a promising approach.

Table 2 (Ref. [21,32,34–36,38,42,45–48]) summarizes the studies that analyzed the effectiveness of corticosteroids in controlling anorexia in adult patients in palliative care. The included studies primarily comprise observational studies and clinical trials that evaluate different drugs and therapeutic regimens. The reported outcomes primarily focus on improved appetite and subjective perception of food intake, with frequent descriptions of early clinical responses following the start of therapy.

Regarding anorexia, the studies included in this review reveal a consistent pattern. Administration of corticosteroids, such as PRE (10–30 mg/day) or DEX (1–4 mg/day), has demonstrated benefits in improving appetite in patients with advanced cancer, frequently observed within the first 48 to 72 hours of treatment [32,34,36,45,46,48].

Paulsen *et al*. (2014) [21] identified a similar effect with MPD, and Matsuo *et al*. (2016) [34] observed a higher probability of response in patients with less inflammation and better baseline performance.

Table 1. Studies on the impact of corticosteroids in patients with chronic fatigue.

Author	Year	Study design	Population	Drug of interest studied and dosage	Main findings in the population of interest	SORT
Yennurajalingam *et al.* [32]	2013	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 84 cancer patients (25 M; 42 F with DEX); average age: 60 years	Dexamethasone 4 mg, 2/day for 14 days	Dexamethasone has demonstrated a significant reduction in overall fatigue in patients with advanced cancer, compared to placebo.	1
Paulsen *et al.* [21]	2014	Double-blind ECR	N = 26 cancer patients (13 M; 13 F); average age: 62.5 years	Methylprednisolone 16 mg, 2/day for 7 days	Significant reduction in fatigue compared to the placebo group.	1
Miyazaki *et al.* [37]	2024	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 70 cancer patients (16 M; 17 F); average age: 79.7 years	Betamethasone 4 mg/day for 7 days	Statistically significant improvement in fatigue in the betamethasone-treated group compared to placebo, at the secondary endpoint.	1
Sandford *et al.* [24]	2023	Systematic review (Cochrane)	N = 297 cancer patients; average age: 60 years	Dexamethasone ≤8 mg/day, for 14 days	Possible benefit in short-term fatigue; however, available data are limited and the risk of bias is high.	2
Yennurajalingam *et al.** [38]	2016	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 114 cancer patients (21 M; 37 F); average age: 63.9 years	Dexamethasone 4 mg, 2/day, for 14 days	Significant improvement in fatigue in the first week, suggesting the short-term effectiveness of dexamethasone.	2
Yennurajalingam *et al.* [33]	2025	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 92 cancer patients (15 M; 32 F); average age: 56 years	Dexamethasone 4 mg/day associated with supervised physical activity (7 days)	Clinically significant improvement on days 8 and 29; the authors highlight the need for studies with greater statistical power.	2
Eguchi *et al.* [35]	2015	Randomized pilot study	N = 35 cancer patients (11 M; 7 F); average age: 71 years	Methylprednisolone 32 mg/day, for 7 days	No statistically significant differences were observed between the methylprednisolone and placebo groups in relieving cancer-related fatigue. The authors emphasize that, being a pilot study, larger trials are needed to confirm efficacy.	2
Matsuo *et al.* [34]	2016	Prospective multicenter observational study	N = 179 cancer patients (85 M; 94 F); average age: 73 years	Betamethasone 1–4 mg/day; Dexamethasone 1–4 mg/day; Prednisolone 10–30 mg/day	Corticosteroids improved fatigue in approximately 48% of patients. The response was more frequent in patients with elevated C-reactive protein (CRP) and better performance status. No predictors were identified that were strong enough to justify isolated clinical use.	2
Koyama *et al.* [39]	2017	Prospective observational study	N = 112 cancer patients (18 M; 6 F); average age: 68 years	Betamethasone 4–8 mg/day	Early administration and administration in patients with better nutritional status were associated with improved fatigue scores. Late initiation, malnutrition, and severe inflammation were associated with less clinical benefit.	2

Table 1. Continued.

Author	Year	Study design	Population	Drug of interest studied and dosage	Main findings in the population of interest	SORT
Miura *et al*. [40]	2021	Phase II clinical trial	N = 32 cancer patients (18 M; 14 F); average age: 65.5 years	Dexamethasone 8 mg/day for 7 days	Significant improvement in fatigue after 7 days, with additional benefits for physical well-being.	2
Ingham *et al*. [41]	2024	Prospective observational study	N = 18 cancer patients (11 M; 7 F); average age: 70 years	Dexamethasone 4 mg/day	Daily administration of dexamethasone was associated with gradual improvement in fatigue scores over time. The drug demonstrated a favorable safety profile and was generally well tolerated.	2
Lundström & Fürst [36]	2006	Transversal observational study	N = 1292 cancer patients (567 M; 725 F); average age: 67 years	Dexamethasone 0.5–16 mg/day	Corticosteroids have been widely used to treat fatigue, with clinical reports of symptomatic benefit, although without standardized measurement. The authors emphasize the need for more uniform and evidence-based clinical protocols.	2
Matsuo *et al*. [42]	2011	Cross-sectional study (national survey of experts)	N = 392 palliative care physicians	Unspecified	Over 97% of experts reported the effectiveness of corticosteroids in improving fatigue and other symptoms in patients receiving palliative care.	3

* study that assessed cachexia.

Table 2. Studies on the effectiveness of corticosteroids in anorexia.

Author	Year	Study design	Population	Drug of interest studied (dosage)	Main findings in the population of interest	SORT
Yennurajalingam *et al.* [32]	2013	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 84 cancer patients (25 M, 42 F); average age: 60 years	Dexamethasone 4 mg 2/day for 14 days	Significant improvement in appetite compared to placebo, as measured by the Edmonton Symptom Assessment Scale (ESAS).	1
Paulsen *et al.* [21]	2014	Double-blind RCT	N = 16 cancer patients (13 M, 3 F); average age: 62.5 years	Methylprednisolone 16 mg twice daily for 7 days	Significant increase in appetite compared to the placebo group.	1
Yennurajalingam *et al.** [38]	2016	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 114 cancer patients (21 M, 37 F), average age: 63.9 years	Dexamethasone 4 mg 2/day	There was an improvement in appetite with dexamethasone, especially in the first week, but without lasting statistical significance.	2
Miller *et al.* [46]	2014	Systematic review	N = 1356 cancer patients (8 studies included)	Dexamethasone 3–25 mg/day; Prednisolone and Methylprednisolone (variable doses)	Corticosteroids have demonstrated short-term efficacy in stimulating appetite; however, these studies had small sample sizes and heterogeneous methodologies. More robust research is needed.	2
Eguchi *et al.* [35]	2015	Randomized pilot study	N = 35 cancer patients (11 M, 7 F), average age: 71 years	Methylprednisolone 32 mg/day for 7 days	No significant differences were observed between methylprednisolone and placebo in relieving anorexia. However, the small sample size limits the generalizability of the results, and further studies are recommended.	2
Hardy *et al.* [47]	2001	Prospective observational study	N = 106 patients with advanced chronic diseases	Dexamethasone 4–16 mg/day	Most patients evaluated reported improved appetite after starting dexamethasone therapy.	2
Mercadante *et al.* [45]	2001	Prospective observational study	N = 376 cancer patients; average age: 68 years	Dexamethasone 4–16 mg/day	Most patients experienced rapid improvement (within 3 days) in appetite and energy levels after starting corticosteroid therapy. The effect was transient, but clinically relevant and well-tolerated.	2
Lundström & Fürst [36]	2006	Cross-sectional observational study	N = 1292 cancer patients (567 M, 725 F); average age: 67 years	Dexamethasone 0.5–16 mg/day	Anorexia was one of the most frequent indications for corticosteroids; most patients had a positive clinical response.	2
Kiani *et al.* [48]	2011	Retrospective observational study	N = 359 adult patients with advanced chronic disease admitted to a Palliative Care unit (190 M, 169 F), average age: 72 years	Dexamethasone 0.5 mg every other day to 16 mg/day	Most patients showed clinical improvement in their anorexia, with good tolerability to the administered corticosteroid.	2
Matsuo *et al.* [34]	2016	Prospective multicenter observational study	N = 180 cancer patients (85 M, 95 F); average age: 74 years	Betamethasone 1–4 mg/day; Dexamethasone 1–4 mg/day; Prednisolone 10–30 mg/day	Corticosteroids have demonstrated benefit in improving anorexia in patients with advanced cancer. Predictive factors: improved functional status, reduced inflammation, and absence of delirium.	2
Matsuo *et al.* [42]	2011	Cross-sectional study (national survey of experts)	N = 392 palliative care physicians	Unspecified	97% of experts reported the effectiveness of corticosteroids in relieving anorexia and other symptoms evaluated.	3

* study that assessed cachexia.

Table 3. Studies on the impact of corticosteroids on anorexia-asthenia and on anorexia-cachexia and asthenia.

Author	Year	Study design	Population	Drug of interest studied (dosage)	Main findings in the population of interest	SORT
Yennurajalingam *et al.** [38]	2016	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 114 cancer patients (21 M, 37 F), average age: 63.9 years	Dexamethasone 4 mg 2/day	Significant improvement in the severity of the FAD (fatigue, anorexia, depression) cluster on days 8 and 15 with dexamethasone. The authors suggest that fatigue, anorexia-cachexia, and depression share common mechanisms and that dexamethasone may be useful in relieving these symptoms together.	2
Paulsen *et al.* [21]	2014	Double-blind RCT	N = 16 cancer patients (13 M, 3 F), average age: 62.5 years	Methylprednisolone 16 mg twice daily for 7 days	Significant improvement in fatigue and anorexia in the methylprednisolone group compared to placebo; no difference in pain.	1
Yennurajalingam *et al.* [32]	2013	Double-blind, placebo-controlled randomized controlled trial (RCT)	N = 84 cancer patients (25 M, 42 F), average age: 60 years	Dexamethasone 4 mg twice daily for 14 days	Significant improvements in fatigue (FACIT-F) and appetite, as well as improvements in physical distress (ESAS); no significant differences in global or psychological distress; similar adverse effects between groups.	1
Eguchi *et al.* [35]	2015	Randomized pilot study	N = 35 cancer patients (11 M, 7 F), average age: 71 years	Methylprednisolone 32 mg/day for 7 days	The corticosteroid was found to have no significant benefit in reducing fatigue compared to the placebo. No relevant improvements in appetite or quality of life were observed either.	2
Hardy *et al.* [47]	2001	Prospective observational study	N = 106 patients with advanced chronic diseases	Dexamethasone 4–16 mg/day	Symptomatic improvement in patients treated for anorexia and fatigue, with reports of increased appetite and energy; response observed even with short-term use.	2
Lundström & Fürst [36]	2006	Cross-sectional observational study	N = 1292 cancer patients (567 M, 725 F); average age: 67 years	Dexamethasone 0.5–16 mg/day	Frequent use of corticosteroids for multiple symptoms (fatigue, anorexia); most patients reported temporary improvement in appetite, energy, and well-being in the first few weeks of use.	2
Matsuo *et al.* [42]	2011	Cross-sectional study (national survey of experts)	N = 392 palliative care physicians	Unspecified	Most experts reported observing symptomatic improvement with the use of corticosteroids for anorexia and fatigue in patients with terminal cancer. The most frequently reported adverse effects were muscle weakness and hyperglycemia. The perceived effectiveness was greater in the areas of anorexia symptoms and overall well-being.	3
Mercadante *et al.* [45]	2001	Prospective observational study	N = 376 cancer patients; average age: 68 years	Dexamethasone 4–16 mg/day	Most patients experienced rapid improvement (within 3 days) in appetite and energy levels after starting corticosteroid therapy. The effect was transient but clinically relevant, with good tolerability.	2

Note: In this table, we distinguish 'weight loss' (patient- or chart-reported bodyweight change) from 'cachexia' (objectively assessed muscle/lean-mass loss or defined using validated cachexia criteria). Studies reporting only weight measurements without objective muscle assessment are labelled under 'weight loss'. * study that assessed cachexia.

In observational studies, anorexia stood out as one of the most frequent indications for corticosteroid prescription [36,45,48]. However, adverse effects, such as hyperglycemia, fluid retention, or muscle weakness, became more relevant with prolonged use. The systematic review by Miller *et al*. (2014) [46], which included 1356 patients, reinforces the use of corticosteroids for anorexia associated with malignancy, although there is no consensus on the ideal dose.

Despite a favorable initial response, most studies describe a loss of effectiveness after 2 to 4 weeks, suggesting that the benefit is primarily short-term. Nevertheless, several authors agree that corticosteroids are a useful option for symptomatic control of anorexia in a palliative setting, especially in patients with limited life expectancy, where the predominant goal is rapid improvement in well-being [21,34].

Table 3 (Ref. [21,32,35,36,38,42,45,47]) presents studies that simultaneously evaluated more than one symptom of ACAS, namely anorexia, asthenia, and, in a smaller number of cases, cachexia. These studies explore the effect of corticosteroids on overall symptom control, enabling an integrated assessment of the therapeutic impact on symptom clusters that frequently coexist in patients with advanced disease in palliative care settings.

This table brings together studies that simultaneously evaluated multiple symptoms in patients with advanced chronic disease, mostly of oncological etiology, undergoing treatment with corticosteroids. In general, the studies reported short-term clinical improvements in multiple outcomes associated with anorexia-cachexia-asthenia syndrome, including appetite, fatigue, and overall well-being [21,32,35,36,38,45,47].

In several studies, clinical response was most frequently observed in the first few weeks after the start of therapy, with variability described in the magnitude of the effect among the patients evaluated [36,45,47].

Regarding harms, the included studies most frequently reported metabolic and neuropsychiatric adverse effects. Metabolic events included hyperglycemia and worsening glycemic control [34,36,45,48], often requiring glucose monitoring or treatment adjustment. Fluid retention/edema and occasional electrolyte disturbances were also described. Neuropsychiatric effects—insomnia, mood changes, agitation and, less commonly, delirium—were reported in randomized trials and observational cohorts [32,34,36]. Muscle weakness/steroid-induced myopathy and increased infection risk with prolonged use were repeatedly noted [36,48]. Most studies did not report uniform incidence rates.

Discussion

This review included 18 studies, with 6306 patients, published between 2001 and 2025 that evaluated the efficacy of corticosteroids in ACAS. Overall, the evidence points to rapid but short-lived clinical benefit, with significant methodological heterogeneity and uncertainty regarding long-term impact [24,47]. The context of care delivery proved to be equally heterogeneous. Most studies were conducted in hospital settings, but there were also investigations conducted in Palliative Care Units, outpatient clinics, and at home. Some studies adopted a multisectoral approach by integrating different levels of care, thereby providing a more comprehensive view of corticosteroid use across stages of the palliative care journey [45,47].

The short-term improvements in appetite and fatigue observed after corticosteroid initiation are consistent with rapid suppression of systemic inflammatory mediators (IL-1, IL-6, TNF-α) and downstream effects on hypothalamic appetite circuits [49–51]. Nevertheless, most included studies did not systematically measure inflammatory biomarkers longitudinally; therefore, linking clinical response to specific cytokine suppression remains inferential. Future trials should incorporate serial biomarker measurements (e.g., IL-6, CRP, lymphocyte counts) to validate these mechanistic hypotheses and identify predictors of response [52,53].

Taken together, this methodological and contextual diversity helps explain the variability observed in the results, reinforcing the need for a descriptive synthesis to better understand patterns of effectiveness and the limitations of the available evidence.

Regarding fatigue, this review consistently indicates a short-term symptomatic benefit of corticosteroid use in patients with advanced pulmonary carcinoma. Included randomized clinical trials demonstrated a significant reduction in fatigue intensity in the first weeks of therapy, particularly in the first 7 to 14 days after the start of treatment, when compared to placebo, especially with DEX [21,32,37].

These findings are corroborated by prospective and retrospective observational studies, which report initial clinical improvement in subgroups of patients, though with variability in response magnitude [34,39,41,47]. These descriptive counts should be interpreted cautiously: outcome instruments, responder definitions and follow-up times differed substantially across studies, precluding quantitative synthesis.

Despite this favorable global trend, the quality of the available evidence remains moderate (LE 2), reflecting important methodological limitations such as the small sample size, the heterogeneity of the instruments used to assess fatigue, and the diversity of therapeutic regimens studied. The beneficial effects described are consistently reported in the literature as transient, with a progressive loss of effectiveness after the first few weeks of treatment, which limits the usefulness of corticosteroids as a sustained strategy for controlling fatigue [24,36,47].

This transient nature of the effect becomes particularly understandable when interpreted in light of the patho-

physiology of cancer-related fatigue, a multifactorial symptom influenced not only by systemic inflammation, but also by metabolic changes, neuroendocrine dysfunction, psychological factors, functional decline, and iatrogenic effects [4,6,9,10,50]. Several authors describe fatigue as partially mediated by pro-inflammatory cytokines, such as interleukin 1, interleukin 6, tumor necrosis factor alpha and interferon gamma, and alterations in the hypothalamic-pituitary-adrenal axis, mechanisms that may explain the initial response to corticosteroids without producing lasting modulation of the underlying processes [3,5,10–13].

The included observational data further suggest that the probability of response is higher in patients with better functional status, less systemic inflammation, and earlier initiation of therapy, reinforcing the importance of careful patient selection and a clear definition of therapeutic goals [34,39].

Previous systematic reviews agree that, despite short-term benefits, the overall evidence remains insufficient to support strong recommendations, highlighting the need for more robust clinical trials with larger samples and longer follow-up [15,24,25,27,46].

It is also important to clarify that, although the term "asthenia" is used in this review, most of the studies analyzed specifically evaluated cancer-related fatigue, as it is a more clearly defined and quantifiable manifestation, which should be considered when interpreting the results.

Taken together, these findings support the idea that corticosteroids may play a useful role in the rapid relief of fatigue in a palliative setting, provided they are used judiciously, for limited periods, and integrated into a multidimensional approach, with frequent reassessment of the clinical benefit obtained [24,32].

With regard to anorexia, the evidence is more consistent. Studies such as those by Yennurajalingam *et al.* (2013; 2016) [32,38] have demonstrated rapid improvements in appetite with DEX, suggesting a possible anti-inflammatory mechanism common to fatigue.

This rapid response is clinically relevant in palliative care, where the therapeutic goal often focuses on immediate relief of suffering and improvement in perceived well-being [54–56]. However, several studies consistently report that this effect tends to be transient, with loss of effectiveness after a few weeks, which limits the role of corticosteroids to short-term strategies [38,45,46].

This rapid, yet poorly sustained nature becomes particularly understandable when considering the pathophysiology of anorexia-cachexia syndrome, in which anorexia is strongly modulated by systemic inflammation and pro-inflammatory mediators, with a central impact on appetite regulation and a peripheral impact on energy metabolism [6,51,52].

Thus, it is plausible that the anti-inflammatory effect of corticosteroids contributes to the initial improvement in appetite by temporarily reducing inflammatory components associated with the symptomatic cluster [38]. In parallel, the observational data point to heterogeneity of response, with a greater likelihood of benefit in patients with better functional status and lower inflammatory burden/clinical impairment at the time of therapy initiation [34,48].

This pattern reinforces the idea that corticosteroids can act as symptomatic modulators in specific subgroups, but hardly alter the sustained biological determinants of anorexia-cachexia, which helps explain the lack of lasting benefit and the need for frequent reassessment [45,46].

In summary, the results of this review support the idea that corticosteroids may have clear utility in anorexia in a palliative setting, especially when a rapid response is needed and life expectancy is limited [34,46]. However, its use should be framed as a temporary and individualized measure, with explicit objectives and close monitoring, taking into account the variability of response and the transient nature of the effect described in the literature [34,46].

The overall quality of the evidence is considered moderate (LE 2), supported mainly by observational studies and clinical trials with methodological limitations, namely small sample sizes, lack of control groups, and heterogeneity in doses and treatment durations. Nevertheless, the overall results support the use of corticosteroids as a short-term pharmacological intervention to stimulate appetite in palliative care [21,32].

Cachexia (i.e., biologically defined syndrome with objective loss of skeletal muscle mass) was the least studied outcome in isolation among included studies. Several studies reported 'weight loss' or changes in bodyweight, but few used objective measures of muscle mass or formal cachexia criteria. Only Yennurajalingam *et al.* (2016) [38] assessed cachexia using integrated endpoints; most other reports provided patient- or chart-reported weight changes without muscle-mass assessment and are therefore reported here as 'weight loss'. This result suggests that pharmacological intervention may exert a simultaneous effect on multiple symptoms that frequently coexist in patients with advanced disease. However, it does not allow for the inference of a sustained benefit on cachexia as an autonomous pathophysiological entity.

Analysis of studies that assessed more than one symptom of ACAS allows for a more integrated perspective on the impact of corticosteroids in PC. These studies consistently describe early clinical improvements in symptoms such as appetite, fatigue, and overall well-being, particularly in the first few weeks after the start of corticosteroid therapy [21,32,35,36,45,47]. These initial effects were observed in both clinical trials and observational studies, reinforcing the notion of rapid symptomatic benefit in a palliative care setting.

This pattern is consistent with the conceptualization of ACAS as an interrelated symptomatic cluster, in which systemic inflammation plays a central role in the simultaneous genesis of anorexia, weight loss, and asthenia [1,5,6].

In this context, the concomitant improvement of several symptoms observed in some studies may reflect the overall anti-inflammatory action of corticosteroids, rather than a specific and sustained effect on each isolated manifestation [34,38,42].

Consistently, the observed benefits tend to be transient, and while some studies reported short-term improvements in appetite or bodyweight (weight loss reversed), there is little evidence of sustained impact on objective structural parameters of cachexia (e.g., muscle mass measured by imaging or validated lean-mass metrics). Thus, symptomatic weight gain does not necessarily equate to reversal of cachexia, reinforcing the distinction between symptomatic improvement and modification of the biological course of the syndrome [45,46].

Observational studies also indicate that the extent of clinical response differs across patients, with more modest benefits typically observed in those with severely impaired functional status, pronounced systemic inflammation, or advanced end-stage disease [34,36].

Surveys of healthcare professionals corroborate this perception, pointing to clinical benefit, especially in less advanced stages of the disease, and reinforcing the need for regular reassessment of therapy [42].

Clinically, our findings suggest that clinicians should monitor for hyperglycemia, fluid retention, neuropsychiatric symptoms, and early signs of infection when prescribing corticosteroids, even for short courses, and remain vigilant for steroid-induced muscle weakness if treatment is prolonged [45,48]. We recommend baseline glucose assessment and regular clinical reassessment during therapy.

This review gains further depth when integrated with the international consensus, which identified DEX as the only corticosteroid to reach formal consensus for the treatment of anorexia in palliative care [57,58]. This designation likely reflects two factors: (1) pharmacologic characteristics—DEX is a potent glucocorticoid with a relatively long biological half-life that supports once-daily dosing and durable receptor exposure; and (2) a larger and more consistent clinical evidence base and clinical experience using DEX in palliative settings compared with other corticosteroids. However, head-to-head comparative trials are lacking, and the consensus therefore indicates relative evidence and practice frequency rather than proven superiority. This consensus suggests that its use should be judicious, short-term, and carefully monitored, given the lack of robust data on long-term safety and inequalities in global access to essential medicines. Where feasible, DEX treatment should be accompanied by monitoring of potential biomarkers (e.g., lymphocyte counts and the CRP/albumin ratio), which may help track therapeutic response and identify early safety signals; future studies should validate their predictive value. In this context, such use should ideally be supported by close monitoring of inflammatory and nutritional biomarkers, namely lymphocyte counts and the C-reactive protein/albumin (CRP/Alb) ratio, which may help to identify patients at higher risk of adverse outcomes and guide timely treatment adjustments [22,58,59].

Equally relevant, the study by Saura *et al*. (2025) [58] offers a contemporary perspective on anorexia-cachexia syndrome in a community setting, showing that this condition is practically universal in patients followed by specialized home-based palliative care teams and that its impact extends beyond the physical domain, affecting emotional, family, and social dimensions. The observed trend towards worsening nutritional status in patients medicated with corticosteroids should be interpreted with caution, as it may reflect their use in more advanced stages of the disease, and not necessarily a direct adverse effect of the therapy.

Taken together, the findings of this review support the view that corticosteroids primarily play a role as a short-term symptomatic intervention, with recognized benefit in the rapid relief of anorexia and fatigue, and a more limited effect on cachexia [34,39].

The marked methodological variability among the studies reinforces the need for adequately powered pragmatic randomized clinical trials, capable of clarifying the ideal dose, the patient profiles that benefit most, and the safe duration of use [24,46]. In the context of palliative care, the introduction of corticosteroids should therefore always be carefully considered and integrated into a multidimensional therapeutic plan, focused on the quality of life, comfort, and dignity of the person with advanced disease [54–56].

We noted that several studies reported daily dexamethasone (DEX) doses in the range of approximately 4–16 mg/day, and these regimens were associated with larger and more sustained clinical improvements compared with lower doses in the included reports.

Dose considerations: Although dexamethasone (DEX) doses between 4 and 16 mg/day were commonly reported, evidence on whether higher doses produce a faster onset of action is limited and inconsistent. Most randomized trials used low-to-moderate doses (4–8 mg/day) and reported rapid onset within days; observational data suggested that higher doses (≈8–16 mg/day) can yield larger or more sustained benefit in some patients, but these signals may reflect confounding by indication and are not supported by head-to-head dose-comparison trials. Importantly, higher daily doses were also more frequently associated with clinically relevant, dose-related harms in palliative populations—notably more pronounced hyperglycemia requiring treatment adjustment, greater fluid retention/edema, increased neuropsychiatric effects (insomnia, mood changes, agitation, delirium), steroid-induced muscle weakness/myopathy, and higher infection risk [34,48]. Given the frailty and comorbidity of many palliative patients, these risks may offset symptomatic gains. Therefore, any decision to escalate dose should be individualized, explicitly document therapeutic goals and stopping rules, and include baseline assessment (glucose,

volume status, neurocognitive risk) with prompt follow-up. If higher doses are used, early monitoring of blood glucose levels and clinical assessment for fluid overload, neuropsychiatric symptoms and signs of infection are recommended. Dose reduction or treatment discontinuation should be considered if the harms of therapy outweigh its benefits.

Limitations and Future Perspectives

Most available studies focus on oncological patients, have small sample sizes, short follow-up periods, and significant variations in the drugs used, doses administered, and outcomes assessed, which makes it difficult to formulate uniform and robust therapeutic recommendations.

Additionally, the scarcity of large-scale randomized clinical trials, as well as the small proportion of multicenter studies, limits the generalizability of the results and contributes to the observed variability.

Also, most investigations address the symptoms in isolation, with the simultaneous assessment of anorexia, cachexia, and asthenia being particularly rare, representing a significant gap in current knowledge.

Moreover, the absence of standardized protocols and the predominance of observational studies increase the risk of bias and hinder comparisons across studies, limiting the strength of currently available clinical recommendations. In particular, cachexia remains insufficiently studied, specifically reflecting the need for more targeted investigations into this component of ACAS.

Another key limitation is the clinical heterogeneity of included populations. Studies often combine distinct underlying conditions (e.g., terminal cancer with differing inflammatory profiles, chronic non-inflammatory diseases), which likely differ in mechanisms driving symptoms such as fatigue and anorexia. This heterogeneity limits the validity of aggregated conclusions about corticosteroid efficacy and safety.

A further limitation is that this is a scoping review and we did not perform a comprehensive formal risk-of-bias assessment; therefore, conclusions regarding effect size and strength of evidence should be interpreted with caution.

We recognize the absence of randomized trials directly comparing dexamethasone doses; heterogeneity in dosing and potential confounding limit any inference about dose–response for onset or durability of effect. In this context, future research should prioritize larger and adequately powered pragmatic randomized clinical trials, ideally multicenter, capable of clarifying the dosage, the safe duration of treatment, and the patient profiles that benefit most from corticosteroid therapy.

Notably, Yennurajalingam *et al*. (2025) [33] reported that combining dexamethasone with supervised physical activity produced clinically significant improvements that persisted longer than steroid alone. We therefore recommend that future pragmatic trials evaluate multimodal strategies (steroid and structured physical activity or rehabilitation) to test whether activity can extend the symptomatic benefit and improve functional outcomes, and include functional and biomarker endpoints.

The inclusion of clinically relevant outcomes and an integrated approach to the different symptoms of ACAS may contribute to a better consolidation of evidence and the development of more effective therapeutic strategies aligned with the principles of person-centered palliative care.

Conclusions

We conclude that corticosteroids—particularly dexamethasone—can be considered a short-term therapeutic option for symptomatic control of refractory anorexia and fatigue in palliative care, but their use must be individualised and time-limited.

Based on available evidence and clinical experience, initial dosing in most patients may reasonably start at low to moderate levels (dexamethasone 4 mg/day or equivalent), with consideration of moderate escalation (up to ≈8 mg/day) when a larger or more durable symptomatic response is needed and tolerated; doses above ≈8–16 mg/day have been reported to produce larger or more sustained effects in some observational reports but are also associated with incrementally higher metabolic, neuropsychiatric and infectious risks. Dose selection should therefore explicitly balance expected symptomatic benefit against patient frailty, comorbidities, baseline glycaemic and volume status, neurocognitive vulnerability, and the patient's prognosis and goals of care.

We recommend: (1) defining clear, measurable therapeutic objectives and stopping rules before initiation; (2) using the lowest effective dose for the shortest feasible period; (3) performing baseline checks (e.g., glucose, volume status, review of neuropsychiatric risk) and early follow-up (days to 1–2 weeks) with targeted monitoring (capillary glucose where appropriate, assessment for fluid retention, delirium, infection, and emerging myopathy); and (4) immediate dose reduction or discontinuation if benefit is absent or harms emerge.

Future research should prioritise randomized dose-finding trials, objective cachexia outcome measures, and evaluation of multimodal interventions (e.g., corticosteroids plus structured physical activity) to better define optimal dosing, duration, and patient selection.

Availability of Data and Materials

Not applicable.

Author Contributions

Conceptualization, CP, MD and HR; methodology, CP, MD, JRN and HR; software, DSS, JRN, CLT and

MMV; validation, VS, ABDT, MD and JRN; formal analysis, CP and HR; investigation, CP, JRN and HR; resources, JRN and HR; data curation, CP, JRN, MMV, CLT and ABDT; writing—original draft preparation, CP, MD and HR; visualization, DSS, MMV, VS, CLT and MD; supervision, HR; project administration, HR; funding acquisition, HR and JRN. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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