

Biochemical Markers of Inflammation, Oxidative Stress, and Nutritional Status in Patients Receiving Palliative Care

Peter Novak^{1*}, Sophie Dubois², Thomas Müller³, Anna Weber⁴, Erik Johansson⁵

¹*Department of Palliative Medicine and Biochemistry, Charles University, Prague, Czech Republic.*

²*Department of Clinical Pharmacy and Nutrition, Utrecht University, Utrecht, Netherlands.*

³*Department of Palliative Care and Laboratory Medicine, University of Vienna, Vienna, Austria.*

⁴*Department of Nursing and Nutritional Status, University of Cologne, Cologne, Germany.*

⁵*Department of Palliative Medicine and Biomarkers, Uppsala University, Uppsala, Sweden.*

Abstract

Biochemical abnormalities are common in advanced illness, yet their meaning becomes increasingly difficult to separate from disease progression, treatment effects, reduced intake, tissue catabolism, systemic inflammation, and the physiological changes that accompany approaching death. This conceptual article develops a multidomain approach to interpreting inflammatory, oxidative-stress, nutritional, and metabolic biomarkers in palliative care. The central premise is that a measured abnormality has several distinguishable meanings: it can indicate a biological process, contribute to prognostic estimation, change over time, coexist with competing explanations, or become clinically relevant because it corresponds with symptoms, function, nutritional burden, or patient goals. These meanings should not be assumed to be interchangeable. Evidence from cancer cachexia, clinical nutrition, inflammatory prognostication, redox biology, body-composition research, and supportive care demonstrates substantial heterogeneity in biomarker definitions, measurement strategies, prognostic horizons, and responsiveness to intervention. The resulting interpretation framework therefore treats laboratory values as context-dependent signals whose clinical usefulness depends on concordance with disease state, treatment exposure, nutritional phenotype, temporal trajectory, bedside assessment, and patient-centred outcomes. This approach preserves the value of biomarkers while limiting overinterpretation of isolated measurements. It also provides a basis for distinguishing prognostic use from longitudinal monitoring and for identifying situations in which laboratory change should prompt reassessment rather than an automatic therapeutic response.

Keywords: Palliative care, Cancer cachexia, Systemic inflammation, Oxidative stress, Nutritional status, Biomarker interpretation

Introduction

Advanced illness frequently produces biochemical, metabolic, nutritional, and inflammatory changes at the same time. Contemporary cachexia literature has consequently moved toward earlier recognition and multimodal supportive care, while also showing that important gaps persist between mechanistic knowledge, clinical assessment, and routine implementation [1-3].

Clinical recommendations reinforce this multidimensional view. Near the end of life, however, clinical value is determined by more than biological plausibility or the capacity to predict mortality. Symptom relief, burden of intervention, quality of life, patient priorities, and the changing goals of care become central to deciding whether additional testing or a response to an abnormal result is worthwhile [4-8].

The interpretive problem is therefore broader than identifying which laboratory abnormality correlates most strongly with adverse outcome. The purpose of this article is to develop a contextual interpretation logic for

Corresponding author: Peter Novak

Address: Department of Palliative Medicine and Biochemistry, Charles University, Prague, Czech Republic.

E-mail: ✉ peter.novak@cuni.cz

Received: 05 October 2024; **Revised:** 02 December 2024;

Accepted: 21 December 2024

How to Cite This Article: Novak P, Dubois S, Müller T, Weber A, Johansson E. Biochemical Markers of Inflammation, Oxidative Stress, and Nutritional Status in Patients Receiving Palliative Care. *J Integr Nurs Palliat Care*. 2024;5(2):409-19. <https://doi.org/10.51847/huPvP8nvDj>

inflammatory, oxidative-stress, nutritional, and metabolic biomarkers in palliative care, with particular attention to the distinction between biological signal, prognosis, longitudinal monitoring, confounding, temporal instability, and clinical actionability.

Conceptual scope

Cachexia biology provides a useful starting point because it demonstrates why a single laboratory value cannot represent the entire physiological state. Biomarker validity is further modified by factors such as age, which can alter both baseline physiology and the relationship between candidate markers and wasting phenotypes [9-11]. The conceptual dispute over whether cachexia should be understood primarily as a nutritional syndrome or as a systemic inflammatory syndrome is itself informative [12, 13]. These accounts overlap but emphasize different mechanisms and different clinical responses. Evidence at one level cannot automatically establish the others.

Why biomarkers require contextual interpretation in palliative care

The biomarker literature does not support treating laboratory measurements as a homogeneous class of endpoints. A systematic review of cancer-cachexia trials identified extensive variation in the biomarkers selected, the biological processes they were intended to represent, and the extent to which they were repeatedly evaluated across interventions [14, 15]. Frequent measurement therefore cannot be equated with validation as a surrogate outcome or with usefulness for bedside decision-making.

Clinical evidence also demonstrates that apparently competing domains can carry independent information. In a large international multicohort analysis, reduced food intake and systemic inflammation were both associated with weight loss and survival, indicating that nutritional and inflammatory states cannot be collapsed into a single explanation [16]. Direct evidence from patients receiving palliative care further shows that inflammatory biomarkers can contribute to short-term prognostic estimation [17, 18]. Such associations are clinically relevant, but they do not establish universal thresholds or determine what should be done for an individual patient.

The practical distinction is summarized in **Table 1**. A laboratory value becomes interpretable only after the question being asked of it is specified.

Table 1. Interpretive distinctions among biomarker signal, clinical state, prognosis, and actionability in palliative care

Interpretive object	Primary question answered	Information required beyond the measured value	What the observation cannot establish by itself
Biological signal	What physiological process may be active?	Disease context, treatment exposure, competing causes, measurement conditions	The patient's complete clinical state
Clinical phenotype	How does the signal relate to symptoms, intake, function, wasting, or nutritional burden?	Bedside assessment, trajectory, body composition, symptom and nutritional information	A single causal mechanism
Prognostic information	Does the observation contribute to estimation of future clinical outcome?	Population, prediction horizon, comparator variables, validated model context	That changing the biomarker will change outcome
Monitoring information	Does change over time plausibly reflect change in the process of interest?	Repeated measurement, timing, treatment exposure, measurement reliability	Therapeutic responsiveness without validation
Clinical actionability	Should the finding change assessment, discussion, testing, or care?	Patient goals, expected benefit, burden, reversibility, alternative explanations	That an abnormal result automatically requires intervention

Systemic inflammation in advanced illness

Systemic inflammation is one of the most extensively studied biological contributors to cancer-associated wasting, but it is generated through interacting rather than isolated pathways. Cytokine signalling, neuroendocrine changes, altered appetite, muscle catabolism, energy expenditure, and tumour-related processes can converge on the cachexia phenotype [19, 20]. This multiplicity helps explain why inhibition of a single inflammatory mediator has not produced a universally effective treatment strategy.

Inflammation becomes more clinically informative when it is interpreted with observable patient state. In advanced cancer cohorts, inflammatory scores and performance status both contribute to survival estimation, supporting the view that biochemical and functional evidence provide related but non-identical information [21, 22]. Prospective work examining emerging cachexia biomarkers has likewise demonstrated associations among inflammatory or metabolic measurements, appetite, quality of life, and cachexia features while also identifying candidate markers that showed weak or absent relationships [23, 24]. Its meaning depends on its relationship with the phenotype in which it occurs.

Inflammatory biomarker domain

Inflammatory biomarkers differ in what they measure and in the questions for which they have been evaluated. These measures should not be treated as interchangeable simply because each has been associated with adverse outcomes.

Recent multicentre work on cancer-cachexia diagnostic criteria illustrates how classification can change according to the variables and definitions used [25, 26]. In terminally ill patients with cancer, comparative evaluation of the Palliative Prognostic Index, Laboratory Prognostic Score, and Palliative Prognostic Score showed that prediction performance varies with the selected time horizon and model characteristics [27, 28]. A marker or score can therefore be informative for one prognostic interval without becoming the preferred measure for another purpose. For palliative interpretation, inflammatory markers are best regarded as signals with several possible functions: characterizing systemic inflammatory burden, contributing to a broader prognostic estimate, or providing longitudinal information when repeatedly measured. None of these functions establishes by itself that the measured inflammatory process is modifiable or that modification would improve symptoms, function, or survival.

Oxidative-stress domain

Oxidative stress adds a second biological domain whose interpretation is especially vulnerable to oversimplification [29]. Reactive oxygen species can damage proteins, lipids, nucleic acids, and cellular structures, but redox processes also participate in signalling and treatment response. Reviews of cancer therapy demonstrate that oxidative stress may contribute to antitumour effects as well as treatment toxicity, depending on dose, location, cellular state, and therapeutic context [30, 31]. The biology is therefore not adequately represented by a simple continuum in which a higher oxidative signal is automatically worse.

Contemporary redox oncology further emphasizes the spatiotemporal and pleiotropic effects of reactive oxygen species across tumour and host biology [32, 33]. Experimental work has identified an inflammatory–redox pathway involving IL-1 β , NBR1-p62-Nrf2 signalling, extracellular superoxide dismutase, and skeletal-muscle responses during cancer cachexia [34, 35]. Such evidence strengthens mechanistic plausibility but does not validate a circulating oxidative-stress marker as a clinical decision tool. The distinction between mechanism and bedside utility must remain explicit.

Nutritional and metabolic biomarker domain

Nutritional status cannot be inferred reliably from a single biochemical measurement. The Global Leadership Initiative on Malnutrition criteria require both phenotypic and etiologic components for malnutrition diagnosis, thereby separating the diagnosis of malnutrition from isolated laboratory abnormalities [36]. Cancer-specific nutrition guidance similarly treats reduced intake, symptoms, body weight, body composition, metabolic demand, and disease state as interacting elements of assessment [37].

This distinction matters because malnutrition in cancer has heterogeneous causes. Inflammation can contribute substantially, but impaired intake, gastrointestinal symptoms, treatment toxicity, altered metabolism, functional decline, and advanced disease may produce overlapping phenotypes through different pathways [38]. Evidence from randomized trials in incurable solid cancer also shows substantial heterogeneity in nutritional interventions, adherence, populations, and outcomes [39]. Nutritional support is therefore clinically meaningful without implying that correcting intake can reverse every catabolic process [40].

Interactions between inflammation, oxidative stress, and nutrition

The three domains interact, but their interaction should not be interpreted as evidence that they are interchangeable. Oxidative pathways can be affected by both tumour biology and treatment. The resulting laboratory pattern may therefore reflect several processes operating simultaneously.

Clinical data support the value of combining rather than collapsing information. Multidimensional assessment incorporating nutritional and inflammatory characteristics can identify prognostically distinct patient states that are not fully explained by tumour variables alone [41]. At the same time, prospective oncology assessment shows that formally measured malnutrition, cachexia, and sarcopenia can be under-recognized when clinicians rely primarily on unaided subjective judgement [42].

Within the present interpretation logic, such discordance is not automatically measurement error. It is a signal to reconsider whether different domains are tracking different components of the illness.

Cachexia and catabolic burden

Cachexia is the clinical setting in which the limits of laboratory reductionism become most apparent. A systematic review of body-weight and body-composition endpoints in cachexia trials documented wide variation across simple weight measures, bioelectrical impedance, dual-energy X-ray absorptiometry, computed tomography, and related approaches [43].

The clinical importance of tissue depletion is supported by systematic evidence associating sarcopenia with adverse treatment outcomes and mortality across cancer populations [44]. However, methodological heterogeneity

in sarcopenia definitions, imaging approaches, thresholds, and tumour populations limits direct interchangeability. Laboratory change may be compatible with worsening catabolism without measuring the magnitude or distribution of tissue loss itself.

Disease severity and treatment effects

Disease burden and treatment can influence the same biological systems that biomarkers are intended to describe. Treatment context must therefore be considered part of interpretation rather than treated as background noise.

Body-composition research demonstrates a related measurement problem. In patients with locally advanced or metastatic pancreatic cancer, longitudinal computed-tomography analysis showed that the prognostic significance of muscle and adipose-tissue change can differ according to sex, compartment, and measurement precision [45]. This finding illustrates a broader principle: apparently objective biological measurements remain sensitive to what is measured, how reliably it is measured, and in whom the relationship is tested.

Table 2 integrates the major sources of modification relevant to the nutritional–metabolic domain without assuming that any observed pattern identifies one mechanism.

Table 2. Nutritional–metabolic findings under competing disease, treatment, and tissue contexts in advanced illness

Observed clinical or biochemical pattern	Plausible modifying processes	Interpretation that remains supportable	Interpretation requiring additional evidence
Reduced food intake	Anorexia, symptoms, treatment toxicity, gastrointestinal dysfunction, fatigue	Nutritional exposure is reduced and may contribute to energy deficit	That reduced intake is the sole driver of wasting
Weight loss	Reduced intake, dehydration, tissue catabolism, fluid redistribution, disease progression	Body mass has declined and requires phenotypic clarification	The proportion of muscle versus fat loss or its mechanism
Muscle depletion	Catabolism, reduced activity, inflammation, treatment effects, inadequate intake	Skeletal-muscle burden may contribute to vulnerability	That one circulating biomarker caused the depletion
Systemic inflammatory abnormality	Tumour activity, infection, tissue injury, treatment, advanced disease	An inflammatory process is present or likely	The specific cause, reversibility, or therapeutic target
Nutritional laboratory abnormality	Inflammation, organ dysfunction, intake, hydration, disease severity	The value may contribute to nutritional and metabolic context	A stand-alone diagnosis of malnutrition
Oxidative-stress signal	Tumour biology, therapy, inflammation, antioxidant defence	Redox balance may be altered	Whether the alteration is beneficial, harmful, or treatment-responsive
Change after intervention	Treatment effect, natural progression, measurement variability, concurrent illness	A temporal association is present	Attribution of the change to the intervention without an appropriate comparator

Prognostic versus monitoring uses

Prognosis and monitoring are distinct uses of biomarker information. A prognostic marker contributes to estimation of what is likely to occur, whereas a monitoring marker must provide interpretable information about change in a biological or clinical state over time. A variable can perform the first function without satisfying the second.

This distinction is visible in cachexia trials. Systematic examination of oncological and survival endpoints shows substantial heterogeneity in overall survival, progression measures, tumour-response outcomes, treatment toxicity, and analytic methods, with comparatively limited evidence that modifying a cachexia endpoint consistently produces corresponding improvement in survival outcomes [46]. Prognostic association should therefore not be treated as proof that a biomarker is a valid surrogate for therapeutic response.

The same issue has become increasingly important in clinical-trial and regulatory discussions. Contemporary cachexia research places greater emphasis on outcomes that represent meaningful patient benefit, including physical function, quality of life, symptom experience, and other dimensions that cannot be substituted automatically by change in body mass or a biochemical measurement [47]. In palliative care, the distinction is especially important because monitoring is worthwhile only when a detectable change can be interpreted and can plausibly inform care.

The appropriate question is therefore not merely whether an inflammatory, oxidative, or nutritional biomarker predicts deterioration. It is whether repeated measurement distinguishes clinically meaningful change from expected biological variability, treatment effects, or progressive disease, and whether that information contributes something beyond direct assessment of symptoms, function, intake, goals, and overall clinical state.

Sources of biological and clinical confounding

Biomarkers are attractive in palliative care because they appear objective, reproducible, and biologically grounded. However, the same biological complexity that produces clinically important signals also creates uncertainty about interpretation.

Age represents one potential modifier because inflammatory regulation, body composition, immune activity, and metabolic responses change across the lifespan. Reviews of cachexia biomarkers have emphasized that candidate markers cannot necessarily be transferred unchanged across age groups because biological context affects both baseline values and relationships with clinical outcomes [10]. Similarly, oxidative-stress pathways are influenced by treatment, tumour biology, and cellular environment rather than operating as a uniform indicator of injury or recovery [30, 32].

Nutritional interpretation introduces additional complexity. Cancer malnutrition reviews have repeatedly emphasized that nutritional decline emerges from interacting biological and clinical mechanisms, including symptoms, treatment effects, metabolic alterations, and inflammatory processes [38]. The consequence is that biomarkers require interpretation alongside clinical information rather than replacement of that information.

Confounding is particularly important when biomarkers are measured around interventions. Serial observations can therefore be valuable while still requiring caution about attribution.

One example comes from patients receiving parenteral nutrition in a palliative-care setting. The observation that a biomarker changes during care does not establish that the intervention caused the change or that modifying the biomarker itself would improve outcome [48].

Temporal variability near end of life

The meaning of a biomarker is not fixed across the illness trajectory. A value measured during active anticancer treatment, during progressive disease, during symptom crisis, or in the final phase of life may represent different combinations of biological processes and clinical priorities.

Prognostic tools in palliative medicine illustrate this temporal dependence. A biomarker that contributes information about short-term mortality may therefore have limited relevance for decisions involving symptom management, nutritional support, or longer-term monitoring [27].

Inflammatory biomarkers measured near the end of life require similar caution. Prospective evidence demonstrates that inflammatory indices can contribute to prognostic assessment in terminal cancer patients [17], but their interpretation must remain connected to the clinical question. The clinical meaning depends on whether the purpose is estimating prognosis, explaining symptoms, evaluating a possible complication, or discussing goals of care.

Temporal interpretation also applies to nutritional and functional changes. Malnutrition, cachexia, and sarcopenia may evolve at different rates, and their trajectories are not always synchronized [42]. The absence of temporal alignment does not necessarily indicate that one measure is incorrect; it may indicate that different domains are changing at different speeds.

Therefore, the framework proposed here treats time as a core interpretive dimension. A biomarker value is a measurement taken within a biological trajectory, not an isolated representation of the entire illness state.

Patient-centered interpretation of laboratory information

Biochemical information becomes clinically meaningful only when connected with the experiences and priorities of the person receiving care. Laboratory information can contribute to these discussions, but it cannot replace patient-reported or clinically observed outcomes.

Cachexia research increasingly recognizes this distinction. Reviews of appetite and dietary-intake endpoints show substantial variation in measurement approaches and emphasize that appetite-related outcomes require careful interpretation rather than simple substitution with laboratory or body-composition measures [49]. Similarly, systematic review of quality-of-life endpoints demonstrates that patient experience represents a separate outcome domain with its own measurement challenges [50].

Longitudinal evidence further illustrates why symptom trajectories matter. Such findings do not imply that appetite measures replace biomarkers. Instead, they demonstrate that patient-centred information provides context that can alter the meaning of biological measurements [51].

For example, an inflammatory abnormality in a patient with stable symptoms, preserved function, and no change in care goals may have a different practical significance from the same abnormality in a patient experiencing rapid functional decline, severe symptom burden, and a need to reassess care priorities. The laboratory value is identical; the clinical meaning is not.

Role of nursing clinical assessment

Nursing assessment provides an essential contextual layer because nurses frequently observe symptom progression, functional change, intake patterns, treatment tolerance, and patient priorities across repeated

encounters. These observations contribute information that cannot be obtained from a single laboratory measurement.

Clinical nutrition guidance emphasizes regular assessment of nutritional status, symptoms, intake, and functional consequences as components of supportive care [37]. Similarly, palliative-care practice requires integration of physical findings, symptom burden, communication, and patient goals rather than isolated disease measurements [6].

Professional practice evidence also demonstrates that implementing multimodal cachexia care depends partly on clinician knowledge, confidence, and coordinated assessment practices. Scoping evidence on cancer-related anorexia further demonstrates that the biological processes underlying appetite loss span inflammatory, metabolic, and other pathways, reinforcing the need for integrated assessment rather than single-domain interpretation [52, 53].

Within this framework, nursing assessment is not positioned as a substitute laboratory method. Its function is complementary: it supplies longitudinal, patient-level information that helps determine whether a biochemical observation corresponds with a clinically meaningful change.

Proposed multidomain biomarker interpretation framework

The evidence reviewed above supports a contextual interpretation framework in which biomarkers are considered through interacting but distinct domains. Instead, it organizes interpretation around three sequential questions.

First, what biological process might the measurement represent? Inflammatory, oxidative-stress, nutritional, and metabolic biomarkers provide information about different aspects of illness biology. Their meanings depend on the mechanisms they capture and the limits of those mechanisms.

Second, what clinical context modifies that meaning? Disease stage, treatment exposure, nutritional phenotype, functional status, symptom burden, and temporal trajectory influence whether a biological signal reflects a clinically relevant transition or an expected consequence of advanced illness.

Third, does the observation alter a meaningful clinical decision? A biomarker may contribute to prognosis, support monitoring, prompt assessment of a possible complication, or provide reassurance that a suspected change is not occurring. These uses require different standards of evidence.

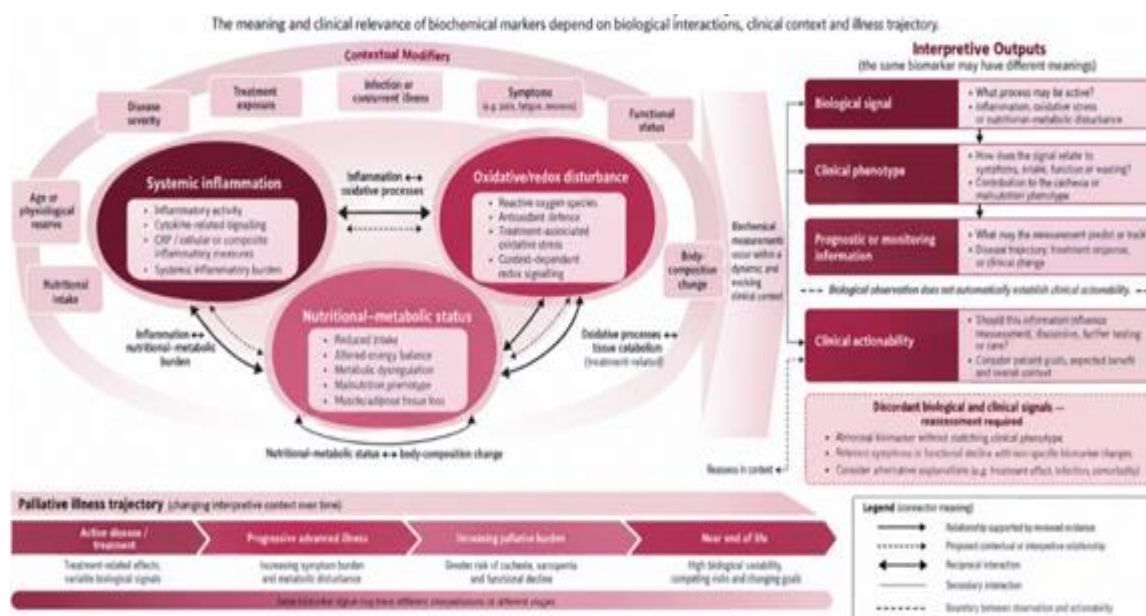


Figure 1. Context-Dependent Interpretation of Inflammatory, Oxidative-Stress, and Nutritional–Metabolic Signals Across the Palliative Illness Trajectory

The framework therefore treats interpretation as a process of contextual integration rather than numerical classification. Conversely, discordance between domains should trigger reassessment of assumptions rather than immediate interpretation as failure.

Interpretation zones and clinical cautions

A practical consequence of this framework is the distinction between different interpretive situations. Biomarkers may occupy a descriptive role, where they indicate that a biological process is present; a prognostic role, where they contribute to estimation of future outcome; a monitoring role, where repeated measurement may assist evaluation of change; or a cautionary role, where uncertainty limits confident interpretation.

These roles should not be converted into fixed thresholds. The available evidence does not support universal laboratory boundaries that automatically determine action across palliative populations. Instead, interpretation requires attention to the relationship between the measurement and the clinical question.

For example, an inflammatory marker may strengthen a prognostic assessment when combined with performance status and other variables [22]. The same marker may be less useful for monitoring response if the intervention does not have a demonstrated relationship with inflammatory change or patient benefit [46, 47]. Similarly, nutritional indicators may identify increased vulnerability while remaining insufficient to determine whether additional intervention will improve outcomes.

The importance of these distinctions is reinforced by evidence showing heterogeneity in cachexia endpoints, prognostic tools, appetite measures, and quality-of-life assessments [14, 27, 43, 49, 50]. A clinically responsible interpretation approach must therefore identify what is known, what remains uncertain, and what additional information is required.

Table 3. Clinical decision, application, and boundary-condition matrix anchored in the multidomain biomarker interpretation framework

Clinical interpretive situation	Biomarker contribution	Required contextual information	Principal caution
Biological characterization	Identifies a possible inflammatory, oxidative, nutritional, or metabolic process	Disease state, treatment exposure, clinical phenotype	Biological signal does not equal clinical diagnosis
Prognostic assessment	May contribute to estimation of future outcome	Validated population, prediction horizon, accompanying clinical variables	Prognostic association does not prove treatment responsiveness
Longitudinal monitoring	May indicate change when repeatedly measured appropriately	Timing, intervention, symptoms, function, competing events	Change does not automatically represent improvement or deterioration
Discordant clinical state	Highlights mismatch between laboratory and patient presentation	Bedside assessment, patient goals, additional evaluation	Discordance should not be resolved through assumption alone
Care decision support	Provides one component of shared interpretation	Expected benefit, treatment burden, patient priorities	Abnormality alone does not mandate intervention

Implications for interprofessional care

Laboratory specialists, physicians, nurses, pharmacists, dietitians, and other members of the care team may contribute different forms of evidence about biological change, symptoms, function, treatment effects, and patient priorities.

Clinical nutrition guidelines support integrated assessment and management rather than isolated nutritional intervention [37]. The growing literature on anorexia and cachexia biomarkers further demonstrates that clinically meaningful interpretation requires integration across biological pathways rather than reliance on one professional perspective or one measurement type [52, 53].

The framework does not assign ownership of biomarker interpretation to one discipline. A laboratory result gains practical meaning when connected with the person's symptoms, function, nutritional status, treatment context, and goals.

Research agenda

Future research should move beyond asking whether individual biomarkers correlate with poor outcomes.

Several research priorities follow from this framework. First, prospective studies should evaluate whether combining inflammatory, oxidative, nutritional, metabolic, functional, and patient-reported information improves clinically meaningful decision-making beyond existing prognostic approaches. Current cachexia-trial literature demonstrates substantial variation in endpoint selection, indicating a continuing need for validated multidimensional outcomes [14, 46].

Second, research should examine whether temporal biomarker trajectories provide information that differs from single measurements. Longitudinal symptom, appetite, body-composition, and laboratory assessments may clarify when biological change corresponds with clinically relevant transitions [49-51].

Third, validation should include patient-centred outcomes. Functional status, quality of life, symptom burden, and treatment burden are increasingly recognized as essential components of meaningful cachexia research [47, 50, 54]. A framework that improves biological prediction but does not improve interpretation of patient benefit would have limited clinical value.

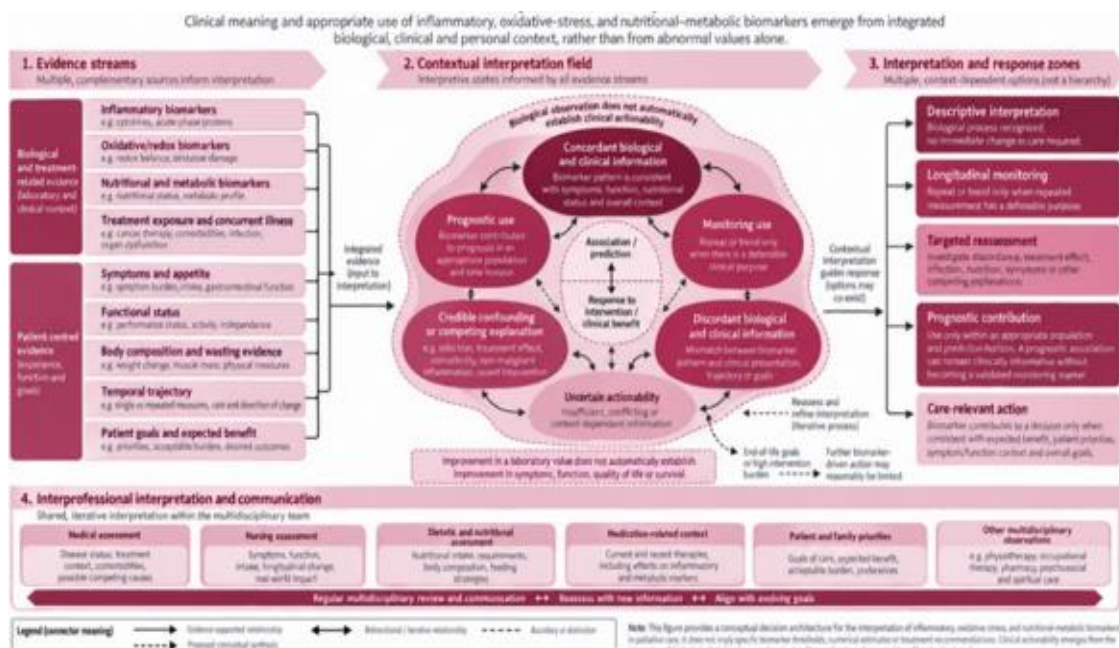


Figure 2. From Biomarker Signal to Clinically Actionable Interpretation: Decision Boundaries and Interprofessional Responses in Palliative Care

Table 4. Research proposition, evidence-priority, and discriminating-test matrix

Research priority	Current limitation	Proposed discriminating test	Meaningful outcome
Context-aware biomarker interpretation	Many biomarkers validated mainly through association studies	Compare isolated biomarkers with multidomain interpretation approaches	Improved clinical decision accuracy or usefulness
Temporal interpretation	Single measurements dominate many studies	Evaluate repeated trajectories linked with clinical transitions	Better distinction of meaningful change from biological variation
Patient-centred validation	Laboratory endpoints may not reflect lived benefit	Integrate function, symptoms, quality of life, and goals	Evidence of patient-relevant utility
Cross-domain integration	Inflammation, oxidative stress, and nutrition often studied separately	Test combined biological-context models prospectively	Clarification of whether domains provide complementary information
Transferability	Many studies are cancer-specific	Validate across broader palliative populations	Definition of appropriate scope and limitations

Results and Discussion

The central contribution of this article is a change in the level at which biomarkers are interpreted. However, these relationships become difficult to apply when a measured abnormality is treated as if it has one universal meaning. Biological mechanisms are separated from clinical decisions; prognostic value is separated from monitoring value; laboratory information is considered alongside patient-centred evidence; and temporal context is treated as a determinant of meaning rather than a secondary consideration.

This approach does not replace validated prognostic instruments or clinical guidelines. The contribution of the framework is different: it addresses situations where clinicians must decide how much meaning to assign to a biomarker result when several biological and clinical explanations remain possible [17 22, 27].

The strongest challenge to this approach is that sufficiently validated prognostic models may already answer many practical questions. If the only purpose is mortality prediction within a defined population and timeframe, additional interpretive complexity may provide limited benefit.

Conceptual limitations

Several limitations require emphasis. First, much of the evidence base is derived from oncology populations, particularly advanced cancer and cancer cachexia. Application to non-cancer palliative populations requires additional validation. Second, the literature includes substantial heterogeneity in biomarker selection, nutritional definitions, prognostic tools, body-composition measures, and patient-reported outcomes. This heterogeneity limits direct comparison and prevents construction of a universal interpretation algorithm.

Third, several mechanistic insights, particularly within oxidative-stress biology, arise from experimental models rather than direct palliative-care cohorts. These findings are valuable for understanding possible pathways but cannot be treated as validated clinical decision rules.

Finally, the framework itself remains a conceptual synthesis. Its value depends on prospective testing. Future studies must determine whether integrating biological signals with clinical context improves decisions, outcomes, or patient-centred care compared with current approaches.

Conclusion

Biochemical markers in palliative care provide important information, but their meaning depends on the biological process they reflect, the clinical context in which they are measured, their timing within the illness trajectory, and their relevance to patient goals. Inflammatory, oxidative-stress, nutritional, and metabolic biomarkers should therefore be interpreted as context-dependent signals rather than isolated representations of disease state.

A clinically useful approach requires integration of laboratory findings with symptoms, function, nutritional phenotype, treatment context, professional assessment, and patient priorities. The strongest application of biomarkers in palliative care is not the search for a single definitive indicator, but the careful interpretation of multiple forms of evidence to support decisions that remain biologically informed and patient centred.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

References

1. Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. *Nat Rev Dis Primers*. 2018;4:17105. doi:10.1038/nrdp.2017.105
2. Bianchini C, Bonomo P, Bossi P, Caccialanza R, Fabi A. Bridging gaps in cancer cachexia care: current insights and future perspectives. *Cancer Treat Rev*. 2024;125:102717. doi:10.1016/j.ctrv.2024.102717
3. Alzahrani MSH. The positive effect of *Artemisia judaica* on immunological and histopathological changes in hepatic rats. *J Biochem Technol*. 2023;14(3):18-22. doi:10.51847/BLLjjAqxzc
4. Roeland EJ, Bohlke K, Baracos VE, Bruera E, Del Fabbro E, Dixon S, et al. Management of cancer cachexia: ASCO guideline. *J Clin Oncol*. 2020;38(21):2438-53. doi:10.1200/JCO.20.00611
5. Arends J, Strasser F, Gonella S, Solheim TS, Madeddu C, Ravasco P, et al. Cancer cachexia in adult patients: ESMO clinical practice guidelines. *ESMO Open*. 2021;6(3):100092. doi:10.1016/j.esmoop.2021.100092
6. Crawford GB, Dzierzanowski T, Hauser K, Larkin P, Luque-Blanco AI, Murphy I, et al. Care of the adult cancer patient at the end of life: ESMO clinical practice guidelines. *ESMO Open*. 2021;6(4):100225. doi:10.1016/j.esmoop.2021.100225
7. Al-Zahrani MH. Colorectal cancer biomarkers discovery approach: a proteomic and genomic perspective. *J Biochem Technol*. 2023;14(3):6-12. doi:10.51847/gVy1I4x9BU
8. Oghenemaro EF, Sochi EO, Oghenovo OF, Michael O. The evaluation of the in-vitro antibacterial and anti-inflammatory potentials of the tender water of *Cocos nucifera* (L.). *World J Environ Biosci*. 2023;12(4):8-13. doi:10.51847/JqUXHGZ6r0
9. Berriel Diaz M, Rohm M, Herzig S. Cancer cachexia: multilevel metabolic dysfunction. *Nat Metab*. 2024;6(12):2222-45. doi:10.1038/s42255-024-01167-9
10. Geppert J, Rohm M. Cancer cachexia: biomarkers and the influence of age. *Mol Oncol*. 2024;18(9):2070-86. doi:10.1002/1878-0261.13590
11. Bianchi MR, Matsumoto Y, Bondar AS. Bidirectional feedback loops linking orthodontic forces to periodontal tissue breakdown. *Asian J Periodontics Orthod*. 2025;5(1):205-13. doi:10.51847/RsKWIKi1RF
12. McGovern J, Dolan RD, Skipworth RJ, Laird BJ, McMillan DC. Cancer cachexia: a nutritional or a systemic inflammatory syndrome? *Br J Cancer*. 2022;127(3):379-82. doi:10.1038/s41416-022-01826-2
13. Seah ACW, Shi S, Xie H, Leung YY, Hu M, An R. Investigating IL-17A's contribution to periodontitis and oral dysbiosis in relation to systemic inflammatory pathways. *Asian J Periodontics Orthod*. 2024;4(1):75-87. doi:10.51847/EAVF5WcGwG
14. Yule MS, Thompson J, Leesahatsawat K, Sousa MS, Anker SD, Arends J, et al. Biomarker endpoints in cancer cachexia clinical trials: systematic review 5 of the cachexia endpoint series. *J Cachexia Sarcopenia Muscle*. 2024;15(3):853-67. doi:10.1002/jcsm.13491

15. Chang SJ, Lee E, Hong G. Exploring the reciprocal link between periodontitis and diabetes through chronic inflammation and glucose regulation. *Asian J Periodontics Orthod.* 2025;5(1):150-63. doi:10.51847/ravyVmxgoR
16. Martin L, Muscaritoli M, Bourdel-Marchasson I, Kubrak C, Laird B, Gagnon B, et al. Diagnostic criteria for cancer cachexia: reduced food intake and inflammation predict weight loss and survival in an international, multi-cohort analysis. *J Cachexia Sarcopenia Muscle.* 2021;12(5):1189-202. doi:10.1002/jcsm.12756
17. da Costa Cunha G, da Costa Rosa KS, Wiegert EVM, de Oliveira LC. Clinical relevance and prognostic value of inflammatory biomarkers: a prospective study in terminal cancer patients receiving palliative care. *J Pain Symptom Manage.* 2021;62(5):978-86. doi:10.1016/j.jpainsymman.2021.04.009
18. Ajiboye BO, Famusiwa CD, Ojelabi AO, Akinola WO, Adeyemi ET, Adejumo AA, et al. Hibiscus sabdariffa leaf extract activates molecular gene expressions of insulin and GLP-I receptor in streptozotocin-induced rats. *Pharmacophore.* 2024;15(5):15-26. doi:10.51847/xSFzqq25OY
19. Clamon G, Byrne MM, Talbert EE. Inflammation as a therapeutic target in cancer cachexia. *Cancers (Basel).* 2022;14(21):5262. doi:10.3390/cancers14215262
20. Hewawitharanage H, Letchuman S. Phytoconstituents docking: exploring anti-inflammatory targets in *Munronia pinnata* and *Andrographis paniculata*. *Pharmacophore.* 2024;15(1):48-56. doi:10.51847/bfXk1DpQRG
21. Soomro S, Sangi S, Nayeem N. Anti-oxidative burst, cytotoxicity, and ADME studies of thiourea compounds. *Pharmacophore.* 2023;14(2):97-105. doi:10.51847/9IrxHHoY81
22. Rocha BMM, Dolan RD, Paiva CE, McGovern J, Paiva BSR, Preto DD, et al. Inflammation and performance status: the cornerstones of prognosis in advanced cancer. *J Pain Symptom Manage.* 2023;65(4):348-57. doi:10.1016/j.jpainsymman.2022.11.021
23. Lipshitz M, Visser J, Anderson R, Nel DG, Smit T, Steel HC, et al. Relationships of emerging biomarkers of cancer cachexia with quality of life, appetite, and cachexia. *Support Care Cancer.* 2024;32(6):349. doi:10.1007/s00520-024-08549-5
24. Omokunle AB. Environmental evaluation of a tropical river based on aquatic insect communities and water quality indicators. *Entomol Lett.* 2024;4(1):8-16. doi:10.51847/joBLkOjCre
25. Huo Z, Chong F, Li N, Luo S, Yin L, Liu J, et al. Diagnostic criteria for cancer-associated cachexia: insights from a multicentre cohort study. *J Cachexia Sarcopenia Muscle.* 2025;16(1):e13703. doi:10.1002/jcsm.13703
26. Wright E, Bennett C, Turner J, Harris O. Systemic depletion and collective burnout in always-on organizations. *J Appl Organ Syst Behav.* 2024;4(2):112-20. doi:10.51847/RovzZKO6l1
27. Yuasa N, Kawai N, Takamizawa J. Comparison of prognostic abilities of Palliative Prognostic Index, Laboratory Prognostic Score, and Palliative Prognostic Score. *J Pain Symptom Manage.* 2024;68(2):153-62.e2. doi:10.1016/j.jpainsymman.2024.04.022
28. Hernandez M, Vega C. Unveiling the anti-inflammatory effects of azithromycin: mechanisms, immune cell interactions, and clinical potential. *J Appl Pharm Technol Syst.* 2023;2:65. doi:10.68159/j331606012
29. Al-Kharabsheh M, Atrooz O, Naik RR. Characterization of *Mirabilis jalapa* seed extract and its effect on human erythrocytes in vitro. *World J Environ Biosci.* 2025;14(3):24-31. doi:10.51847/SXo7IEc7XL
30. Jiang H, Zuo J, Li B, Chen R, Luo K, Xiang X, et al. Drug-induced oxidative stress in cancer treatments: angel or devil? *Redox Biol.* 2023;63:102754. doi:10.1016/j.redox.2023.102754
31. Pereira L, Martins B. Impact of dimethyl sulfoxide on hippocampal function in a rat model of Parkinson's disease induced by rotenone. *J Appl Pharm Technol Syst.* 2025;4:118. doi:10.68159/c100518093
32. Wu K, El Zowalaty AE, Sayin VI, Papagiannakopoulos T. The pleiotropic functions of reactive oxygen species in cancer. *Nat Cancer.* 2024;5(3):384-99. doi:10.1038/s43018-024-00738-9
33. Benali A, Boudiaf K, Touati S. Digital firms as learning systems: continuous organizational knowledge development through data interaction and market feedback. *J Digit Bus Manag Stud.* 2023;3:26. doi:10.68159/u140122078
34. Yamada M, Warabi E, Oishi H, Lira VA, Okutsu M. Muscle-derived IL-1 β regulates EcSOD expression via the NBR1-p62-Nrf2 pathway in muscle during cancer cachexia. *J Physiol.* 2024;602(17):4215-35. doi:10.1113/JP286460
35. Chen W, Zhang L. A conceptual framework for trustworthy AI decisions across the materials design lifecycle. *J Artif Intell Mater Sci.* 2024;3:44. doi:10.68159/p426656712
36. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition—a consensus report from the global clinical nutrition community. *Clin Nutr.* 2019;38(1):1-9. doi:10.1016/j.clnu.2018.08.002
37. Muscaritoli M, Arends J, Bachmann P, Baracos V, Barthelmy N, Bertz H, et al. ESPEN practical guideline: clinical nutrition in cancer. *Clin Nutr.* 2021;40(5):2898-913. doi:10.1016/j.clnu.2021.02.005
38. Bozzetti F. The role of the nutrition in malnourished cancer patients: revisiting an old dilemma. *Clin Nutr.* 2024;43(6):1320-8. doi:10.1016/j.clnu.2024.03.018

39. McLuskie A, Bowers M, Bayly J, Yule MS, Maddocks M, Fallon M, et al. Nutritional interventions in randomised clinical trials for people with incurable solid cancer: a systematic review. *Clin Nutr.* 2025;44:201-19. doi:10.1016/j.clnu.2024.12.008
40. Compton SLE, Heymsfield SB, Brown JC. Nutritional mechanisms of cancer cachexia. *Annu Rev Nutr.* 2024;44(1):77-98. doi:10.1146/annurev-nutr-062122-015646
41. Renard J, Durand JP, De Percin S, Arrondeau J, Noel J, Thomas-Schoemann A, et al. Early nutritional and inflammation assessment predicts prognosis in patients with cancer across tumor origin and metastatic status. *Clin Nutr.* 2025;52:313-22. doi:10.1016/j.clnu.2025.07.029
42. Rasschaert M, Vandecandelaere P, Marechal S, D'hondt R, Vulsteke C, Mailleux M, et al. Malnutrition prevalence in cancer patients in Belgium: the ONCOCARE study. *Support Care Cancer.* 2024;32(2):135. doi:10.1007/s00520-024-08324-6
43. Brown LR, Sousa MS, Yule MS, Baracos VE, McMillan DC, Arends J, et al. Body weight and composition endpoints in cancer cachexia clinical trials: systematic review 4 of the cachexia endpoints series. *J Cachexia Sarcopenia Muscle.* 2024;15(3):816-52. doi:10.1002/jcsm.13478
44. Zhang Y, Zhang J, Zhan Y, Pan Z, Liu Q, Yuan W. Sarcopenia is a prognostic factor of adverse effects and mortality in patients with tumour: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle.* 2024;15(6):2295-310. doi:10.1002/jcsm.13629
45. Davis MP, Bader N, Basting J, Vanenkevort E, Koppenhaver N, Patel A, et al. Are muscle and fat loss predictive of clinical events in pancreatic cancer? The importance of precision metrics. *J Pain Symptom Manage.* 2025;69(2):141-51. doi:10.1016/j.jpainsymman.2024.10.004
46. Dajani O, Philips I, Størkson EK, Balstad TR, Brown LR, Bye A, et al. Oncological and survival endpoints in cancer cachexia clinical trials: systematic review 6 of the cachexia endpoints series. *J Cachexia Sarcopenia Muscle.* 2025;16(2):e13756. doi:10.1002/jcsm.13756
47. Fioretti F, von Haehling S, Coats AJS, Butler J, Del Fabbro E, Skipworth RJE, et al. Cachexia and wasting in chronic illness: regulatory and clinical trial update. *J Cachexia Sarcopenia Muscle.* 2025;16(6):e70128. doi:10.1002/jcsm.70128
48. Kieler M, Kössler P, Milovic M, Meyer E, Křižanová K, Kum L, et al. C-reactive protein and white blood cell count are adverse prognostic markers for patients with advanced cancer on parenteral nutrition in a palliative care unit setting: a retrospective cohort study. *Palliat Med.* 2022;36(3):540-8. doi:10.1177/02692163211073939
49. Vagnildhaug OM, Balstad TR, Ottestad I, Bye A, Greil C, Arends J, et al. Appetite and dietary intake endpoints in cancer cachexia clinical trials: systematic review 2 of the cachexia endpoints series. *J Cachexia Sarcopenia Muscle.* 2024;15(2):513-35. doi:10.1002/jcsm.13434
50. Hjemstad MJ, Jakobsen G, Arends J, Balstad TR, Brown LR, Bye A, et al. Quality of life endpoints in cancer cachexia clinical trials: systematic review 3 of the cachexia endpoints series. *J Cachexia Sarcopenia Muscle.* 2024;15(3):794-815. doi:10.1002/jcsm.13453
51. Zhou J, Muluneh B, Li Q, Wagner LI, Wang Y, Hughes JH. From symptom to outcome: defining clinically meaningful patient-reported appetite loss in non-small-cell lung cancer. *J Cachexia Sarcopenia Muscle.* 2025;16(6):e70150. doi:10.1002/jcsm.70150
52. Amano K, Koshimoto S, Arakawa S, Oyamada S, Ishiki H, Morita T, et al. Factors associated with multimodal care practices for cancer cachexia among registered dietitians. *Support Care Cancer.* 2024;32(4):213. doi:10.1007/s00520-024-08417-2
53. Sun X, Chen Y, Zhang Z, Tang C, Hu X, Wu L, et al. Biomarkers associated with cancer-related anorexia in lung cancer: a scoping review. *Support Care Cancer.* 2025;33(7):596. doi:10.1007/s00520-025-09670-9
54. Crawford J, Fallon M, Fang J, Groarke JD, Smoyer K, Naito T, et al. Functional outcomes and quality of life for patients with cachexia and solid tumour cancers: findings of a systematic literature review. *J Cachexia Sarcopenia Muscle.* 2026;17(4):e70319. doi:10.1002/jcsm.70319