# Exercise Recommendation for People With Bone Metastases: Expert Consensus for **Health Care Providers and Exercise Professionals**

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QUESTION ASKED: What are the best practice recommendations for exercise programming for people with bone metastases?

**SUMMARY ANSWER:** People with bone metastases should be supported and encouraged to engage in regular physical activity, including structured exercise, to obtain the well-established general health benefits and as a strategy to manage side effects related to cancer and treatments. Perceived risks of skeletal complications should be weighed against the potential health benefits in consultation between the person with bone metatases, health care team, and exercise professional.

WHAT WE DID: The International Bone Metastases Exercise Working Group (IBMEWG) developed best practice recommendations on the basis of published research, clinical experience, and expert opinion using (1) modified Delphi survey, (2) systematic review, (3) cross-sectional survey to physicians and nurse practitioners, (4) inperson meeting, and (5) stakeholder engagement.

WHAT WE FOUND: On the basis of the review of available evidence and expert consensus, the IBMEWG developed five key recommendations: (1) Before exercise testing or training, perform a risk assessment to inform the likelihood of a skeletal complication from exercise. (2) Consultation with the medical team is strongly encouraged to obtain key medical information and establish bidirectional communication. (3) Exercise professionals best suited for this population are physical therapists and clinical exercise physiologists (or equivalent) who have additional cancer exercise training. (4) Professional judgement should be used to consider if exercise testing is necessary. (5) Exercise prescription

should follow the standard exercise recommendations as outlined by the International Exercise Guidelines for Cancer Survivors, with greater emphasis on postural alignment, controlled movement, proper technique, and consideration of the bone lesion location and presentation.

BIAS, CONFOUNDING FACTORS: Some authors of this paper are employed by entities that provide physical activity programming for people with cancer, are involved in professional organizations that promote the role of exercise professionals within health care settings, and/or were authors for the International Exercise Guidelines for Cancer Survivors. Although these are strengths in terms of expertise, they may also lead to bias.

REAL-LIFE IMPLICATIONS: Exercise has been underutilized in people with advanced or incurable cancer despite the potential to improve physical function and reduce psychosocial morbidity, especially for people with bone metastases because of concerns over skeletal complications. These recommendations provide a framework and starting point for members of the medical team and exercise professionals to improve the integration of physical activity into the care of people with bone metastases. It is anticipated that the recommendations provided here will continue to evolve as more literature is available. Fundamental limitations remain around a lack of definitive literature on standardized approaches to predict the risk of skeletal complications and a paucity of data on the safety and efficacy of exercise for specific people that may be at increased risk of skeletal complications with exercise (ie, elderly individuals with multiple myeloma).

### **ASSOCIATED** CONTENT

**Appendix** 

Author affiliations and disclosures are available with the complete article at ascopubs.org/ journal/op.

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contributions

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**PURPOSE** Exercise has been underutilized in people with advanced or incurable cancer despite the potential to improve physical function and reduce psychosocial morbidity, especially for people with bone metastases because of concerns over skeletal complications. The International Bone Metastases Exercise Working Group (IBMEWG) was formed to develop best practice recommendations for exercise programming for people with bone metastases on the basis of published research, clinical experience, and expert opinion.

**METHODS** The IBMEWG undertook sequential steps to inform the recommendations: (1) modified Delphi survey, (2) systematic review, (3) cross-sectional survey to physicians and nurse practitioners, (4) in-person meeting of IBMEWG to review evidence from steps 1-3 to develop draft recommendations, and (5) stakeholder engagement.

**RESULTS** Recommendations emerged from the contributing evidence and IBMEWG discussion for pre-exercise screening, exercise testing, exercise prescription, and monitoring of exercise response. Identification of individuals who are potentially at higher risk of exercise-related skeletal complication is a complex interplay of these factors: (1) lesion-related, (2) cancer and cancer treatment-related, and (3) the person-related. Exercise assessment and prescription requires consideration of the location and presentation of bone lesion(s) and should be delivered by qualified exercise professionals with oncology education and exercise prescription experience. Emphasis on postural alignment, controlled movement, and proper technique is essential.

CONCLUSION Ultimately, the perceived risk of skeletal complications should be weighed against potential health benefits on the basis of consultation between the person, health care team, and exercise professionals. These recommendations provide an initial framework to improve the integration of exercise programming into clinical care for people with bone metastases.

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# INTRODUCTION

People living with advanced or incurable cancers are treated with sequential cancer therapies to improve survival and quality of life, but treatment burden can be high, including fatigue, reduced physical function, and psychosocial morbidity. In this context, people with advanced or incurable cancer highlight that maintaining functional independence and managing symptom burden are top priorities.2,3

Exercise (ie, planned and structured physical activity aimed to improve health) has been shown to improve fatigue, physical function, and psychosocial morbidity in people with early-stage cancers. 4 In the advanced or incurable cancer setting, the presence of bone metastases complicates prescribing exercise and promoting physical activity because of concerns about potential skeletal complications such as pathologic fracture, hypercalcemia, or spinal cord compression.<sup>5</sup> Although people with bone metastases regularly express an interest in information on exercise, 6-8 health care professionals report uncertainties regarding risk management.9-11 Recent systematic reviews in advanced or incurable cancer generally show exercise to be safe, feasible, and beneficial for quality of life, physical function, and fatigue. 12-18 However, these

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systematic reviews have not focused specifically on the safety or efficacy of exercise for people with bone metastases.

The International Bone Metastases Exercise Working Group (IBMEWG) was formed on the basis of the recognition that people with bone metastases could potentially benefit from exercise and are not receiving direction from the health care team, as they may be reticent because of lack of guidance in the literature or clinical practice. This group aimed to develop best practice recommendations on the basis of existing research evidence, clinical experience, and expert opinion.

#### **METHODS**

The IBMEWG is a multidisciplinary, international panel of physicians, physical therapists, clinical exercise physiologists, and researchers. Sequential steps (Fig 1) were taken to inform the recommendations: (1) modified Delphi survey to ascertain the practical considerations of implementing exercise for people with bone metastases in the outpatient oncology setting<sup>19</sup> (all participants provided informed consent, Research Ethics Board approval, University of British Columbia; H19-00379); (2) systematic review to assess the safety, feasibility, and efficacy of exercise in controlled trials that included people with bone metastases (International Prospective Register of Systematic Reviews: CRD42019121958)<sup>20</sup>; (3) cross-sectional survey to physicians and nurse practitioners to understand the attitudes toward exercise for people with bone metastases and components required to promote exercise referral<sup>21</sup> (all participants provided informed consent, Research Ethics Board approval, University of British Columbia; H19-00379); (4) in-person meeting of IBMEWG to review evidence from steps 1-3 to develop recommendations; and (5) stakeholder engagement, first with people with bone metastases (draft recommendations) and second with clinician peers (penultimate recommendations).

# **RESULTS**

#### Recommendation 1

Before exercise testing or training, perform a risk assessment to inform the likelihood of a skeletal complication from exercise.

The Delphi identified consensus on information that respondents deemed key to determine exercise suitability (Table 1). However, reliance on an individual's *self-reported* bone lesion details did not reach consensus. The systematic review showed that randomized controlled trials of exercise involving people with bone metastases commonly exclude people deemed to have structurally unstable bone lesion(s) or pain associated with bone lesion(s).<sup>20</sup> Determination of lesion stability was either undefined<sup>22,23</sup> or two randomized controlled trials used Taneichi's subtype A-C scoring for osteolytic thoracic and lumbar spine lesions, with computed tomography or magnetic resonance

imaging assessed independently by a radiologist and orthopedic surgeon. <sup>24,25</sup> In the survey, most respondents agreed that exercise for people with bone metastases was safe (82%) and these individuals look to their health care providers to provide exercise referral and recommendations (74%). To facilitate respondents providing an exercise recommendation to individuals, the most frequently cited resource identified was a set of clinical guidelines for exercise in this population (25%), an easy-to-use screening scale (20%), and a consult with a qualified exercise professional (13%). <sup>21</sup>

The IBMEWG acknowledged that in the absence of literature, all people with bone metastases can be at risk of an exercise-related skeletal complication, but this should not preclude prescribing exercise. Identification of individuals who are potentially at higher risk of exercise-related skeletal complication is a complex interplay of these factors: (1) lesion-related, (2) cancer and cancer treatment-related, and (3) person-related (Table 2). Furthermore, it was acknowledged that bone scan reports may not consistently provide information on lesion volume and that a computed tomography and magnetic resonance imaging may be more reliable for structural qualities of the bone and preferable for people deemed higher risk. Finally, more research is required to confirm the utility of pre-exercise skeletal assessment scales to guide risk assessment. Stakeholders with bone metastases reported that they were keen to exercise but fearful, lacking in confidence for self-guidance, and uncertain where to look for exercise advice. They confirmed that discussion with the health care team on how to manage risk was of key interest to people with bone metastases.

## Recommendation 2

Consultation with the medical team is strongly encouraged before an exercise professional provides structured exercise for a person with bone metastases, to obtain key medical information and establish bidirectional communication for initial assessment and exercise training throughout care.

The primary reason reported by exercise professionals to seek medical clearance or guidance was to obtain key medical information, such as results of bone scan reports to guide exercise prescription and to establish two-way communication (ie, to allow for information sharing with the goal of better safety and overall care). When asked if a primary reason for seeking medical clearance or guidance was a requirement for professional liability (ie, signed approval by a physician), only 39% of exercise professionals strongly agreed or agreed (Table 1). In the systematic review, 24% of trials required medical clearance by a physician. For the remainder, exclusion criteria specific to lesion characteristics of bone metastases were used, such as excluding people with unstable bone metastases (24%) or pain associated with the bone lesion (41%).<sup>20</sup> Most

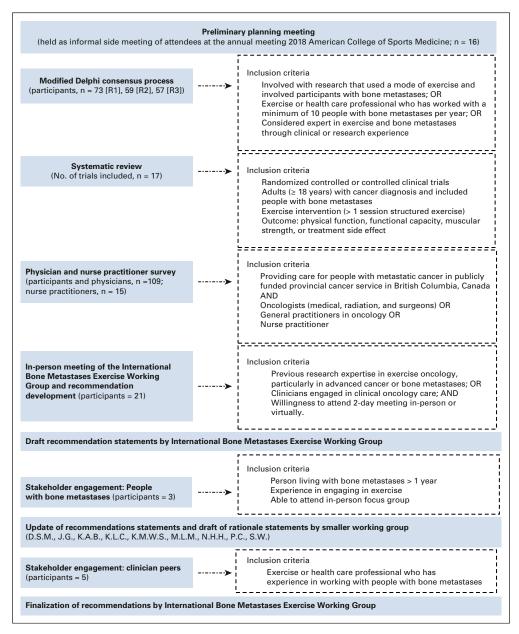


FIG 1. Information gathering and recommendation development process.

survey respondents agreed that people with bone metastases expected their physician to provide physical activity recommendations (74%), and these recommendations would be well received (66%) and followed (58%). However, less than half of the physicians and nurse practitioners (43%) felt confident to recommend exercise to people with bone metastases.<sup>21</sup>

The IBMEWG agreed that the term medical consultation versus clearance was the most appropriate term for communication between the exercise professional and health care provider. The goal of such medical consultation is to establish two-way communication to assess the cost to benefit-risk of an exercise prescription, as it can be difficult

for health care providers to feel that they have enough understanding of exercise to provide medical clearance and for exercise professionals to obtain or interpret all the desired clinical information to assess risk, especially without access to the medical chart (Appendix Table A1, online only).

# Recommendation 3

Exercise professionals best suited to prescribe exercise to people with bone metastases are physical therapists and clinical exercise physiologists (or equivalent), who have additional cancer exercise training and appropriate experience in working with people with a cancer diagnosis.

TABLE 1. Modified Delphi Survey Results and Future Research Directions

DR	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	Consensus (%)	
		A. Pre	-exercise screening	g questions (Recomi	mendation 1)		
DR2	uses the following lesion location, ty	g information to on the pe, progression, a	determine exercise and history; (2) bone	suitability: (1) bone	STRONGLY RECOMMENDED lesion details, ideally from a crest, ADLs, or physical activity pone lesions	diagnostic report that includes	
	91%	9%	0%	0%	0%	100% agree	
DR2	that an exercise p medications or tro	orofessional also u eatments specific	ses the following inf	ormation to determir ) history of fractures	n an individual with MBD, it is ne exercise suitability: (1) detai and falls, (4) bone mineral der	led medical history, (2) curren	
	86%	12%	2%	0%	0%	98% agree	
DR2	In the absence of a bone lesion(s) Al		(or a similar diagnos	stic report or letter fro	om medical doctor), an individu	ual's self-reported details of the	
	2%	14%	23%	35%	26%	No consensus reached	
		B. Medica	I clearance and Me	edical guidance (Red	commendation 2)		
DR3	As an exercise profe an individual witl	, ,	ary objective when	seeking a medical cl	learance or medical guidance	from a physician, in relation to	
	a. Medical inforn	nation (eg, report	s from recent scan	s or tests and any u	pcoming treatments)		
	65%	28%	5%	0%	2%	93% agree	
	b. Establish two-	way communicat	ion				
	53%	23%	7%	16%	2%	76% agree	
	c. Recommenda	tions for exercise	prescription				
	10%	23%	23%	33%	11%	No consensus reached	
	d. Professional li	ability					
	12%	27%	12%	33%	16%	No consensus reached	
DR3	Individuals with MBD who meet any of the following conditions REQUIRE medical guidance from the individual's medical professional prio to commencing a structured exercise program with a clinical exercise professional: (1) bone lesions that are unstable or of unknown stability, (2) bone pain or medical treatment of bone pain in the past 3 months, and (3) history of disease-related fractures within the past 12 months						
	63%	26%	2%	5%	4%	89% agree	
		C. Sı	iitable exercise pro	fessionals (Recomm	endation 3)		
DR2	Please select all the exercise professionals that you feel are suitable to safely prescribe exercise to an individual with metastatic bond disease who is deemed HIGHER RISK OF FRACTURE (eg, multiple bone lesion locations, unknown stability, and symptomatic)						
	disease who is d						
	a. Physical thera	eemed HIGHER					
		eemed HIGHER pist	RISK OF FRACTUE			stability, and symptomatic)	
	a. Physical thera	eemed HIGHER pist pist with cancer	RISK OF FRACTUE			stability, and symptomatic) 39	
	<ul><li>a. Physical thera</li><li>b. Physical thera</li><li>c. Exercise physi</li></ul>	eemed HIGHER pist pist with cancer ologist	RISK OF FRACTUE	RE (eg, multiple bon		stability, and symptomatic) 39 95	
	a. Physical thera b. Physical thera c. Exercise physi d. Exercise physi	eemed HIGHER pist pist with cancer ologist ologist with canc	RISK OF FRACTUR	RE (eg, multiple bon		stability, and symptomatic) 39 95 20	
	a. Physical thera b. Physical thera c. Exercise physi d. Exercise physi e. Kinesiologist o	eemed HIGHER pist pist with cancer ologist ologist with canc r exercise or spo	exercise training er exercise training trs scientist or exer	RE (eg, multiple bon	e lesion locations, unknown s	stability, and symptomatic)  39  95  20  85	
	a. Physical thera b. Physical thera c. Exercise physi d. Exercise physi e. Kinesiologist o	eemed HIGHER pist pist with cancer ologist ologist with canc r exercise or spo r exercise sports	exercise training er exercise training trs scientist or exer	RE (eg, multiple bon	e lesion locations, unknown s	stability, and symptomatic) 39 95 20 85	
	a. Physical thera b. Physical thera c. Exercise physi d. Exercise physi e. Kinesiologist of	eemed HIGHER pist pist with cancer ologist ologist with cancer r exercise or spo r exercise sports er	exercise training er exercise training rts scientist or exercise	RE (eg, multiple bon	e lesion locations, unknown s	stability, and symptomatic)  39  95  20  85  13  52	
	a. Physical thera b. Physical thera c. Exercise physi d. Exercise physi e. Kinesiologist o f. Kinesiologist o g. Personal traine	eemed HIGHER pist pist with cancer ologist ologist with cancer r exercise or spo r exercise sports er er with cancer ex	exercise training er exercise training rts scientist or exercise	RE (eg, multiple bon	e lesion locations, unknown s	stability, and symptomatic) 39 95 20 85 13 52 0	
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**TABLE 1.** Modified Delphi Survey Results and Future Research Directions (continued)

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	Consensus (%)			
			D. Exercise testin	g (Recommendatio	n 4)				
DR2	In an individual with MBD who is at a LOWER risk of fracture, I recommend exercise testing, but there are some tests that are contraindicated								
	70%				30%	70% agree			
	In an individual with contraindicated	n MBD who is at a	a HIGHER risk of f	racture, I recomme	end exercise testing, but there	are some tests that are			
	88%				12%	88% agree			
DR3	When considering strength testing for a person with bone metastases, I would								
	a. Avoid any strength testing (7%)								
	b. Avoid any strength testing that places stress on the lesion site (44%)								
	c. Use caution wi	th any testing tha	t places stress on	the lesion site (379	%)				
	d. Not make any	considerations (7	%)						
	e. I am not an ex	ercise professiona	al and do not feel	can answer this q	uestion (2%)				
		E	. Exercise prescrip	otion (Recommenda	ation 5)				
DR2	If an individual is deemed UNSAFE TO EXERCISE (aka "high" risk), it is appropriate for an exercise professional to provide physical active education or movement prescription that is modified to specifically suit the individual and is provided in collaboration with the individuals' medical team								
	65%	26%	2%	4%	4%	91% agree			
DR3	Exercise Physiological Instructor) may be	gist with cancer e e appropriate. The	xercise training), r	eferral to a less qua ercise professional v	highly qualified exercise profes alified exercise professional (eg vould administer and monitor t	g, Personal Trainer or Fitne			
	16%	49%	12%	16%	7%	No consensus reache			
DR3	For individuals with lower risk MBD (eg, stable and asymptomatic), exercise prescription is normally safe if it USES CAUTION with exercise that place stress on the bone lesion site								
	54%	39%	5%	0%	2%	93% agree			
	0.70	What does the term "use caution" mean to you, in the context of the question above?							
DR3		"use caution" me	ean to you, in the	context of the ques	tion above?				
DR3	What does the term			context of the ques					
DR3	What does the term  a. Start by avoidir  b. For exercises the	ng any exercises t	hat place stress or on site, start with ac	n the lesion site (14		ss slowly, provided there is I			
DR3	What does the term  a. Start by avoidin  b. For exercises th  exacerbation of  c. For exercises th	ng any exercises t nat target the lesion f pain or adverse	hat place stress or on site, start with ac symptoms (47%) site, start with low	n the lesion site (14 ctive movement and	1%)				
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DR3	What does the term  a. Start by avoidir  b. For exercises the exacerbation of  c. For exercises the exacerbation of  d. Other (10%)  Clinical prediction in	ng any exercises that target the lesion from adverse at target the lesion from or symptom.  F. Direction for nodels for adverse.	hat place stress or on site, start with ac symptoms (47%) site, start with low as (28%) future exercise re e event risk during	the lesion site (14 ctive movement and loads (eg, theraband search for people v	1%) I no load or weight and progres d or light dumbbells) and progre				
DR3	What does the term  a. Start by avoidir  b. For exercises the exacerbation of  c. For exercises the exacerbation of  d. Other (10%)  Clinical prediction in	ng any exercises to the lesion of pain or adverse at target the lesion of pain or symptom.  F. Direction for models for adverse of people with adverse of people	hat place stress or on site, start with ac symptoms (47%) site, start with low as (28%) future exercise re e event risk during	the lesion site (14 ctive movement and loads (eg, theraband search for people v	1%) I no load or weight and progres d or light dumbbells) and progre vith bone metastases				
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Abbreviations: ADL, activity of daily living; DR, Delphi Round; MBD, metastatic bone disease.

 TABLE 2. Recommendation for Team-Based Approach to Provision of Exercise Programming to People Living With Bone Metastases

	Medical communication		
Communication with current medical team (eg, Oncologist) is recommended to	Obtain any necessary medical guidance or additional information (eg, specific bone lesion details, previo and current cancer therapies, etc)		
	Establish and maintain a two-way communication pathway to share information on		
	New presentation of pain		
	Other symptoms		
	Functional concerns		
access to information on lesion-specific factors	Most recent bone scan report or other diagnostic report that describes the following:		
	Type of lesion (osteolytic, sclerotic, or mixed)		
	Number of lesion (s)		
	Location of lesion(s) (ie, load-bearing areas such as femur, spine, pelvic ring, acetabulum, and tib plateau)		
	Size of lesion(s) (ie, small <i>v</i> large)		
	Series of reports to determine status of the lesion(s), rate of progression, and structural stability of bone ( any evidence of vertebral compression)		
	Pre-exercise history		
Cancer and cancer treatment-related factors to cons	sider		
Cancer diagnosis	Prognosis or progression of disease		
	Metastases to other organ systems (ie, brain and lung)		
	History of fractures since cancer diagnosis		
Management of bone metastases	Planned or prior treatment approach to management of bone metastases (ie, surgical, radiation, and medical)		
	Planned or prior treatment approach to management or for SSE (ie, surgical, radiation, and medical		
	Current use of bone agents (eg, denosumab and bisphosphonates > 6 months)		
	Current use of agents that may increase risk of SSE (ie, corticosteroids, hormonal therapy, and anticoagulants)		
General bone health	Bone health risk factors (ie, smoking and family history of osteoporosis)		
	Diagnosis and severity of osteoporosis		
	Pharmaceutical management of osteoporosis (eg, bisphosphonates)		
Pain	Severity		
	Location		
	Use of pain medication related to site of lesion(s)		
	Triggers (eg, functional pain, during ADLs, loading, at rest, and at night)		
	Change in quality or location of pain (ie, new pain with weight bearing, transitional pain when performi ADLs, and pain worsening at night)		
Neurologic	Sudden or recent muscle weakness in any region		
	Sudden, new or recent change in bowel and/or bladder control (ie, progressive urinary retention, bladder bowel incontinence)		
	New or progressive gait or balance impairment		
	Loss of sensation or reflexes in any region		
Falls	Occurrence within the past 12 months		
	If positive, number of falls		
	If positive, injuries consequent to fall		
erson-related factors to consider			
Overall medical and symptom profile (eg, comorbi	d condition, fatigue, and cachexia)		
Worse ECOG PS			
Limitations in ADLs or instrumental ADLs			
Cognitive impairment (eg, making adherence to pr	recautions unreliable)		

Abbreviations: ADL, activity of daily living; ECOG PS, Eastern Cooperative Oncology Group Performance Status; SSE, symptomatic skeletal event.

The Delphi showed consensus that the exercise professionals best suited to prescribe exercise to people with bone metastases were university qualified with clinical expertise, namely, physical therapists (95% agree) and clinical exercise physiologists (85% agree), provided that each has additional cancer exercise education and training (Table 1). In the systematic review, exercise supervision was provided predominantly by university-trained exercise professionals, including physical therapists and clinical exercise physiologists. All but one trial included at least one session of in-person supervised exercise instruction (ie, individualized demonstration and practice).<sup>20</sup>

The IBMEWG recommended that all people are assessed by a physical therapist or clinical exercise physiologist, with additional cancer exercise education and ideally experience in working with people who have bone metastases (Appendix Table A1). This may necessitate that exercise professionals initially are advised or supervised by a more experienced colleague, and these recommendations may need to be adapted in different jurisdictions and clinical settings. Stakeholders with bone metastases endorsed the importance of members of the health care team being able to guide people to qualified professionals. The IBMEWG highlighted that considerable work is needed to establish a referral pathway to improve equitable access to qualified exercise professionals. Each exercise professional must consider their own training and experience, as well as the setting in which they work, to determine if it is appropriate to work with that client or to refer. Finally, the results of the systematic review suggest that an element of supervised exercise instruction should be initially included before the addition of unsupervised exercise for individuals with bone metastases. Although this supports the potential feasibility of delivering supervised virtual exercise programs in light of the COVID-19 pandemic, research is needed to determine the overall safety profile of virtual exercise for individuals with bone metastases.26

# Recommendation 4

Professional judgment should be used to consider if exercise testing at baseline and follow-up is necessary by weighing the risks and benefits of including the test or if the testing protocols may need to be modified.

In the Delphi, for lower and higher risk examples, the statement that "exercise testing was recommended but there were some tests that were contraindicated" met consensus. Specific to strength testing, there was consensus to avoid tests or use caution with a test that places stress on a lesion site (Table 1). In the systematic review, few studies provided sufficient details on which participants completed the tests outlined in the methods and why a test may or may not be used for select participants. For the four studies exclusively in people with bone metastases, all

outlined specific adjustments to the testing protocol.<sup>20</sup> For example, Galvao et al<sup>27</sup> excluded people with metastatic bone lesion(s) in the proximal femur from completing the 1-RM leg press and 400-m walk tests, and people with lesions in ribs, thoracic spine, or humerus were excluded from completing the 1-RM chest press and 1-RM seated row.

The IBMEWG assessed that there was insufficient evidence to guide specific recommendations on a standardized approach for safe exercise testing. To provide additional expert guidance, the recommendation is to focus on the goal of exercise testing and to follow the testing guidance in the International Exercise Guidelines for Cancer Survivors<sup>4</sup> until further evidence is available to update this approach (Appendix Table A1). In addition, exercise practitioners should use professional judgment to consider if a test is necessary and consistent with the person's goals, while providing written justification for inclusion of the test as part of the treatment plan in an appropriate charting location.

#### Recommendation 5

Exercise prescription should follow the standard exercise recommendations as outlined by the International Exercise Guidelines for Cancer Survivors, with greater emphasis on postural alignment, controlled movement, and proper technique, as well as consideration given to the location and presentation of the bone lesion(s). Formal monitoring of exercise response and adjustment of exercise prescription should be ongoing.

The Delphi shows a 91% consensus that education and advice on safe movement patterns for activities of daily living is important for all people with bone metastases (Table 1). Specific to prescribing an exercise that could directly place stress on the lesion site, most respondents agreed that the correct approach was to use caution. Respondents defined this as "start with active movement and no load or weight and progress slowly, provided there is no exacerbation of pain or adverse symptoms" (47%) or "start with low loads and progress slowly, provided there is no exacerbation of pain or adverse symptoms (28%)." This is a notable departure from approaches outlined originally by Cormie et al<sup>28</sup> and Galvao et al,<sup>27</sup> in which exercise involving the affected bone region was avoided altogether. In the systematic review, exercise prescription modifications specific to the presence of bone metastases were included in 41% of trials, whereas the remainder of trials did not report exercise modifications specific to bone metastases. How a participant's response to exercise was monitored and the related adjustments made to the exercise prescription were not uniformly reported.<sup>20</sup>

The IBMEWG discussed the available literature that could be used to inform specific guidance around exercise prescription approaches. Exercise prescription for resistance exercises that prevent direct stress on the site of bone lesions has been published by IBMEWG members (P.C.,

N.H.H., and R.U.N.).<sup>27,28</sup> It was acknowledged that these previously published approaches were conservative and provided a starting point, while evidence regarding safety continued to emerge. The challenge in applying these generic prescription approaches is that individuals with widespread metastatic disease may be recommended to engage in limited exercise options that do not target the overall function or the goals of the individual. The approved movements can also be more restrictive than many activities of daily living that place considerable load on the body, including sites of bone metastases, such as descending stairs.

The IBMEWG recommendation aims to move beyond the initial and restrictive approaches to exercise testing and prescription with the goal better informing the development of efficacious exercise prescriptions for people with bone metastases in the clinical setting. The standard approach to exercise prescription for people living with and beyond cancer as outlined by the International Exercise Guidelines for Cancer Survivors from the American College of Sports Medicine<sup>4</sup> should be used, with ongoing monitoring of individual response to adjust the exercise prescription or to send the person for further review. It was also deemed important to take additional guidance from exercise literature in osteoporosis that has sought to reduce the risk of skeletal-related complications, especially in vertebral bodies and hip.<sup>29,30</sup> This includes an emphasis on correct technique and postural alignment with all exercises; avoidance of rapid or loaded end-range movements, such as rotation, flexion, or extension movements that involve the area of the lesions; consideration of impact loading of an exercise along with the type of movement (ie. concentric. eccentric, and plyometric) in the area of the bone lesion(s); and education and precautions to minimize the risk of falls. An additional consideration is that people with bone metastases may be deconditioned, because of treatment or higher symptom burden, and exercise volume should be adjusted accordingly.

### **Overarching Recommendation**

Regular exercise has the potential to maintain or improve physical function and health-related quality of life in people with bone metastases, and the perceived risk of skeletal complication should be weighed against the potential health benefits.

On the basis of the review of available evidence and expert consensus, the IBMEWG has concluded that people with bone metastases should be supported and encouraged to engage in physical activity, including structured exercise, to obtain the well-established general health benefits, as a strategy to manage side effects related to cancer and treatments.<sup>4</sup> Overall, the perceived risk of skeletal complications should be weighed against the potential health benefits of regular physical activity, including prevention of further loss of functional capacity. Exercise professionals

should communicate with the health care team to minimize participant risk while providing sufficient exercise stimulus to improve or maintain function or to slow decline, while prioritizing the goals of the person. The IBMWG also identified research priorities to allow for the continuous evolution of evidence-based guidelines (Table 1).

This recommendation was strongly endorsed by our stakeholders, both people with bone metastases and clinician peers, who felt it essential for members of the health care team to initiate a conversation about exercise, explain why exercise is important for people with bone metastases, and frame exercise as a range of activities, spanning from activities of daily living to sports. Stakeholders with bone metastases also highlighted the need to increase the availability of exercise services led by qualified exercise professionals and the provision of more information on how to access services.

#### **DISCUSSION**

These recommendations aim to provide a framework for improved integration of exercise programming into the care of people with bone metastases. The overarching recommendation is that routine exercise has the potential to improve or maintain physical function and quality of life and reduce treatment side effects, while also potentially increasing resilience for future treatments. To achieve provision of exercise programming, a collaborative relationship between the health care team and qualified exercise professionals is optimal. This approach is intended to improve the health care team's confidence in encouraging people with bone metastases to engage in regular exercise and provide navigation on how to access qualified exercise professionals who can develop appropriate and individualized exercise programming.

Determining the ideal approaches to pre-exercise screening, exercise testing, and exercise programming related to safety and skeletal-related events (SREs) remains a challenge. The IBMEWG recommends that exercise programming for people with bone metastases is administered by qualified exercise professionals, namely, physical therapists and clinical exercise physiologists, who have additional training and experience in working with people with a cancer diagnosis. These exercise professionals have university-level training (or equivalent) in most countries and a scope of practice that includes working with individuals with complex medical conditions.

A specific risk stratification tool to evaluate the appropriateness of exercise participation for an individual is desired by the health care team, exercise professionals, and people with bone metastases. However, the utility to apply existing screening tools used to predict the risk of fracture or guide decisions on prophylactic surgical fixation (ie, Taneichi, Mirels, and Spinal Instability Neoplastic Score<sup>31</sup>) within the exercise screening process for people with bone metastases

is unknown. These have not been trialed extensively as part of the pre-exercise screening process to date and cannot be scored independently by an exercise professional. More research into the practical use of such a screening tool or newly developed tool is needed to determine if a standardized approach is feasible. Confounding this issue, the initial detection of bone metastasis is evolving with the advent of new imaging modalities. Unlike soft tissue tumors where Response Evaluation Criteria in Solid Tumors are clear, the response of bone metastasis to cancer treatment remains poorly understood.<sup>32</sup> A recently proposed algorithm for the investigation of bone metastasis was proposed by the European Society for Medical Oncology in 2020, and this could be considered for future exercise studies.<sup>32</sup>

The impact of cancer therapy and bone-modifying agents (BMA) on bone remodeling remains an area of intense study. With respect to BMA, zoledronic acid remains to date the only bisphosphonate to show broad efficacy in reducing SREs in people with bone metastases from almost all malignancies (including lung carcinoma and other solid tumor types: prostate, breast, thyroid, head and neck, thyroid, and renal cell).32 Data also show decreased SREs with the use of RANK ligand inhibitors (denosumab) for cancers of the prostate, breast, and renal cell, non-smallcell lung cancer, and multiple myeloma. 32 In the future, the use of BMA should be clearly documented in exercise studies to develop a better understanding of their potential influence on bone remodeling. Furthermore, future studies should explore the use of bone biomarkers and imaging, especially positron emission tomography in exploring potential risk indicators and treatment response of exercise interventions.

A key strength of the IBMEWG was the process to merge a systematic understanding of the current literature with a formalized Delphi process and stakeholder input. The IBMEWG recommendations are consistent with two existing publications. Sheill et al<sup>33</sup> published a narrative review of considerations for exercise prescription for people with bone metastases, and the support organization Macmillan Cancer Support in the United Kingdom developed a user-friendly guidance document for health care professionals.<sup>34</sup> The IBMEWG aimed to address gaps in these documents by documenting the specific information gathering and decision-making processes used to generate the recommendations.

A fundamental limitation is a lack of definitive literature on standardized approaches to safety screening, exercise testing and prescription, and safety reporting of minor or major complications with exercise, including between exercise sessions (ie, pain, disability, and need for analgesia). In addition, there is a paucity of data on specific individuals that may be at increased risk of fracture with exercise (ie, elderly individuals with multiple myeloma).

In conclusion, these recommendations provide a framework and starting point for exercise professionals and members of the health care team to improved integration of physical activity into the care of individuals with bone metastases. It is anticipated that the recommendations provided here will continue to evolve as more literature is available.

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#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

#### Exercise Recommendation for People With Bone Metastases: Expert Consensus for Health Care Providers and Exercise Professionals

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#### **APPENDIX**

TABLE A1. Guidance for Exercise Testing Approach and Monitoring Exercise Response With Examples of Qualified Exercise Professionals

	Guidance for exercise testing approach	ch			
Is the test necessary?	Consideration should be given to why the test is being conducted, weighing the risks against the benefits, in discussion with patient and healthcare team				
Criteria for specific test selection:	Testing should inform clinical decision making and exercise prescription				
	Testing should be adapted according to patient goals				
	Individuals must be informed and feel comfortable to perform the test safely				
Practical considerations	Avoid tests that place high loads on site(s) of bone metastasis (ie, 1-RM leg press for individual with lesion in proximal femur or vertebrae) <sup>4</sup>				
	Consider potential of fall risk when using treadmill or other ambulatory machines (ie, handrails must be available and blood pressure monitoring should be done with consideration of not compromising balance				
	Consider forces testing approach on site(s) of bone metastasis (ie, eccentric concentric, or isometric, including open <i>v</i> closed chain)				
	Consider the compressive forces of testing approach (ie, pressure on lumbar spine from backrest of leg press machine or repeated chair rise causing rapid/forceful impact onto the chair)				
	Be mindful of movement and forces needed to get into position for tests not just the test itself (ie, range of hip flexion needed to get into position for leg press in a leg press machine) as this can inadvertently cause unsafe movement related to risk of skeletal complication				
	Guidance for monitoring response to exercise	e training			
Observation	Exercise professionals should continuously mor prescription as appropriate to reduce poten	nitor overall response to each exercise prescribed and adjust tial risk of exercise-related adverse event			
Self-reported response	Exercise professionals must ask the individual	before and after each session about			
	Pain <sup>a</sup>	New or increased pain; or Change in quality or location of pain; or Unexplained pain; or Change in pain medication (dose and/or type) prior to or following an exercise session Ideally using a standardized tool, such as a visual analog scale			
	Neurological symptoms <sup>a</sup>	New symptom or change in symptom (eg, muscle weakness, loss of sensation or change in bladder/bowe function, balance or gait)			
	ADL	New limitation or change in limitations			
Exa	mples of qualified exercise professionals and can	ncer certifications			
Professional title <sup>b</sup>	Regulatory or professional body	Examples of additional cancer training or certifications			
Licensed or registered physical therapist or physiotherapist	Colleges of Physical Therapy (State, Province, or National)	Specialist Certification in Oncology from the American Physical Therapy Association <sup>35</sup>			
		Clinical Specialist from Canadian Physiotherapy Association <sup>36</sup>			
ACSM-CEP	ACSM	ACSM Cancer Exercise Trainer <sup>37</sup>			
		CanRehab <sup>38</sup>			
CSEP-CEP	CSEP	Thrive Cancer and Exercise Training <sup>39</sup>			
ESSA-AEP	ESSA	ExMedCancer <sup>40</sup>			
		Exercise Medicine Research Institute <sup>41</sup>			

Or equivalent in a given jurisdiction

Abbreviations: ACSM, American College of Sports Medicine; ADL, activity of daily living; AEP, Accredited Exercise Physiologist; CEP, Clinical Exercise Physiologist; CSEP, Canadian Society for Exercise Physiology; ESSA, Exercise and Sport Science Australia; RM, repetition maximum.

<sup>&</sup>lt;sup>a</sup>For individuals with complex presentation, exercise professional should consider asking the individual before and after each exercise performed, especially if it is a new exercise.

<sup>&</sup>lt;sup>b</sup>There is currently no single standardized licensing examination or number of clinic hours identified as optimal credentials for exercise professionals, specific to working with people with bone metastases.