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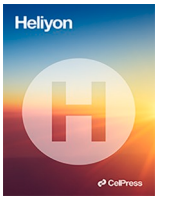

Review article

Current landscape and support for practical initiation of oncological prehabilitation translatable to thyroid cancer: A position paper

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ABSTRACT

Despite a growing body of evidence for the effectiveness of prehabilitation, the uptake of prehabilitation in Europe remains low. Contributing factors range from limited awareness and understanding of prehabilitation to a lack of supporting infrastructure and reimbursement challenges. In this position paper, the authors propose a new comprehensive definition of prehabilitation and identify differentiated thyroid cancer as a type of cancer particularly well-suited for prehabilitation. To support clinicians with the implementation of prehabilitation programs in their clinics, the authors discuss the following practical solutions: a) find the most appropriate prehabilitation program for each patient; b) raise awareness among peers; c) develop evidence to demonstrate the effectiveness of prehabilitation; d) expand the interdisciplinary team; e) expand your network and make use of existing assets; f) utilize learnings from the COVID-19 pandemic.

1. Introduction

Traditionally in oncology, adverse outcomes of physiological and psychological stress associated with cancer and cancer treatment have been managed with rehabilitation [1]. Prehabilitation is a newer approach with a focus on improving patient reserve and

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resilience so that they are better prepared to withstand an anticipated stress [1–6].

Historically, prehabilitation has been associated with the surgical field, and this is where the majority of evidence for multimodal prehabilitation currently exists [3,7,8]. Prehabilitation can also be applied to other acute treatments, such as stem cell transplant, chemotherapy, and radiotherapy, or long-term treatment, for example, in patients anticipating chronic hormone therapy or systemic anti-cancer therapy, which can include immunotherapy or tyrosine kinase inhibitor use [2,3,9–12].

Despite the growth of cancer prehabilitation research in recent years [3,7,9,13–16], awareness of prehabilitation within the medical and patient communities remains low, as evidenced by the infrequent use of the term "prehabilitation" in the literature and a lack of consensus on its definition. Low awareness, alongside financial and organizational barriers, significantly limits the uptake of prehabilitation across countries [9,17,18].

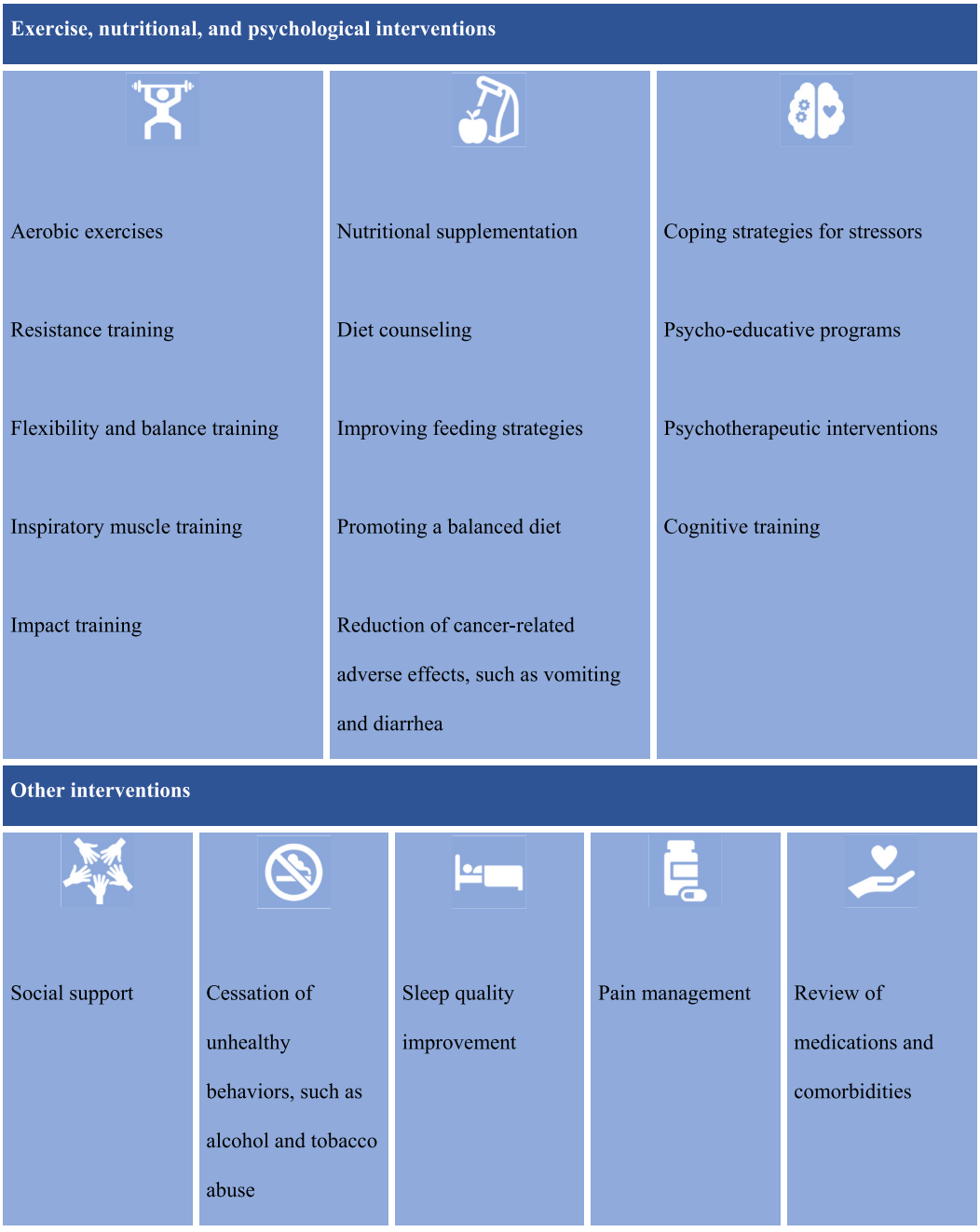

Fig. 1. Examples of prehabilitation interventions.

There is an increasing amount of evidence to support the importance of prehabilitation for all oncology patients [2,19]. However, certain cancer types, such as testicular cancer, malignant melanoma, prostate cancer, Hodgkin lymphoma, breast cancer, and differentiated thyroid cancer (DTC), may be particularly well-suited for prehabilitation, especially in the early stages, due to their excellent prognosis and relatively slow progression, which allows planning for treatment and prehabilitation ahead of time [20,21]. This article aims to increase awareness and understanding of prehabilitation as a concept and to support its wider implementation. Since there is an unmet need in patients with DTC, including hormonal imbalance, tiredness, and weight gain [20,22], and because they are particularly well-suited for prehabilitation, the emphasis is placed on these patients.

2. Defining prehabilitation

In the academic literature, there are two dominant definitions of prehabilitation [9]: "The process of enhancing the functional capacity of the individual to enable him or her to withstand a stressful event" [23], and "A process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment, includes physiological and psychological assessments that establish a baseline functional level, identifies impairments, and provides targeted interventions that improve a patient's health to reduce the incidence and the severity of current and future impairments" [2].

Although both definitions include important messages, the former is too brief and non-specific and does not provide sufficient information on prehabilitation in this context. While the latter provides more detail, it does not apply to long-term treatment or other diseases, since it is focused on acute cancer [2]. Establishing a more meaningful definition of prehabilitation is important for inspiring and empowering the medical community to use such programs in clinical practice [9]. As such, we propose a new, comprehensive definition: *Prehabilitation is the process of preparing a patient by prescribing multimodal needs-based interventions initiated at the time of diagnosis to minimize the negative impact of the disease and future treatments.* This definition succinctly covers all forms of prehabilitation, is tailored to individual patient needs, is not limited to a treatment or disease type, and highlights prehabilitation as part of a continuum of care. This will make it more accessible for increased numbers in the medical community, while maintaining the core principals of prehabilitation.

Prehabilitation should include exercise and nutritional and psychological interventions underpinned by behavior-change techniques, delivered by an interdisciplinary team (IDT) across the continuum of care [3,4,7,10,13,24–34]. As the first step to prevent and alleviate treatment-related side effects and toxicities and to preserve quality of life (QoL), prehabilitation complements rehabilitation and simultaneous care [35–40]. The impact of prehabilitation, however, goes beyond that, as emerging evidence suggests that prehabilitation may be associated with higher rates of tumor regression [15,41]. Prehabilitation interventions must be tailored to the needs of the individual [10,24] and may involve the various activities and procedures summarized in Fig. 1 [3–5,7–9,17,25–27,33,34,42–50]. Responsiveness to these interventions and patient progression must be monitored at all times [10,24,51].

3. Current prehabilitation landscape

The benefit of surgical prehabilitation to patients is well established and includes positive impacts on mortality and morbidity, post-operative complication rates, recovery and health-related QoL, the need for further care, the length of hospital stays, and the number of short-notice surgery cancellations [2,3,6–8,10,13,51–59]. Although lifestyle factors are not specifically prehabilitation interventions, the benefits of reduction in alcohol consumption and smoking cessation on post-operative outcomes have long been known [60]. These factors should be considered as standard care and an adjunct to the delivery of the needs-based prescribed pillars of prehabilitation previously described. Existing evidence indicating the effectiveness of perioperative multimodal prehabilitation suggests that similar outcomes might be expected for prehabilitation in non-acute, non-surgical contexts, such as stem cell transplant, chemotherapy and radiotherapy [2,3,9–12]; however, a more established evidence base for non-surgical interventions is needed [3,9,10]. One of the reasons for this is that markers of efficacy for non-surgical prehabilitation may be different from those for perioperative interventions (e.g. relative dose intensity, dose tolerance, discontinuation of treatment course, patient-reported health) as sequelae of treatments such as chemotherapy or radiotherapy may have a more gradual onset than the acute stress of surgery [3]. An emerging knowledge base has begun to demonstrate the benefit of prehabilitation ahead of various treatments, including systemic therapy, justifying further exploration [3,61]. One small proof-of-concept, randomized, controlled trial in women with breast cancer showed that 30 min of vigorous-intensity exercise 24 h prior to anthracycline administration attenuated cardiac damage [3,62]. A retrospective study on patients with head and neck cancer illustrated better-preserved swallowing function 3 months post-treatment in patients who had received swallowing exercises prior to chemoradiation therapy versus patients who had received the exercises after treatment [63], with similar evidence demonstrated in other studies [64]. In patients with gastrointestinal cancer, those receiving QoL interventions led by a psychologist or a psychiatrist, such as social (e.g. communication strategies, interpersonal relationships), cognitive (e.g. healthy lifestyle choices, goal setting) and emotional (e.g. stress management, assertiveness) support, were more likely to complete their planned chemoradiation regimens than those in the control group [49]. The same study also reported higher rates of completed chemoradiation and fewer required hospitalizations in the intervention versus control group [49]. Potential benefits of multimodal prehabilitation have also been found in patients with refractory DTC treated with lenvatinib [61]. While research to date is encouraging, prospective, randomized, high-powered studies are needed to verify the findings and increase their generalizability [3,42,51,55].

4. Prehabilitation in DTC

The incidence rate of thyroid cancer is rising, with 586,202 new cases observed globally in 2020 [65,66]. DTC, which includes papillary thyroid carcinoma and follicular thyroid carcinoma, comprises over 90 % of all thyroid cancers [67,68]. Patients with DTC may be particularly well-suited to prehabilitation because of the patient and disease characteristics. The 10-year survival rate of patients with papillary thyroid carcinoma is about 80–95 %, and it is about 70–95 % in patients with follicular thyroid carcinoma [67,69]. Such favorable prognoses, as well as the indolent nature of DTC in the majority of patients, allow sufficient time to introduce multimodal prehabilitation ahead of primary and secondary DTC treatments [70]. Patient well-being affected by the disease is another factor making thyroid cancer particularly suitable for prehabilitation: patients with thyroid cancer are at risk of developing symptoms of anxiety and fatigue [71,72], and self-reported QoL in thyroid cancer survivors is either similar to or worse than that of other cancer survivors [73]. Hormonal imbalance during treatment is common in DTC, resulting in fatigue, weight gain, and reduced exercise capacity [22,74]. Exercise, nutrition, and psychological or emotional interventions underpinned by behavior-change techniques have the potential to counter these stresses.

Despite its potential suitability for prehabilitation, little evidence exists in the literature, with only one study on radioactive iodine-refractory DTC published so far [61]. Moreover, there are currently no ongoing clinical trials on prehabilitation in thyroid cancer. Out of four active Phase 3 and 4 studies on prehabilitation in adults, there are two studies on gynecological cancer, one on pancreatic cancer and one on colorectal cancer (as per clinicaltrials.gov, December 2023). Prehabilitation uptake may be significantly limited by a lack of other reports on the effectiveness of prehabilitation in patients with DTC, as well as the aforementioned low awareness of the concept [9], lack of an exhaustive, widely recognized definition [9], and sparse research on non-surgical prehabilitation in general [3,61]. Other potential barriers to uptake in DTC as well as other cancers are presented in Table 1 [10,17,18,24,75–83].

The barriers may vary across countries.

5. Proposed solutions to increase the uptake of prehabilitation

Solutions to widespread adoption of prehabilitation may be time-consuming and resource-heavy and are yet to be implemented [17,24]. In the absence of a structured approach to prehabilitation [17,24,84], here we propose steps for the immediate initiation of prehabilitation and encourage healthcare professionals to implement the solutions that they find applicable in their clinics. Since the literature on prehabilitation in thyroid cancer is sparse and a targeted literature review conducted of the PubMed database returned only four results, the recommendations are largely based on the authors' clinical experience (see the supplementary materials for the search strategies and results). An outline of relevant prehabilitation and rehabilitation interventions discussed below, including key findings and the level of evidence, is available in the supplementary materials.

5.1. Solution 1: find the most appropriate prehabilitation program for each patient

It is highly unlikely that a "one size fits all" approach to prehabilitation would be universally beneficial, feasible, and acceptable to patients. In a recent study on prehabilitation in patients with colorectal cancer, a compliance rate of $\geq$80 % to both the exercise and nutritional interventions was achieved in only 67 % of participants [85]. Notably, of the patients who were eligible for inclusion, 67 % declined to participate, citing reasons including the program being too much (40 %), role of informal caregiver, diet restrictions, difficulty traveling to the hospital, living too far from the hospital, and moderate physical condition. This low participation rate is consistent with previous studies [86,87]. Additional visits for exercise sessions can be a burden to those who are already attending multiple hospital appointments, with transport-related problems presenting a significant barrier to uptake [88].

The prehabilitation program should be tailored and prescribed but should also where possible largely address the needs, capabilities, and preferences of the patient and should consider the patient's individual comorbidities, physical condition, nutritional status, frailty, and social role, as well as psychological burden, psychosocial concerns, and the expected treatment modality. It is also important to prevent unnecessary interventions and to ensure optimal use of limited healthcare resources [27]. An optimized

Table 1
Barriers to the uptake of prehabilitation.

Related to healthcare system	•**Reimbursement challenges and delivering "return on investment" which are recognized as tangible cost saving for the health systems involved** •**Health inequalities and disparity in access to prehabilitation**
Related to infrastructure	•Lack of institution-wide commitment and supporting infrastructure •Limited access to space to screen and assess patients together with the delivery of the interventions [personal communication]
Related to healthcare professionals	•Lack of established assessment tools •Apprehension or discomfort in providing exercise guidance among many healthcare professionals •Lack of educational opportunities highlighting the benefits of exercise
Related to patients	•Limiting comorbidities •Transport-related problems •Time and financial worries •Lack of motivation •Feeling overwhelmed •Lack of technical abilities required to effectively participate in virtual aspects of prehabilitation

recommendation should be formulated based on current guidelines and recommendations and adapted to the individual patient following an intake assessment of the patient by a dedicated IDT. There is a lot of traction in the further development of guidelines and ongoing Delphi processes to address the lack of evidence and consensus around the utilization of screening and assessment tools. Moreover, the patient, and eventually their caregiver, should be actively encouraged and supported to participate in crafting the program and to give feedback on its feasibility. Ideally, this setting should be available in all clinics treating patients with malignant tumors, and the execution or guidance of the prescription should not be limited to one specific institution.

In contrast with typical cancer patients undergoing prehabilitation, patients with thyroid carcinoma are often of a younger age but are expected nonetheless to undergo significant metabolic changes due to changed hormonal status after thyroid surgery. Treatment with iodine-131 following thyroid surgery requires, in some patients, withdrawal of thyroid hormone substitution for up to 6 weeks, rendering the patients hypothyroid. During this period, patients are expected to follow an iodine-restrictive diet to improve the efficacy of treatment. This can pose significant challenges. Patients often feel tired, gain weight, and have a reduced exercise capacity. Even after recommencing thyroid hormone substitution, many patients receive a supraphysiological dosage of levothyroxine, as thyroid-stimulating hormone–suppressive therapy, for a period ranging from a few months to lifelong; this can affect mood, exercise capacity, body composition, and body weight. The short-term surgical outcome for these patients is generally very good, and the complication rate, which was often the endpoint of studies investigating the effectiveness of prehabilitation, is low and is therefore not an adequate parameter to assess prehabilitation impact. Understanding whether, and in which form, prehabilitation is helpful for these patients is mandatory in order to harness its full potential. For patients with advanced disease or for those who require systemic treatment, prehabilitation can be expected to reduce fatigue (which may be present in this context), reduce drug toxicity, and improve adherence to treatment. Patients with thyroid cancer also report shoulder complaints after surgery [89], which may be mitigated by the inclusion of physical exercises to optimize shoulder function.

In order to maximize the benefit to the patient, healthcare providers may consider the following [25]:

- Start on an individual basis or with a small group of patients and plan individualized interventions.
- Prepare a pragmatic, feasible protocol with your team that targets the patient's needs based on their screening and assessment outcomes.
- Identify outcomes meaningful to the patient, funders, and other stakeholders.
- Identify patients who could be independent and those who need closer supervision and more interaction.
- Consider delivering prehabilitation in community settings to increase its cost-effectiveness and to ensure patients' comfort and autonomy.
- Establish regular contact with patients and determine whether they are compliant.

Table 2
Screening and assessment tools used in prehabilitation programs.

Application	Exemplar tools
Nutrition	Malnutrition screening tool [92]
	Nutrition Risk Screening 2002 [93]
	Patient-Generated Subjective Global Assessment [94]
	Food Frequency Questionnaires [95]
	Bioelectrical impedance analysis [96]
	Biochemical measurements [97]
Cardiorespiratory fitness	Cardiopulmonary exercise testing [98]
	Six-minute walk test [7]
	Incremental shuttle walk test [99]
Muscle strength and functionality	One-repetition maximum strength test [100]
	Hand grip [101]
	30-s sit to stand test [102]
Physical activity	International Physical Activity Questionnaire Short Form [103]
	Accelerometery [104]
Balance	Unipedal stance test [105]
	Y Balance Test [106]
Psychological well-being	Generalized Anxiety Disorder-7 questionnaire [107,108]
	Patient Health Questionnaire-9 [109,110]
Frailty	Geriatric 8 questionnaire [111,112]
QoL	EORTC QLQ-C30 [113]
	EORTC QLQ-THY34 [114]
Adverse events assessment[a]	Common Terminology Criteria for Adverse Events version 5.0 [115]
Fluctuations in hormone levels associated with certain treatments, such as thyroxine withdrawal, supraphysiological levothyroxine doses [22,74]	Assessment of thyroid function with thyroid-stimulating hormone and free thyroxine tests when drug adjustments are anticipated

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life of Cancer Patients core questionnaire; EORTC QLQ-THY34, European Organisation for Research and Treatment of Cancer Quality of Life Thyroid Cancer questionnaire; QoL, quality of life.
[a]This includes but is not limited to the assessment of adverse cardiac events, pulmonary complications, delirium, and cognitive post-operative functioning.

- Utilize existing screening and risk assessment tools to evaluate patients' physical and psychological conditions, barriers that patients may encounter when asked to participate in the program, and solutions to these barriers [10,42,90,91]. Existing tools are presented in Table 2.

To gain a clearer understanding of the treatment landscape and patient needs, healthcare providers should consider conducting surveys for patients and clinicians and involving patient representatives in the process of developing prehabilitation programs.

Useful examples:

- The Peri Operative Program (POP) – practical patient-centered approach to prehabilitation [25,116].
- The Person-Based Approach – patient-centered methods and tools designed to develop effective health interventions [25,117].
- Three sets of interviews with cancer patients encouraged to exercise prior to their treatment, which informed the design of the WesFit pilot program [118].
- Holistic Needs Assessment – questionnaire for patients at any stage of the cancer pathway designed to help identify patients' concerns and needs and develop a Personalized Care and Support Plan [119].

5.2. Solution 2: raise awareness among peers

Increasing awareness is vital to improve uptake, and peer-to-peer communication plays an important role. Methods to achieve this can include national and international cancer congresses, local/departmental seminars, workshops, journal clubs, and lunch and learn events.

The "learning community" model of group learning can support the dissemination and implementation of healthcare innovations [120]. In this model, participants work together with content experts, or "champions" to identify challenges and strategies that could help overcome barriers to adoption, with the goal of sharing learnings with a broader audience. This model provides a collaborative, motivational environment for discussion that can bring about meaningful organizational change.

In order to increase uptake and improve outcomes of prehabilitation in DTC, increasing awareness via peer-to-peer communication is vital. For example, in a qualitative study of prehabilitation in colorectal cancer, low awareness of the importance and potential of a prehabilitation program in healthcare professionals was identified as a major barrier to implementation, highlighting the importance of knowledge exchange. Raising awareness among patients is also of key importance: patients often believe that sedentary behavior is appropriate following a cancer diagnosis and are unaware of the potential impact of surgery on their physiological, metabolic, and psychological condition.

Useful examples of knowledge dissemination:

- Case study on the "Lunch and Learn" initiative organized by Health Education England [121].
- Conference abstract discussing a successful implementation of the journal club activity [122].
- Talk by Ceinwen Giles about her experiences as a cancer patient and how health services often reflect the priorities of providers and not patients [123].
- UK conference on prehabilitation [124].
- Prehabilitation World Congress [125].

5.3. Solution 3: develop evidence to demonstrate the effectiveness of prehabilitation

Providing high-quality evidence from prospective intervention studies for the effectiveness of multimodal prehabilitation is paramount. This can advance our understanding of how to tailor prehabilitation, both in generic terms and to respond specifically to the needs of patients with particular forms of cancer, e.g. thyroid carcinoma. Most current evidence in the field covers the application of various prehabilitation programs, often a combination of physical training and nutritional interventions, in patients preceding major surgery, such as abdominal surgery (for colorectal cancer and for gynecological malignancies) and thoracic surgery. Patients eligible for inclusion in these studies were mostly physically and nutritionally frail elderly patients. The most-assessed primary endpoints represent an improvement in short-term outcomes for patients, such as reduced complication rates and hospital length of stay, and an improvement in short-term recovery rates. Although prehabilitation has been shown to improve these outcomes in the aforementioned patient categories, its potential impact in other cancer patient groups and the effect of prehabilitation on other endpoints such as short- and long-term QoL, self-efficacy, and coping remain to be determined. These outcomes may be particularly important in those patients who become long-term survivors.

Prehabilitation programs can pose problems with reimbursement in many countries. Demonstrating the efficacy of responsible and sustainable prehabilitation programs may help to mitigate this problem. Studies that probe the cost-effectiveness of prehabilitation, considering not only medical costs but also total societal costs, in differing cancer patient populations are important.

Ultimately, demonstrating the efficacy of affordable prehabilitation programs will improve their acceptability and uptake and incorporation as an integral part of the care continuum for cancer patients and the patient journey.

Therefore, conducting randomized clinical trials to generate prospective data firstly on the efficacy, which is yet to be proven in patients with DTC, and then effectiveness of prehabilitation in this patient cohort would provide the strongest evidence for the increased uptake and acceptance in the field. The need for clear research priorities to inform the design of future prehabilitation trials has been recognized in a recently published international Delphi study [126]. The top research priorities in prehabilitation for patients

undergoing cancer surgery identified by a panel of prehabilitation experts included the effect of prehabilitation on surgical outcomes, identifying populations most likely to benefit from prehabilitation and optimal composition of prehabilitation programs [126]. In the absence of randomized clinical trials, healthcare providers may consider establishing a small independent study using existing study protocols and practical tips from other researchers.

Useful protocols and practical examples:

- PREHAB clinical trial protocol [127].
- SafeFit [128]/WesFit [129].
- FIT4TREAT study protocol [130,131].
- "From theory to practice: an international approach to establishing prehabilitation programs" – practical suggestions on conducting prehabilitation programs and studies from across countries [25].

5.4. Solution 4: expand the IDT

Growing evidence emphasizes the importance of interdisciplinary and multidisciplinary rehabilitation, which address the complex needs of patients with cancer through a more comprehensive approach compared with monodisciplinary care. In the rehabilitation setting, a systematic review of the effects of multidisciplinary outpatient cancer rehabilitation showed positive effects on the physical and/or psychosocial status of cancer patients [132]. In the context of prehabilitation, in frail colorectal cancer, preoperative evaluation by an IDT (consisting of at least one representative core medical specialist, a clinical pharmacist, a physiotherapist, a dietician, and a nurse specialist) was shown to improve risk stratification and prehabilitation, resulting in post-operative outcomes comparable with those of non-frail patients [133]. A systematic review of multimodal prehabilitation in patients with breast cancer indicated that prehabilitation improved physical function, QoL, and psychosocial variables, with a preference for multimodal versus unimodal provision. However, multimodal prehabilitation models are heterogeneous and diverse in the mode of administration, the professionals involved, the duration of intervention, and how the results are assessed, which can make comparing outcomes difficult [134].

An effective prehabilitation team should be multi/interdisciplinary, including professionals specializing in the range of modalities required to optimize patient outcomes, including specialized nurses, oncologists, surgeons, exercise physiologists/instructors, sports physicians, physiotherapists and/or physiatrists, nutritionists and/or dieticians, psychologists, and behavioral scientists to support with adherence and motivation. The patient, carer, and family are an integral part of this team and essential in the shared decision-making process. Working as a team from the outset will ensure the IDT has adequate knowledge on the disease and the anti-cancer treatments that are discussed/decided upon and that all team members are aware of the prehabilitation strategy to allow ample opportunity for discussion on aspects of patient care.

Importantly, patients' partners/families can be critical supports during the distressing phases of the continuum of cancer care and may be integrated into prehabilitation programs [135].

Examples of multimodal prehabilitation from across the globe:

- The Peri Operative Program at McGill University – a structured, personalized prehabilitation program in Canada involving a team of surgeons, anesthesiologists, internists, nurses, physiotherapists, exercise physiologists, nutritionists, psychologists, volunteers, and a patient representative [25,116].
- Involvement of an IDT in the prehabilitation program at the Maxima Medical Centre in the Netherlands [25,136].
- Multimodal prehabilitation pilot program involving an IDT in patients with radioactive iodine refractory DTC ahead of a systemic therapy at Germans Trias I Pujol University Hospital [61].
- PeriopFit: a Prehabilitation Medicine Service funded by University Hospital Southampton NHS Foundation Trust [137].

5.5. Solution 5: expand your network and make use of existing assets

In addition to building a network with other healthcare experts, healthcare providers may consider gaining the insight of patient advocacy groups and charities on prehabilitation programs. Many relevant resources have already been developed; relevant existing patient-focused materials can be promoted to patients where appropriate.

- International Prehabilitation and Perioperative Exercise Testing Society. https://ipoetts.org/– the purpose of the organisation is to support the gathering and sharing of knowledge about prehabilitation, create a support network for stakeholders in prehabilitation, and facilitate the implementation of prehabilitation programs [125].
- Shine Cancer Support – a cancer support charity for young people [138].
- Online workshop for healthcare professionals organized by Shine [139].
- pRosPer – a cancer prehabilitation and rehabilitation program [140].
- Fit4Surgery – a program that helps patients prepare for and recover after surgery [141].
- Prehab4Cancer and Recovery Programme – an exercise, nutrition, and well-being scheme in Greater Manchester [11,13,142].
- SafeFit – online exercise and well-being programs for cancer patients during lockdown (online version of WesFit) [143].
- PeriopFit: Wessex Prehabilitation Medicine Service in University Hospital Southampton NHS Foundation Trust [137].

- Getting It Right First Time – a program designed to improve medical care within the NHS by reducing variability in service delivery [144].
- Kent & Medway Prehab – a prehabilitation program utilizing a multidimensional telehealth resource to help prepare cancer patients for treatment [145].
- PREPARE – a program helping patients get ready for an esophago-gastric surgery [146].
- MeFit – the Medway prehabilitation service supporting patients to improve their health before an operation [147].
- The prehabilitation program at the Maxima Medical Centre in the Netherlands, focused on colorectal surgery [25,136].
- The lung cancer prehabilitation program at Barts Health [148].
- ONCOMOVE – a prehabilitation and rehabilitation program for cancer patients created by the Oncology Supportive Care Research Association in Portugal [149].
- Alvie – digital health coaching and expert guidance to support patients through all diagnosis and treatment stages [150].
- GM Active – a collaboration of 12 leisure and community organizations from across Greater Manchester aiming to get more people physically active [151].
- Existing guidelines, such as "Principles and guidance for prehabilitation within the management and support of people with cancer" by Macmillan Cancer Support [10].
- Prepwell – a community-based prehabilitation service in the UK [152,153].

Examples of materials developed for patients:

- University College London Hospitals Surgical School video for prostate cancer patients [154].
- Life Kitchen cookery school for people whose taste and smell have been affected by cancer, cancer treatment, or COVID-19 [155].
- Activity videos (e.g. yoga, Pilates, well-being break) by Shine Cancer Support [156].
- Prehabilitation leaflet for patients by MeFit (the Medway prehabilitation service) [147].
- Exercises for patients diagnosed with cancer by The Royal Marsden [157].
- "Eating well" booklet for patients with cancer by The Royal Marsden [158].
- The Macmillan booklet for patients who struggle with maintaining their weight during and after cancer treatment [159].
- "Eat well during cancer" booklet by World Cancer Research Fund, helping patients cope with cancer and cancer treatment side effects [160].
- ONCOMOVE manual and online materials for cancer patients [161,162].

5.6. *Solution 6: utilize learnings from the COVID-19 pandemic*

The COVID-19 pandemic transformed clinical practice, leading to an accelerated introduction of technology specifically in the field of telemedicine. Health centers are now equipped with computer-based communication systems, and contact with patients by this method is now more common. In addition, many clinician agendas now allow the possibility of a virtual visit. These changes in the healthcare system offer great potential, and learnings from the pandemic can be incorporated into the prehabilitation model.

The successes of a digital approach are already becoming evident in the literature. In the rehabilitation setting, a systematic review of telerehabilitation in older adults during the COVID-19 pandemic found that a digital strategy could overcome many of the field's obstacles; in some cases, it was found to be more effective than traditional methods [163]. The PROACTIVE trial, exploring experiences with telehealth in patients with head and neck cancer, reported the learning experience was not compromised when speech language pathology interventions were rapidly transitioned from in-person to teleconference sessions as a result of the pandemic [164]. A study on an exercise-based telerehabilitation program in adult cancer survivors found overall satisfaction of participants and no reports of major adverse events, demonstrating that virtual rehabilitation programs may be a successful alternative to the traditional in-person approach [165]. The California Health Care Foundation established the Connected Care Accelerator program, a quality improvement initiative to support health centers to quickly make changes to technology, workflows, and staffing to accommodate telehealth visits. This initiative demonstrated that telehealth can deliver accessible, convenient, patient-focused care. However, the authors caution that further research is needed to ensure effective implementation, particularly with regard to health equity [166].

Healthcare providers should consider how digital technology can be adopted in the prehabilitation space, for example, by identifying elements of prehabilitation programs that could be delivered to patients in their homes (see SafeFit trial [128]). Existing approaches within institutions can be audited and small changes implemented, building on relevant measures taken during the pandemic. For inspiration, healthcare providers may consider participating in events providing updates on COVID-19 to learn from healthcare leaders and to facilitate networking with peers.

Useful examples/resources:

- Prehabilitation interventions utilizing technology, for example, in-home physical exercise, personal apps, computerized cognitive training, remote fitness assessment monitored by web-camera, teleconsulting [1,5,7,13,45,46,143,167–172].
- Fit4SurgeryTV – an at-home prehabilitation program developed for frail older colorectal cancer patients [170].
- Webinar series by The Royal Society of Medicine aiming to provide healthcare workers with updates on COVID-19 [173].
- SafeFit Trial – NIHR COVID-19 Priority Trial: virtual clinics to deliver a multimodal intervention to improve physiological and psychological well-being for people with cancer (or suspicion of cancer) [129].

6. Discussion

Prehabilitation is the process of improving patients' physiological and psychological resilience so that they are better prepared to cope with a disease or treatment-associated stress [1–6] This approach is demonstrative of a shift from reactive to proactive healthcare and, together with rehabilitation and simultaneous care, forms a holistic approach to cancer patient support [1–6,38,40]. Having recognized a lack of consensus on the meaning of prehabilitation as one of the main barriers to its adoption [9], we propose a new definition to convey the meaning of prehabilitation in the hope of inspiring clinicians to develop and implement relevant interventions in their practices. Clinical evidence thus far has demonstrated the benefit of prehabilitation ahead of various surgical treatments, yet research on prehabilitation prior to non-surgical and systemic treatments is sparse, which may contribute to limited prehabilitation uptake [3,61]. In the absence of a structured approach to prehabilitation [17,24,84], we propose six solutions for the immediate initiation of prehabilitation programs and share examples of successful interventions to date. We encourage healthcare professionals to assess the applicability of the proposed solutions and implement one or many of them in their clinics as they see fit. Although the interventions should be considered for all oncological patients, certain cancer types are particularly well-suited for prehabilitation due to their excellent prognosis [20,21]. One such cancer type is DTC, as its relatively slow progression allows sufficient time to introduce multimodal prehabilitation ahead of primary and secondary treatments [67,69,70]. However, to our knowledge, only one study on prehabilitation in DTC has been published so far [61], highlighting an urgent need for future research in the thyroid cancer space and other under-researched cancer types. The future of prehabilitation landscape will likely evolve to integrate emerging technologies and virtual and or/home-based interventions [174], in line with the adoption of telemedicine in wider patient care, as long as these interventions have proven beneficial, safe, and are aligned with patient needs. The advancements in digital interventions have the potential to empower patients and increase their participation in health management and recovery, contributing to sustainable adoption of prehabilitation [174]. The development of new guidelines and consensus processes will aim to deliver core outcome sets around screening, assessment, delivery, and description of the pillars of prehabilitation. All in all, future studies and step-by-step implementation of prehabilitation on a local scale, alongside an ongoing digital transformation of medicine, have the potential to change the treatment landscape and constitute prehabilitation as a standard of cancer care.

CRediT authorship contribution statement

S. Jack: Writing – review & editing, Validation, Supervision, Methodology. **E. Andritsch:** Writing – review & editing, Validation, Supervision, Methodology. **A. Joaquim:** Writing – review & editing, Validation, Supervision, Methodology. **M.C. Kreissl:** Writing – review & editing, Validation, Supervision, Methodology. **L. Locati:** Writing – review & editing, Validation, Supervision, Methodology. **R.T. Netea-Maier:** Writing – review & editing, Validation, Supervision, Methodology. **J.L. Reverter:** Writing – review & editing, Validation, Supervision, Methodology. **R. Elisei:** Writing – review & editing, Validation, Supervision, Methodology.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Rossella Elisei reports financial support was provided by Eisai Europe Ltd. Rossella Elisei reports a relationship with Eisai Inc that includes: consulting or advisory. Rossella Elisei reports a relationship with Ipsen that includes: consulting or advisory. Rossella Elisei reports a relationship with Bayer that includes: consulting or advisory. Rossella Elisei reports a relationship with Lilly that includes: consulting or advisory. Rossella Elisei reports a relationship with Roche that includes: consulting or advisory. J.L. Reverter reports a relationship with Eisai Inc that includes: consulting or advisory. R.T. Netea-Maier reports a relationship with Eisai Inc that includes: consulting or advisory. L. Locati reports a relationship with Eisai Inc that includes: consulting or advisory, funding grants, and speaking and lecture fees. L. Locati reports a relationship with MSD that includes: consulting or advisory, funding grants, and speaking and lecture fees. L. Locati reports a relationship with Merck Serono that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Lilly that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Sanofi that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Sun Pharmaceutical Industries Ltd that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Ipsen that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Bayer that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Roche that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with Instituto Gentili Srl that includes: consulting or advisory and speaking and lecture fees. L. Locati reports a relationship with New Bridge that includes: consulting or advisory and speaking and lecture fees. E. Andritsch reports a relationship with Eisai Inc that includes: consulting or advisory. A. Joaquim reports a relationship with Bristol Myers Squibb that includes: consulting or advisory. A. Joaquim reports a relationship with Eisai Inc that includes: consulting or advisory and speaking and lecture fees. A. Joaquim reports a relationship with Merck that includes: consulting or advisory and speaking and lecture fees. A. Joaquim reports a relationship with MSD that includes: consulting or advisory and speaking and lecture fees. A. Joaquim reports a relationship with Novartis that includes: consulting or advisory. A. Joaquim reports a relationship with Pfizer that includes: consulting or advisory and speaking and lecture fees. A. Joaquim reports a relationship with Roche that includes: consulting or advisory. A. Joaquim reports a relationship with Daiichi Sankyo Inc that includes: speaking and lecture fees. A. Joaquim reports a relationship with Gillead that includes: speaking and lecture fees. A. Joaquim reports a relationship with GlaxoSmithKline Inc that includes: speaking and lecture fees. A. Joaquim reports a relationship with Lilly that includes: speaking and

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Appendix A. Supplementary data

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