


Original Article

Development of Care Pathway for Assessment and Treatment of Fatigue in Palliative Care

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ABSTRACT

Objectives: Fatigue is a frequent and burdensome symptom in patients with advanced disease in palliative care. However, it is under-assessed and undertreated in clinical practice, even though many treatment options have been identified in systematic reviews. Care pathways with defined and standardised steps have been recommended for effective management in the clinical setting. This paper describes a care pathway for managing fatigue in palliative care patients. This study aims to develop a care pathway with detailed guidance for screening, assessment, diagnosis, and treatment of fatigue in palliative care patients.

Material and methods: A collaborative effort of multidisciplinary clinicians participated in constructing the care pathway. The care pathway was developed using the following steps: (a) Developing an intervention; (b) piloting and feasibility; (c) evaluating the intervention; (d) reporting; and (e) implementation. This paper covers the first step, which includes the evidence base identification, theory identification/development, and process/outcomes modeling. A literature search was conducted to understand the extent of the fatigue problem in the palliative care setting and identify existing guidelines and strategies for managing fatigue. Consistent recommendations emanating from the included papers were then contributed to a care pathway. Patient representatives and palliative care professionals provided feedback on the draft.

Results: The care pathway address the following care processes: (1) Screening for the presence of fatigue; (2) assessment to evaluate the severity of fatigue; (3) diagnostic procedure, including history, physical examination, and laboratory finding; (4) therapeutic management pathway for clinical decision-making; and (5) valuation of treatment effect, using questionnaires, diaries and physical activity monitoring with body-worn sensors.

Conclusion: The development of a care pathway will help to implement regular and structured assessment, diagnosis, and treatment of fatigue for healthcare professionals treating palliative care patients. Reviewing the pathway with a multidisciplinary expert group and field testing the pathway will be the next steps toward implementation.

Keywords: Care pathway, Fatigue, Weakness, Tiredness, Palliative care, Complex interventions, Advanced illness

INTRODUCTION

Fatigue has been defined as a subjective feeling of tiredness, weakness, or lack of energy.^[1] Qualitative differences between fatigue in cancer patients and healthy controls have been proposed, but these differences seem only to express the overwhelming intensity of cancer-related fatigue.^[1] Almost 80% of cancer patients and up to 99% of patients following radio- or chemotherapy have reported suffering from fatigue.^[1] In a study of 1000 patients in an American

palliative care programme, fatigue, weakness, and lack of energy were three of the five most frequently reported symptoms, averaging 84%, 66%, and 61%, respectively.^[2] A German nationwide study reported moderate or severe weakness in 86% of patients at the time of admission to a palliative care unit and 73% at the end of treatment. Moderate or severe tiredness was reported in 70% of the patients at the time of admission and 59% at the end of treatment.^[3] When associated with cachexia and anorexia,

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fatigue increases mortality, morbidity, and reduced response to therapy.^[4]

Managing fatigue in palliative care remains challenging for physicians and healthcare services. The European Association for palliative care has published recommendations for treating of fatigue in palliative care, describing useful assessment procedures and pharmacological and non-pharmacological interventions.^[1] Given the complex and multi-faceted nature of fatigue in palliative care, a care pathway seems suitable for differentiated management.

A care pathway is a task-orientated care plan that outlines the primary clinical intervention for specified groups of patients with a particular diagnosis, aiding the coordination and delivery of high-quality care.^[5] Care pathways have been suggested as an excellent tool for the transfer from guidelines into local protocols and clinical practice.^[6] The utilisation of care pathways is expected to promote interprofessional teamwork and optimise resource allocation, thus leading to better organisation of care processes, increasing the efficiency and effectiveness of healthcare, and lower healthcare costs.^[6] This study describes the development of a care pathway for managing fatigue in patients requiring palliative care. The care pathway has been developed for the Department of Palliative Care of the University Hospital of Bonn, with the clinical care team of the department providing expert input.

MATERIAL AND METHODS

The care pathway will be developed using the following steps from the MRC model:^[7]

1. Developing an intervention
2. Piloting and feasibility
3. Evaluating the intervention
4. Reporting
5. Implementation.

This paper covers the first step of developing an intervention, which includes the evidence base identification, theory identification/development, and process/outcomes modelling.

Structural development of the care pathway

The care pathway was developed as a comprehensive method of planning, delivering, and monitoring care for patients with fatigue in palliative care. The care pathway illustrates the following process of care:

1. Screening for fatigue
2. A diagnostic procedure, including a fatigue questionnaire, history, physical examination, laboratory findings, and tests
3. Therapeutic management
4. Evaluation of effectiveness.

Users of the care pathways

The care pathway is designed to be explicitly used in the palliative care department, where they often need to treat

advanced illness patients with fatigue problems in the inpatient palliative care unit. The care pathway is also suitable for patients with fatigue treated in collaboration with the comprehensive cancer centre and patients seen with the consultation service in other hospital departments. It is expected that practitioners and administrators would work together to incorporate similar and compatible features of this care pathway.

User involvement

Two focus groups were planned to solicit feedback from potential pathway users. One focus group included healthcare professionals (physicians, nurses, psychologists, and social workers) working in different palliative care settings (university-hospital palliative care unit and consultation service, community-hospital palliative care unit, and home care team). A second focus group was planned with representatives of self-help groups identified from an online directory of self-help groups in the city of Bonn. All 12 self-help groups related to cancer were contacted and invited to participate. However, due to a lack of responses, only two representatives of self-help groups and a breast cancer care nurse were recruited for individual interviews.

Focus groups and interviews were organised through Zoom. The care pathway was presented to the participants, and feedback on the patient's needs and priorities related to fatigue and its treatment, additional burden from diagnostic or therapeutic interventions, presumed effectiveness, and overall evaluation of the pathway were discussed. The discussion was recorded, and a protocol was written and sent to participants to offer an opportunity for additional comments.

The chair of the Research Ethics Committee of the University Hospital of Bonn was informed of the focus group evaluation and confirmed that this was not a biomedical research intervention and, thus, did not require ethical approval.

RESULTS

Diagnostic management

Screening

Patients with severe life-limiting illnesses such as advanced cancer should be screened repeatedly for fatigue from diagnosis until completion of treatment.^[8] Screening should be performed and documented using simple instruments. Screening questions such as 'Do you feel unusually tired or weak?' or 'How weak are you?'/ 'How tired are you?' are recommended. Quantitative assessment of fatigue intensity can be done on a categorical (none, mild, moderate and severe) or numerical rating scale (NRS 0 = no fatigue and 10 = worst fatigue imaginable). Patients with moderate or severe fatigue or an intensity NRS >5 should receive a more detailed assessment. Patients with a high-risk but low intensity should be offered counseling and physical activity enhancement

to prevent or delay the development of fatigue.^[9] Screening steps are shown in [Figure 1].

In our German palliative care unit setting the minimal documentation system for palliative care patients (MIDOS), the German version of the Edmonton Symptom Assessment System will be used as a screening instrument. MIDOS consists of categorical scales for pain, dyspnoea, nausea, constipation, tiredness, weakness, depression, and anxiety (none, slight, moderate, and severe) and a categorical scale for well-being (very bad, bad, average, good, and very good). Patients are asked to rate these items on the day of assessment and the day before. Patients rating tiredness or weakness as moderate or severe for fatigue screening will be offered a more detailed assessment.^[10]

Assessment

The Brief Fatigue Inventory (BFI) will be utilised to assess our department's severity and impairment of fatigue. The BFI measures the severity of fatigue and impairment caused by fatigue using 0–10 numeric rating scales. The BFI consists of an initial question asking the patient whether he feels more than usual fatigue or tired. The three following questions asking for the intensity of fatigue on average, at its worst and at the moment (0 no fatigue, 10 worst you can imagine). Six more questions ask for the impairment of general activity, mood, walking ability, normal work and relations with others, and enjoyment of life during the past 24 h.^[10,11]

Malnutrition will be assessed with the short form of the patient-generated subjective global assessment of nutrition (PG-SGA), using the first four items of the instrument.

A thorough health history is necessary [Figure 2] to obtain data not only about the fatigue history, including type, severity, and temporal course of fatigue, but also other symptoms such as pain, dyspnoea, appetite loss, weight loss, sleep disorders, existential distress or depression that might contribute to fatigue.^[12] Comorbidities, as well as medication with sedative properties, should be documented. Social and environmental factors and alcohol, tobacco, or substance use should also be assessed.

A general physical examination is needed, checking for signs of infection, assessing hydration and nutritional status, and excluding any neurological deficits [Figure 3]. The body mass index should be calculated to assess cachexia. The examination should also include a functional test of the performance status of patients that are not bedridden. The time up and go (TUG) is suitable as a standard instrument. The patient sits on a chair and is asked to stand up, walk 2 meters, turn around and sit down as fast as possible. Grip strength can be measured with a dynamometer. Continuous physical activity assessment should also be included, for example, using body-worn sensors that record the position or smartwatch apps recording the number of steps. However, functional tests such as TUG or grip strength might not be appropriate for patients with low-performance scores due to advanced disease or temporary impairment, such as chemotherapy.

Several laboratory assessments are required to control organ dysfunctions that could cause or aggravate fatigue [Figure 4]. Additional diagnostic procedures that add to the patient's burden are rarely indicated in palliative care. Diagnosis of

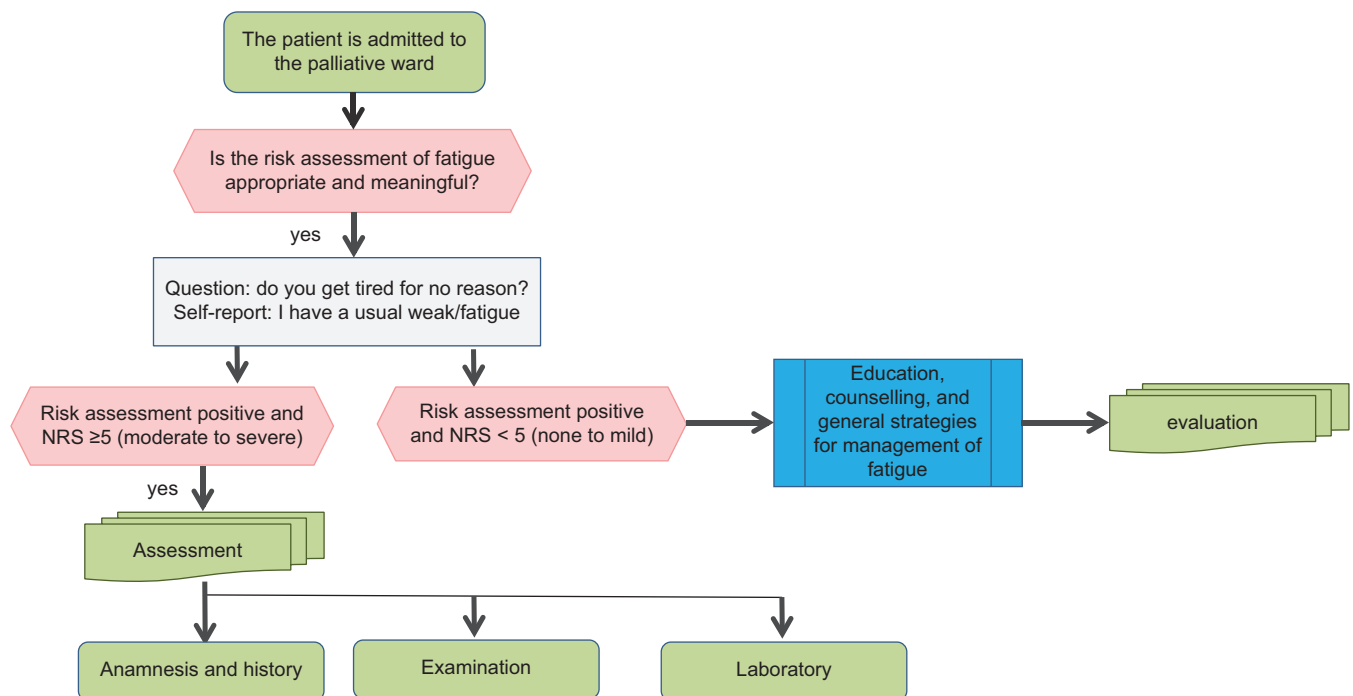


Figure 1: Screening process (adaptation from Cuhls *et al.*^[9] SOP - Fatigue).

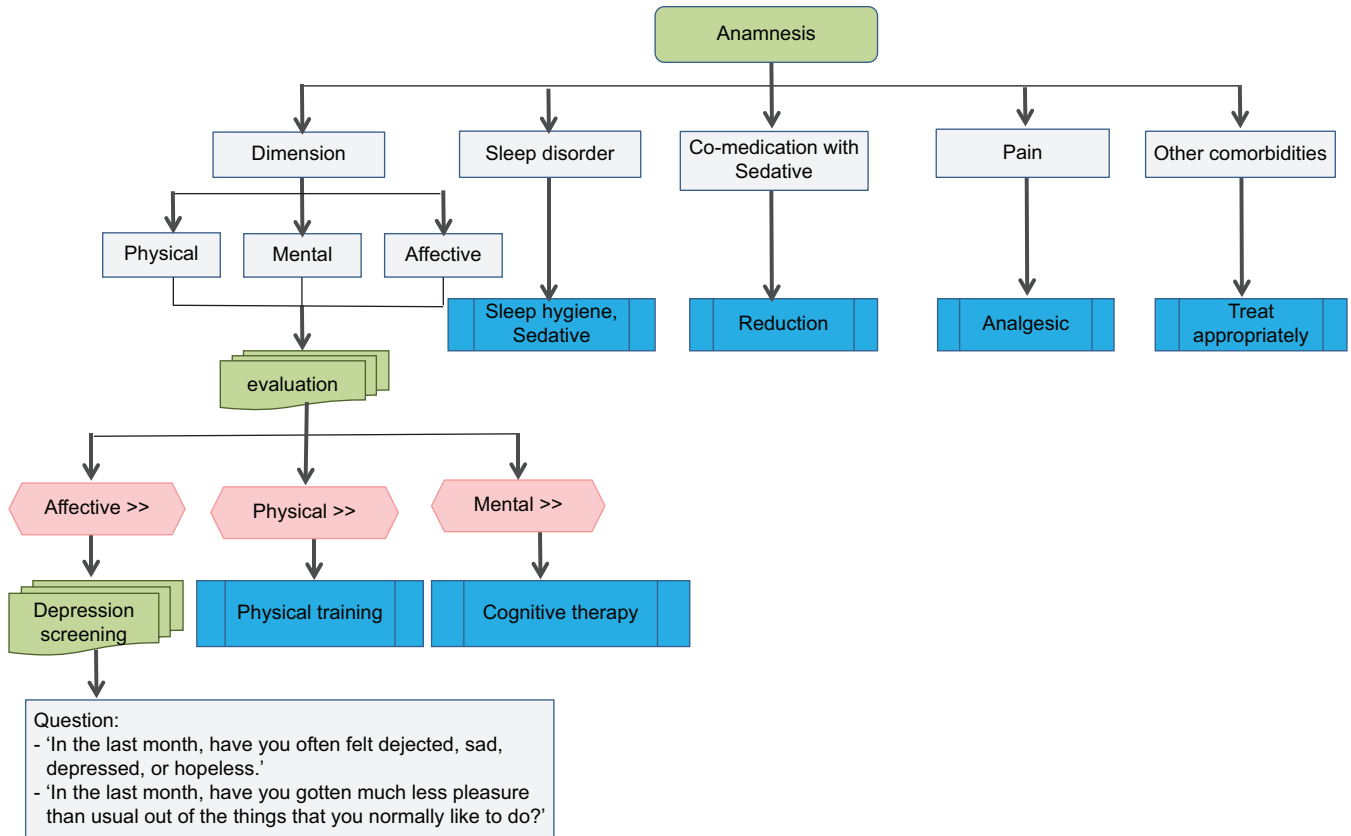


Figure 2: Diagnostic – anamnesis process (adaptation from Cuhls *et al.*,^[9] SOP - Fatigue).

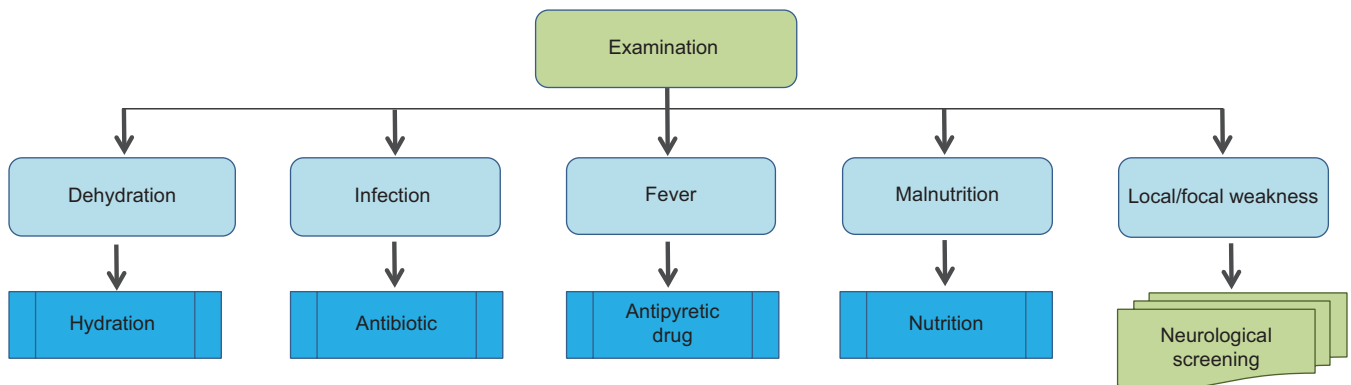


Figure 3: Diagnostic – Physical examination process (adaptation from Cuhls *et al.*,^[9] SOP - Fatigue).

cachexia is better made from a calculation of the appendicular muscular mass index from dual-energy X-ray absorptiometry or the skeletal muscle mass index from a lumbar CT scan. Still, both procedures usually are not performed in palliative care patients. However, if a lumbar CT scan has been done in the past weeks, a secondary evaluation might provide this index without additional burden to the patient. Feedback from the focus group with palliative care professionals highlighted the low-performance status of

many patients receiving specialist palliative care, which could render even short and simple functional tests impossible. This situation raised the question of whether these patients with very reduced performance status should be eligible for the fatigue pathway, or at least with careful consideration of the balance between the diagnostic and therapeutic burden and the potential benefit. Table 1 provides a checklist for use in clinical practice as a minimal dataset documentation sheet.

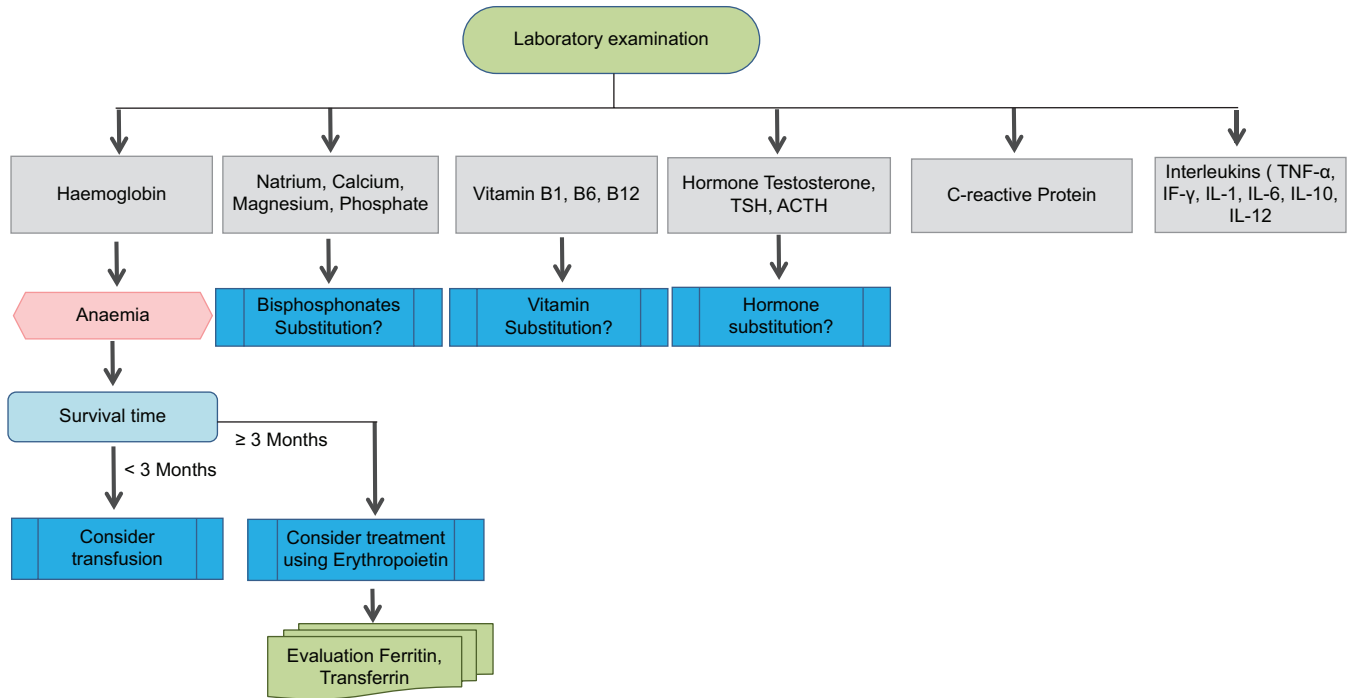


Figure 4: Diagnostic – laboratory examination process (adaptation from Cuhls *et al.*;^[9] SOP - Fatigue).

Therapeutic management

Before the therapeutic approach's planning, the patient and healthcare team must consent to treatment goals. As usual in palliative care symptom management, the therapeutic approach towards fatigue should consider first causal therapies if possible and pharmacological and non-pharmacological treatments if these causal therapies are ineffective. As most patients will not have one single aetiology of fatigue but rather a plethora of contributing and aggravating factors in addition to primary fatigue, the treatment regimen will have to include causal and symptomatic therapies for most patients [Table 2].

Causal therapy

Treatment of the underlying cause should be initiated in patients with secondary fatigue [Figure 5]. Some causes of secondary fatigue, such as anaemia, depression, infection, dehydration, malnutrition, electrolyte disbalance or treatment with opioids or other sedative medications can be treated. Effective causal treatment should alleviate fatigue. For example, blood transfusions can relieve fatigue in anaemic patients undergoing chemotherapy, or nutritional supplements can alleviate fatigue in patients with the early stages of cachexia.^[9]

However, any additional burden caused by these therapies has to be balanced carefully against the therapeutic benefit. For example, transfusions can alleviate fatigue but usually have to be repeated regularly, sometimes requiring the patient to continue with inpatient treatment to continue receiving the

transfusions. This prolongation might not be acceptable for a patient wanting to spend this last stage of life in a familiar setting at home. Aggressive treatment of potential causes of fatigue could lead to side effects or complications, resulting in a negative net effect of these therapies on the patient's health status.

Symptomatic pharmacological treatment

A recent Cochrane systemic review^[13] highlighted that some medications, such as corticosteroids, methylphenidate, and modafinil, might be beneficial for treating fatigue associated with palliative care. However, due to the limited evidence, there is no strong recommendation for a specific medication in this setting. An individual therapeutic trial could be indicated, with careful evaluation of the effectiveness and discontinuation of the medication if ineffective.

The psychostimulant methylphenidate has been demonstrated to affect fatigue in cancer patients positively. Several randomised controlled trials have demonstrated that the administration of methylphenidate improved fatigue compared to a placebo assessed by FACIT-F or BFI.^[14,15] Methylphenidate was also superior to a placebo in hospice patients with different types of advanced diseases.^[16]

Another medication used for the symptomatic treatment of fatigue is modafinil. Modafinil has initially been used for sleep disorders and narcolepsy but has been explored for the treatment of fatigue in recent studies of cancer patients. It appeared to be effective in alleviating fatigue for lung cancer patients using FACIT-F scores^[17] and in various

Table 1: Diagnostic checklist for fatigue.

Item	Norm values	Result
History		
Weight loss in last two months	>2kg	
Weight loss in last 6 months	>5kg	
Sleep	No sleep disorders	
Appetite	No appetite loss	
Nutritional intake	>1000 kcal	
Depression	No Depression	
Grief, anxiety, loss of meaning	No excessive distress	
Brief fatigue inventory		
PG-SGA	Total score<4	
Sedative medication		
Family, social network, caregivers		
Examination		
Height, weight	BMI>18.5 kg/m ²	
Time Up and Go (TUG)	<20 s	
Body temperature	< 37.5°C	
Neurological status	No sensory or motor deficits	
Grip strength	>20 kg (male) >15 kg (female)	
Laboratory		
Haemoglobin	11.7–15.5 gr/dL	
Haematocrit	35.0–47.0%	
Leucocytes	4.0–11.0×10 ³ /μL	
C-reactive Protein	<1.0 mg/dL	
Testosterone (for males)	300–1000 ng/dL	
TSH	0.5–5.0 mIU/L	
ACTH	10–50 pg/mL at 8 a.m	
Sodium	135–147 mEq/L	
Potassium	3.5–5.0 mEq/L	
Calcium	8.6–10.3 mg/dL	
Creatinine	0.7–1.3 mg/dL	
Other		
Lumbar skeletal muscle index (CT scan)	males>55 cm ² /m ² , females>39 cm ² /m ²	
Activity assessment with body-worn sensors (ActivPal)	Normal profile with standing, sitting and laying down	

cancer patients using BFI.^[18] Another study using modafinil to treat fatigue in multiple sclerosis patients demonstrated a clear beneficial effect of modafinil, although the participant numbers were small.^[19]

However, patients often do not continue with these two medications in clinical practice. Even with careful dose titration, restlessness seems to be a major side effect that offsets the therapeutic benefit.

At least for short-time relief, corticosteroids could improve fatigue in patients with advanced cancer.^[20,21] Dexamethasone 4 mg was compared with a placebo in a recent study to treat fatigue in 84 advanced cancer patients. In this study, dexamethasone was significantly superior to placebo,^[22] while methylprednisolone (16 mg twice daily for seven days) was used with significant effect in a study of patients with advanced cancer.^[23] Therapy with corticosteroids could be initiated with a high dose, with subsequent gradual tapering towards a maintenance dose.^[9] However, steroids such as

dexamethasone may lead to proximal myopathy after several weeks of application and, thus, should not be used for prolonged periods.^[24] Steroids seem to indicate specific short-term treatment goals rather than continuous treatments.

Symptomatic non-pharmacological treatment

Several studies have demonstrated that physical activity may decrease fatigue and improve palliative care patients' quality of life.^[25,26] A recent systematic review and meta-analysis reported that aerobic exercise interventions have the best result.^[27] The mode, intensity, and timing of exercise differed across the studies. The duration of training ranged from 6 weeks to 6 months.

In addition to physical exercise, the interviews named yoga and QiGong as other therapeutic options. Energy conservation has also been shown as an effective non-pharmacological intervention. Implementing a plan for energy conservation by prioritising tasks and managing

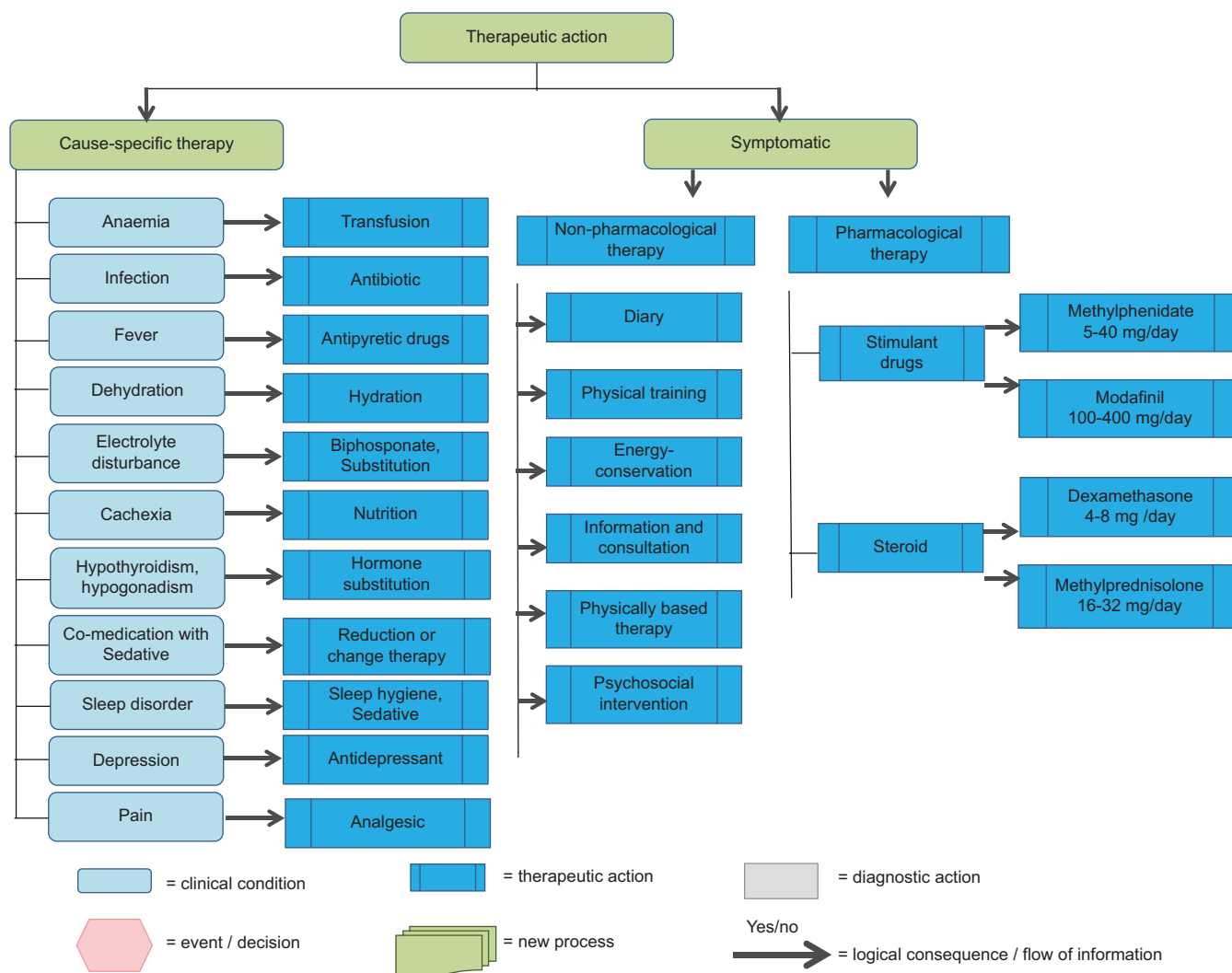


Figure 5: Therapeutic management (adaptation from Cuhls et al.,^[8] SOP - Fatigue).

activities could reduce fatigue and promote a healthy lifestyle.^[28]

Energy conservation can be supported with a fatigue diary [Figure 6] documenting activities and symptom intensity regularly throughout the day, which could point out particularly burdening activities or daytimes with less fatigue. Psychosocial therapy, such as cognitive behavioural therapy (CBT), has also been described as having a considerable role in treating fatigue. CBT helps to identify and cope rapidly with specific challenges. Several trials have demonstrated that CBT relieves fatigue in cancer patients.^[29]

DISCUSSION

Care pathways have been proven to be cost-effective while improving the quality of care and maintaining standardised outcome-oriented care.^[30,31] Pathways are a means towards efficient resource management, provision of more patient information, and a clinical audit tool. We describe the

Time	Activity	How tired	How weak	Comment
		0 = no	0 = no	
		1 = mild	1 = mild	
		2 = moderate	2 = moderate	
		3 = severe	3 = severe	

Figure 6: Example of diary for fatigue patient (adaptation from Cuhls et al.,^[8] SOP - Fatigue).

construction of a care pathway for fatigue in the palliative care setting. In developing the pathway, we integrated available published evidence, guidelines, and clinical experience. As a next step, the care pathway will be piloted in a specialist palliative care setting in the University Hospital Bonn as the first step towards implementation.

Fatigue in palliative care patients usually has a multifactorial aetiology and often is influenced by multiple cognitive, psychosocial, and biological factors. A structured approach

Table 2: Therapeutic checklist for fatigue.

	Therapeutic option?	Initiated (date)	Effectiveness/Comment
Treatment goal			
Causal therapy			
Transfusions	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Erythropoietin	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Antibiotics	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Antipyretics	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Hydration (Infusion)	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Electrolyte infusion	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Testosterone	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Thyroid hormone	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Antidepressant	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Sleep-inducing med.	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Pain medication	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Other:	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Pharmacological therapy			
Modafinil	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Methylphenidate	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Corticosteroids	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Other:	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Non-pharmacological therapy			
Physical training	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Yoga	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
QiGong	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Restoration therapy	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Energy conservation measures	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Psychoeducational intervention	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Cognitive behavioural therapy	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Self-help group contact (f.e. online)	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Information material for caregivers	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Information material for health-care professionals	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Case management	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Social Security Counselling	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Nutritional counselling	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Fatigue diary	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Day/week plan	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Other:	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	
Other:	<input type="checkbox"/> Yes <input type="checkbox"/> No	--/--/--	

to screening, assessment, and therapy is required for optimal treatment. A variety of different interventional approaches have been suggested to treat fatigue. Causal therapies are useful for some patients, but most will require symptomatic therapy with a combination of non-pharmacological and pharmacological interventions to alleviate fatigue adequately. However, the evidence base for most fatigue interventions is small and often restricted to cancer patients. Little evidence has been published on fatigue therapies in patients with other life-limiting diseases. This obscurity might raise a concern about their effectiveness and, in turn, whether the costs incurred for implementing a care pathway would be worthwhile. Considering the limited or not available evidence of causal therapies, expensive diagnostic or therapeutic approaches such as routine assessment of

cytokines or regular neurological or radiological screening is not warranted. However, considering the cost-benefit ratio, the direct and indirect costs of unrelieved fatigue must be considered. Considering the huge burden of fatigue reported by patients and their caregivers, even small therapeutic benefits would lead to a positive cost-benefit relationship. Studies have repeatedly demonstrated for a range of medical procedures that implementing a care pathway in patients was cost-effective compared to patients managed before implementing the clinical pathway.^[32,33]

A secondary aim of a care pathway is to improve the quality of care by optimising the use of resources. Given the complexity of the treatment of fatigue, a care pathway is expected to improve resource utilisation in the tertiary hospital and peripheral healthcare settings.

Finally, implementing this pathway is expected to raise awareness of fatigue as a major burdening symptom that greatly burdens patients and caregivers. It will increase healthcare professionals' understanding of their role as part of the interdisciplinary team as effective agents in treating this symptom. This will contribute to the relief of suffering and might prove as pivotal as implementing effective pain management 50 years since.

CONCLUSION

Guidelines for assessing and treating fatigue in palliative care patients have been published, but these have not yet been translated into clinical practice. We have developed a care pathway as a prerequisite for implementing structured fatigue management in palliative care patients. The next steps in the implementation will be piloting the care pathway in a tertiary hospital setting to evaluate the impact on clinical care, feasibility, acceptance, barriers to implementation, and costs related to the care pathway. Subsequent steps will include implementation and dissemination of the care pathway, surveillance and monitoring, and long-term follow-up that require a collaborative effort with a multidisciplinary approach – including palliative care, psychotherapy, physiotherapy, nutritional support, and self-help experts for implementing this complex intervention.

Declaration of patient consent

Patient consent is not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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