

Keep Fit and Have Fun(*ction*): The Importance of Cancer Prehabilitation

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Presenter Disclosure

- **Faculty/Speaker: Lindsey Woodrow**

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- **Other:** None

Mitigating Potential Bias

- Not Applicable

Equity Commitment

- In preparing for this presentation, I have considered the Health Equity Resource for Presenters provided by the conference planning committee.
- This was provided to help presenters reflect on how these topics and content can have good effects or bad effects on people or populations that are underserved.

Learning Objectives

- At the end of this session, participants will be able to:
 - Define prehabilitation
 - Identify the components of a prehabilitation program
 - Describe how prehabilitation impacts patient outcomes
 - Describe physical activity guidelines for cancer survivors

Agenda

- Terminology
- *Exercise Is Medicine*
- Defining prehabilitation
- Components of a prehabilitation program
- Physical activity guidelines for cancer survivors
- Evidence for cancer prehabilitation
- Safety considerations
- Summary

Terminology

- Physical activity (PA):
 - Any bodily movement produced by skeletal muscles that results in energy expenditure. The energy expenditure can be measured in kilocalories. Physical activity in daily life can be categorized into occupational, sports, conditioning, household, or other activities.
- Exercise:
 - A subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective of the improvement or maintenance of physical fitness.
- Physical fitness:
 - A set of attributes that are either health- or skill-related. The degree to which people have these attributes can be measured with specific tests.

(Caspersen, 1985)

**So, while we're talking about
"exercise" as medicine, we're
really referring to "physical
activity" as medicine...**

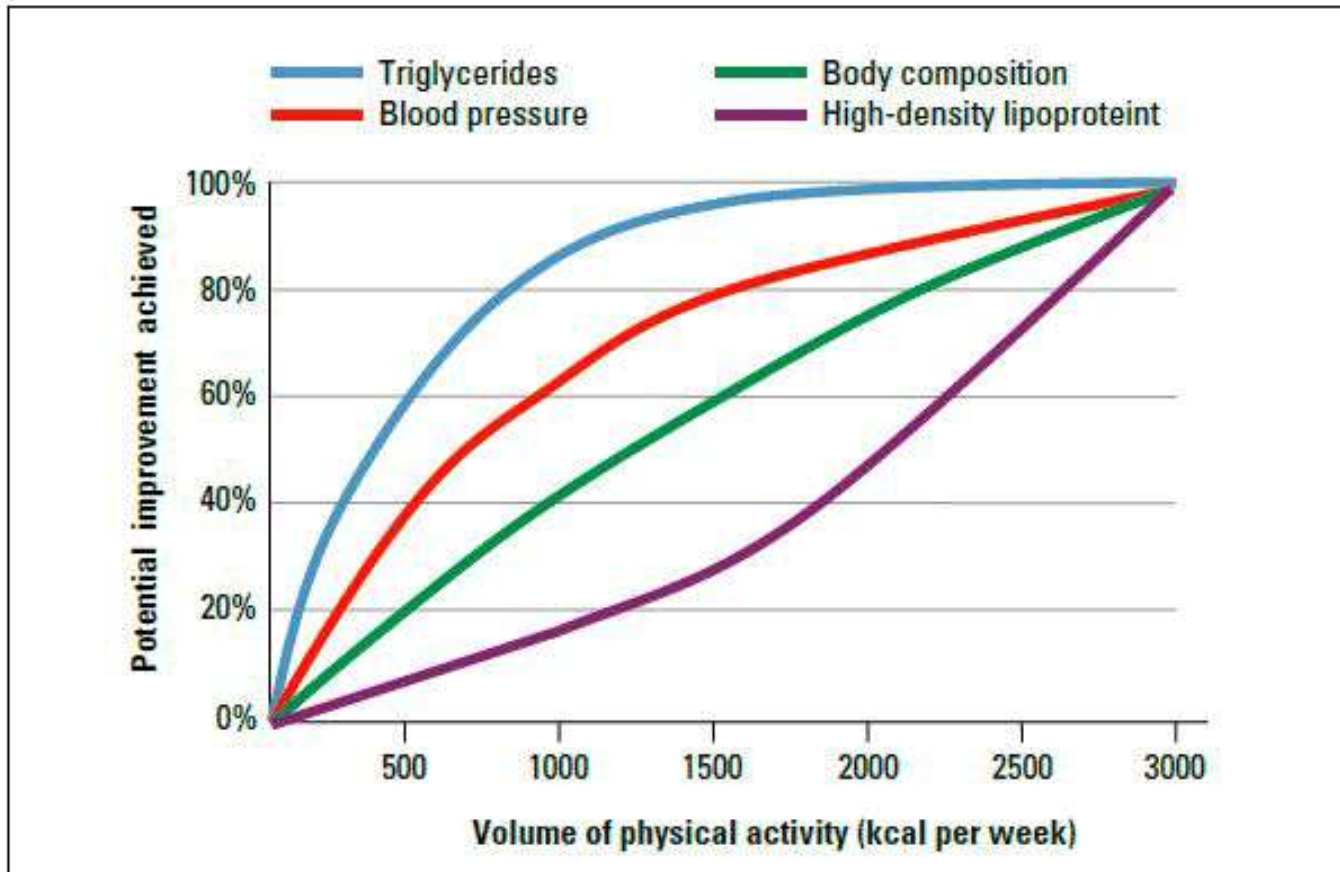
Exercise Is Medicine

- Movement launched by ACSM in 2007
 - With support from AMA, Office of US Surgeon General
 - Movement brought to Canada by CSEP in 2011
- Goal:
 - To mobilize healthcare professionals (including physicians) to promote PA to prevent, reduce, manage or treat diseases that impact health and quality of life
- Done by:
 - Assessing current PA levels
 - PA as a vital sign!
 - Prescribing PA (or referring to qualified exercise professional)

(Tipton, 2014; MacIntosh, 2017)

What is the goal of physical activity?

It depends...

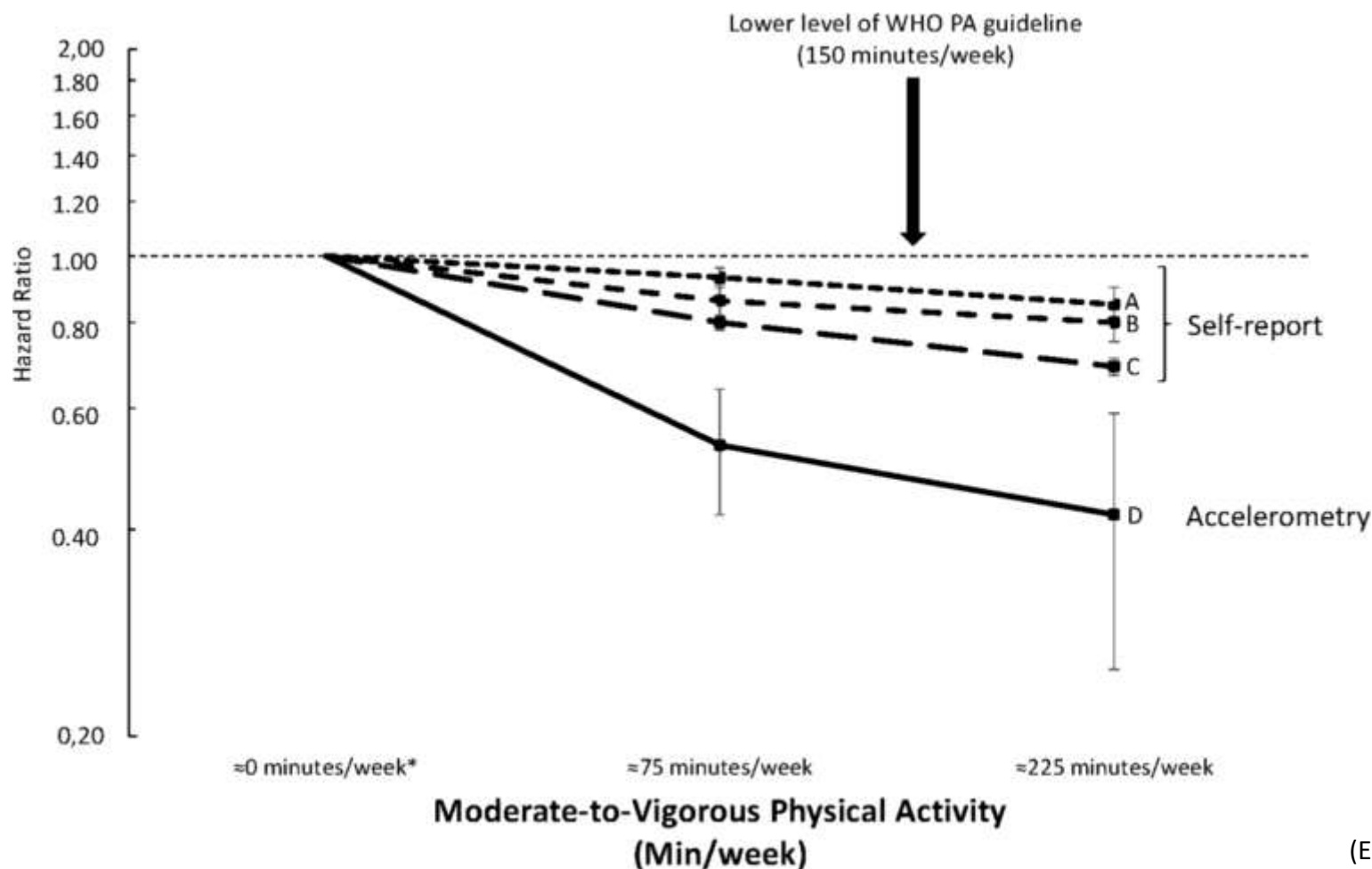


Physical Activity and Mortality

- Level of PA inversely related to risk of all-cause mortality
 - Non-linear relationship
 - Similar relationship seen in patients with T2DM, breast cancer, ischemic heart disease and COPD
- Amount of sedentary time directly related to all-cause mortality
 - Non-linear relationship
- Biggest “bang for your buck” in lower PA quartiles
 - Suggests that modest increases in PA substantially reduce risk of death
 - Threshold likely lower than current PA recommendations
 - Least active individuals should be targeted in public health interventions

(Ekelund, 2020; Geidl, 2020; Wen, 2011)

Physical Activity and Mortality



(Ekelund, 2020)

Functional Independence

- Estimated VO_2 max required for functional independence
 - Women: 15 mL/kg/min
 - Men: 18 mL/kg/min
- VO_2 max declines with age
 - 5 mL/kg/min decrease each decade starting in 20s-30s
 - Most sedentary elderly people slip below threshold for independence between 80 and 90 years of age
 - 90% of cancer diagnoses in patients \geq age 50
- Training can increase VO_2 max by 5-10 mL/kg/min in middle-aged adults
 - Reduces biologic age by \geq 10 years
 - Prevents loss of functional independence

(Shephard, 2009, Canadian Cancer Society)

Frailty

- “Frailty is a state of vulnerability to poor resolution of homeostasis following a stressor event. It develops as a consequence of cumulative decline across multiple physiological systems and increases the risk of adverse outcomes.”
- Prevalence in older cancer patients
 - Frailty → 42%
 - Pre-frailty → 43%
- Outcomes of frailty/pre-frailty in older cancer patients:
 - Increased all-cause mortality
 - Increased post-operative complications, mortality
 - Increased chemotherapy intolerance

(Clegg, 2013; Handforth, 2015)

Health Benefits

- Health benefits of 150-300 minutes of moderate-intensity PA/week:
 - ↓ risk of developing new chronic health condition/progression of existing condition
 - T2DM, HTN, heart disease, stroke, OA
 - **↓ risk of cancers**
 - **Bladder, breast, colon, endometrium, esophagus, kidney, stomach**
 - **↓ cancer mortality**
 - ↓ risk of dementia
 - ↓ risk of depression, anxiety
 - Improved symptoms
 - Improved weight maintenance
 - ↓ risk of falls, fall-related injuries in older adults
- Other benefits:
 - ↑ sleep quality
 - ↓ sleep latency
 - ↑ sleep maintenance
 - ↑ time in deep sleep
 - ↑ daytime energy
 - ↑ QoL, function

(2018 Physical Activity Guidelines Advisory Committee Scientific Report)

Effects of Exercise on Health-Related Outcomes in Those with Cancer









What can exercise do?

- **Prevention of 7 common cancers***
Dose: 2018 Physical Activity Guidelines for Americans: 150-300 min/week moderate or 75-150 min/week vigorous aerobic exercise
- **Survival of 3 common cancers****
Dose: Exact dose of physical activity needed to reduce cancers-specific or all-cause mortality is not yet known; Overall more activity appears to lead to better risk reduction

*bladder, breast, colon, endometrial, esophageal, kidney and stomach cancers

**breast, colon and prostate cancers

Overall, avoid inactivity, and to improve general health, aim to achieve the current physical activity guidelines for health (150 min/week aerobic exercise and 2x/week strength training).

Outcome	Aerobic Only	Resistance Only	Combination (Aerobic + Resistance)
Strong Evidence	Dose	Dose	Dose
 Cancer-related fatigue	3x/week for 30 min per session of moderate intensity	2x/week of 2 sets of 12-15 reps for major muscle groups at moderate intensity	3x/week for 30 min per session of moderate aerobic exercise, plus 2x/week of resistance training 2 sets of 12-15 reps for major muscle groups at moderate intensity
 Health-related quality of life	2-3x/week for 30-60 min per session of moderate to vigorous	2x/week of 2 sets of 8-15 reps for major muscle groups at a moderate to vigorous intensity	2-3x/week for 20-30 min per session of moderate aerobic exercise plus 2x/week of resistance training 2 sets of 8-15 reps for major muscle groups at moderate to vigorous intensity
 Physical Function	3x/week for 30-60 min per session of moderate to vigorous	2-3x/week of 2 sets of 8-12 reps for major muscle groups at moderate to vigorous intensity	3x/week for 20-40 min per session of moderate to vigorous aerobic exercise, plus 2-3x/week of resistance training 2 sets of 8-12 reps for major muscle group at moderate to vigorous intensity
 Anxiety	3x/week for 30-60 min per session of moderate to vigorous	Insufficient evidence	2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity
 Depression	3x/week for 30-60 min per session of moderate to vigorous	Insufficient evidence	2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity
 Lymphedema	Insufficient evidence	2-3x/week of progressive, supervised, program for major muscle groups does not exacerbate lymphedema	Insufficient evidence
Moderate Evidence			
 Bone health	Insufficient evidence	2-3x/week of moderate to vigorous resistance training plus high impact training (sufficient to generate ground reaction force of 3-4 time body weight) for at least 12 months	Insufficient evidence
 Sleep	3-4x/week for 30-40 min per session of moderate intensity	Insufficient evidence	Insufficient evidence

Citation: bit.ly/cancer_exercise_guidelines

Moderate intensity (40%-59% heart rate reserve or VO₂R) to vigorous intensity (60%-89% heart rate reserve or VO₂R) is recommended.

Exercise is Medicine® AMERICAN COLLEGE of SPORTS MEDICINE

Phases of Cancer Rehabilitation

- Dietz Classification
 - Preventative
 - → “prehabilitation”
 - Restorative
 - Supportive
 - Palliative

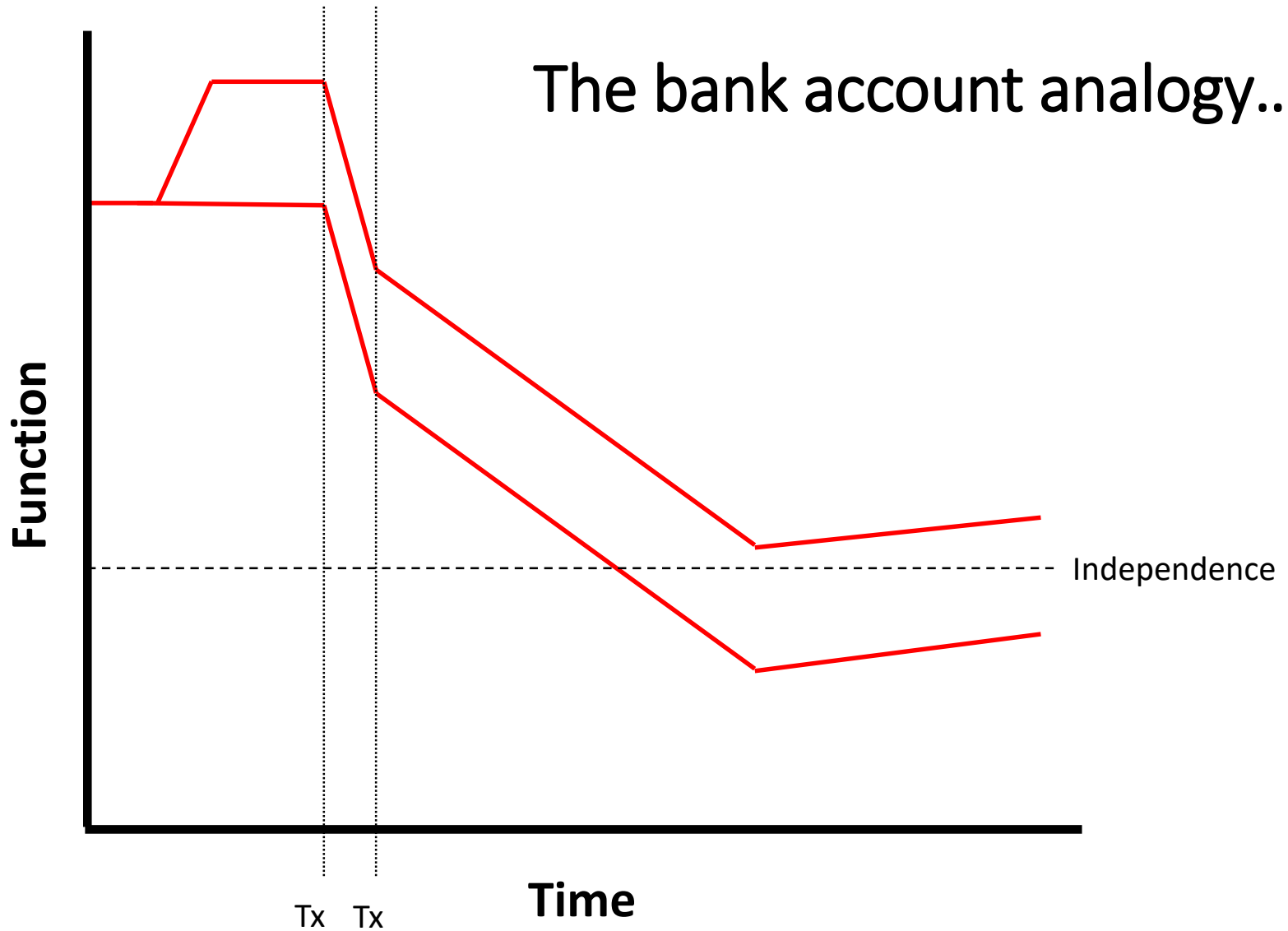
(Dietz, 1981)

Prehabilitation

- Prehabilitation is an area of medicine *“concerned with strategies to optimize patients’ pre-treatment physiological, functional, and psychological risk profiles, such that post-treatment recovery trajectories are boosted.”*

(Silver, 2014)

The bank account analogy...



The Army's need for recruits and the growing opinion that imperfection of this kind could be corrected by appropriate means, led to the establishment of two substandard recruits physical development depots. To those such as could be expected to profit were sent, there to encounter those health- and growth-promoting agencies that had been absent from their civilian environments. There they received the raw materials of health, growth, and development—an objective in living, a sense of being of value to society, good food, lodging, hygiene, and recreation, combined with controlled physical training and general education.

These centres are concerned with prehabilitation—that is to say, with the metamorphosis of the substandard recruit into the standard recruit, who can then enter a primary training centre and profit from the military training that he will there undergo. Men up to the age of 35 of poor physique or exhibiting minor remedial defects of locomotion form the bulk of those who are sent to these physical development centres. Of the rest many are cases of postural spinal defect and of foot defect. Young officers in need of physical development or restoration were also accommodated.

Goals of Prehabilitation

- Goals of prehab:
 - Assess baseline level of function
 - Objective measures, body composition
 - Recognize impairments present at baseline
 - Prescribe interventions to:
 - Promote function
 - Address underlying impairments
 - Mitigate anticipated impairments (from cancer/Tx)
 - Reassess function following interventions
 - Objective measures, body composition

(Silver, 2015)

Components of a Prehab Program

- Multimodal
 - Exercise Rx → ACSM*/CSEP guidelines
 - Managing barriers to exercise
 - Medical, psychological, access, etc.
 - Nutritional counselling
 - Alcohol reduction
 - Smoking cessation
 - Stress reduction

(Silver, 2015; Campbell, 2019; USDHHS, 2018; Moore, 2015; Chaoul, 2014)

Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable

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Exercise Guidelines for Cancer Survivors

- Aerobic
 - **F**requency
 - ≥ 3 times / week
 - **I**ntensity
 - Moderate intensity
 - **T**ime
 - ≥ 30 minutes / session
 - **T**ype
 - Continuous, rhythmic activity that uses large muscles
- Resistance
 - **F**requency
 - ≥ 2 times / week
 - **I**ntensity
 - $\geq 60\%$ 1RM
 - **T**ime
 - 2 sets x 8-15 reps
 - **T**ype
 - Exercises involving all major muscle groups

(Campbell, 2019)

Components of a Prehab Program

- Multidisciplinary
 - Physical Medicine and Rehabilitation*
 - *Anesthesia
 - Oncology, Family Medicine
 - Nursing
 - Occupational therapy
 - Physiotherapy
 - Speech language pathology
 - Respiratory therapy
 - Dietetics
 - Psychology
 - Social work
 - Recreation therapy
 - Music therapy
 - ...

(Silver, 2015; Campbell, 2019; USDHHS, 2018; Moore, 2015; Chaoul, 2014)

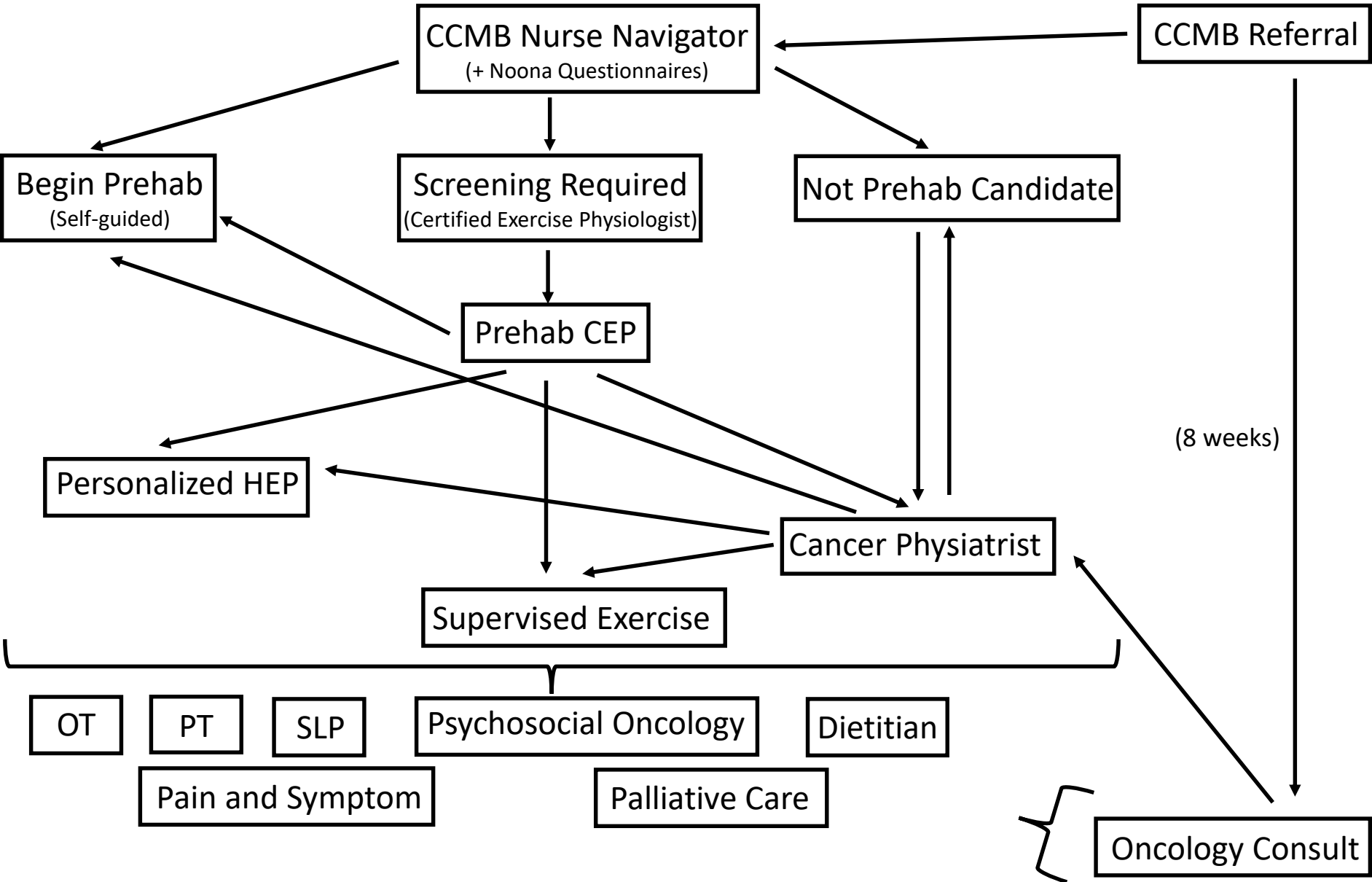
Benefits of Cancer Prehabilitation

- Improved quality of life, symptom burden, function
- Reduced complications, readmissions
- Reduced length of stay
- Reduced mortality and improved survival
- Reduced healthcare costs!

Good for the patient and the healthcare system!

(Silver, 2015; Silver, 2013; Kotz, 2012; Kullbersh, 2006; Cavalheri, 2017; Lai, 2017; Morano, 2013; Boujibar, 2018; Salvi, 2016; Souwer, 2018; Dewberry, 2019; Hattori, 2018; Huisman, 2015; Benzo, 2011; Pehlivan, 2011; Trepanier, 2019; Dholakia, 2021)

Prehabilitation in Manitoba

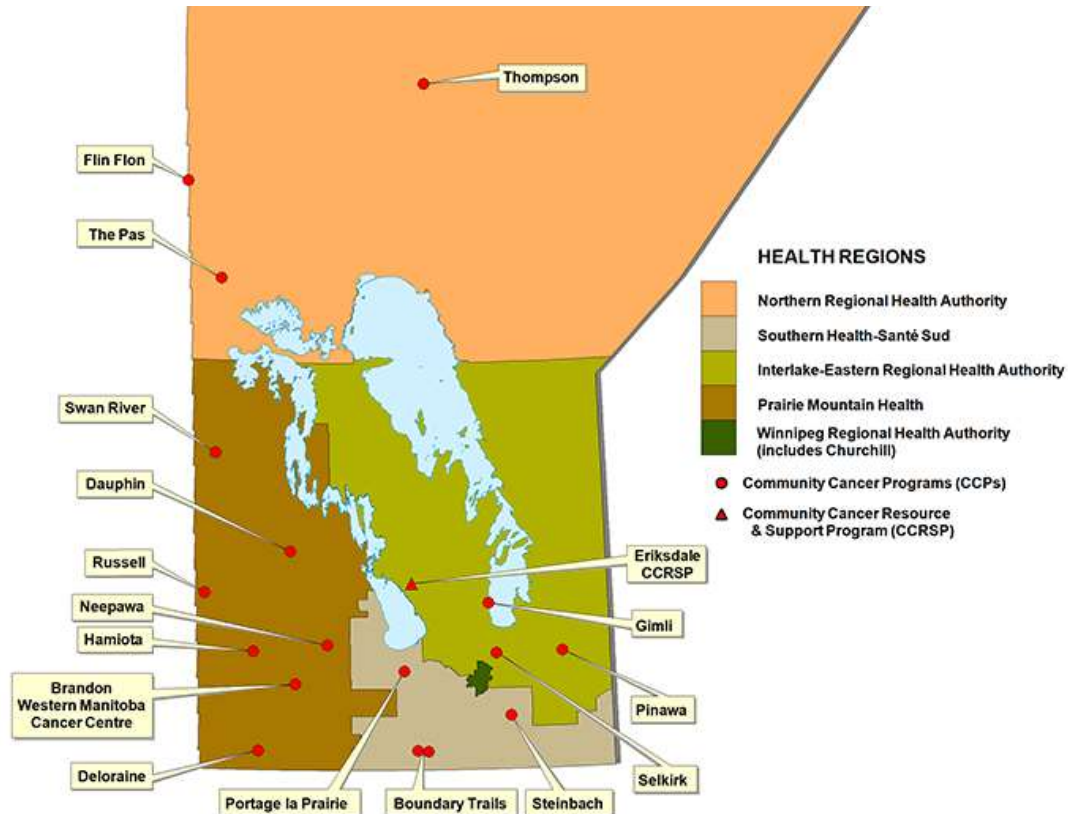


Prehabilitation in Manitoba

- Received CCMF Grant Funding for 2022-2023
- Developing materials for prehab package
 - Including home exercise program requiring minimal equipment/space
 - In future: ?videos, ?website, ?app
 - Consider translations, access to internet, technology
- ?Addition of certified exercise physiologist
 - In future: ?more prehab supports, ?services outside of Winnipeg
- Developing frailty index for CCMB Prehab
 - Demonstrate CCMB model can work in other locations where geography/access a challenge

Prehabilitation Telemedicine in Neoadjuvant Surgical Oncology Patients During the Novel COVID-19 Coronavirus Pandemic

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Safety Considerations

- ?Pre-exercise medical clearance
 - Cancer population flagged on PAR-Q/CSEP Get Active Questionnaire
 - When in doubt, refer

TABLE 4. Adapted national comprehensive cancer network triage approach based on risk of exercise-induced adverse events.

Description of Patients	Evaluation, prescription, and programming recommendations
No comorbidities	No further preexercise medical evaluation ^a Follow general exercise recommendations
Peripheral neuropathy, arthritis/musculoskeletal issues, poor bone health (e.g., osteopenia or osteoporosis), lymphedema	Recommend preexercise medical evaluation ^a Modify general exercise recommendations based on assessments Consider referral to trained personnel ^b
Lung or abdominal surgery, ostomy, cardiopulmonary disease, ataxia, extreme fatigue, severe nutritional deficiencies, worsening/changing physical condition (i.e., lymphedema exacerbation), bone metastases	Preexercise medical evaluation ^a and clearance by physician before exercise Referral to trained personnel ^b

^aMedical evaluation—per NCCN guidelines for specific symptoms and side effects. ^bRehabilitation specialists (i.e., physical therapists, occupational therapists, physiatrists) and certified exercise physiologists (i.e., ACSM Certified Clinical Exercise Physiologist (ACSM-CEP), Canadian Society for Exercise Physiology Certified Exercise Physiologist (CSEP-CEP), Exercise & Sport Science Australia Accredited Exercise Physiologist (ESSA-AEP)).

(Campbell, 2019)

Safety Considerations

General Rehabilitation Considerations in the Context of Hematological Compromise^{13,16,19}

Blood Count	Rehabilitation Considerations
White Blood Cells	<p>> 11.0 10⁹/L: Symptom-based approach, monitor for fever</p> <p>< 4.0 10⁹/L: Symptom-based approach, monitor for fever</p> <p>< 1.5 10⁹/L (Neutropenia): Symptom-based approach, neutropenic precautions based on facility guidelines.</p> <ul style="list-style-type: none"> Mild < 1.5 10⁹/L Moderate 0.5 – 1.0 10⁹/L Severe < 0.5 10⁹/L
Platelets	<p>< 150,000 cells/uL (Thrombocytopenia): Symptom-based approach, monitor tolerance to activity.</p> <p>> 50,000 cells/uL: Progressive exercise as tolerated, aerobic and resistive with monitoring for symptoms associated with bleeding.</p> <p>> 30,000 cells/uL: Active range of motion exercises, moderate exercise, aquatic therapy based on immune status.</p> <p>> 20,000 cells/uL: Light exercise, walking, activities of daily living without strenuous effort; Assess fall risk and implement safety plan for falls prevention</p> <p>< 20,000 cells/uL: Understand transfusion status or plan of care, walking, light activities of daily living, symptom monitoring, precaution for falls.</p>
Hemoglobin	<p>Reference Values:</p> <p>Male: 14 – 17.4 g/dL</p> <p>Female: 12 – 16 g/dL</p> <p>< 11 g/dL (anemia): Establish baseline vital signs; may be tachycardic or present with orthostatic hypertension; symptom-based approach to intervention, monitoring self-perceived exertion</p> <p>< 8 g/dL (severe anemia): Close monitoring of symptoms and vital signs with intervention; transfusion may or may not be indicated based on individual presentation; short periods of intervention, symptom-limited; education for energy conservation</p>

Mirels Criteria

Score	Site of lesion	Size of lesion	Nature of lesion	Pain
1	Upper limb	< 1/3 of cortex	Blastic	Mild
2	Lower limb	1/3–2/3 of cortex	Mixed	Moderate
3	Trochanteric region	> 2/3 of cortex	Lytic	Functional

General Safety Measures with Bone Metastasis

No manual muscle testing in affected limb
No progressive resistive exercises in affected limb
Offloading affected limb with assisted device
Avoid excessive spinal flexion, extension and rotation. Clarify need for bracing.
Monitor for increasing functional pain

(Maltser, 2017)

Take Home Messages

- Physical activity is important to reduce mortality, improve function, and for health benefits
 - Excellent evidence that physical activity is safe and beneficial for many medical conditions, including cancer
- Prehabilitation is a multimodal, team-based approach to improve pre-treatment profile and post-treatment recovery in cancer patients
 - Takes advantage of lead time prior to oncology consult!
- Cancer prehabilitation has been demonstrated to improve symptoms, reduce mortality and decrease healthcare costs
 - Phased rollout of CCMB Prehab Program to start in 2023!



“Too many things, too much to know...”

References

1. Caspersen, C. J., Powell, K. E., & Christenson, G. M. (1985). Physical activity, exercise and physical fitness: definitions and distinctions for health-related research. *Public Health Reports*, 100(2), 126-131.
2. Tipton, C. M. (2014). The history of "Exercise Is Medicine" in ancient civilizations. *Advances in Physiology Education*, 38(2), 109-117.
3. Macintosh, B. R., Boreskie, S., Petrella, R. J., Dasgupta, K., & Fowles, J. (2017). Historical perspective: Research supporting Exercise is Medicine in Canada. Canadian Society for Exercise Physiology. <https://csep.ca/2017/07/05/historical-perspective-research-supporting-exercise-is-medicine-in-canada/>
4. Ekelund, U., Dalene, K. E., Tarp, J., & Lee, I.-M. (2020). Physical activity and mortality: what is the dose response and how big is the effect? *British Journal of Sports Medicine*, 54(19), 1125-1126.
5. Geidl, W., Schlesinger, S., Mino, E., Miranda, L., & Pfeifer, K. (2020). Dose-response relationship between physical activity and mortality in adults with noncommunicable diseases: a systematic review and meta-analysis of prospective observational studies. *International Journal of Behavioral Nutrition and Physical Activity*, 17(1), 109.
6. Wen, C. P., Wai, J. P. M., Tsai, M. K., Yang, Y. C., Cheng, T. Y. D., Lee, M.-C., Chan, H. T., Tsao, C. K., Tsai, S. P., & Wu, X. (2011). Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet*, 378(9798), 1244-1253.
7. Shephard, R. J. (2009). Maximal oxygen intake and independence in old age. *British Journal of Sports Medicine*, 43(5), 342-346.
8. Canadian Cancer Statistics 2021. (2021). Canadian Cancer Society. <https://cdn.cancer.ca/-/media/files/research/cancer-statistics/2021-statistics/2021-pdf-en-final.pdf>
9. Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. *Lancet*, 381(9868), 752-762.
10. Handforth, C., Clegg, A., Young, C., Simpkins, S., Seymour, M. T., Selby, P. J., & Young, J. (2015). The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Annals of Oncology*, 26(6), 1091-1101.
11. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. (2018). Department of Health and Human Services. https://health.gov/sites/default/files/2019-09/PAG_Advisory_Committee_Report.pdf
12. Dietz, J. H. (1980). Adaptive rehabilitation of the cancer patient. *Current Problems in Cancer*, 5(5), 1-56.
13. Silver, J. K. (2014). Cancer rehabilitation and prehabilitation may reduce disability and early retirement. *Cancer*, 120(14), 2072-2076.
14. Silver, J. K. (2015). Cancer prehabilitation and its role in improving health outcomes and reducing health care costs. *Seminars in Oncology Nursing*, 31(1), 13-20.
15. Campbell, K. L., Winters-Stone, K. M., Wiskeemann, J., May, A. M., Schwartz, A. L., Courneya, K. S.,...Schmitz, K. H. (2019). Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. *Medicine & Science in Sports & Exercise*, 51(11), 2375-2390.
16. Moore, D. R., Churchward-Venne, T. A., Witard, O., Breen, L., Burd, N. A., Tipton, K. D., & Phillips, S. M. (2015). Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 70(10), 57-62.
17. Chaoul, A., Milbury, K., Sood, A. K., Prinsloo, S., & Cohen, L. (2014). Mind-body practices in cancer care. *Current Oncology Reports*, 16(12), 417-429.
18. Silver, J. K., & Baima, J. (2013). Cancer prehabilitation: an opportunity to decrease treatment related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes.
19. Kotz, T., Federman, A. D., Kao, J., Milman, L. Packer, S., Lopez-Prieto, C.,...Genden, E.M. (2012). Prophylactic swallowing exercises in patients with head and neck cancer undergoing chemoradiation: a randomized trial. *Archives of Otolaryngology – Head & Neck Surgery*, 138(4), 376-382.
20. Kulbersh, B. D., Rosenthal, E. L., McGrew, B. M., Duncan, R. D., McColloch, N. L., Carroll, W. R., & Magnuson, J. S. (2006). Pretreatment, preoperative swallowing exercises may improve dysphagia quality of life. *The Laryngoscope*, 116(6), 883-886.
21. Cavalheri, V., & Granger, C. (2017). Preoperative exercise training for patients with nonsmall cell lung cancer (review). *Cochrane Database of Systematic Reviews*, 6, i-40.
22. Lai, Y., Su, J., Qiu, P., Wang, M., Zhou, K., Tang, Y., & Che, G. (2017). Systematic shortterm pulmonary rehabilitation before lung cancer lobectomy: a randomized trial. *Interactive Cardiovascular and Thoracic Surgery*, 25(3), 476-483.
23. Morano, M. T., Araujo, A. S., Nascimento, F. B., da Silva, G. F., Mesquita, R., Pinto, J. S.,...Pereira, E. D. (2013). Preoperative pulmonary rehabilitation versus chest physical therapy in patients undergoing lung cancer resection: a pilot randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, 94(1), 53-58.
24. Boujibar, F., Bonnevie, T., Debeaumont, D., Bubenheim, M., Cuvellier, A., Peillon, C.,...Baste, J. M. (2018). Impact of prehabilitation on morbidity and mortality after pulmonary lobectomy by minimally invasive surgery: a cohort study. *Journal of Thoracic Disease*, 10(4), 2240-2248.
25. Salvi, R., Meoli, I., Cennamo, A., Perrotta, F., Cerqua, F. S., Montesano, R.,...Bianco, A. (2016). Preoperative high-intensity training in frail old patients undergoing pulmonary resection for NSCLC. *Open Medicine (Warsaw, Poland)*, 11(1), 443-448.
26. Souwer, E. T. D., Bastiaannet, E., de Bruijn, S., Breugom, A. J. van den Bos, F., Portielje, J. E. A., & Dekker, J. W. T. (2018). Comprehensive multidisciplinary care program for elderly colorectal cancer patients: "from prehabilitation to independence". *European Journal of Surgical Oncology*, 44(12), 1894-1900.
27. Dewberry, L. C., Wingrove, L. J., Marsh, M. D., Glode, Ashley, E., Scheffter, T. E., Leong, S.,...McCarter, M. D. (2019). Pilot prehabilitation program for patients with esophageal cancer during neoadjuvant therapy and surgery. *Journal of Surgical Research*, 235, 66-72.
28. Hattori, K., Matsuda, T., Takagi, Y., Nagaya, M., Inoue, T., Nishida, Y.,...Ito, S. (2018). Preoperative six-minute walk distance is associated with pneumonia after lung resection. *Interactive Cardiovascular and Thoracic Surgery*, 26(2), 277-283.
29. Huisman, M. G., Audisio, R. A., Ugolini, G., Montroni, I., Vigano, A., Spiliotis, J.,...van Leeuwen, B. L. (2015). Screening for predictors of adverse outcome in onco-geriatric surgical patients: A multicenter prospective cohort study. *European Journal of Surgical Oncology*, 41(7), 844-851.
30. Benzo, R., Wagle, D., Novotny, P., Wetzstein, M., Nichols, F., Shen, R. K.,...Deschamps, C. (2011). Preoperative pulmonary rehabilitation before lung cancer resection: results from two randomized studies. *Lung Cancer*, 73(3), 441-445.
31. Pehlivan, E., Turna, A., Gurses, A., & Gurses, H. N. (2011). The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. *Annals of Thoracic and Cardiovascular Surgery*, 17(5), 461-468.
32. Trepanier, M., Minnella, E. M., Paradis, T., Awasthi, R., Kaneva, P., Schwartzman, K.,...Lee, L. (2019). Improved disease-free survival after prehabilitation for colorectal cancer surgery. *Annals of Surgery*, 270(3), 493-501.
33. Dholakia, J., Coh, D. E., Straughn Jr., J. M., & Dilley, S. E. (2021). Prehabilitation for medically frail patients undergoing surgery for epithelial ovarian cancer: a cost-effectiveness analysis. *Journal of Gynecologic Oncology*, 32(6), e92.
34. Maltzer, S., Cristian, A., Silver, J. K., Morris, G. S., & Stout, N. L. (2017). A Focused Review of Safety Considerations in Cancer Rehabilitation. *PM&R*, 9(Supplement 2), S415-S428.