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High specificity clinical signs of impending death: A scoping review

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ABSTRACT

Background: Accurate diagnosis of impending death is essential to provide proper care in the last days and hours of life. Recognising the death situation immediately allows adjustment of care goals, ensuring that they suit the patient's condition, as well as tuning the team's and family's expectations.
Objective: To map and describe evidence on high specificity clinical signs of impending death in cancer and noncancer hospitalised patients over 18 years of age.
Methods: A comprehensive search of the published literature was conducted According to Joanna Briggs Institute's methodology for scoping reviews. Online databases, including MEDLINE, CINAHL complete, SCOPUS, WEB OF SCIENCE, and the Cochrane Database of Systematic Reviews, and the search for unpublished studies included OpenGrey, DART-Europe, and RCAAP. Publications in English, French, Portuguese, and Spanish were included, and no period was set. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis extensions to scoping review guidelines were used to report the results. The review protocol was registered in Open Science Framework (Simões et al., 2022).
Results: The 15 studies included in this review were published in English between 2013 and 2023. In addition to identifying the clinical signs of impending death, some researchers intend to develop accurate prognostic models for this clinical situation. Only two studies in the noncancer population met the inclusion criteria. Twelve articles were prospective observational studies (seven were multicentre studies), one was a retrospective cohort study, and two were narrative reviews. A clinical sign that is common to studies in both populations is respiration with mandibular movement, particularly in the last 12 h of life.
Conclusions: Clinical signs of impending death and prediction models can help clinicians identify impending death. However, they should not replace clinical judgement. Further research is required to understand whether the dying process differs among different patient populations and care settings.

What is already known

- The diagnosis of impending death is key to understanding and clarifying care goals for patients in their final hours and days of life.
- Identifying evidence of high specificity clinical signs of impending death may improve clinical practice.
- Despite the importance of this topic, scoping reviews addressing this purpose are yet to be published, highlighting the urgent need for further research in this area.

What this paper adds

- This review, which maps and describes the clinical signs of impending death in both cancer and noncancer patients, has the potential to significantly improve patient care.
- In cancer patients, the clinical signs identified have a remarkably high specificity for impending death, with a rate above 95 % within 72 h.
- It is crucial to note that there are currently no evidence-based data regarding the specific elements of diagnosing dying situations in noncancer patients, highlighting the urgent need for further research in this area.

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1. Background

An accurate diagnosis of impending death is essential for providing appropriate end-of-life care. Recognising the signs of impending death is crucial for tailoring treatment goals and managing the expectations of patients' families and care teams.

Caring for individuals approaching the end of their life is a crucial skill for all healthcare professionals, especially physicians and nurses. Recognising the signs of impending death is essential for making critical decisions such as discharging patients from hospitals, discontinuing futile interventions, and prioritising immediate patient comfort (Hosoi et al., 2021; Ikari et al., 2021a; Mori et al., 2021; Hui et al., 2015a, 2015b). As patients approach the end of their lives, critical decisions must be made to ensure that they receive the most appropriate care according to their situation. At the same time, it is essential to provide the best possible support to family members who are likely to experience difficult times (Chi et al., 2016).

Sensitivity and specificity are standard terms for evaluating the accuracy of clinical tests. However, a clinician's judgement regarding the value of the test, as indicated by its positive and negative predictive values, is more crucial. This emphasises the audience's responsibility and engagement in the test evaluation process (Trevethan, 2017). The use of highly specific clinical signs is crucial to ensure accurate diagnosis, particularly when dealing with low false-positive clinical clues. However, our current knowledge does not provide a clear understanding of these signs for the differential diagnosis of impending death, especially in noncancer patients. This lack of clarity underscores the importance of our research in this field.

The *More Care, Less Pathway Report* highlights that the accurate prediction of impending death, for instance, in noncancer patients, is challenging due to the lack of specific clinical signs and variability in disease progression. The review panel recommends the promotion of evidence-based prognostic tools and evidence-based education and training (Independent Review of the Liverpool Care Pathway, 2013).

This scoping review aimed to map and describe the high specificity clinical signs of impending death in hospitalised patients aged >18 years. The research questions were as follows: (1) What are the high specificity clinical signs of impending death? and (2) Are there differences in the clinical signs of impending death between cancer and noncancer patients?

2. Methods

This scoping review was conducted in accordance with the JBI methodology (Peters et al., 2024), described in a previous study (Simões et al., 2022). A preliminary search of CINHAL (EBSCOhost), MEDLINE (PubMed), the Cochrane Database of Systematic Reviews, and *JBI Evidence Synthesis* conducted in March 2022 identified no current or in-progress systematic or scoping reviews.

2.1. Selecting the literature (i.e. inclusion-exclusion criteria)

The articles included in this scoping review met the specified inclusion criteria and were carefully chosen to ensure the relevance of the included studies. Participants were all hospitalised adults over 18 years old; the situation of impending death was defined as the period of the last 72 h of life, high specificity clinical signs of impending death were related to a specificity of at least 95 %. The studies included in this scoping review were not limited to one particular country or healthcare system. However, owing to our limited financial resources, restricted access to international databases, and the low quality of automatic translation, we focused on papers written in English, French, Portuguese, and Spanish.

A broad range of quantitative and qualitative research designs was considered for inclusion. This review considered literature reviews and descriptive observational study designs, including prospective and retrospective cohort, case–control, and cross-sectional studies. Grey literature such as dissertations, conference proceedings, and reports were considered for inclusion but none that were eligible were found.

2.2. Search process

The search for primary studies and reviews used a comprehensive 3-step strategy. Following JBI guidelines, an initial preliminary search was conducted in MEDLINE (PubMed) and CINAHL (EBSCO) for clinical signs of impending death in hospitalised patients over 18. The retrieved studies were analysed based on their titles, abstracts, and index terms, which informed the development of a customised search strategy for each database. Two authors determined the key terms and reviewed them by a third author and a librarian. The complete search strategy for MEDLINE is provided in the Supplementary Material. Additionally, the reference lists of all the included studies were screened for supplementary evidence.

The search was conducted without a specific end date and concluded on 12 September 2023. The databases searched included MEDLINE (PubMed), CINAHL Complete (EBSCO), SCOPUS, WEB OF SCIENCE, and Cochrane Database of Systematic Reviews. Unpublished studies were searched using OpenGrey, DART-Europe, and RCAAP. Following the search, all identified records were collated and uploaded to Endnote X9 3.3 (Clarivate Analytics, US), and duplicates were removed. After conducting a pilot test, two reviewers (CS and ACT) independently screened the titles and abstracts of the studies against the inclusion criteria for the review. If there was ambiguity, they included studies in the next phase. Two independent reviewers assessed the full text of the selected citations in detail against the inclusion criteria. Finally, the references of all included studies were manually searched. No disagreements were found between the reviewers during the selection process. Patients were excluded following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (Page et al., 2021). Finally, the PRISMA extension for Scoping Reviews checklist (PRISMA-ScR) (Tricco et al., 2018) was used to ensure that all pertinent elements of the scoping review methods were reported (Fig. 1).

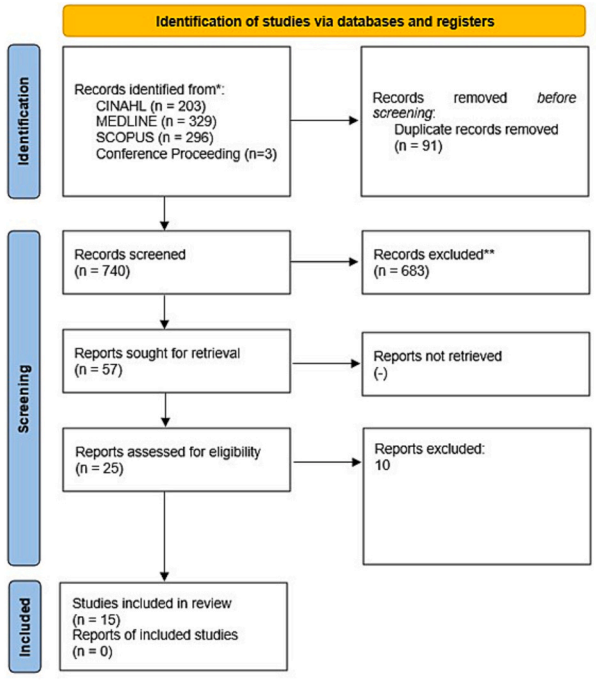

Fig. 1. PRISMA flow diagram.

The authors compared the results of each article until they identified preliminary themes and discussed them as the data extraction and thematic synthesis progressed. Two authors used a data extraction tool to extract data from the papers in the scoping review. The extracted data included specific details about the population, concept, context, methods, and critical findings relevant to the review questions (Tables 1, 2, and 3). This enabled a logical and descriptive summary of the results, aligned with the objective of the review and facilitated the identification of gaps in the literature (Lockwood et al., 2015; Vaismoradi et al., 2013).

3. Results

We found 831 articles. Ninety-one duplicates were removed and 683 articles were excluded after screening the titles and abstracts. A total of 25 full-text articles were assessed and screened, and 15 were included in this scoping review.

3.1. Included papers

The 15 studies (Table 1) included in this review were published between 2013 and 2023. Five studies were performed in Japan (Hosoi et al., 2021; Ikari et al., 2021a, 2021b; Mori et al., 2021; Matsunami et al., 2018), one in the United States (Hui et al., 2019), one in South Korea (Hwang et al., 2013), four in the United States and Brazil (multicentre studies) (Hui et al., 2015a, 2015b, 2014; Bruera et al., 2014), one in the United Kingdom (White et al., 2019), one in Switzerland (Christ et al., 2022), and two narrative reviews were included (Ijaopo et al., 2023; Mori et al., 2022). Twelve articles were prospective observational studies (seven were multicentre studies) (Hui et al., 2015a, 2015b; Hwang et al., 2013; Bruera et al., 2014), and one was a retrospective cohort study (Christ et al., 2022). Twelve studies were conducted in palliative care units or teams (Hosoi et al., 2021; Ikari et al., 2021a, 2021b; Mori et al., 2021; Hui et al., 2015a, 2015b, 2014; Matsunami et al., 2018; Hwang et al., 2013; Bruera et al., 2014; Christ et al., 2022). Three studies included cancer and noncancer patients (Matsunami et al., 2018; White et al., 2019; Christ et al., 2022), and one was specifically in a respiratory medicine ward (Matsunami et al., 2018). The sample sizes of the studies ranged from 50 to 1411 participants. Most studies only included patients with cancer, and only one study attempted to identify clinical signs of impending death in noncancer patients (Tables 2 and 3).

3.2. High specificity clinical signs of impending death in noncancer patients

Researchers have developed a prediction model for imminent death in noncancer patients based on clinical signs, such as pulselessness of the radial artery, respiration with mandibular movement, and a shock index

Table 1
Summary of included papers.

Authors (year)	Local	Study type	Aim and objectives	Population (n)	Context
Hwang et al. (2013)	South Korea	Prospective observational study	To determine what events herald the onset of the dying process using the length of time from "any change" to death	Cancer patients (n = 181)	Palliative care unit
Hui et al. (2014)	Brazil and USA	Prospective observational study	To determine the frequency and onset of 10 clinical signs associated with impending death	Cancer patients (n = 203)	Palliative care unit
Bruera et al. (2014)	Brazil and USA	Prospective, longitudinal, observational study	To determine the variation in vital signs in the final two weeks of life among cancer patients To determine the association between the changes in vital signs and impending death	Cancer patients (n = 203)	Palliative care unit
Hui et al. (2015a)	Brazil and USA	Prospective observational study	To examine the frequency and onset of an additional 52 bedside physical signs and their diagnostic performance for impending death	Cancer patients (n = 357)	Palliative care unit
Hui et al. (2015b)	Brazil and USA	Prospective observational study	To develop and assess a diagnostic model for impending death based on bedside physical signs.	Cancer patients (n = 357)	Palliative care unit
Hui et al. (2019)	USA	Prospective observational study	To determine the association between phase angle and survival	Cancer patients (n = 204)	Palliative care unit
Matsunami et al. (2018)	Japan	Prospective longitudinal observational study	To determine the onset time of changes in both physical signs and clinical findings in the final days and hours of life in elderly patients who were admitted to the Respiratory Ward with a prognosis of impending death To investigate whether the changes in the profile and timing of both HR and SpO_2 in the last hours and minutes of life can indicate the cause of impending death	Cancer and non-cancer patients (n = 70)	Respiratory Ward
White et al. (2019)	United Kingdom	Prospective observational study	To document the clinical condition of patients considered to be in the last 2 weeks of life To compare patients who did or did not survive for 72 h	Cancer and non-cancer patients (n = 50)	
Hosoi et al. (2021)	Japan	Prospective longitudinal observational study	To investigate the prevalence and onset of SID and to develop models that predict death within seven days, 72 h, and 24 h in noncancer patients.	Non-cancer patients (n = 50)	Hospital setting
Ikari et al. (2021a, 2021b)	Japan	Multicenter prospective observational study	To clarify the efficacy of the "3-Day Surprise Question" in predicting the prognosis for advanced cancer patients with impending death	Cancer patients (n = 1411)	Palliative care unit
Ikari et al. (2021a, 2021b)	Japan	Multicenter prospective observational study	To examine the usefulness of the 1-Day Surprise Question	Cancer patients (n = 1411)	Palliative care unit
Mori et al. (2021)	Japan	Multicenter prospective cohort study	To develop diagnostic models to predict death $\leq$3 Days in cancer patients.	Cancer patients (n = 1396)	Inpatient hospices
Mori et al. (2022)	NA	Narrative Review	To summarise the current evidence on prognostication and communication regarding the last days of life of patients with cancer	Cancer patients	NA
Christ et al. (2022)	Switzerland	Retrospective single-center observational case-control study	To quantify the prevalence of patient transfer 72 h before death onto the acute palliative care unit and to identify factors predictive of 72-h mortality.	Cancer and non-cancer patients (n = 188)	Acute palliative care unit
Ijaopo et al. (2023)	NA	Narrative Review	To evaluate the clinical signs and symptoms that show end-of-life is imminent in individuals with advanced illness.	Individuals With Advanced Illness	NA

Table 2
Prevalence of clinical signs of ID.

	Hwang et al. (2013)[a]	Hui et al. (2014)[a]	Hui et al. (2015b)[a]	Bruera et al. (2014)[a]	Hui et al. (2015a)[a]	Matsunami et al. (2018)[a]	Hui et al. (2019)[a]	White et al. (2019) [a] & [b]	Hosoi et al. (2021)[b]	Ikari et, al. (2021a)[a]	Ikari et al. (2021b)[a]
Sample	n = 181	n = 357		n = 357	n = 357	n = 70	n = 204	n = 24[c]	n = 50	n = 1411	n = 847
Death within	48 h	72 h		72 h	72 h	12 h	72 h	72 h	72 h	72 h	24 h
Increased heart rate	76.2 %			52 %	92 %					82.6 %	
Pulselessness of radial artery		38 %						8 %	40 %		53.9 %
Decreased blood pressure	90.1 %			20 %[d]/ 10 %[e]	82 %[f]/62 %[e]						
Capillary refill >3 s					87 %						
Peripheral edema	7.2 %				94 %						28 %
Dysphagia of liquids		90 %									46.9 %
Loss of oral intake/ poor appetite					95 %			25 %			
Decreased urine output	40.3 %	72 %[d]						71 %			42.7 %[g]
Apnea periods		46 %									26.8 %
Cheyne-Stokes breathing		41 %						17 %	16 %		34 %
Death rattle	45.9 %	66 %						54 %	30 %		
Peripheral cyanosis		59 %						21 %	32 %	69.2 %	39.3 %
Low oxygen saturation (<90 %)	73.5 %			45 %	90 %					57.8 %	22.4 %
Respiration with mandibular movement		56 %				78 %		8 %	44 %	94 %	66 %
High respiratory rate (<20 CPM)				16 %	72 %					71 %	
Decreased conscious level					97 %						
Decreased response to verbal stimuli					69 %				76 %	70.5 %	37.1 %
Decreased response to visual stimuli					70 %				74 %	68 %	36.1 %
Non-reactive pupils					38 %						
Inability to close eyelids					57 %				22 %		37.7 %
RASS ≤−2		90 %									
Temperature <36 °C				15 %	60 %						
Fever	61.9 %			2 %							
Drooping of nasolabial fold					78 %				24 %		
Hyperextension of neck					46 %				28 %		42.2 %
Grunting of vocal cords					54 %						43.9 %
PPS ≤20 %		93 %									

[a] Cancer patients.
[b] Non-cancer patients.
[c] n reported to patients died in <72 h (n total = 50).
[d] Urine output <100 mL/12 h.
[e] Diastolic blood pressure.
[f] Systolic blood pressure.
[g] Urine output <200 mL/12 h.

greater than one.

Studies have investigated the occurrence and timing of signs indicating impending death in noncancer patients. They analysed data from 50 noncancer patients and developed prediction models for death within seven days, three days, and 24 h. The model that included 'pulselessness of the radial artery OR respiration with mandibular movement OR shock Index greater than one' demonstrated an impressive accuracy, predicting death within seven days in 83.9 % of cases. However, the accuracy of the models for predicting death within 72 and 24 h was 65.0 % or less. The median onset of all signs was within three days of death (Hosoi et al., 2021). However, this study did not specify the clinical signs used in the model.

In the Respiratory Ward, researchers conducted a study on both cancer and noncancer patients to document the physical assessments and timing of ECG and SpO2 changes before death. They found that patients displaying respiration with mandibular movement died on the same day in 78 % of cases, with an average of 12 h (range: 1–56 h) observed before death (Matsunami et al., 2018).

3.3. High specificity clinical signs of impending death in cancer patients

Seventeen clinical signs indicate impending death, including confusion, decreased blood pressure, increased pulse pressure, low oxygen saturation, death rattle (sounds due to an accumulation of secretions in the pharynx and/or airways when the patient cannot swallow or cough) (Hwang et al., 2013), and reduced consciousness level in one of the

Table 3
High specificity clinical signs of Impending Death.

	Hui et al. (2014)	Bruera et al. (2014)	Hui et al. (2015a)	Hui et al. (2015b)	Hui et al. (2019)	Ikari et al. (2021a)	Ikari et al. (2021b)	Mori et al. (2021)
Death within	72 h	72 h	72 h					
Increased heart rate		80 %	65 %					
Pulselessness of the radial artery	99.3 %							
Decreased blood pressure		90 %[a]/88 %[b]	88.2 %[a]/94.9 %[b]					
Dysphagia of liquids	78.8 %							
Upper gastrointestinal bleed			99.7 %					
Decreased urine output	98.2 %[c]							
Apnea periods	95.3 %							
Respiratory rate decrease		96 %						
Cheyne-Stokes breathing	98.5 %							
Death rattle	97.1 %							
Peripheral cyanosis	94.9 %							
Low oxygen saturation		95 %	86 %					
Respiration with mandibular movement	97.5 %							
Decreased level of consciousness			66.1 %					
Decreased response to verbal stimuli			96 %					
Decreased response to visual stimuli			94.9&					
Non-reactive pupils			99 %					
Inability to close eyelids			97.9 %					
RASS -2	89.3 %							
Temperature increase		83 %						
Temperature decrease			85.2 %					
Drooping of the nasolabial fold			95.5 %					
Hyperextension of neck			96.7 %					
Grunting of vocal cords			97.9 %					
Phase angle $<3^{o}$					90 %			
PPS $\leq$20 %	81.3 %							
3-Day Surprise Question						26.3 %		
1-Day Surprise Question							45.5 %	
P3did $\geq$1								37.6 %
$\geq$2								72.6 %
$\geq$3								91 %
4								98.2 %

Legend:
[a] Systolic blood pressure.
[b] Diastolic blood pressure.
[c] Urine output $<$100 mL/12 h.

studies (Hwang et al., 2013). Decreased blood pressure and low oxygen saturation were the most predictable events for death within 48 h, with a positive predictive value of 95.0 % and a negative predictive value of 81.4 %. Impending death within three days was significantly associated with increased heart rate, decreased systolic and diastolic blood pressure, and reduced oxygen saturation (Bruera et al., 2014). However, these changes have limited predictive value and many patients have unchanged vital signs during the last few days of life (Bruera et al., 2014).

Hui et al. (2014) identified clinical signs of impending death such as pulselessness of the radial artery, respiration with mandibular movement, decreased urine output, Cheyne-Stokes breathing, and death rattle. Further research found additional indicators, including non-reactive pupils, decreased response to stimuli, inability to close eyelids, drooping of the nasolabial fold, hyperextension of the neck, vocal cord grunting, and upper gastrointestinal bleeding (Hui et al., 2015b, 2014).

In a comparison between patients who survived longer than 72 h and those who did not, researchers observed various changes in breathing, circulatory patterns, physical condition, skin integrity, excretion, oral intake, pain, consciousness, and psychological or spiritual conditions. The findings revealed that patients who lived for only 72 h or less presented with symptoms such as a rapid decline in overall health, reduced urine output, faecal incontinence, noisy respiratory secretions, Cheyne-Stokes breathing, peripheral cyanosis, and food refusal. Additionally, two symptoms were found to be unique to patients who died within 72 h: respiration with mandibular movement and pulselessness of the radial artery (Mori et al., 2022).

Data regarding the prevalence of these symptoms are presented in Table 2, and their specificities are presented in Table 3.

Excluding the predictive models developed by selected authors (Hosoi et al., 2021; Ikari et al., 2021a, 2021b; Mori et al., 2021; Hui et al., 2015a), only a handful of studies have obtained data on the specificity of clinical signs of impending death, with a specificity rate of over 95 %. These signs include pulselessness of the radial artery (Hui et al., 2014), upper gastrointestinal bleed (Hui et al., 2015c), decreased urine output (Hui et al., 2014), apnoea periods (Hui et al., 2014), respiratory rate decrease (Bruera et al., 2014), Cheyne-Stokes breathing (Hui et al., 2014), death rattle (Hui et al., 2014), peripheral cyanosis (Hui et al., 2014), low oxygen saturation (Bruera et al., 2014), respiration with mandibular movement (Hui et al., 2014), decreased response to verbal stimuli (Hui et al., 2015b), non-reactive pupils (Hui et al., 2015b), inability to close eyelids (Hui et al., 2015b), drooping of the nasolabial fold (Hui et al., 2015b), hyperextension of the neck (Hui et al., 2015b), and grunting of vocal cords (Hui et al., 2015b). Low performance status and albumin levels have been validated as having a predictive value for short-term survival (Christ et al., 2022).

3.4. *Prognostication models*

Several studies have attempted to create diagnostic models for predicting impending death based on clinical signs. One such model, presented in a study focusing on noncancer patients, utilised the criteria of "pulselessness of the radial artery OR respiration of mandibular movement OR the shock Index (SI) >1.0" to predict death within seven days with an impressive 83.9 % accuracy. However, models designed to predict death within 72 or 24 h were found to have an accuracy of 65 % or less (Hosoi et al., 2021). A diagnostic model based on two clinical signs (Palliative Performance Scale and drooping of the nasolabial fold) (Hui et al., 2015a) took advantage of the higher sensitivity of an early sign (Palliative Performance Scale ≤ 20 %) and the higher specificity of a late clinical sign (drooping of nasolabial fold). Patients with Palliative Performance Scale ≤ 20 % who also showed drooping of the nasolabial fold had a remarkably high risk of 3-day mortality (94 %).

The "3-Day Surprise Question" is a reliable tool in identifying patients nearing death within three days, with a sensitivity of 94.3 % but low specificity of 26.3 % (Ikari et al., 2021a). The "1-Day Surprise Question" had a high sensitivity of 82 % and a specificity of 45.5 % in predicting death (Ikari et al., 2021b). One study identified five variables associated with death within one day: decreased urine output, decreased response to visual stimuli, respiration with mandibular movement, pulselessness of the radial artery, and SpO2 $<$ 90 %. The P3did score is a prediction system, based on ten clinical signs, that has shown good diagnostic properties with high specificity (over 90 % for death ≤ 3 days in patients with PPS $\leq$ 20) but with an accuracy rate that needs to be improved (68.6 % for death ≤ 3 days).

4. Discussion

All healthcare professionals must demonstrate clinical competence in diagnosing the dying process and it should be included in academic training (Croxon et al., 2018; Smith et al., 2018; Zheng et al., 2018). Clinicians must avoid conveying ambiguous information as it can lead to misunderstandings and uncertainty among patients and their families. Ambiguity in healthcare communication may result in incorrect assumptions, hinder informed decision making, and contribute to heightened anxiety or confusion. Therefore, it is essential for clinicians to aim for clear, precise, and easily understandable communication to support patients and their families effectively (Ijaopo et al., 2023). As death is often accompanied by the failure of multiple organs or systems, it is expected that signs of impending death will reflect this. Clinicians in palliative care are not just task oriented; they are critical thinkers who provide individualised and compassionate care. Their roles transcend specific tasks such as vital signs, treatments, and interventions (Schroeder and Lorenz, 2018).

Clinicians in palliative care play a crucial role in managing the complexity of end-of-life care. Their knowledge of the physiology of dying, particularly the clinical signs of impending death, empowers them to navigate through this complexity and provide the best possible care. It is crucial to acknowledge the progression from active patient participation in daily activities to the gradual deterioration of the disease in the final weeks and days of life and the rapid decline in the last hours of life. Recognising this trajectory can assist clinicians in predicting disease decline and tailoring treatment plans (Ijaopo et al., 2023). When family members do not have access to information that their loved one is facing imminent death, they are less able to cognitively prepare for loss (Sallnow et al., 2022). Furthermore, the ability to identify high specificity signs of impending death may lead to the need for anticipation of care needs and better planning, and ultimately, to improve end-of-life care as well as better bereavement adjustment, as mentioned previously. Families are reportedly more stressed during the unexpected death of patients (Ikari et al., 2021a).

According to the Lancet Report on the Value of Death (Sallnow et al., 2022), the early recognition of imminent death can have important implications for patients, families, and healthcare professionals involved in a person's care.

In compiling the evidence on imminent death, Mori *et al* went further and reflected on future challenges, such as the clinically important outcomes that result from prognosticating this situation. These may include goal-directed care, aggressive end-of-life care interventions, completion of end-of-life tasks, patient and family satisfaction with care, preferred place of death, quality of dying and quality of life. The authors say it is important that these are clear and, where appropriate, validated (Mori et al., 2022).

Good end-of-life care has been defined as being able to die in the place of choice, free from pain, respected in dignity and supported by the best possible care, but people still receive less than optimal end-of-life care (McGlinchey et al., 2023).

The International Collaborative for Best Care for the Dying Person (The Collaborative) supports ensuring a world where all people experience a good death as an integral part of their individual life, supported by the very best personalised care (Ellershaw and Lakhani, 2013) as a

vision and incorporated 10 key elements into a model of care for best care for the dying, called the 10/40 Model, which recently had a new version updated and validated (McGlinchey et al., 2023). This model is being used in several countries and recently saw its Portuguese version validated (Carneiro et al., 2024). The first key principle is Recognition that the person is in the last few days and hours of life should be made by the multidisciplinary team (ideally a doctor and a nurse) and documented by a senior healthcare professional responsible for the person's care (McGlinchey et al., 2023).

Researchers have shown that mandibular movement during respiration, although with different prevalence data, is the most specific indicator of impending death, regardless of the presence or absence of cancer (Hosoi et al., 2021; Mori et al., 2021; Matsunami et al., 2018; Hui et al., 2014; White et al., 2019). Other cardiovascular parameters, such as changes in blood pressure, can also help diagnose impending death within 2–3 days (Hwang et al., 2013; Bruera et al., 2014). However, changes in vital signs may not always accurately predict impending death and may cause discomfort, anxiety, and additional burden on patients and caregivers. Associated with this general deterioration, researchers have identified other signs, namely respiratory (decreased oxygen saturation, apnea periods, respiratory rate decrease, Cheyne-Stokes breathing, grunting of vocal cords, and death rattle) and subsequent peripheral cyanosis (Hui et al., 2015b, 2014; Bruera et al., 2014); and neurological, such as nonreactive pupils and decreased responses to stimuli, which can also provide valuable clues for identifying impending deaths. Upper gastrointestinal bleeding was found only in patients who were actively dying of cancer (Hui et al., 2015b). Other clinical signs, such as decreased urine output (Hui et al., 2014), and neck hyperextension (Hui et al., 2015c) may be present. The nasolabial fold sign is a relatively new predictor of impending death, and further research is needed to investigate its validity and reliability among terminally ill patients of various ethnicities, as differences in age and race may affect its accuracy (Hosoi et al., 2021).

Next step will actually be to move on to a systematic review.

4.1. Limitations

Although some studies only provided data on prevalence, we included them in this review because there is little evidence regarding specificity. We hope to contribute to future research by mapping this information.

Only few studies have focused on defining the specificity of clinical signs, particularly in noncancer patients, and have only presented their prevalence. Although this information is helpful, it does not allow healthcare professionals to diagnose impending deaths accurately. Most studies were conducted in palliative care cancer populations; therefore, these results may not be applicable to noncancer patients or other care settings. One of the main difficulties in identifying clinical signs of impending death, particularly in noncancer patients, is that these signs have low sensitivity. This means that their presence strongly suggests impending death, but their absence does not necessarily mean that death will not occur within 72 h.

4.2. Implications for practice and research

In this review, we intend to map the evidence of the clinical signs of impending death. Therefore, we do not make any unequivocal recommendations for practice. In the last few days and hours of life, clinicians play a crucial role in adopting an urgent and effective interdisciplinary approach, clarifying the goals of care, ensuring compassionate communication, and facilitating shared decision making. The predictors of impending death depend on the needs of patients, families, and clinicians. Recognising impending death provides an opportunity for patients and their families to address unfinished matters and share their feelings.

It is important to conduct additional research within the realm of palliative care, specifically focusing on the provision of care during the terminal stages of life, and exploring methodologies for making accurate prognostic decisions in situations where data may be incomplete (White et al., 2019). Despite the growing body of research on impending death, many questions remain unanswered. Subsequent studies should aim to help clinicians improve their ability to predict impending death, effectively communicate with patients and their families, and enhance clinically significant outcomes. Some questions remain unanswered and are important outcomes of prognostication and require further research (Mori et al., 2022), namely, the aims of prognostication of impending death, clinically important outcomes, validation of prognostic models, novel biomarkers for the prediction of impending death, and artificial intelligence and prediction of impending death.

5. Conclusion

There is still a lack of evidence regarding the highly specific clinical signs of impending death, particularly in noncancer patients. In the cancer population, certain clinical signs have proven to be highly specific for predicting impending death within 72 h, with a specificity above 95 %. It is essential to focus on assisting clinical professionals in diagnosing impending deaths, while accurately minimising false-positive cases. Further studies are needed to better understand and compare the clinical signs of impending death, especially in noncancer patients, and determine whether the process is similar in different care settings.

CRediT authorship contribution statement

Catarina Simões: Writing – original draft, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Rui Carneiro:** Writing – review & editing, Validation. **Abílio CardosoTeixeira:** Writing – review & editing, Validation, Methodology, Data curation.

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Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijnurstu.2025.105015.

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