

ONS LYMPHEDEMA SYMPTOM MANAGEMENT GUIDELINE

Supplementary Material

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1. Guideline panel conflict of interest disclosures

Guidelines Panel Member	Conflict of Interest
Jane M. Armer, PhD, RN, FAAN, CLT Professor Sinclair School of Nursing University of Missouri, Ashland	No conflicts listed
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Bonnie B. Lasinski, MA, PT, CLT-LANA Clinical Directory of Lymphedema Therapy, Woodbury, New York	No conflicts listed
Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN Associate Dean for Nursing and Nurse Anesthesia and Director of the Center for Oncology Education and Research Harris College of Nursing and Health Sciences Texas Christian University, Fort Worth	No conflicts listed
Pamela Lynne Ostby, PhD, RN, OCN®, CLT Research Collaborator Sinclair School of Nursing University of Missouri-Columbia	No conflicts listed
Joan White Patient Representative Lighthouse Lymphedema Network	No conflicts listed

2. PICO questions

PICO Components			
Population	Intervention(s)	Comparator	Patient-important outcomes (objective and subjective)
Prospective Surveillance			
Patients receiving cancer-related surgery	Prospective surveillance	No surveillance	Development of lymphedema Missed work or cost of coming in for prospective surveillance Number of patients referred for treatment to lymphedema specialist (surrogate for development of lymphedema)
Risk Reduction			
Patients who are at risk for extremity or truncal lymphedema from cancer surgery	Programmed (supervised) exercise	No programmed exercise	Development of persistent stage of lymphedema versus transient Change in physical activity Functional impairments (ROM, grip)
Patients receiving cancer surgery	Compression garments	No compression garments	Development of persistent stage of lymphedema versus transient Change in physical activity Functional impairments (ROM, grip)

Patients with cancer at risk of developing lymphedema	Massage of scar tissue	No massage of scar tissue	Development of persistent vs transient stage of lymphedema Change in physical activity Functional impairments (ROM, grip)
Treatment			
Patients with cancer-related secondary lymphedema	Additional active treatment along with self-management (Phase II Complete Decongestive Therapy (CDT)) Additional active treatments: Manual lymphatic drainage (MLD), compression pumps, resistance exercise, aerobic exercise, water-based or yoga exercise	Self-management (Phase II CDT)	Reduction of lymphedema swelling and symptoms Return to work and usual activities of daily living Decrease in physical activity Fatigue Functional disability (ROM, grip) Mortality Quality of life (depression, anxiety) Adverse events related to the intervention
Patients with cancer-related secondary lymphedema	Resistance exercise plus self-management (Phase II CDT)	Self-management (Phase II CDT)	Reduction of lymphedema swelling and symptoms Return to work and usual activities of daily living Decrease in physical activity Fatigue Functional disability (ROM, grip) Mortality

			Quality of life (depression, anxiety) Adverse events related to the intervention
Patients with cancer-related secondary lymphedema	Supervised water-based/yoga exercise plus self-management (Phase II CDT)	Self-management (Phase II CDT)	Reduction of lymphedema swelling and symptoms Return to work and usual activities of daily living Decrease in physical activity Fatigue Functional disability (ROM, grip) Mortality Quality of life (depression, anxiety) Adverse events related to the intervention

3. Evidence-to-Decision Frameworks (Developed using GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. McMaster University, 2015 (developed by Evidence Prime, Inc.). Available from grade.pro.org.)

- Prospective surveillance to detect lymphedema
- Programmed (supervised) exercise to delay or minimize the risk of lymphedema
- Compression garments to delay or minimize the risk of lymphedema
- Massage of scar tissue to delay or minimize the risk of lymphedema
- Active treatment with self-management (Phase II CDT) for treatment of lymphedema
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- Supervised water-based/yoga exercise plus self-management (Phase II CDT) for treatment of lymphedema


Prospective surveillance to detect lymphedema

RECOMMENDATION

Among patients receiving cancer-related surgery, should prospective surveillance rather than no prospective surveillance be conducted to detect lymphedema?	
POPULATION:	Persons receiving cancer-related surgery and are at risk for lymphedema
INTERVENTION:	Prospective surveillance
COMPARISON:	No surveillance
MAIN OUTCOMES:	Development of lymphedema; Missed work or cost of coming in for prospective surveillance; Number of patients referred to lymphedema specialist (surrogate for development of lymphedema)
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Patients with lymphedema experience physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019); lymphedema and has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, RN, MSN, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Poage, FNP-C, MSN, MPH, CLT-LANA , Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, Pamela Ostby, PhD, RN, OCN®, CLT Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem																	
Is the problem a priority?																	
JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS												
<div><div><div><div></div><div>No</div></div><div><div></div><div>Probably no</div></div><div><div></div><div>Probably yes</div></div><div><div></div><div>Yes</div></div><div><div></div><div>Varies</div></div><div><div></div><div>Don't know</div></div></div></div>	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart, 2010); at five years, 43–94% (Armer & Stewart, 2010); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015).</p> <p>The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et. al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et. al., 2010).</p>				<p>The panel noted that there is delayed identification of patients with lymphedema, and that earlier treatment should be provided compared to the current practices.</p> <p>The panel said a surveillance program involves measuring patients before and after surgery.</p> <p>In a proposed prospective surveillance model (Ostby et al., 2014), everyone having breast cancer treatment would be assessed pre-op, post-op, quarterly the first year, then semi-annually in years 1 – 3. The assessment visits would be coordinated with MD visits.</p>												
Desirable Effects																	
How substantial are the desirable anticipated effects?																	
JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS												
<div><div><div><div></div><div>Trivial</div></div><div><div></div><div>Small</div></div><div><div></div><div>Moderate</div></div><div><div></div><div>Large</div></div><div><div></div><div>Varies</div></div><div><div></div><div>Don't know</div></div></div></div>	<table><tr><th>Outcomes</th><th>№ of participants (studies) Follow up</th><th>Certainty of the evidence (GRADE)</th><th>Relative effect (95% CI)</th><th colspan="2">Anticipated absolute effects* (95% CI)</th></tr><tr><td rowspan="2">Diagnosis of reversible lymphedema follow up: 6 months</td><td rowspan="2">203 (1 observational study)</td><td rowspan="2">⊕○○○ VERY LOW^a</td><td rowspan="2">RR 2.06 (1.54 to 2.76)</td><td>Risk with no surveillance</td><td>Risk difference with prospective surveillance</td></tr><tr><td>390 per 1,000</td><td>413 more per 1,000 (210 more to 686 more)</td></tr></table>	Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Diagnosis of reversible lymphedema follow up: 6 months	203 (1 observational study)	⊕○○○ VERY LOW ^a	RR 2.06 (1.54 to 2.76)	Risk with no surveillance	Risk difference with prospective surveillance	390 per 1,000	413 more per 1,000 (210 more to 686 more)	<p>The panel prioritized the outcome of diagnosis of reversible lymphedema as a measure of catching lymphedema earlier and providing the ability for treatment/management earlier. Also, the cumulative incidence of advanced (stage 3) lymphedema at 5 years is less in the surveillance group vs. the historical control. Historical control patients were diagnosed with lymphedema based on clinical observation or patient symptom reports--they may have underestimated the events of lymphedema that would have been categorized as edge cases or through regular measurement methods.</p> <p>The Yang et al. (2016) study was conducted among a high baseline risk (~45.7%) historical control population.</p>	
Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)													
Diagnosis of reversible lymphedema follow up: 6 months	203 (1 observational study)	⊕○○○ VERY LOW ^a	RR 2.06 (1.54 to 2.76)	Risk with no surveillance	Risk difference with prospective surveillance												
				390 per 1,000	413 more per 1,000 (210 more to 686 more)												

Cumulative incidence of advanced lymphedema	203 (1 observational study)	 LOW	-	The overall 5-year cumulative incidence of advanced LE (greater than stage 3) was 25 (95 % CI 15.4–34.6 (6.4 %) in the SLYM group and 48 (95 % CI 15.4–34.6) (15.1 %) in the HC group. ^b	The panel noted that a similar preference for prospective surveillance exists between persons developing mild lymphedema and advanced lymphedema.
<p>a. The event number does not meet the optimal information size, suggesting some fragility in the estimate.</p> <p>b. Yang 2016 reports the same 95% CI for the 5-year cumulative incidence in the intervention and control arms, most likely an error in publication given that the control arm 95% CI does not fall around the point estimate of 48. Author was contacted, no response received.</p> <p>References:</p> <p>Yang, E.J., Ahn, S., Kim, E.K., Kang, E., Park, Y., Lim, J.Y., & Kim, S.W. (2016). Use of a prospective surveillance model to prevent breast cancer treatment-related lymphedema: A single-center experience. <i>Breast Cancer Research and Treatment</i>, 160, 269–276. https://doi.org/10.1007/s10549-016-3993-7</p> <p>In a large, observational, case-control study (Stout Gergich et al., 2008), 196 women with breast cancer had limb volume measured preoperatively and every 3 months after surgery. If limb volume increased 3% or more (which occurred in 43 women), lymphedema was diagnosed, and a compression garment was prescribed for 4 weeks. The garment was used thereafter only when visible swelling or heaviness occurred or during strenuous activity. At onset of lymphedema, the mean limb volume increase was 83 ml. After the intervention, mean volume was decreased by 48 ml, which was statistically significant. The reduction was sustained an average of 4.8 months after the intervention.</p>					

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS	
<div>○ Large</div> <div>○ Moderate</div> <div>● Small</div> <div>○ Trivial</div> <div>○ Varies</div> <div>○ Don't know</div>	Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	<div>The panel noted that prospective surveillance adds to patient burden because of the psychological stress of another potential diagnosis.</div> <div>In order to reduce the burden on the patient, the guideline panel decided that the prospective surveillance should be at the same time as the regular check-ups.</div> <div>The panel noted that there are no expected harms from the actual measurement techniques.</div>	
					Risk with no surveillance		Risk difference with prospective surveillance
	Diagnosis of reversible lymphedema follow up: 6 months	203 (1 observational study)	<div>⊕○○○</div> <div>○</div> <div>VERY LOW^a</div>	RR 2.06 (1.54 to 2.76)	Study population		
					390 per 1,000		413 more per 1,000 (210 more to 686 more)
	Cumulative incidence of advanced lymphedema	203 (1 observational study)	<div>⊕⊕○○</div> <div>LOW</div>	-	The overall 5-year cumulative incidence of advanced LE (greater than stage 3) was 25 (95 % CI 15.4–34.6 (6.4 %) in the SLYM group and 48 (95 % CI 15.4–34.6) (15.1 %) in the HC group. ^b		
<div><div>a.</div><div>The event number does not meet the optimal information size, suggesting some fragility in the estimate.</div></div> <div><div>b.</div><div>Yang 2016 reports the same 95% CI for the 5-year cumulative incidence in the intervention and control arms, most likely an error in publication given that the control arm 95% CI does not fall around the point estimate of 48. Author was contacted, no response received.</div></div>							
<div>References:</div> <div>Yang, E.J., Ahn, S., Kim, E.K., Kang, E., Park, Y., Lim, J.Y., & Kim, S.W. (2016). Use of a prospective surveillance model to prevent breast cancer treatment-related lymphedema: A single-center experience. <i>Breast Cancer Research and Treatment</i>, 160, 269–276. https://doi.org/10.1007/s10549-016-3993-7</div>							

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Very low○ Low○ Moderate○ High○ No included studies		The certainty in the evidence was rated as very low due to the imprecision and for risk of bias.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Important uncertainty or variability● Possibly important uncertainty or variability○ Probably no important uncertainty or variability○ No important uncertainty or variability	<p>In a qualitative phenomenological study (Río-González, Molina-Rueda, Palacios-Ceña, & Alguacil-Diego, 2018) in Spain of life with lymphedema, 11 patients with gynecological or urological cancer-related lymphedema were assessed. Physical issues related to work, leisure activities, and sports were reported. Compression garments made tasks difficult and were frequently a nuisance. Appearance requirements at work were a problem because of the garments. Participants found it difficult to psychologically deal with lymphedema, which they described as a traumatic event and a chronic condition.</p> <p>In a population-based cohort study (Ahmed, Rizment, Lazovich, Schmitz, & Folsom, 2008) of the health-related quality of life of 1,287 female breast cancer survivors, women diagnosed with lymphedema or having arm symptoms without a lymphedema diagnosis had lower physical and mental health-related quality of life than women without lymphedema or arm symptoms, based on data reported using the Medical Outcomes Study Short Form-36.</p> <p>In a qualitative analysis (Anbari, Wanchai, & Armer, 2019) of 97 women diagnosed with breast cancer-related lymphedema and quality of life during seven years of survivorship, the women reported pain, fatigue, being less active, an impact on their jobs and roles, concerns with body image, frustration, depression, and irritability.</p>	<p>The panel noted that patients may prefer to have measures taken versus considering the process a burden.</p> <p>There is lifetime risk of lymphedema.</p> <p>In panel members' experience, no patients decline prospective surveillance.</p> <p>Based on the identification of the burden on the patient, patients at lower risk may prefer to not have the increased burden with the lower risk of development.</p>

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention● Favors the intervention○ Varies○ Don't know		The panel decided that in the balance of effects, there is no difference for the high and low risk groups: the benefits still outweigh the harms.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large costs● Moderate costs○ Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know	<p>In a study (Dean et al., 2019) regarding long-term out-of-pocket expenses for patients having breast cancer-related lymphedema, 129 women completed a survey. The annual adjusted health-related out-of-pocket costs (not including productivity losses) for survivors with lymphedema were \$2306 versus \$1090 for survivors without lymphedema. The figures including productivity losses were \$3325 with lymphedema and \$2792 without lymphedema.</p> <p>National average price for an established patient MD office visit: \$218 (https://www.mdsave.com/procedures/established-patient-office-visit/d785f4ce)</p>	<p>Resource costs depend on the programming.</p> <p>Measurements take more than 10 minutes of the clinicians' time.</p> <p>Costs include equipment cost, personnel, and data collection.</p> <p>Everyone would be surveilled--this is made in comparison to other costs in the area.</p> <p>There would be one extra visit at the preoperative time or they are seen as part of the preoperative process. Even with extra preoperative visits, the resource requirements would be moderate.</p> <p>If prospective surveillance is smoothly integrated into the regular visits, then the cost could be lower than moderate.</p>

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Very low○ Low○ Moderate○ High● No included studies	<p>No research evidence identified.</p>	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention● Favors the intervention○ Varies○ No included studies	<p>In a perspective article (Stout et al., 2012), direct treatment costs associated with a prospective surveillance model and a traditional model of impairment-based care for the managing of breast cancer-related lymphedema were examined. It was assumed that one third of each group would develop lymphedema within a year. Cost estimates were based on the 2009 Medicare physician fee schedule. The cost per year with the prospective surveillance model was \$636.19 (including \$344.00 for ready-made compression garments); the traditional impairment-based care model, \$3,124.92 (including \$1,400.00 for custom-made compression garments).</p> <p>In a study (Dean et al., 2019) regarding long-term out-of-pocket expenses for patients having breast cancer-related lymphedema, 129 women completed a survey. The annual adjusted health-related out-of-pocket costs (not including productivity losses) for survivors with lymphedema were \$2306 versus \$1090 for survivors without lymphedema. The figures including productivity losses were \$3325 with lymphedema and \$2792 without lymphedema.</p>	<p>There is a smaller cost with surveillance because the swelling is caught earlier.</p>

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Reduced○ Probably reduced● Probably no impact○ Probably increased○ Increased○ Varies○ Don't know	<p>In an analysis (Morehead-Gee et al., 2012) of Caucasian and African American breast cancer survivors (in a military health system) comparing health status, health-related quality of life, and incidence of physical impairments after treatment, there were no differences regarding breast cancer type, stage, grade, or tumor size; type of surgery; or number of lymph nodes sampled. African American survivors experienced more estrogen/progesterone receptor-negative tumors and had radiation treatment more often. African American survivors reported more frequent social activities but fewer recreational activities. More African American survivors were employed and had higher rates of cording and lymphedema postoperatively.</p> <p>In a retrospective study (Black, Jiang, Kuerer, Buchholz, & Smith) of 31,274 women from 2002 to 2007 having pathologically node-negative breast cancer, sentinel lymph node biopsy was used for 73.7% of white patients and 62.4% of black patients. The 5-year cumulative risk of developing lymphedema was 8.2% in white patients, 12.3% in black patients. Data was drawn from the Surveillance, Epidemiology, and End Results – Medicare-linked database.</p> <p>In a study (Dean et al., 2016) of 296 overweight breast cancer survivors, black race and BMI were not associated with interlimb volume difference (ILD). College attendance was the strongest factor associated with greater ILD.</p> <p>In a prospective cohort study (the Pathways Study) (Kwan et al., 2010) of 997 early breast cancer survivors, being African American or more educated was associated with an increased risk of breast cancer-related lymphedema (BCRL). Obesity at diagnosis was suggestive of an elevated risk.</p> <p>In a multiethnic prospective cohort study (the Pathways Study) (Kwan et al., 2016) of 2953 patients with breast cancer, self-reported breast cancer-related lymphedema (BCRL) status was examined along with self-reported race/ethnicity and estimated genetic ancestry. A younger age at diagnosis and a higher BMI at baseline were associated with higher BCRL risk. African American patients had a</p>	<p>Included in equity considerations were accessibility, cost, and insurance coverage.</p> <p>The panel decided there was no impact on equity when prospective surveillance was coupled with the regular visit.</p>

	<p>two-fold increased risk compared to white patients. An association with increased risk was found with African genetic ancestry and with Hispanic ethnicity in nonobese women.</p> <p>A retrospective study (Eversley et al., 2005) of 116 mainly low-income women who had undergone breast cancer surgery found that African American, Latina, and other (comprised of Asian, Pacific Islander, mixed race heritage, and two women whose ethnicity was not reported) women were more likely to report lymphedema than white women.</p> <p>In an Australian retrospective study (Svensson & Thrift, 2010) of 79 women who had undergone breast cancer surgery, women living 50+ km from the rural lymphedema service were less likely to have a lymphedema diagnosis and developed lymphedema later than women living ≤49 km away. No explanation for this result was determined.</p>	
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><input type="radio"/> No</div><div><input type="radio"/> Probably no</div><div><input checked="" type="radio"/> Probably yes</div><div><input type="radio"/> Yes</div><div><input type="radio"/> Varies</div><div><input type="radio"/> Don't know</div></div>	In an Australian pilot study (Nicholson, Eaton, & Wong Shee, 2019) of the acceptability and feasibility of a regional lymphedema surveillance program, 32/35 patients and 9/9 staff members answered surveys about the program. Generally, the patients and staff reported a positive experience with the program.	<p>Clinicians will find it acceptable if they have more knowledge about the risk of lymphedema and the assessment that occurs at regular MD visits.</p> <p>Nurses will find it acceptable if they have more knowledge about the risk of lymphedema and if the assessment occurs at regular physician visits.</p> <p>Institutional acceptability is "probably yes."</p>

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><input type="radio"/> No</div><div><input type="radio"/> Probably no</div><div><input type="radio"/> Probably yes</div><div><input checked="" type="radio"/> Yes</div><div><input type="radio"/> Varies</div><div><input type="radio"/> Don't know</div></div>	In the discussion section of a case control study (Stout Gergich et al., 2008), the authors noted that few clinical sites have access to optoelectronic measurement technology, though they said other assessment tools may prove to be efficacious in diagnosing subclinical lymphedema.	It is feasible because the clinician just needs a perimeter, or even simple measurements could be taken.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

Among persons who have had cancer-related surgery, the ONS guideline panel *suggests* prospective surveillance, including an educative-component, rather than no prospective surveillance, for detection of lymphedema. (Conditional recommendation, very low certainty of evidence)

Remarks: Persons receiving surgeries that have a higher baseline risk for development of lymphedema may place greater value on participating in prospective surveillance programs and less value on the resources required to participate in such programs.

Persons may have a greater acceptance of prospective surveillance programs when institutions and practices integrate prospective surveillance components into regular pre- and post-operative care and wellness visits throughout survivorship.

Justification

The panel determined that there is low certainty in the evidence for a net health benefit from surveillance, but that the desirable anticipated effects were large, and the balance of effect favors surveillance, rather than no surveillance. Based on this evidence, the panel issued a conditional recommendation in favor of prospective surveillance in patients at risk for cancer -related LE. Table 3 includes considerations for components of a prospective surveillance program. Additional research is needed to inform specific components and identify outcomes from prospective surveillance programs.

Subgroup considerations

No subgroup considerations.

Implementation considerations

The goal for implementation is to have surveillance incorporated as a routine check, similar to the taking of patients’ blood pressure.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

- Improve the level of evidence in prospective surveillance programs
- Examine cost effectiveness of prospective surveillance programs

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Programmed (supervised) exercise to delay or minimize the risk of lymphedema

RECOMMENDATION

Among patients who are at risk for extremity or truncal lymphedema from cancer surgery, should programmed (supervised) exercise rather than no programmed exercise be initiated to delay or minimize the risk of lymphedema development?	
POPULATION:	Persons who are at risk for extremity or truncal lymphedema from cancer surgery
INTERVENTION:	Programmed (supervised) exercise
COMPARISON:	No programmed exercise
MAIN OUTCOMES:	Development of persistent vs. transient stage of lymphedema; Change in physical activity; Functional impairments (ROM, grip)
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Patients with lymphedema experience physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019); lymphedema also has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, RN, MSN, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Poage, FNP-C, MSN, MPH, CLT-LANA, Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, Pamela Ostby, PhD, RN, OCN®, CLT Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart); at five years, 43–94% (Armer & Stewart); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et. al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015).</p> <p>The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et. al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et. al., 2010).</p>	<p>The panel made two comparison: delayed versus early and programmed versus no exercise. Then they compared extremity/truncal versus head/neck.</p> <p>The body of the evidence is from breast cancer patients and is too indirect to inform the PICO about head/neck cancer.</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Trivial○ Small○ Moderate○ Large○ Varies○ Don't know	<p>For evidence, see Ding, J.F., Hasan, B., Malandris, K., Farah, M.H., Manolopoulos, A., Ginex, P., ... Murad, M.H. (2020). Prospective surveillance and risk reduction of cancer treatment-related lymphedema: Systematic review and meta-analysis. <i>Oncology Nursing Forum</i>, 47(5).</p>	<p>The early versus delayed exercise evidence informs the potential harms of early movement.</p> <p>When exercise is delayed, risk of lymphedema is reduced and range of motion is also less. Todd et al. (2008) delayed 7 days; Bendz and Olsen (2002) delayed 14 days.</p> <p>Delayed vs. early:</p> <p>The panel decided there were moderate desirable effects with delayed exercise.</p> <p>There was almost a 50% reduction in the development of lymphedema, an important outcome.</p> <p>Programmed vs. no intervention:</p> <p>The panel decided the desirable effects of programmed exercise were small.</p>

		<p>The focus was on range of motion and change in physical activity. The panel decided that about less than a 10-degree change in range of motion is small.</p> <p>The evidence about other benefits of exercise (well-being, etc.) were not measured in the evidence.</p>
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large○ Moderate● Small○ Trivial○ Varies○ Don't know	<p>For evidence, see Ding, J.F., Hasan, B., Malandris, K., Farah, M.H., Manolopoulos, A., Ginex, P., ... Murad, M.H. (2020). Prospective surveillance and risk reduction of cancer treatment-related lymphedema: Systematic review and meta-analysis. <i>Oncology Nursing Forum</i>, 47(5).</p>	<p>Delayed vs early</p> <p>The panel determined the undesirable effects of delayed exercise were small.</p> <p>The panel decided that the grip strength may not be meaningfully different and that the range of motion effects were small.</p> <p>Programmed vs not:</p> <p>The panel determined that the undesirable effects of programmed exercise were small.</p> <p>Different programs/regimens were used.</p>
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Very low○ Low○ Moderate○ High○ No included studies		<p>Delayed vs early:</p> <p>For the question of delayed compared to early exercise, the certainty in the evidence was rated as very low due to imprecision from the potential of both benefits and harms and for risk of bias.</p> <p>Programmed vs no exercise:</p> <p>For the question of programmed exercise compared to no exercise, the certainty of evidence across the body of evidence for the outcomes was low due to concerns with inconsistency between the findings from the RCTs and non-randomized studies, as well as imprecision.</p>
Values Is there important uncertainty about or variability in how much people value the main outcomes?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Important uncertainty or variability○ Possibly important uncertainty or variability○ Probably no important uncertainty or variability○ No important uncertainty or variability	In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), challenges to behavioral changes included symptoms such as lymphedema, chronic weight retention, depression symptoms, and personal barriers including lack of time and resources and little knowledge about how to start incorporating physical activity in their lives.	<p>The panel noted that risk reduction for lymphedema is more important to patients than it is to doctors.</p> <p>Delayed vs early:</p> <p>The panel determined there was no important uncertainty in the valuing the main outcomes.</p> <p>Programmed vs no exercise:</p> <p>The panel determined there was possibly important uncertainty or variability in valuing the main outcomes—this was based on the dosing of the exercise regimen, whether it was supervised or not supervised, and whether it was the same regimen or not.</p>

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ Don't know		<p>Delayed vs early:</p> <p>The panel decided the balance of effects favored delayed exercise.</p> <p>Programmed vs no exercise:</p> <p>The panel decided the balance of effects does not favor either.</p>

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know 	<p>Exercise, preventative:</p> <ul style="list-style-type: none"> • Initial instruction on exercises, billed as MD visit—National average price for established patient office visit: \$218 (https://www.mdsave.com/procedures/established-patient-office-visit/d785f4ce) • National average price for physical therapy (does not specify lymphedema-related): \$162 (https://www.mdsave.com/procedures/physical-therapy-visit/d787f9ce) <p>Exercise, therapeutic (resistance training, lymphedema exercises, aqua lymphatic exercise, deep breathing)</p> <ul style="list-style-type: none"> • Initial instruction on lymphedema exercises, resistance training, deep breathing, billed as MD visit—National average price for established patient office visit: \$218 (https://www.mdsave.com/procedures/established-patient-office-visit/d785f4ce) • “Aquatic therapy” national average: \$116 (https://www.mdsave.com/procedures/aquatic-therapy/d286ff) • Black Mountain Products Loop Resistance Bands Set of 5 with Carrying Case: \$9.07 (https://www.walmart.com/ip/Black-Mountain-Products-Loop-Resistance-Exercise-ands-Set-of-5-with-Carrying-Case/835430849) • Weider Neoprene Dumbbell, 1 – 10 lbs.: \$1.10 - \$9.48 (https://www.walmart.com/ip/Weider-Neoprene-Dumbbell-1-10lbs-with-Compact-Design/54997678) 	<p>Delayed vs early:</p> <p>The panel decided that the resources required for delayed exercise would be negligible. They noted that the difference in the costs and savings between the delayed and early exercise would be negligible because the costs and savings would be the same, just starting later for the delayed group.</p> <p>Programmed vs no exercise:</p> <p>The panel decided that the resources required for programmed exercise would be moderate. They would include the cost of the trainer and a gym.</p>

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ○ Low ○ Moderate ○ High ● No included studies 	<p>No research evidence identified.</p>	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention● Varies○ No included studies	No research evidence identified.	<p>Delayed vs early exercise:</p> <p>The panel decided the cost effectiveness favored delayed exercise because of the decreased long-term cost associated with treatment.</p> <p>Programmed vs no:</p> <p>The panel determined that the cost effectiveness varied. They considered the moderate cost versus the cost of lifetime treatment of lymphedema. Money would be saved from a reduction in lymphedema.</p>
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Reduced○ Probably reduced○ Probably no impact○ Probably increased○ Increased○ Varies○ Don't know	No research evidence identified.	<p>Delayed vs early:</p> <p>The panel decided there would be no impact on health equity with delayed exercise.</p> <p>Programmed vs no:</p> <p>The panel determined that equity would be reduced with programmed exercise. There are accessibility, coverage, transportation, and socio-economic status issues.</p>
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes○ Yes○ Varies○ Don't know	<p>In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), preferred components of a physical activity program would include personal interactions with group or individual counseling, activities suited for physical limitations and comorbidities, peer partners, leaders who understand that emotions can affect motivation, and access to public facilities.</p> <p>In a study (Hayes, Reul-Hirche, & Turner, 2009) of exercise and secondary lymphedema, 32 women with breast cancer-related lymphedema were randomly allocated to a supervised, aerobic, and resistance exercise group or a control group (continued habitual activities). In self-reported questionnaires, women in the exercise group noted a greater sense of well-being. Women in the intervention group were concerned that exercise would adversely affect the lymphedema. Six women in the exercise group were concerned that changes in arm symptoms indicated a worsening of the lymphedema (The changes did not actually indicate that. Because of the women's concerns, reassessment with BIS around week 6 was performed. It showed</p>	<p>Delayed vs early:</p> <p>The panel determined that delayed exercise would be acceptable to key stakeholders. They noted that reimbursement is affected by whether the person is staying in the hospital or making a clinical visit.</p> <p>Programmed vs no:</p> <p>The panel determined that acceptability varies for programmed exercise among key stakeholders. It would be variable depending on the exercise program involved</p>

	improvement in 5 of the women and no change in the 6th.). Women in both the intervention and control groups noted that heavy or repetitive use or heavy lifting caused problems with the arm.	and the associated costs. There are specialty needs for exercise programs.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes○ Yes○ Varies○ Don't know	<p>In a Turkish qualitative study (Cal & Bahar, 2016) of barriers prophylaxis of lymphedema after breast surgery and of home care needs, 14 women having lymphedema were interviewed. Few reported they were given adequate information about the prophylaxis of lymphedema and protective exercises. Most of the women did not follow recommended practices after lymphedema developed even though they had been informed about them. Women noted that personal factors (e.g., diligence) were an important variable when it came to performing self-management. They found that meeting with peers encouraged them to follow their prophylaxis measures. Comorbidities were another factor they said affected compliance.</p> <p>In a hybrid Type 1 effectiveness-implementation trial (Beidas et al., 2014) of a physical therapy-based group strength training program for breast cancer survivors with and without lymphedema (Strength After Breast Cancer), referring physicians, nurse practitioners, and physical therapists reported barriers to success involving the varying abilities of participants, insurance coverage/cost, understanding eligibility criteria, the referral process, and the need for a champion to gain support for the program.</p>	<p>Delayed vs early:</p> <p>The panel decided that delayed exercise would be feasible to implement.</p> <p>Programmed vs no:</p> <p>The panel decided that programmed exercise would probably be feasible. Training/certifications would be required of providers of the programmed exercise regimens.</p>

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

Delayed vs early:

Among persons with cancer who are at risk of extremity/truncal lymphedema from cancer surgery, the ONS guideline panel *suggests* delaying the initiation of programmed (supervised) exercise for no less than seven days following surgery (immediately post-op). (Conditional recommendation, very low certainty of evidence).

Programmed vs no:

Among persons with cancer who are at risk for extremity/truncal lymphedema from cancer surgery, the ONS guideline panel *suggests* initiating programmed (supervised) exercise including resistance and strengthening exercises rather than no programmed exercise following the post-operative 7-day period, and a favorable physical assessment by the patient’s surgeon and lymphedema therapist (Conditional recommendation, low certainty of evidence).

Justification

The ONS guideline panel determined there was very low certainty in the evidence for net health harms from delayed exercise compared to early post-operative exercise. Overall, the panel judged that the desirable outcomes were greater than the undesirable outcomes and made a conditional recommendation for delayed exercise rather than immediate post-operative exercise.

Subgroup considerations

No subgroup considerations.

Implementation considerations

Programmed exercise should be under the supervision of a lymphedema specialist and a physical therapist.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

- Determine optimal regimens of lymphedema risk-reduction practice/behaviors/strategies
- Examine risk reduction, treatment, and management of lymphedema at other (non-arm) anatomical sites, such as head and neck, leg, truncal, genitals, and abdomen

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Compression garments to delay or minimize the risk of lymphedema

RECOMMENDATION

Should patients receiving cancer surgery use compression garments rather than no use of compression garments to delay or minimize the risk of lymphedema development?	
POPULATION:	Persons receiving cancer surgery who are at risk for developing lymphedema
INTERVENTION:	Use of compression garments
COMPARISON:	No use of compression garments
MAIN OUTCOMES:	Development of persistent stage of lymphedema vs.transient; Change in physical activity; Functional impairments (ROM, grip)

SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Patients with lymphedema experience physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019); lymphedema and has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	<p>ONS conflict of interest declaration and management policies were applied, and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Gordon Poage, MSN, FNP-C, MPH, CLT-LANA®, Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, and Pamela Ostby, PhD, RN, OCN®, CLT.</p> <p>Panel members recused as a result of risk of conflicts of interest: None</p>

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div><div><div><div></div></div><div>No</div></div><div><div><div></div></div><div>Probably no</div></div><div><div><div></div></div><div>Probably yes</div></div><div><div><div></div></div><div>Yes</div></div><div><div><div></div></div><div>Varies</div></div><div><div><div></div></div><div>Don't know</div></div></div></div></div>	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart); at five years, 43–94% (Armer & Stewart); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et. al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015).</p> <p>The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et. al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et. al., 2010).</p>	
Desirable Effects		

How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know 	For evidence, see Ding, J.F., Hasan, B., Malandris, K., Farah, M.H., Manolopoulos, A., Ginex, P., ... Murad, M.H. (2020). Prospective surveillance and risk reduction of cancer treatment-related lymphedema: Systematic review and meta-analysis. <i>Oncology Nursing Forum</i> , 47(5).	Sleeves were used post-operatively.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know 	For evidence, see Ding, J.F., Hasan, B., Malandris, K., Farah, M.H., Manolopoulos, A., Ginex, P., ... Murad, M.H. (2020). Prospective surveillance and risk reduction of cancer treatment-related lymphedema: Systematic review and meta-analysis. <i>Oncology Nursing Forum</i> , 47(5).	<p>There are other potential harms that may include skin allergies from the compression garments, too much pressure when the garments are not applied correctly, and the risk of edema if the garments do not fit properly. There possibly may also be post-operative harms related to the garments.</p> <p>The guideline panel determined the undesirable effects to be small, which incorporated their belief that the harms are underreported.</p>
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 		The panel rated the certainty in these estimated effects as very low owing to serious imprecision and risk of bias.
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important 	In a qualitative phenomenological study (Río-González, Molina-Rueda, Palacios-Ceña, & Alguacil-Diego, 2018) in Spain of life with lymphedema, 11 patients with gynecological or urological cancer-related lymphedema were interviewed. Participants reported that compression garments made tasks difficult and were frequently a nuisance. Appearance requirements at work were a problem because of the garments.	The panel determined there is some variability in the patient values surrounding the aesthetics and comfort of the garments but that there is a smaller risk involved when wearing them for risk reduction versus for treatment.

<p>uncertainty or variability</p> <p>○ No important uncertainty or variability</p>	<p>In a study (Ochalek, Gradalski, & Partsch, 2017) of light arm compression sleeves with 23 women wearing the sleeves about 10 hours a day, compliance was good, and there were no reports that the garments were uncomfortable or that the women had problems in donning and doffing.</p> <p>In a focus group qualitative study (Ostby, Armer, Smith, & Stewart, 2018) of 9 women experiencing breast cancer-related lymphedema, negative comments were made about compression garments being uncomfortable or too hot.</p>	
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Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p>○ Favors the comparison</p> <p>○ Probably favors the comparison</p> <p>○ Does not favor either the intervention or the comparison</p> <p>● Probably favors the intervention</p> <p>○ Favors the intervention</p> <p>○ Varies</p> <p>○ Don't know</p>		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large costs● Moderate costs○ Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know	Compression garments (Not covered by Medicare (https://lymphedematreatmentact.org/increase-awareness)): <ul style="list-style-type: none">• Initial instruction on garment use, billed as MD visit—National average price for established patient office visit: \$218 (https://www.mdsave.com/procedures/established-patient-office-visit/d785f4ce)• Various garments for extremities, standard-fit per piece, average retail price: \$67 - \$159 (http://lymphedematreatmentact.org/wp-content/uploads/2017/12/Cost-and-Utilization-of-Compression-Garments.pdf)• Various garments for extremities, custom-fit per piece, average retail price: \$161 - \$960 (http://lymphedematreatmentact.org/wp-content/uploads/2017/12/Cost-and-Utilization-of-Compression-Garments.pdf)	Custom garments may be needed. The garments need to be replaced every six months.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Very low○ Low○ Moderate○ High● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison● Probably favors the intervention○ Favors the intervention○ Varies○ No included studies	In a perspective article (Stout et al., 2012), direct treatment costs associated with a prospective surveillance model and a traditional model of impairment-based care for the managing of breast cancer-related lymphedema were examined. It was assumed that one third of each group would develop lymphedema within a year. Cost estimates were based on the 2009 Medicare physician fee schedule. The cost per year with the prospective surveillance model was \$636.19 (including \$344.00 for ready-made compression garments); the traditional impairment-based care model, \$3,124.92 (including \$1,400.00 for custom-made compression garments).	The panel decided there are moderate direct costs for lymphedema risk reduction—about 8% reduction for lymphedema.

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<ul style="list-style-type: none">○ Reduced● Probably reduced○ Probably no impact○ Probably increased○ Increased○ Varies○ Don't know	No research evidence identified.	The panel considered insurance coverage, accessibility to compression garments or custom garments, and access to a provider/fitting when discussing equity.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know	<p>In a study (Hayes, Reul-Hirche, & Turner, 2009) of exercise and secondary lymphedema, 32 women with breast cancer-related lymphedema participated. The investigators collected quantitative data about lymphedema changes and qualitative data about the exercise program and about the participants' lymphedema experience. One woman noted that the need to wear a compression garment causes people to ask questions she finds hard to answer. Another woman noted it was difficult to hide her compression garment, so she usually did not use it.</p> <p>In a qualitative phenomenological study (Río-González, Molina-Rueda, Palacios-Ceña, & Alguacil-Diego, 2018) in Spain of life with lymphedema, 11 patients with gynecological or urological cancer-related lymphedema were interviewed. Patients reported that compression garments made tasks difficult and were frequently a nuisance. Appearance requirements at work were a problem because of the garments.</p>	<p>For clinicians, there is an increase in overall time with patients because of the need to fit the garments and to teach about their use.</p> <p>The panel determined that nurses and therapists would accept the intervention.</p> <p>The panel discussed the need for reimbursement policy.</p>
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know	<p>In an English qualitative study (Jeffs et al., 2016), 21 women with breast cancer-related lymphedema were interviewed about self-management of lymphedema. Several issues were identified as influencing the patients' ability to succeed in self-management: incorporating self-management into their daily routine, acknowledging the benefit of self-management/consequence of neglecting self-management, taking ownership of self-management, knowledge and understanding of lymphedema and its treatment, the ability to problem solve, time pressures, and the aesthetics of their compression garments.</p> <p>In a Turkish qualitative study (Cal & Bahar, 2016) of barriers prophylaxis of lymphedema after breast surgery and of home care needs, 14 women having lymphedema were interviewed. Few reported they were given adequate information about the prophylaxis of lymphedema and protective exercises. Most of the women did not follow recommended practices after lymphedema developed even though they had been informed about them. Women noted that personal factors (e.g., diligence) were an important variable when it came to performing self-management. They found that meeting with peers encouraged them to follow their prophylaxis measures. Comorbidities were another factor they said affected compliance.</p>	<p>The panel considered the availability of trained providers, adherence by patients, and the availability of compression at the immediate post-operative period when discussing feasibility.</p>

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

Among persons with cancer who are at risk for lower extremity lymphedema, the ONS guideline panel *suggests* use of compression garments rather than no use of compression garments to delay or minimize lymphedema development. (Conditional recommendation, very low certainty of evidence).

Remarks: Persons placing greater value on avoiding the appearance or discomfort of wearing compression garments may prefer to not wear them to delay or minimize lymphedema because of smaller potential benefit for risk reduction.

Among persons with cancer who are at risk for truncal, upper extremity, or head and neck lymphedema, the ONS guideline panel *recommends* use of compression garments to delay or minimize lymphedema development *only in the context of a clinical trial*. (Knowledge gap, research recommendation).

Justification

The ONS guideline panel determined there was very low certainty in the evidence for net health harms from compression garments for risk reduction of lower extremity LE. Overall, the panel judged that the desirable outcomes, although minimal, were greater than undesirable outcomes and made a conditional recommendation for compression garments for reducing risk of lower extremity LE. The panel considered the limited evidence on prophylactic use of lower extremity compression garments with the risk of LE following inguinal lymph node dissection and acknowledged that this is a situation where shared decision-making between the patient and their health care provider should occur in weighing individual risks and harms.

The panel decided that the evidence for the benefits was too indirect to inform a recommendation for persons at risk of truncal, upper extremity, or head and neck cancer; however, the harms associated with the compression garment may be similar. Therefore, the panel decided to make a research recommendation that compression garments to delay or minimize the risk of LE in patients with truncal, upper extremity or head and neck cancer be used only in the context of a clinical trial.

Subgroup considerations

No subgroup considerations.

Implementation considerations

No implementation considerations.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

- Determine optimal regimens of lymphedema risk-reduction practice/behaviors/strategies
- Investigate the effect of prophylactic use of compression garments on minimization of lymphedema risk, including dosing, frequency of use, adverse events, and patient comfort
- Examine risk reduction, treatment, and management of lymphedema at other (non-arm) anatomical sites, such as head and neck, leg, truncal, genitals, and abdomen

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Massage of scar tissue to delay or minimize the risk of lymphedema

RECOMMENDATION

Among patients with cancer at risk of developing lymphedema, should massage of scar tissue rather than no massage of scar tissue be performed?	
POPULATION:	Persons with cancer at risk of developing lymphedema
INTERVENTION:	Massage of scar tissue
COMPARISON:	No massage of scar tissue
MAIN OUTCOMES:	Development of persistent vs. transient stage of lymphedema; Change in physical activity; Functional impairments (ROM, grip)
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Lymphedema affects patients with physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019) and has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	<p>ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, RN, MSN, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Poage, FNP-C, MSN, MPH, CLT-LANA , Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, Pamela Ostby, PhD, RN, OCN®, CLT</p> <p>Panel members recused as a result of risk of conflicts of interest: None</p>

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div><div><div></div><div>No</div></div><div><div></div><div>Probably no</div></div><div><div></div><div>Probably yes</div></div><div><div></div><div>Yes</div></div><div><div></div><div>Varies</div></div><div><div></div><div>Don't know</div></div></div></div></div>	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart, 2010); at five years, 43–94% (Armer & Stewart, 2010); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et. al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015).</p> <p>The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et. al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et. al., 2010).</p>	<p>Fibrosis was raised as an additional consideration.</p>
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div><div><div></div><div>Trivial</div></div><div><div></div><div>Small</div></div><div><div></div><div>Moderate</div></div><div><div></div><div>Large</div></div><div><div></div><div>Varies</div></div><div><div></div><div>Don't know</div></div></div></div></div>	<p>In a review (Shin & Bordeaux, 2012) of ten publications that included 144 patients who received scar massage at various timepoints after surgery (non-cancer-specific), 45.7% were reported to have experienced clinical improvement based on one or more of the following: Patient Observer Scar Assessment Scale score, Vancouver Scar Scale score, range of motion, pruritus, pain, mood, depression, or anxiety. Ninety percent of 30 scars treated with massage had improved appearance or Patient Observer Scar Assessment Scale score.</p>	<p>The panel decided that range of motion may be a surrogate for daily function. The degrees of motion may not be a clinically meaningful difference—a 2.5-degree difference.</p> <p>The panel noted that range of motion is a subjective measure and that precision and reliability is an issue. Range of motion is critical to patients because it relates to daily function.</p> <p>Temur and Kapucu (2019) and Torres Lacomba et al. (2010) were considered for evidence.Torres Lacomba et al. (2010) includes scar tissue massage. Temur and Kapucu (2019) had an exercise regimen as a co-intervention. The panel decided the Temur and Kapucu</p>

		<p>(2019) and Torres Lacomba et al. (2010) studies were too indirect-- the studies refer to manual lymph drainage (MLD), which is different than scar massage.</p> <p>One clinical trial (ClinicalTrials.gov ID:NCT00760123) was conducted among breast cancer patients; however, the study ended in 2009 and no results were posted.</p> <p>The panel considered indirect evidence from a systematic review (Shin & Bordeaux, 2012) on scar massage for burns. The outcomes were clinical improvement, range of motion, quality of life (depression/anxiety), and appearance.</p> <p>The panel noted that people who have scars are concerned with its appearance. That could be a surrogate for quality of life/self-image.</p>
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large○ Moderate● Small○ Trivial○ Varies○ Don't know	<p>In a review (Shin & Bordeaux, 2012) of ten publications that included 144 patients who received scar massage at various timepoints after surgery (non-cancer-specific), 45.7% were reported to have experienced clinical improvement based on one or more of the following: Patient Observer Scar Assessment Scale score, Vancouver Scar Scale score, range of motion, pruritus, pain, mood, depression, or anxiety. Ninety percent of 30 scars treated with massage had improved appearance or Patient Observer Scar Assessment Scale score.</p>	<p>The panel said there could be harm associated with scar therapy following surgery because too much pressure may damage the tissue.</p> <p>During massage, there is some sharp pain/stabbing, but it is generally temporary and resolves quickly. However, pain can appear years later. A constant inflammatory response is experienced when the massage is delivered, and then it is residual.</p> <p>Improvement in chronic pain is a goal from the treatment. Could massage lead to nerve regeneration?</p> <p>Persons having head and neck cancer may experience greater severity of chronic pain.</p> <p>The panel noted that during self-massage, the pain would be less than when a professional massage is received. All the patients experience pain with professional massage.</p> <p>The harms of the intervention and of the scar need to be separated.</p>

Certainty of evidence		
What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Very low○ Low○ Moderate○ High○ No included studies		The panel determined the certainty of evidence to be very low for this question because of the indirectness of the evidence, which was not specifically from persons with surgery from cancer or in radiation treated tissue, as well as the lack of evidence around the potential harms from massage of scar.
Values		
Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Important uncertainty or variability○ Possibly important uncertainty or variability● Probably no important uncertainty or variability○ No important uncertainty or variability	No research evidence identified.	This question was answered for persons having cancer in the extremities. Research is required to investigate the population having head and neck cancer.
Balance of effects		
Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention● Favors the intervention○ Varies○ Don't know		The panel noted that harms are underreported/not reported in the literature, but they are expected to be minimal and resolve quickly, with a large expected benefit from the intervention.

Resources required		
How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div>○ Large costs</div><div><div>● Moderate costs</div></div><div>○ Negligible costs and savings</div><div>○ Moderate savings</div><div>○ Large savings</div><div>○ Varies</div><div>○ Don't know</div></div>	Initial instruction on prophylactic massage, billed as an MD visit—National average price for an established patient office visit: \$218 (https://www.mdsave.com/procedures/established-patient-office-visit/d785f4ce)	
Certainty of evidence of required resources		
What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div>○ Very low</div><div>○ Low</div><div>○ Moderate</div><div>○ High</div><div><div>● No included studies</div></div></div>	No research evidence identified.	
Cost effectiveness		
Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div>○ Favors the comparison</div><div>○ Probably favors the comparison</div><div>○ Does not favor either the intervention or the comparison</div><div><div>● Probably favors the intervention</div></div><div>○ Favors the intervention</div><div>○ Varies</div><div>○ No included studies</div></div>	No research evidence identified.	The panel considered the cost of an office visit. They noted that there would be no cost for self-massage, and with the reduction of fibrosis, range of motion could possibly increase.

Equity		
What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div>○ Reduced</div><div><div>● Probably reduced</div></div><div>○ Probably no impact</div><div>○ Probably increased</div><div>○ Increased</div><div>○ Varies</div><div>○ Don't know</div></div>	No research evidence identified.	The panel determined there would be an increase in equity because patients could do it at home—the only cost would be an office visit. However, the office visit may not be covered (reducing equity), especially if services were provided by an occupational therapist, physical therapist, and speech therapist. Access to a properly trained provider/teacher could be a source for reduced equity. Scar massage may necessitate more visits.
Acceptability		
Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div>○ No</div><div>○ Probably no</div><div>○ Probably yes</div><div><div>● Yes</div></div><div>○ Varies</div><div>○ Don't know</div></div>	No research evidence identified	
Feasibility		
Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div>○ No</div><div>○ Probably no</div><div>○ Probably yes</div><div><div>● Yes</div></div><div>○ Varies</div><div>○ Don't know</div></div>	In a Turkish qualitative study (Cal & Bahar, 2016) of barriers prophylaxis of lymphedema after breast surgery and of home care needs, 14 women having lymphedema were interviewed. Few reported they were given adequate information about the prophylaxis of lymphedema and protective exercises. Most of the women did not follow recommended practices after lymphedema developed even though they had been informed about them. Women noted that personal factors (e.g., diligence) were an important variable when it came to performing self-management. They found that meeting with peers encouraged them to follow their prophylaxis measures. Comorbidities were another factor they said affected compliance.	

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		Varies	Don't know

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

Among persons with cancer at risk for extremity, truncal or head and neck lymphedema, the ONS guideline panel *suggests* massage of post-surgical scar tissue rather than no massage of post-surgical scar tissue. (Conditional recommendation, very low certainty of evidence).

Remarks: Massage of the scar tissue may be uncomfortable or painful and should be initiated only after recovery from acute tissue injury by a trained lymphedema therapist who can teach patients proper technique. If pain is too intense or for patients valuing to not experience pain during the massage, they may choose not to do this.

Justification

Currently, there is a lack of evidence regarding the effect of massage of scar in radiation-treated tissue. Thus, this recommendation is only applicable to postsurgical scar management. The panel determined that there is very low certainty in the evidence for a net health benefit from massage, but that the desirable anticipated effects were large, and the balance of effects favors massage, rather than no treatment. Based on this evidence, the panel issued a conditional recommendation in favor of scar massage in patients at risk for cancer-related LE.

Subgroup considerations

No subgroup considerations.

Implementation considerations

No implementation considerations.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

- Evaluate the impact of risk-reduction practice/behaviors/strategies (e.g., prophylactic massage of scar) on lymphedema management
- Determine optimal regimens of lymphedema risk-reduction practice/behaviors/strategies

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RECOMMENDATION

POPULATION:	Persons with cancer-related secondary lymphedema
INTERVENTION:	Any additional active treatment in addition to self-management (Phase II CDT)
COMPARISON:	Self-management alone
MAIN OUTCOMES:	Reduction of lymphedema swelling and symptoms; Return to work and usual activities of daily living; Decrease in physical activity; Fatigue; Functional disability (ROM, grip); Mortality; Quality of life (depression, anxiety); Adverse events related to the intervention
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Lymphedema affects patients with physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019) and has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	<p>ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, RN, MSN, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Poage, FNP-C, MSN, MPH, CLT-LANA , Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, Pamela Ostby, PhD, RN, OCN®, CLT</p> <p>Panel members recused as a result of risk of conflicts of interest: None</p>

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know 	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart, 2010); at five years, 43–94% (Armer & Stewart, 2010); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm</p>	

	<p>lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et. al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015). The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et. al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et. al., 2010).</p>	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Trivial○ Small○ Moderate○ Large○ Varies○ Don't know	<p>For evidence, see Lytvyn, L., Zeraatkar, D., Anbari, A., Ginex, P., Zoratti, M., Niburski, K., ... Morgan, R. (2020). Conservative intervention strategies for adult cancer-related lymphedema: A systematic review and network meta-analysis of randomized controlled trials. <i>Oncology Nursing Society</i>, 47(5).</p>	<p>The panel determined that the network results may not show meaningful differences between the active interventions.</p> <p>They determined the evidence has much variability in the underlying patient population and the timing of the lymphedema. The underlying population's lymphedema duration was approximately at least 12 months, but there were variable levels of lymphedema. The analysis does not address initial lymphedema experienced by patients.</p> <p>The panel decided there was a trivial difference between the comparisons and CDT.</p> <p>The panel decided that self-management varies across the comparisons, which may impact the comparative efficacy shown. In the included studies, self-management contained varieties of SLD, remedial exercise, skin/nail care, compression bandages, and compression garments.</p>

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large○ Moderate○ Small○ Trivial● Varies○ Don't know	For evidence, see Lytvyn, L., Zeraatkar, D., Anbari, A., Ginex, P., Zoratti, M., Niburski, K., ... Morgan, R. (2020). Conservative intervention strategies for adult cancer-related lymphedema: A systematic review and network meta-analysis of randomized controlled trials. <i>Oncology Nursing Society</i> , 47(5).	<p>None of the studies reported on the adverse effects of compression pumps, but the panel identified discomfort and the small possibility of severe harm—the lymphatic fluid could go retrograde into the genitals/chest.</p> <p>The panel determined that cellulitis could possibly be found with any intervention but that the intervention may not be the cause.</p> <p>The panel noted a small risk of mild skin reactions/allergy with water-based exercise, CDT, self-care (bandages), and compression pumps. They also noted a small risk of muscle strain/soreness with water-based exercise/yoga, resistance exercise, and resistance+aerobic.</p> <p>The panel added that all interventions may have some discomfort.</p> <p>The panel decided there was small concern with compression pump in comparisons and trivial concern with harms in other comparisons.</p>

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Very low○ Low○ Moderate○ High○ No included studies		<p>The panel rated the certainty in these estimated effects as very low owing to serious imprecision from the potential for both benefit and harm and risk of bias. We had concerns with the studies included in the network meta-analysis because many did not provide standard intervention components and had considerable variability in the baseline LE volume/stage among participants within the same study. The panel also noted some issues with trial design, including lack of blinding of patients, influencing reporting of subjective outcomes, lack of independent outcome assessment; as well as small sample sizes and participant withdrawals leading to incomplete outcome data.</p>

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Important uncertainty or variability○ Possibly important uncertainty or variability● Probably no important uncertainty or variability○ No important uncertainty or variability	In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), challenges to behavioral changes included symptoms such as lymphedema, chronic weight retention, depression symptoms, and personal barriers including lack of time and resources and little knowledge about how to start incorporating physical activity in their lives.	<p>The panel agreed that relief of symptoms is important to the patients and is related to daily functioning. They noted that patients may prefer different activities or self-management. Patients with wounds cannot be in the water.</p> <p>The panel discussed the burden on the patient with all the interventions—they all have a time commitment. For CDT, the standard definition is 3 to 5 days per week with bandage changes, so multiple office visits would be required. Patients need to learn how to apply bandages, and it takes time to learn the proper technique. The bandages may be uncomfortable. Pumps require half an hour per day, and patients may give up eventually. There is a cost for the pumps.</p> <p>The panel determined that preference may vary across all interventions based on the complexity of treatment; however, the main outcomes remain reduction or stabilization of lymphedema.</p>

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison● Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ Don't know		The panel decided the balance of effects did not favor either the interventions or the comparator, and that determination included the small harm of the pump.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large costs○ Moderate costs○ Negligible costs and savings		The guideline panel made the following observations about resource requirements for the various interventions:

<ul style="list-style-type: none">○ Moderate savings○ Large savings● Varies○ Don't know		<p>The compression pump is expensive but may be reimbursed.</p> <p>Compression garments and bandages are an expense but less than the pump.</p> <p>CDT is expensive upfront, but over a lifetime, it costs less than compression garments/bandages.</p> <p>MLD costs less than garments/bandages.</p> <p>Self-management includes the expense of an office visit.</p> <p>Water-based/yoga/resistance/aerobic exercise may be more negligible because of lifestyle factors.</p> <p>The cost of self-management versus CDT varies depending on the implementation of the self- management. With the definition of self-management as the second phase of CDT, there would be moderate savings.</p> <p>For CDT + resistance exercise vs CDT, there would be negligible savings.</p> <p>For CDT + compression pump vs CDT, there would be moderate costs.</p> <p>For MLD vs CDT, there would be moderate savings.</p> <p>For compression pump vs CDT, there would be moderate costs.</p>
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Very low○ Low○ Moderate○ High● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies● No included studies	No research evidence identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Reduced○ Probably reduced○ Probably no impact○ Probably increased○ Increased● Varies○ Don't know	No research evidence identified	The panel determined that equity would vary by community, individual, coverage, and accessibility. They decided that access and coverage would probably be similar across interventions.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes○ Yes● Varies○ Don't know	<p>In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), preferred components of a physical activity program would include personal interactions with group or individual counseling, activities suited for physical limitations and comorbidities, peer partners, leaders who understand that emotions can affect motivation, and access to public facilities.</p> <p>In a study (Hayes, Reul-Hirche, & Turner, 2009) of exercise and secondary lymphedema, 32 women with breast cancer-related lymphedema were randomly allocated to a supervised, aerobic, and resistance exercise group or a control group (continued habitual activities). In self-reported questionnaires, women in the exercise group noted a greater sense of well-being. Women in the intervention group were concerned that exercise would adversely affect the lymphedema. Six women in the exercise group were concerned that changes in arm symptoms indicated a worsening of the lymphedema (The changes did not actually indicate that. Because of the women's concerns,</p>	<p>The panel determined that clinicians have their favored interventions—some prefer high-touch, others prefer high-tech. Some have ties to industry.</p> <p>The panel noted that all the interventions have a time burden.</p> <p>The panel used the definition of self-management as the second phase of CDT and observed that self-management tapers off over the years.</p> <p>The panel determined that all the interventions would be acceptable except a compression pump as sole treatment because it is generally used as an adjunct.</p>

	reassessment with BIS around week 6 was performed. It showed improvement in 5 of the women and no change in the 6th.). Women in both the intervention and control groups noted that heavy or repetitive use or heavy lifting caused problems with the arm.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know	In a hybrid Type 1 effectiveness-implementation trial (Beidas et al., 2014) of a physical therapy-based group strength training program for breast cancer survivors with and without lymphedema (Strength After Breast Cancer), referring physicians, nurse practitioners, and physical therapists reported barriers to success involving the varying abilities of participants, insurance coverage/cost, understanding eligibility criteria, the referral process, and the need for a champion to gain support for the program.	With the definition of self-management being the second phase of CDT, the panel decided the intervention would be feasible to implement but that feasibility changes when the components are not standardized, as in the published studies.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

JUDGEMENT							
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

Among persons with cancer-related secondary lymphedema, the ONS guideline panel *suggests* an active treatment intervention* in addition to self-management (Phase II CDT) rather than self-management alone. (Conditional recommendation, very low certainty of evidence).

*interventions reviewed: MLD; compression pumps; resistance exercise; aerobic plus resistance exercise; water-based or yoga exercise; CDT plus resistance exercise; CDT plus compression pumps; or CDT plus compression pumps plus aerobic and resistance exercise

Remarks: Due to the potential small harms, burden, and comparative cost of compression pumps, patients may wish to try other conservative treatments before compression pumps.

Justification

The ONS guideline panel determined there was very low certainty in the evidence for net health harms from MLD, aerobic and resistance exercise, compression pumps, water-based (aqua lymphatic) exercise, yoga and tai-chi-like exercise, in addition to self-management. Overall, the panel judged that the desirable outcomes outweighed the undesirable outcomes and made a conditional recommendation for any one or a combination of the interventions listed above in addition to self-management.

Subgroup considerations

No subgroup considerations.

Implementation considerations

No implementation considerations

Monitoring and evaluation

No monitoring and evaluation considerations

Research priorities

- Assess the effect of clearly defined/standardized exercise programs on lymphedema, including types, doses, timing, qualifications/training of providers
- Determine the additional benefits of an active treatment (e.g., aerobic exercises, resistance exercises, and water-based exercises) along with Phase II of CDT (self-management)

IN-TEXT REFERENCES

Anbari, A.B., Wanchai, A., & Armer, J.M. (2019). Breast cancer-related lymphedema and quality of life: A qualitative analysis over years of survivorship. *Chronic Illness*. Advance online publication. <https://doi.org/10.1177/1742395319872796>

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Hayes, S.C., Reul-Hirche, H., & Turner, J. (2009). Exercise and secondary lymphedema: Safety, potential benefits, and research issues. *Medicine & Science in Sports & Exercise*, 41, 483–489. <https://10.1249/MSS.0b013e3181818b98fb>

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Sagen, A., Kaaresen, R., Sandvik, L., Thune, I., & Risberg, M.A. (2014). Upper limb physical function and adverse effects after breast cancer surgery: A prospective 2.5-year follow-up study and preoperative measures. *Archives of Physical Medicine and Rehabilitation*, 95, 875–881. <https://doi.org/10.1016/j.apmr.2013.12.015>

Resistance exercise plus self-management (Phase II CDT) for treatment of lymphedema

RECOMMENDATION

Among patients with cancer-related secondary lymphedema, should resistance exercise plus self-management (Phase II CDT) rather than self-management alone be used for lymphedema treatment?	
POPULATION:	Persons with cancer-related secondary lymphedema
INTERVENTION:	Resistance exercise plus self-management (Phase II CDT)
COMPARISON:	Self-management alone
MAIN OUTCOMES:	Reduction of lymphedema swelling and symptoms; Return to work and usual activities of daily living; Decrease in physical activity; Fatigue; Functional disability (ROM, grip); Mortality; Quality of life (depression, anxiety); Adverse events related to the intervention
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Lymphedema affects patients with physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019) and has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, RN, MSN, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Poage, FNP-C, MSN, MPH, CLT-LANA , Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, Pamela Ostby, PhD, RN, OCN®, CLT Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div><div><div></div><div>No</div></div><div><div></div><div>Probably no</div></div><div><div></div><div>Probably yes</div></div><div><div></div><div>Yes</div></div><div><div></div><div>Varies</div></div><div><div></div><div>Don't know</div></div></div></div></div>	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart, 2010); at five years, 43–94% (Armer & Stewart, 2010); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015).</p> <p>The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et al., 2010).</p>	
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div><div><div></div><div>Trivial</div></div><div><div></div><div>Small</div></div><div><div></div><div>Moderate</div></div><div><div></div><div>Large</div></div><div><div></div><div>Varies</div></div><div><div></div><div>Don't know</div></div></div></div></div>	<p>For evidence, see Lytvyn, L., Zeraatkar, D., Anbari, A., Ginex, P., Zoratti, M., Niburski, K., ... Morgan, R. (2020). Conservative intervention strategies for adult cancer-related lymphedema: A systematic review and network meta-analysis of randomized controlled trials. <i>Oncology Nursing Society</i>, 47(5).</p>	<p>Resistance exercise was not included in the network meta-analysis.</p> <p>Schmitz et al. (2009) were explicit about the details of the standard of care: remedial exercise/nail care/compression garments; Cormie et al. (2013) did not list the components (The panel assumed patients had previously been taught self-management.).</p> <p>Cormie et al. (2013) used two instruments to measure quality of life but data was only extracted for one. In addition, the baseline may not have been equivalent for both groups.</p>

		<p>Cormie et al. (2013) and Schmitz et al. (2009) both used supervised exercise.</p> <p>Desirable effects of resistance exercise included a decrease in lymphedema swelling/symptoms, an increase in functional measures, and a decrease in pain.</p> <p>The panel noted that the standard mean difference (SMD) is difficult to interpret in this situation. SMD had to be used in this case because there are not reporting standards.</p>
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large○ Moderate● Small○ Trivial○ Varies○ Don't know	<p>For evidence, see Lytvyn, L., Zeraatkar, D., Anbari, A., Ginex, P., Zoratti, M., Niburski, K., ... Morgan, R. (2020). Conservative intervention strategies for adult cancer-related lymphedema: A systematic review and network meta-analysis of randomized controlled trials. <i>Oncology Nursing Society</i>, 47(5).</p>	<p>The panel noted that resistance exercise can involve soreness and a risk of injury such as muscle strain.</p> <p>The panel also noted that there may be the additional burden of travel to a gym but that home training options are available as well.</p> <p>The panel decided that the FACT-B + 4 result for quality of life was not a significant harm.</p>

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Very low○ Low○ Moderate○ High○ No included studies		<p>The panel rated the certainty in these estimated effects as very low owing to very serious imprecision from the potential for both benefit and harm and few participants included in the studies.</p>

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Important uncertainty or variability○ Possibly important uncertainty or variability● Probably no important uncertainty or variability○ No important uncertainty or variability	<p>In a qualitative phenomenological study (Río-González, Molina-Rueda, Palacios-Ceña, & Alguacil-Diego, 2018) in Spain of life with lymphedema, 11 patients with gynecological or urological cancer-related lymphedema were assessed. Physical issues related to work, leisure activities, and sports were reported. Compression garments made tasks difficult and were frequently a nuisance. Appearance requirements at work were a problem because of the garments. Participants found it difficult to psychologically deal with lymphedema, which they described as a traumatic event and a chronic condition.</p> <p>In a population-based cohort study (Ahmed, Rizment, Lazovich, Schmitz, & Folsom, 2008) of the health-related quality of life of 1,287 female breast cancer survivors, women diagnosed with lymphedema or having arm symptoms without a lymphedema diagnosis had lower physical and mental health-related quality of life than women without lymphedema or arm symptoms, based on data reported using the Medical Outcomes Study Short Form-36.</p> <p>In a qualitative analysis (Anbari, Wanchai, & Armer, 2019) of 97 women diagnosed with breast cancer-related lymphedema and quality of life during seven years of survivorship, the women reported pain, fatigue, being less active, an impact on their jobs and roles, concerns with body image, frustration, depression, and irritability.</p> <p>In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), challenges to behavioral changes included symptoms such as lymphedema, chronic weight retention, depression symptoms, and personal barriers including lack of time and resources and little knowledge about how to start incorporating physical activity in their lives.</p>	<p>The panel determined that patient preference based on the outcomes may vary but not the priority on the outcomes.</p>

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison● Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large costs○ Moderate costs● Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know		The panel noted that patients would not have constant supervision at a gym and that a similar amount of time would be required with a gym trainer as compared to a self-care trainer.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Very low○ Low○ Moderate○ High● No included studies	No research evidence identified.	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies● No included studies	No research evidence identified.	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Reduced○ Probably reduced● Probably no impact○ Probably increased○ Increased○ Varies○ Don't know	No research evidence identified	The panel noted that resistance exercises can be done at home.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know	<p>In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), preferred components of a physical activity program would include personal interactions with group or individual counseling, activities suited for physical limitations and comorbidities, peer partners, leaders who understand that emotions can affect motivation, and access to public facilities.</p> <p>In a study (Hayes, Reul-Hirche, & Turner, 2009) of exercise and secondary lymphedema, 32 women with breast cancer-related lymphedema were randomly allocated to a supervised, aerobic, and resistance exercise group or a control group (continued habitual activities). In self-reported questionnaires, women in the exercise group noted a greater sense of well-being. Women in the intervention group were concerned that exercise would adversely affect the lymphedema. Six women in the exercise group were concerned that changes in arm symptoms indicated a worsening of the lymphedema (The changes did not actually indicate that. Because of the women's concerns, reassessment with BIS around week 6 was performed. It showed improvement in 5 of the women and no change in the 6th.). Women in both the intervention and control groups noted that heavy or repetitive use or heavy lifting caused problems with the arm.</p>	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<div><div><div>○ No</div><div>○ Probably no</div><div>○ Probably yes</div><div>● Yes</div><div>○ Varies</div><div>○ Don't know</div></div></div> <div>In a hybrid Type 1 effectiveness-implementation trial (Beidas et al., 2014) of a physical therapy-based group strength training program for breast cancer survivors with and without lymphedema (Strength After Breast Cancer), referring physicians, nurse practitioners, and physical therapists reported barriers to success involving the varying abilities of participants, insurance coverage/cost, understanding eligibility criteria, the referral process, and the need for a champion to gain support for the program.</div> <div></div>
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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
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○	○	●	○	○
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CONCLUSIONS

Recommendation

Among persons with cancer-related secondary lymphedema, the ONS guideline panel *suggests* resistance exercises in addition to self-management (Phase II CDT) rather than self-management alone. (Conditional recommendation, very low certainty of evidence.)

Remarks: Preference for resistance exercises may be driven by cost and accessibility.

Justification

The ONS guideline panel determined there was very low certainty in the evidence for net health harms from resistance exercises in addition to self-management. The panel noted the importance of the inclusion of a trained professional to supervise the exercise program. Overall, the panel judged that the desirable outcomes were greater than undesirable outcomes and made a conditional recommendation for resistance exercise in addition to self-management.

Subgroup considerations

No subgroup considerations.

Implementation considerations

No implementation considerations

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

- Assess the effect of clearly defined/standardized exercise programs on lymphedema, including types, doses, timing, qualifications/training of providers
- Determine the additional benefits of an active treatment (e.g., aerobic exercises, resistance exercises, and water-based exercises) along with Phase II of CDT (self-management)

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Supervised water-based/yoga exercise plus self-management (Phase II CDT) for treatment of lymphedema

RECOMMENDATION

Among patients with cancer-related secondary lymphedema, should supervised water based/yoga exercise plus self-management (Phase II CDT), rather than self-management alone be used for lymphedema treatment?	
POPULATION:	Persons with cancer-related secondary lymphedema
INTERVENTION:	Water-based/yoga exercise plus self-management (Phase II CDT)
COMPARISON:	Self-management alone
MAIN OUTCOMES:	Reduction of lymphedema swelling and symptoms; Return to work and usual activities of daily living; Decrease in physical activity; Fatigue; Functional disability (ROM, grip); Mortality; Quality of life (depression, anxiety); Adverse events related to the intervention
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Patients with lymphedema experience physical symptoms such as pain, fatigue, and decrease in activity (Anbari, Wanchai, & Armer, 2019); lymphedema and has a negative psychosocial impact (Anbari, Wanchai, & Armer, 2019; Fu et al., 2013). Survivors with lymphedema have higher out-of-pocket health-related costs, including productivity losses, compared to survivors without lymphedema (Dean et al., 2019).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Jane Armer, PhD, RN, FAAN, CLT, Marcia Beck, RN, MSN, ACNS-BC, CLT-LANA®, Jie Deng, PhD, RN, OCN®, FAAN, Mei R. Fu, PhD, RN, FAAN, Ellen Poage, FNP-C, MSN, MPH, CLT-LANA , Suzy Lockwood, PhD, MSN, RN, OCN®, FAAN, Pamela Ostby, PhD, RN, OCN®, CLT Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know	<p>The incidence of lymphedema varies by type of cancer and procedure. At 1 year post-surgery, 22–66% of breast cancer patients experienced lymphedema (Armer & Stewart, 2010). At 2 years, the figure was 35–81% (Armer & Stewart, 2010); at five years, 43–94% (Armer & Stewart); and at seven years, 36% (Clough-Gorr, Ganz, & Silliman, 2010). Rupp et al. (2019) found that lymphedema persisted through a 10-year follow-up for more than 23% of patients. Also, incidence of breast cancer-related lymphedema in the arm varied by the type of surgery performed. At the 2.5-year follow-up, 3% of patients who underwent sentinel lymph node biopsy experienced arm lymphedema (Sagen, Kkaaresen, Sandvik, Thune, & Risberg, 2014); 17% of patients who underwent axillary lymph node dissection had that adverse effect (Sagen et al., 2014).</p> <p>Cormier et al. (2010) found the incidence of gynecologic cancer-related lymphedema to be 20% (Cormier et al., 2010). Bae et al. (2016) reported that almost 70% of patients with endometrial cancer experienced lymphedema within the first 12 months after surgery and that the lymphedema continued beyond 12 months in about 80% of patients.</p> <p>Cormier et al. (2010) found the incidence of melanoma-related lymphedema to be 16% (Cormier et al., 2010). Melanoma-related upper extremity lymphedema incidence was noted as 5% (Cormier et al., 2010) and 31% (Cromwell et al., 2015); lower extremity as 28% (Cormier et al., 2010) and 40% (Cromwell et al., 2015).</p> <p>The incidence of lymphedema in patients with genitourinary cancer was reported as 10% (Cormier et. al., 2010) and in patients with head and neck cancer patients, 4% (Cormier et. al., 2010).</p>	
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">● Trivial○ Small○ Moderate○ Large○ Varies○ Don't know	<p>For evidence, see Lytvyn, L., Zeraatkar, D., Anbari, A., Ginex, P., Zoratti, M., Niburski, K., ... Morgan, R. (2020). Conservative intervention strategies for adult cancer-related lymphedema: A systematic review and network meta-analysis of randomized controlled trials. <i>Oncology Nursing Society</i>, 47(5).</p>	<p>The panel determined the magnitude of the desirable effects to be trivial based on their interpretation of the SMD values.</p>
Undesirable Effects		
How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large○ Moderate○ Small● Trivial○ Varies○ Don't know	<p>For evidence, see Lytvyn, L., Zeraatkar, D., Anbari, A., Ginex, P., Zoratti, M., Niburski, K., ... Morgan, R. (2020). Conservative intervention strategies for adult cancer-related lymphedema: A systematic review and network meta-analysis of randomized controlled trials. <i>Oncology Nursing Society</i>, 47(5).</p>	<p>Quality of life is on the side of self-management (Lytvyn et al., 2020).</p> <p>The panel noted a small risk of skin rash from contact with the pool, not from the exercise itself. They also noted muscle strain</p>

		as a potential side effect of yoga. They decided that some muscle strain/soreness points to the need for conditioning.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 		The panel rated the certainty in these estimated effects as very low, owing to very serious imprecision from the potential for both benefit and harm, few participants included in the studies, and serious risk of bias due to high loss to follow-up.
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability 	<p>In a qualitative phenomenological study (Río-González, Molina-Rueda, Palacios-Ceña, & Alguacil-Diego, 2018) in Spain of life with lymphedema, 11 patients with gynecological or urological cancer-related lymphedema were assessed. Physical issues related to work, leisure activities, and sports were reported. Compression garments made tasks difficult and were frequently a nuisance. Appearance requirements at work were a problem because of the garments. Participants found it difficult to psychologically deal with lymphedema, which they described as a traumatic event and a chronic condition.</p> <p>In a population-based cohort study (Ahmed, Rizment, Lazovich, Schmitz, & Folsom, 2008) of the health-related quality of life of 1,287 female breast cancer survivors, women diagnosed with lymphedema or having arm symptoms without a lymphedema diagnosis had lower physical and mental health-related quality of life than women without lymphedema or arm symptoms, based on data reported using the Medical Outcomes Study Short Form-36.</p> <p>In a qualitative analysis (Anbari, Wanchai, & Armer, 2019) of 97 women diagnosed with breast cancer-related lymphedema and quality of life during seven years of survivorship, the women reported pain, fatigue, being less active, an impact on their jobs and roles, concerns with body image, frustration, depression, and irritability.</p> <p>In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), challenges to behavioral changes included symptoms such as lymphedema, chronic weight retention, depression symptoms, and personal barriers including lack of time and resources and little knowledge about how to start incorporating physical activity in their lives.</p>	<p>The panel decided patients may prefer different activities or self-management.</p> <p>The panel determined that patients with wounds cannot be in the water.</p>

Balance of effects		
Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div>○ Favors the comparison</div><div>○ Probably favors the comparison</div><div>● Does not favor either the intervention or the comparison</div><div>○ Probably favors the intervention</div><div>○ Favors the intervention</div><div>○ Varies</div><div>○ Don't know</div></div></div>		The panel had decided there was a negligible difference between the efficacy of the intervention and comparison and that the intervention had trivial benefit.
Resources required		
How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div>○ Large costs</div><div>● Moderate costs</div><div>○ Negligible costs and savings</div><div>○ Moderate savings</div><div>○ Large savings</div><div>○ Varies</div><div>○ Don't know</div></div></div>		The panel noted a cost to access a pool and that yoga can be done at home.
Certainty of evidence of required resources		
What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<div><div><div>○ Very low</div><div>○ Low</div><div>○ Moderate</div><div>○ High</div><div>● No included studies</div></div></div>	No research evidence identified.	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies● No included studies	No research evidence identified.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Reduced● Probably reduced○ Probably no impact○ Probably increased○ Increased○ Varies○ Don't know	No research evidence identified.	The panel determined equity could be affected by the cost of and access to a pool/facilities and that the cost would likely not be covered by insurance.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know	In a qualitative study (Black et al., 2018) of perceived barriers and preferred components for physical activity interventions among 20 African American patients with type 2 diabetes who were survivors of breast or endometrial cancer (percentage of participants having lymphedema unknown), preferred components of a physical activity program would include personal interactions with group or individual counseling, activities suited for physical limitations and comorbidities, peer partners, leaders who understand that emotions can affect motivation, and access to public facilities.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ No○ Probably no○ Probably yes	No research evidence identified.	

<div><div>● Yes</div><div>○ Varies</div><div>○ Don't know</div></div>		
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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

Among persons with cancer-related secondary lymphedema, the ONS guideline panel *suggests* supervised water-based activities or yoga in addition to self-management (Phase II CDT) rather than self-management alone. (Conditional recommendation, very low certainty of evidence).

Remarks: Preference for water-based exercise or yoga or self-management may be driven by cost and accessibility.

Justification

The ONS guideline panel determined there was very low certainty in the evidence for net health harms from supervised water-based exercises or yoga in addition to self-management. Overall, the panel judged that the desirable outcomes were greater than the undesirable outcomes and made a conditional recommendation for either supervised water-based exercise or yoga, in addition to self-management.

Subgroup considerations

No subgroup considerations.

Implementation considerations

No implementation considerations.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

- Assess the effect of clearly defined/standardized exercise programs on lymphedema, including types, doses, timing, qualifications/training of providers
- Determine the additional benefits of an active treatment (e.g., aerobic exercises, resistance exercises, and water-based exercises) along with Phase II of CDT (self-management)

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