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Effectiveness of the WHO analgesic ladder for malignancy pain: Systematic literature review

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Abstract

Background: Inadequately managed malignancy pain severely compromises patients' quality of life. This study synthesizes scientific evidence regarding the effectiveness of standard and modified WHO Analgesic Ladders in reducing pain intensity.
Method: Following PRISMA guidelines, 15 quantitative studies (RCTs and cohorts) published between 2010–2025 were identified via PubMed, ScienceDirect, and Cochrane Library, and manual searches via Google.
Results: Methodological quality was assessed using JBI Critical Appraisal Tools, revealing 4 studies with a low risk of bias (score ≥75%) and 11 with a moderate risk (50–75%). The standard WHO ladder remains highly effective in pediatric populations, achieving 85%–100% pain control. In adults, a modified two-step approach (bypassing weak opioids) demonstrated significant superiority, with pain reduction response rates of 76.5%–88.2%, compared to only 32.35%–54.7% for weak opioids. Standard adult application yielded 64.5%–73.8% effectiveness, which rose to 91.25% when supported by strict management cycles. Integrating multimodal therapies further reduced daily opioid requirements while significantly improving Quality of Life (QOL). Precise assessment using Wong-Baker (children) or NRS/VAS (adults) remains essential.
Conclusion: Transitioning to a two-step approach and integrating multimodal therapies offers a more optimal, faster, and statistically superior strategy for modern malignancy pain management.

Keywords: malignancy; pain management; WHO Analgesic Ladder; chronic pain.

INTRODUCTION

Pain is a highly prevalent and debilitating symptom among patients with malignancies, affecting approximately 44.5% of the general oncology population and surging to 54.6% in those with advanced, metastatic, or terminal disease (1). Inadequately managed cancer pain serves not merely as an indicator of physical suffering, but profoundly compromises patients' overall quality of life by triggering sleep disturbances, chronic fatigue, and severe emotional distress (2,3). In response to the substantial global burden of cancer-related pain, the World Health Organization (WHO) introduced the Analgesic Ladder in 1986, a three-step framework designed to rationalize and facilitate a stepwise approach to pain relief, progressing from non-opioid analgesics to strong opioids (4,5). Due to its simplicity and wide applicability, this guideline has historically served as the cornerstone and gold standard for malignancy pain management worldwide (6,7).

Despite its widespread historical adoption, the application of the WHO Analgesic Ladder in contemporary clinical practice increasingly encounters challenges driven by the evolving complexity of malignancy pain. Evidence suggests that the standard application of these guidelines remains highly effective, particularly within pediatric populations (8,9). However, recent literature highlights gaps that a rigid adherence to the three-step approach is not universally optimal for adult patients presenting with complex and multifaceted pain profiles (10,11). Accumulating clinical

evidence indicates that strict adherence to Step 2 (the administration of weak opioids) frequently results in therapeutic inefficiency; notably, over 50% of these patients experience analgesic failure, necessitating rapid escalation to strong opioids (12). Furthermore, discrepancies in real-world prescribing adherence (13) and serious risks such as opioid misuse and dependency, with an estimated combined risk prevalence of 12.3% among cancer patients (14), underscore the critical need for a comprehensive re-evaluation of this intervention's efficacy in the modern era.

In response to the limitations inherent in the standard guidelines, contemporary clinical practice is gradually shifting towards modified applications of the WHO Analgesic Ladder, such as the adoption of a "two-step approach" (which bypasses weak opioids) and the early integration of multimodal therapies (15–17). The novelty of this study lies in its systematic compilation and synthesis of current literature spanning from 2010 to 2025 using a Systematic Literature Review methodology. It directly evaluates and compares the effectiveness of the standard WHO guidelines against its contemporary modifications, focusing on both the rapidity of pain reduction and the enhancement of patients' quality of life. Consequently, the primary objective of this research is to systematically synthesize scientific evidence regarding the efficacy of the WHO Analgesic Ladder, evaluating both its standard and modified applications, in reducing pain intensity among patients with malignancies.

METHODS

This study utilized a quantitative Systematic Literature Review (SLR) design, structured around the Population, Intervention, Comparison, and Outcome (PICO) framework. To ensure transparency and enable methodological reproducibility, the literature search and selection processes were rigorously conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

A comprehensive literature search was executed between October 2025 and February 2026 across three primary electronic databases: PubMed, ScienceDirect, and the Cochrane Library. To ensure consistency and full reproducibility across all platforms, an identical search string using free-text keywords was applied to all three databases. Medical Subject Headings (MeSH) were not utilized in the final search strings because the specific primary keywords, particularly "WHO Analgesic Ladder," yielded "items not found" or no relevant results when restricted to MeSH terminology. The exact, reproducible search string used was: (malignancy OR cancer) AND ("WHO Analgesic Ladder" OR "Three-Step Pain Management" OR "Stepwise Analgesic") AND "pain management". Furthermore, to ensure a comprehensive capture of data across all age demographics, a supplemental manual search was conducted via Google, specifically targeting studies involving pediatric populations, which yielded 4 additional relevant records.

The literature search was restricted to original research published between 2010 and 2025 to capture clinical practices reflecting the modern era. All identified records were systematically managed using reference management software; Zotero was specifically utilized for the identification and removal of duplicate records, whereas Mendeley was employed for article organization, in-text citation management, and the automated generation of the bibliography.

Literature was deemed eligible for inclusion if it met the following predetermined criteria: 1) original quantitative research, specifically Randomized Controlled Trials (RCTs) or cohort studies; 2) available as a full-text PDF in either English or Indonesian; 3) explicitly evaluated the application of the WHO Analgesic Ladder (standard or modified); and 4) provided empirical data on pain reduction utilizing standardized tools such as VAS, NRS, or the Wong-Baker FACES Scale. Studies addressing non-malignant pain were strictly excluded.

The methodological quality of each selected article was independently evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Tools. The assessment employed a binary scoring system (yes = 1, no/unclear = 0), and eligibility was calculated as a percentage: low risk of bias (≥75%), moderate risk (50–75%), and high risk of bias (<50%).

The results of this critical appraisal for the 15 included studies are as follows: 4 studies (26.7%) were categorized as having a low risk of bias, while 11 studies (73.3%) presented a moderate risk of bias. Specifically, high-quality evidence with a low risk of bias was identified in studies by Amr & Makharita (92%), Biji et al. (91%), Kim & Lee (85%), and Shilpakar et al. (77%). The remaining 11 studies, including Cai et al. and Fallon et al., maintained a consistent moderate risk profile with scores ranging from 64% to 73%.

Data analysis was conducted using a narrative synthesis technique coupled with critical analysis. The results of the risk of bias appraisal directly influenced the narrative synthesis; findings from studies identified as having a low risk of bias were prioritized and given greater weight when formulating the primary conclusions regarding the superior efficacy of the two-step approach and multimodal integrations. Through this critical analysis, the researchers evaluated the strengths and limitations of each study, ensuring that the ultimate conclusions remained methodologically grounded and aligned with the research objectives.

RESULTS

Literature Search and Selection. The comprehensive literature search yielded a total of 1,149 articles. Initial identification was conducted across three primary electronic databases: PubMed (n = 228), ScienceDirect (n = 872), and the Cochrane Library (n = 45), supplemented by a manual search via Google (n = 4). To ensure consistency with Figure 1, all supplemental articles are hereafter referred to as identified through Google manual searches. Following deduplication via Zotero, 1,145 records remained for screening.

The preliminary screening of titles and abstracts excluded 1,130 articles based on predetermined exclusion criteria, such as publication date (n = 471), ineligible study design (n = 580), and non-malignancy populations (n = 23). Consequently, 15 articles underwent full-text eligibility assessment and were all (n = 15) included in the final qualitative synthesis as illustrated in the PRISMA Flow Diagram (Figure 1).

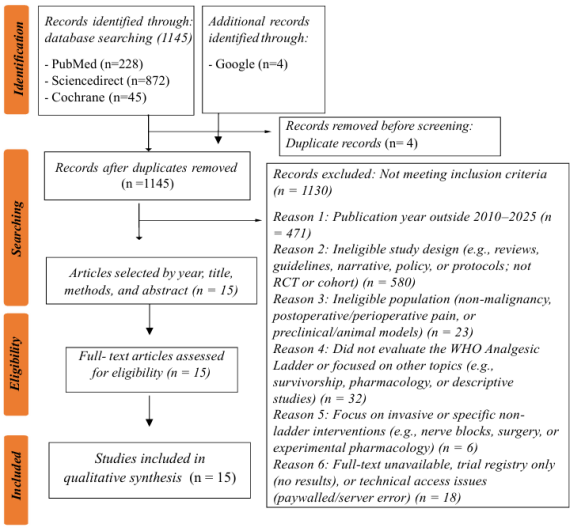

Figure 1. PRISMA Flow Diagram for Systematic Literature Review

Methodological Quality Appraisal (JBI Scores) In direct follow-up to the quality appraisal criteria described in the Methods, the results of the JBI assessment are detailed in Table 1. Four studies (26.7%) achieved a low risk of bias (score ≥75%), while 11 studies (73.3%) presented a moderate risk of bias (50–75%).

Table 1. Methodological Quality Appraisal (JBI Scores)

No	Author	Country	Title	Scoring	Overall Apraisal
1	(Cai et al., 2018)	China	A Chinese medicine warm compress (Wen Jing Zhi Tong Fang), combined with WHO 3-step analgesic ladder treatment for cancer pain relief	69%	include
2	(Fallon et al., 2022)	Multinational (international) → The UK, Israel, Mexico, and Uganda	An international, open-label, randomised trial comparing a two-step approach versus the standard three-step approach of the WHO analgesic ladder in patients with cancer	69%	include
3	(Bandieri et al., 2016)	Italy	Randomized Trial of Low-Dose Morphine Versus Weak Opioids in Moderate Cancer Pain	69%	include
4	(W. Luo et al., 2025)	China	Implementation of pharmaceutical strategies using the PDCA cycle for standardized management of cancer pain medications	69%	include
5	(Biji et al., 2019)	India	Pain Management in Children With Cancer Using World Health Organization Guidelines at a Tertiary Cancer Center in Rural India	91%	include
6	(Begum et al., 2023)	Bangladesh	Pain Management of Pediatric Cancer Patients at BSMMU and Utilization of WHO Analgesic Ladder	73%	include
7	(Geeta et al., 2010)	India	Management of Pain in Leukemic Children using the WHO Analgesic Ladder	64%	include
8	(Hadi et al., 2014)	Egypt	Impact of pain management using the WHO analgesic ladder in children with cancer in South Egypt Cancer Institute, Assiut University	73%	include
9	(Amr & Makharita , 2014)	Egypt	Neurolytic Sympathectomy in the Management of Cancer PaindTime Effect: A Prospective, Randomized Multicenter Study	92%	include
10	(Armeanu et al., 2025)	Romania	Modeling Pain Dynamics and Opioid Response in Oncology Inpatients: A Retrospective Study with Application to AI-Guided Analgesic Strategies in Colorectal Cancer	73%	include
11	(Kim & Lee, 2018)	South Korea	Intradermal Acupuncture Along with Analgesics for Pain Control in Advanced Cancer Cases: A Pilot, Randomized, Patient-Assessor-Blinded, Controlled Trial	85%	Include
12	(Nunes et al., 2014)	Brazil	Morphine as first medication for treatment of cancer pain	69%	Include
13	(Kashyap et al., 2022)	India	Scrambler Therapy Enhances Quality of Life in Cancer Patients in a Palliative Care Setting: A Randomised Controlled Trial	69%	Include
14	(Konopka -Filippow et al., 2015)	Poland	Pain management during radiotherapy and radiochemotherapy in oropharyngeal cancer patients: single-institution experience	64%	include
15	(Shilpakar et al., 2025)	Nepal	Comparison of the effectiveness of oral morphine versus oral tramadol on early pain control in opioid-naive patients with moderate cancer pain	77%	Include

Summary of Included Studies and Primary Outcomes Table 2 provides a streamlined summary of the 15 included studies. As requested, the "Results" column focuses on primary statistical outcomes, such as pain reduction scores and response rates.

Characteristics of Included Studies The 15 included articles encompassed a diverse array of research designs, primarily including Randomized Controlled Trials (RCTs), prospective and retrospective observational studies, as well as comparative studies. The investigated populations comprised both adult and pediatric oncology patients. All selected articles specifically evaluated the effectiveness of the WHO Analgesic Ladder, encompassing both its standard three-step application and contemporary modifications, such as the two-step approach and combinations with multimodal therapies. The comprehensive characteristics and primary findings of each individual study are sequentially summarized in (Table 2).

Characteristics of Pain Measurement Instruments Findings from this review indicate that the selection of pain measurement tools is highly dependent on patient demographics, particularly age. Among the four studies focusing on pediatric populations, all (100%) utilized the visual Wong-Baker FACES Pain Rating Scale due to its ease of interpretation for children; in certain instances, this was combined with the FLACC Scale for preschool-aged children (8,9,17,19).

Conversely, within the 11 studies targeting adult populations, the primary instruments were predominantly the Numeric Rating Scale (NRS) (64%) and the Visual Analog Scale (VAS) (45%) (13,15,20). Beyond unidimensional pain assessments, the synthesis also revealed a growing trend in measuring Quality of Life (QOL). Notably, 73% of the adult studies integrated multidimensional instruments, such as the EORTC QLQ-C30, WHOQOL-BREF, and the Edmonton Symptom Assessment System (ESAS), to holistically evaluate the impact of pain interventions on the patients' overall physical well-being (21–23).

Effectiveness of Standard Application vs. Modified Approaches An analysis of the findings from the 15 extracted studies categorizes the effectiveness of these interventions into three primary clinical approaches:

1. **Standard Three-Step Application:** This approach demonstrated a high level of effectiveness, particularly among pediatric patients. Approximately 85% to 94.6% of children reportedly achieved adequate pain control utilizing solely Step 1 and Step 2 interventions (8,19). In adult populations, the standard application also recorded clinical pain improvements in 64.5% to 73.8% of patients (20), an efficacy rate that could surge to 91.25% when rigorously governed by a strict Plan-Do-Check-Act (PDCA) pharmaceutical management cycle (13).
2. **Two-Step Approach Modification:** This modified strategy, which bypasses Step 2 (weak opioids) to directly initiate low-dose morphine (Step 3), consistently proved to offer superior analgesic efficacy. Highly significant pain reduction response rates were reported to range between 76.5% and 88.2%, standing in stark contrast to the efficiency of weak opioids, which ranged only from 32.35% to 54.7% (15,23). Although this approach is significantly more efficient and cost-effective (12), several findings noted a higher susceptibility to early-onset adverse effects (such as nausea and sedation) if the initial strong opioid dose is not meticulously titrated (24).
3. **Invasive and Non-Pharmacological Combination Therapy Modification:** The early integration of adjunctive therapies significantly minimized the required daily opioid dosage. Non-pharmacological interventions, such as warm compresses, enhanced the Overall Response Rate to 70.97% and mitigated severe constipation (16). Similarly, the implementation of neuromodulation (Scrambler Therapy) and early invasive procedures (Neurolytic Sympathectomy) demonstrated a massive reduction in morphine consumption, which directly correlated with a substantial improvement in the patients' QOL (21,22).

Table 2. Data Extraction of the Systematic Literature Review

No	Author and Year	Sample Size / Population	Study Design	Results	Pain Measurement Instruments
1	(Cai et al., 2018) (16)	62 cancer patients with mild–severe pain (31 intervention, 31 control)	RCT (Standard vs. Standard + CMWC)	ORR 70.97% (intervention) vs 29.03% (control); significant VAS reduction ($p < 0.001$).	VAS and NRS
2	(Fallon et al., 2022) (12)	153 cancer patients with pain ≥4/10	Open-label RCT (2-step vs. 3-step)	No significant diff. in time to stable control ($p = 0.667$); >50% of 3-step group failed and required escalation.	NRS, BPI, NCCN Distress Thermometer, EQ-5D-5L
3	(Bandieri et al., 2016) (15)	240 opioid-naïve adult cancer patients with moderate pain	Multicenter RCT (2-step vs. 3-step)	88.2% responders (morphine) vs 54.7% (weak opioids); $p < 0.001$; OR 6.18.	NRS, Edmonton Symptom Assessment System (ESAS)
4	(W. Luo et al., 2025) (13)	160 advanced cancer patients and >4000 prescriptions	Mixed-methods (PDCA implementation)	Compliance 92.92% vs 72.32% ($p < 0.05$); VAS 2.26 vs 3.07 ($p < 0.01$).	VAS
5	(Biji et al., 2019) (8)	59 children (290 inpatient episodes) with hematological malignancies	Retrospective cohort	94.6% pain-controlled at discharge; Step 1 effective in 55.9%, Step 2 in 34.4%.	Wong-Baker Faces Scale (<8 yrs); NRS (>8 yrs)
6	(Begum et al., 2023) (9)	120 pediatric cancer patients	Prospective observational	100% pain-free within 2 weeks following the WHO ladder; mild side effects only.	Wong-Baker Faces Pain Scale (4–8 yrs); NRS (>8 yrs)
7	(Geeta et al., 2010) (19)	39 children with leukemia	Prospective observational	85% controlled with Step 1 (31%) & Step 2 (54%); only 15% required morphine.	NRS; Wong-Baker Faces Scale
8	(Hadi et al., 2014) (17)	94 pediatric cancer patients (133 pain cycles)	Prospective comparative (2-step vs. 3-step)	Median pain 1.33 (2-step) vs 3.33 (3-step); $p = 0.002$; 77.6% pain reduction.	FLACC Scale; Wong-Baker FACES Scale
9	(Amr & Makharita, 2014) (21)	109 patients with inoperable abdominal/pelvic cancer and visceral pain	Randomized multicenter (Early vs. Late Block)	Significant pain reduction ($p < 0.05$); Opioid consumption decreased ($p < 0.0001$).	VAS 0–100; EORTC QLQ-C30; DN4
10	(Armeanu et al., 2025) (20)	107 oncology inpatients (42 colorectal cancer subgroup)	Retrospective observational (AI Modeling)	64.5% pain improvement (mean ↓1.78 pts); 73.8% improvement in colorectal cancer.	Numerical Pain Rating Scale (NPRS 0–10)
11	(Kim & Lee, 2018) (25)	30 advanced cancer patients	Pilot RCT (Standard vs. Standard + Acupuncture)	Pain response 64.3% vs 38.5% ($p < 0.001$); Mean score reduction -1.54 ± 1.45.	NRS, EORTC QLQ-C30
12	(Nunes et al., 2014) (24)	60 adult cancer patients	Prospective RCT (Early Morphine vs. Stepwise)	No significant difference in pain intensity; higher incidence of early nausea ($p = 0.0088$).	Visual Analogue Scale (VAS), WHOQOL-brief
13	(Kashyap et al., 2022) (22)	80 head, neck, and thorax cancer patients	Open-label RCT (Standard vs. Standard + Scrambler)	Morphine consumption ↓ by 22.12 mg; significant QOL improvement across all domains ($p < 0.01$).	NRS, WHOQOL-BREF
14	(Konopka-Filippow et al., 2015) (26)	42 oropharyngeal cancer patients	Retrospective observational	50% required strong opioids; 23.8% experienced breakthrough pain.	Dische scale and Visual Analogue Scale (VAS)
15	(Shilpakar et al., 2025) (23)	68 opioid-naïve cancer patients with moderate pain	Phase II RCT (2-step vs. 3-step)	Initial response 94.1% (morphine) vs 55.9% (tramadol); $p < 0.001$. NRS ↓≥5 pts: 76.5% vs 32.3%.	NRS, Edmonton Symptom Assessment Scale (ESAS)

DISCUSSION

This systematic review comprehensively evaluates the research question regarding the effectiveness of the WHO Analgesic Ladder in the management of malignancy pain. The synthesis of 15 studies confirms that, in general, the WHO guidelines remain highly effective in alleviating cancer pain; however, findings indicate that in the modern era, this effectiveness is no longer achieved through rigid adherence to the classic three-step structure, but rather through a more dynamic, modified approach. This interpretation addresses the gaps identified in previous reviews, which highlighted that a uniformly applied standard guideline fails to consistently provide optimal pain control for patients presenting with complex and variable pain profiles (10,11).

Striking differences in effectiveness were observed across different population groups. Among pediatric populations, the standard three-step guideline is consistently effective and aligns with existing protocols, yielding pain control rates between 85% and 100% (8,9,19). Conversely, in adult populations, strict adherence to Step 2 (the administration of weak opioids) frequently leads to unnecessary analgesic failure, forcing over 50% of patients into a rapid escalation to Step 3 (12). Scientifically, this inefficiency can be attributed to the ceiling effect of weak opioids, coupled with the pharmacokinetic inability of drugs such as tramadol and codeine to suppress the transmission of progressive visceral or neuropathic pain signals that are prevalent in adults. Consequently, modifying the framework via a "two-step approach", bypassing Step 2 to directly initiate low-dose morphine, consistently yields a markedly superior pain reduction response rate (76.5% to 88.2%) and achieves pain control significantly faster (15,23). These findings align with recent clinical investigations advocating for the elimination of Step 2 in cancer patients experiencing moderate to severe pain.

Beyond stepwise pharmacotherapy, these findings reveal that the early integration of multimodal and invasive interventions is crucial to addressing the substantial risk of opioid misuse, which has an estimated prevalence of 12.3% among chronic cancer patients (14). Combination therapies, ranging from warm compresses (Chinese Medicine) and Scrambler Therapy to early neurolytic sympathectomy, have proven highly effective in reducing daily morphine requirements while significantly boosting patients' Quality of Life (QOL) scores (16,21,22). The biological rationale for this success lies in the ability of multimodal therapies to interrupt nociceptive pathways locally or via peripheral neuromodulation. This reduces nerve excitability without solely burdening systemic opioid receptors, which ultimately mitigates adverse effects such as chronic constipation.

Analysis of pain measurement instruments indicates that verifying therapeutic effectiveness relies heavily on utilizing tools tailored to the patient's age and cognitive capacity. The application of the Wong-Baker FACES and FLACC scales proved essential for children who have not yet grasped numerical abstraction (17), whereas the Numeric Rating Scale (NRS) is essential for adults (20). A crucial finding from this review is the growing trend of integrating multidimensional instruments, such as the ESAS and EORTC QLQ-C30, alongside standard numerical scales. This underscores that evaluating the success of modern cancer pain management is no longer confined merely to reducing physical pain scores; rather, it must be measured by the holistic restoration of biopsychosocial functioning.

Furthermore, this literature review challenges and modifies long-established fundamental theories of pain management. The WHO Analgesic Ladder, introduced in 1986, should no longer be interpreted as "steps" that must be climbed rigidly and sequentially. Based on the accumulated evidence, this theory has now evolved into a dynamic platform; modifying it into a two-step approach is the primary, more ethical, and pharmacologically rational choice for patients with moderate to severe pain, provided it is accompanied by standardized and quality-controlled pharmaceutical prescribing

management, such as the implementation of the Plan-Do-Check-Act (PDCA) cycle (13).

In a broader context, the implications of these findings provide medical justification for anesthesiology nurses and oncology teams to confidently initiate low-dose strong opioid therapies earlier. Although this upfront approach has proven clinically and economically efficient (12), healthcare professionals must remain vigilant regarding the higher risk of early-onset nausea and sedation resulting from direct morphine initiation, which demands meticulous titration and extra monitoring (24). For future research directions, it is highly recommended that larger-scale experimental Randomized Controlled Trials (RCTs) utilizing cluster designs be conducted to compare the long-term effectiveness and toxicity of the two-step approach head-to-head against the standard three-step guidelines. Such clinical trials should specifically focus on patient demographics with distinct cancer pain subtypes (e.g., predominantly neuropathic pain or bone metastases), which have frequently been overlooked in the majority of observational studies.

Study Limitations Despite providing significant clinical insights into the evolution of pain management, this systematic literature review has several inherent limitations that must be acknowledged. First, there is a high degree of methodological heterogeneity among the 15 included studies, which encompass a mix of Randomized Controlled Trials (RCTs), prospective observational studies, and retrospective cohort analyses. This diversity in study designs may introduce varying levels of evidence strength and potential confounding factors. Second, the review is subject to potential publication biases, as the search strategy was restricted to three primary electronic databases and limited to full-text articles available in English and Indonesian, potentially overlooking relevant grey literature or studies published in other languages.

Finally, the findings were synthesized using a narrative approach rather than a statistical meta-analysis. While this descriptive synthesis effectively maps clinical patterns and trends, the lack of a pooled quantitative estimate limits the ability to determine the precise overall effect size of the modified two-step approach compared to the standard WHO Analgesic Ladder across all demographics.

Conclusion

Based on this systematic literature review of current clinical evidence, the application of the WHO Analgesic Ladder in malignancy pain management remains an empirically effective foundation; however, its clinical practice has evolved significantly from a rigid three-step structure to a more dynamic, modified approach. The primary findings of this review indicate that the two-step approach modification, which directly initiates low-dose strong opioids by bypassing weak opioids, is the most highly recommended contemporary strategy, as it is statistically proven to be significantly superior and faster in achieving adequate pain control compared to the standard application (15,23). Furthermore, integrating this foundational guideline with multimodal combination therapies, such as warm compresses, Scrambler Therapy, and invasive procedures like neurolytic sympathectomy, has demonstrably minimized daily opioid consumption while comprehensively enhancing physical well-being outcomes (21,22). The success of these interventions is also heavily dependent on the selection of demographically standardized measurement tools: the Wong-Baker FACES scale is strictly required for pediatric populations (9), whereas the Numeric Rating Scale (NRS) or Visual Analog Scale (VAS), integrated with multidimensional Quality of Life (QOL) assessment instruments, is absolutely essential for evaluating therapeutic impacts in adult patients (20).

Conceptually, shifting implementation toward this modified approach provides highly advantageous clinical effects, including reduced analgesia response times, decreased incidence of opioid complications such as severe constipation, and the achievement of optimal pain control when supported by a standardized pharmaceutical

management system (13). Nevertheless, implementing this modification does carry limitations, namely the risk of early-onset adverse effects like nausea and somnolence if strong opioid initiation is not meticulously titrated and monitored by the medical team (24). Conversely, maintaining rigid adherence to the standard guidelines yields detrimental effects through a high rate of inefficiency at Step 2, where the majority of patients inevitably experience therapeutic failure and require rapid escalation to morphine use (12). Ultimately, the WHO Analgesic Ladder in the modern clinical era must be interpreted as a responsive and flexible framework, wherein a modified two-step approach, integrated with age-appropriate assessment and multimodal therapies, represents the most optimal therapeutic strategy for managing malignancy pain.

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