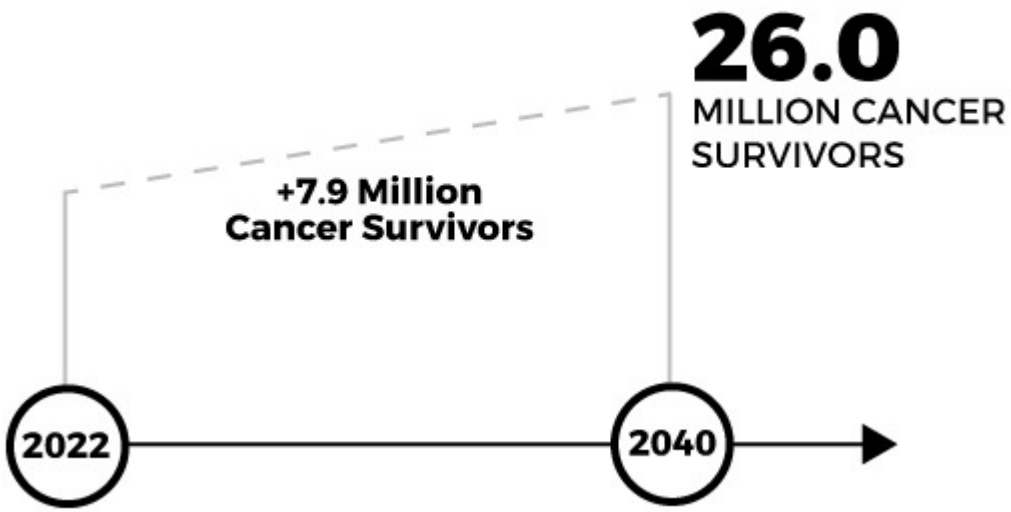
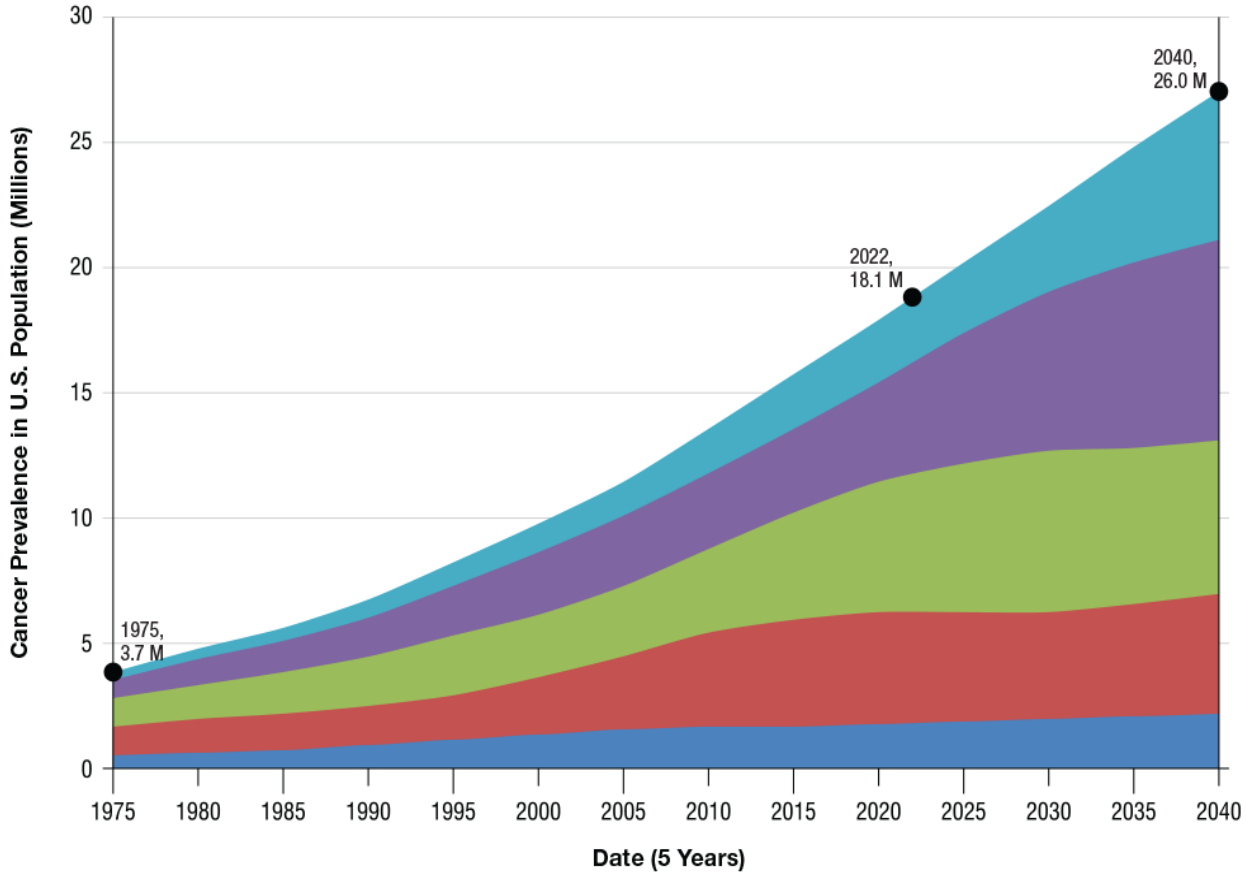
Using Digital Tools to Improve Physical Function in Cancer Patients and Survivors

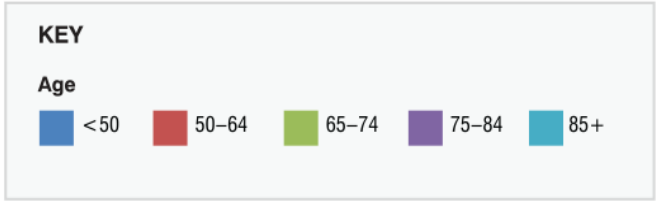
Maria C. Swartz, PhD, MPH, RD, LD
Assistant Professor
Department of Pediatrics-Research

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®



Cancer Prevalence and Projections in U.S. Population from 1975–2040



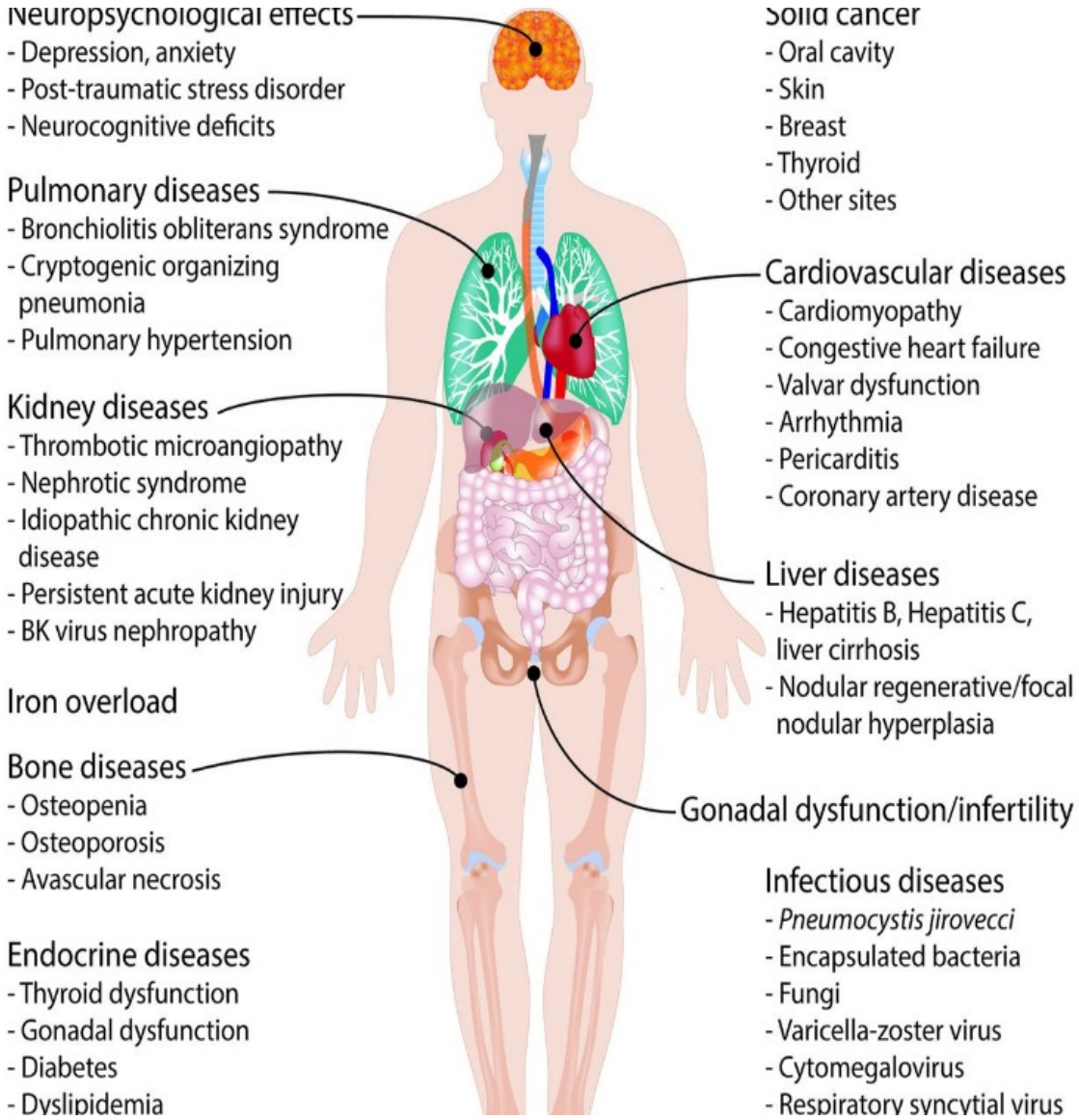


REFERENCES

Bluethmann SM, Mariotto AB, Rowland JH. Anticipating the "Silver Tsunami": Prevalence Trajectories and Comorbidity Burden among Older Cancer Survivors in the United States. Cancer Epidemiol Biomarkers Prev. 2016 Jul;25(7):1029-36.

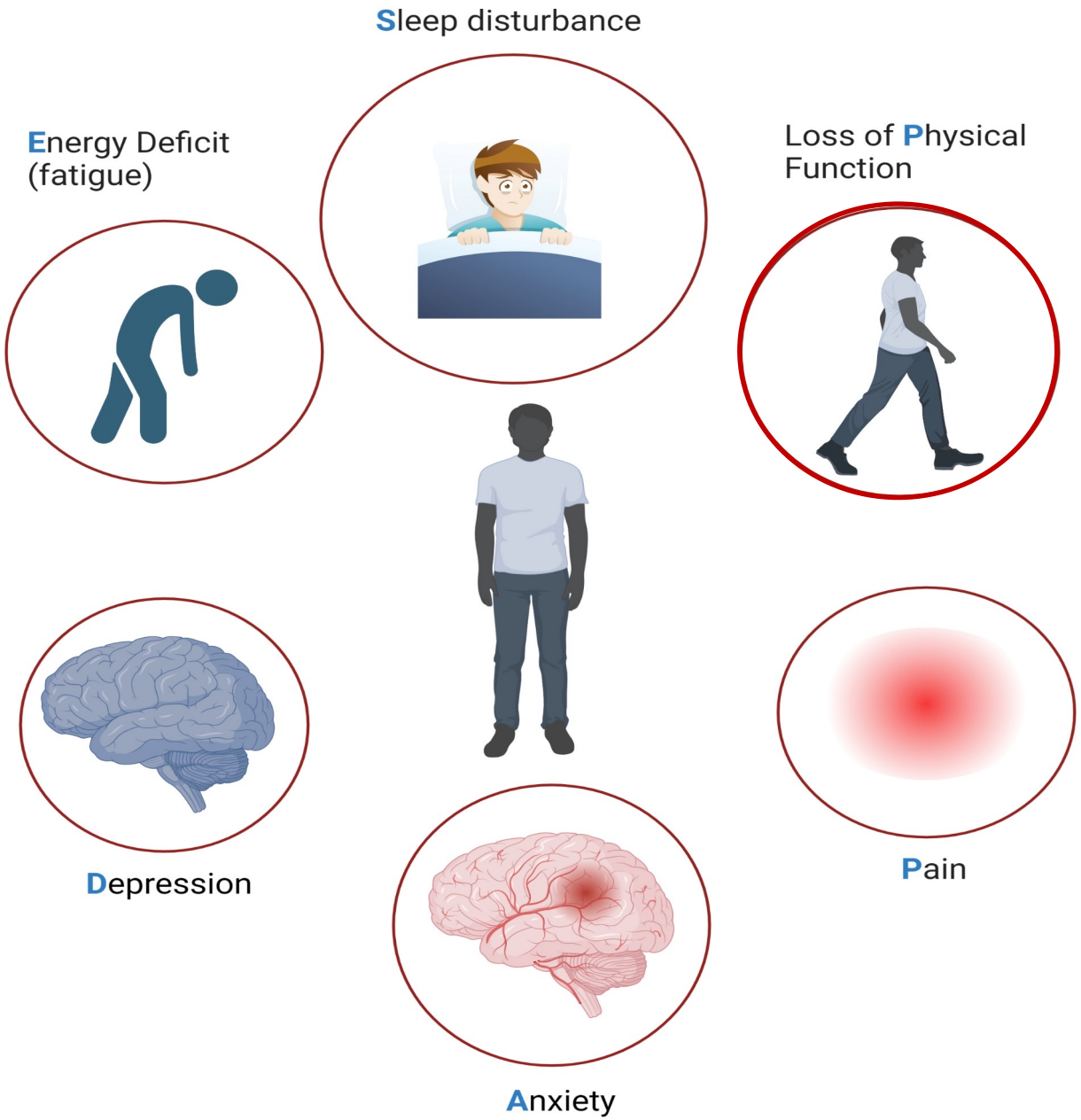
Miller KD, Nogueira L, Devasia T, Mariotto AB, Yabroff KR, Jemal A, Kramer J and Siegel RL. Cancer Treatment and Survivorship Statistics. CA A Cancer J Clin. 2022.

Short and long-term side effects[1]



[1]Rowland et al. (2014)

Common symptoms during and after cancer treatment: SPPADE[1]



[1]Kroenke et al. (2023)

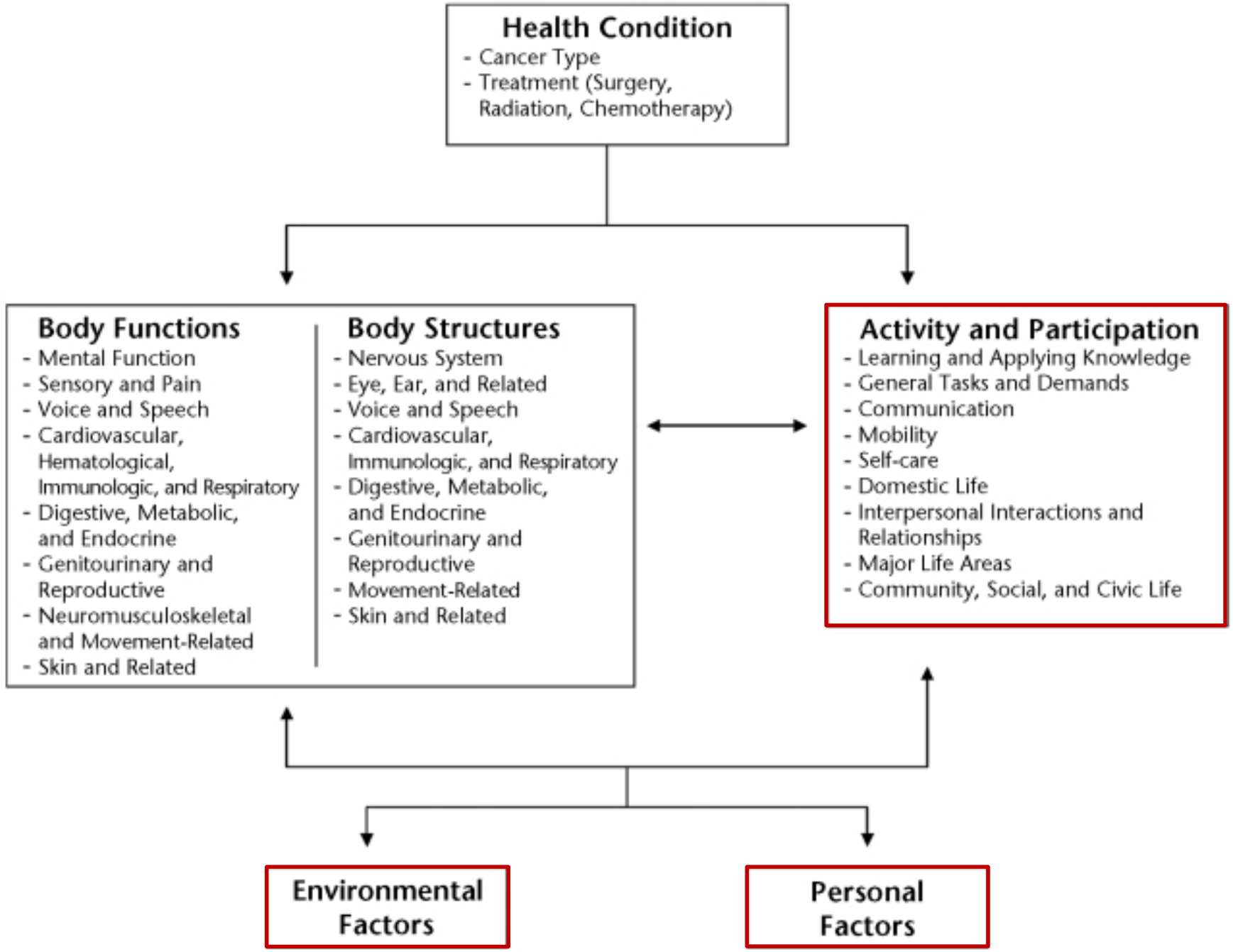
Functional issues in cancer survivors

- 53% of adult cancer survivors reported functional issues[1,2]
  - Activities of Daily Living-related problems were documented less frequently than symptoms (e.g., pain) and signs (e.g., weight loss)
    - 11.4% patients reported difficulty standing from chair/toilet
    - 4.4% documented in the electronic medical record

  - A range of 36% to 88% of young adult childhood cancer survivors (18-39 years old) reported symptoms associated with frailty phenotype expected of older adults (e.g., walking limitations and exhaustion)[3,4,5, 6]

[1]Cheville et al. (2009); [2]Cheville et al. (2017); [3]Hayek et al. (2019); [4]Fitch et al. (2020); [5]Tai et al. (2012); [6]Jones et al. (2020)

Applying WHO's ICF Framework for Oncologic Rehabilitation Care[1]



[1]Gilchrist et al. (2009)

Consequences of poor physical function

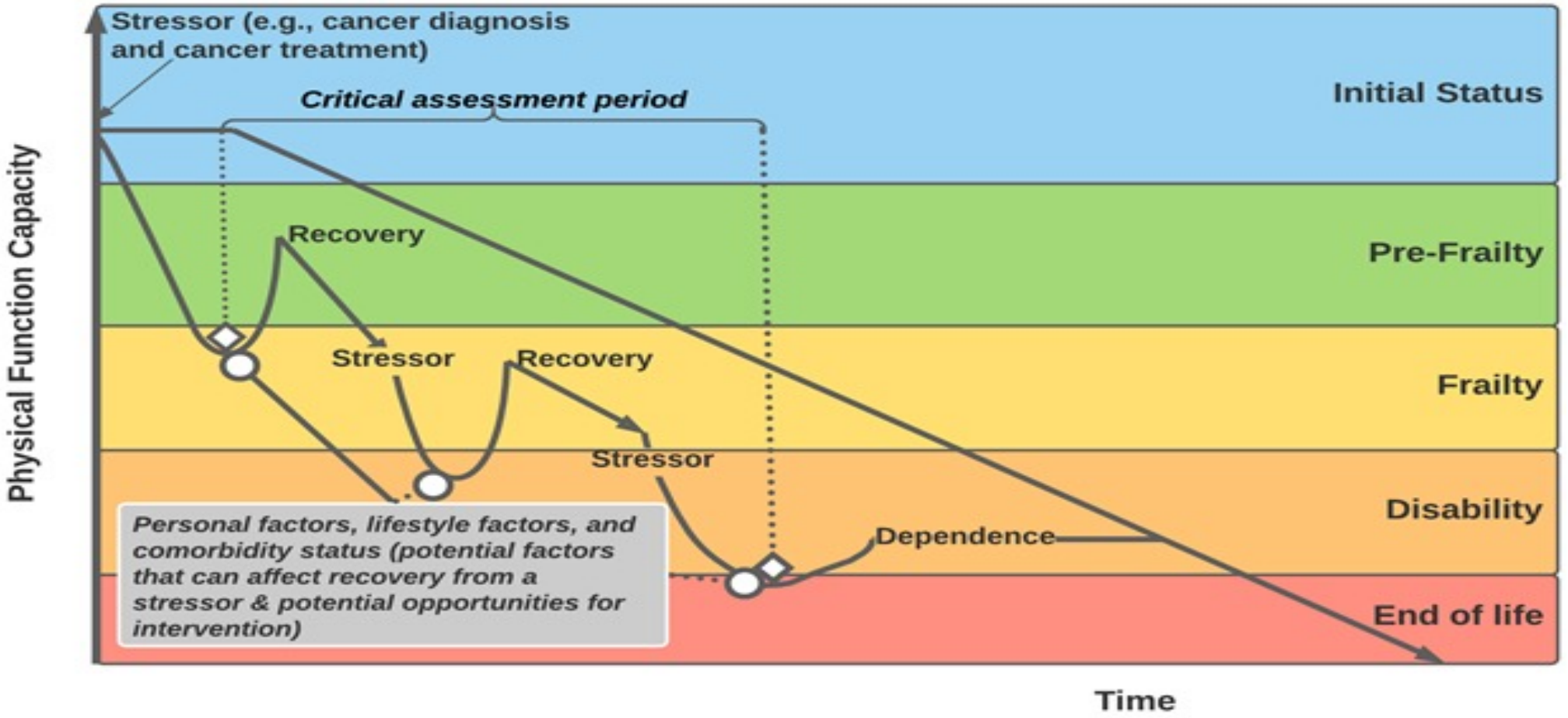


Figure 2. The cascade of functional decline (adapted from Dent et al. [2019])

Feliciano et al. (2020), doi: 10.1001/jamanetworkopen.2020.16747

Disability Rate at Different Time Points and Median Time to Disability (N=13,225 matched pairs using administrative data)

Cohort	Disability rate (95% CI)			Median year (95% CI)	Log-rank p-value
	3 Years	5 Years	9 Years		
Colorectal cancer	0.27 (0.2–0.28)	0.37 (0.36–0.38)	0.54 (0.53–0.56)	7.92 (7.58–8.33)	<0.01
Non–cancer	0.21 (0.20–0.22)	0.32 (0.31–0.33)	0.48 (0.46–0.49)	—	

Colorectal cancer diagnosis: HR = 1.07 (1.02; 1.13)

Zhang et al. (Unpublished results)

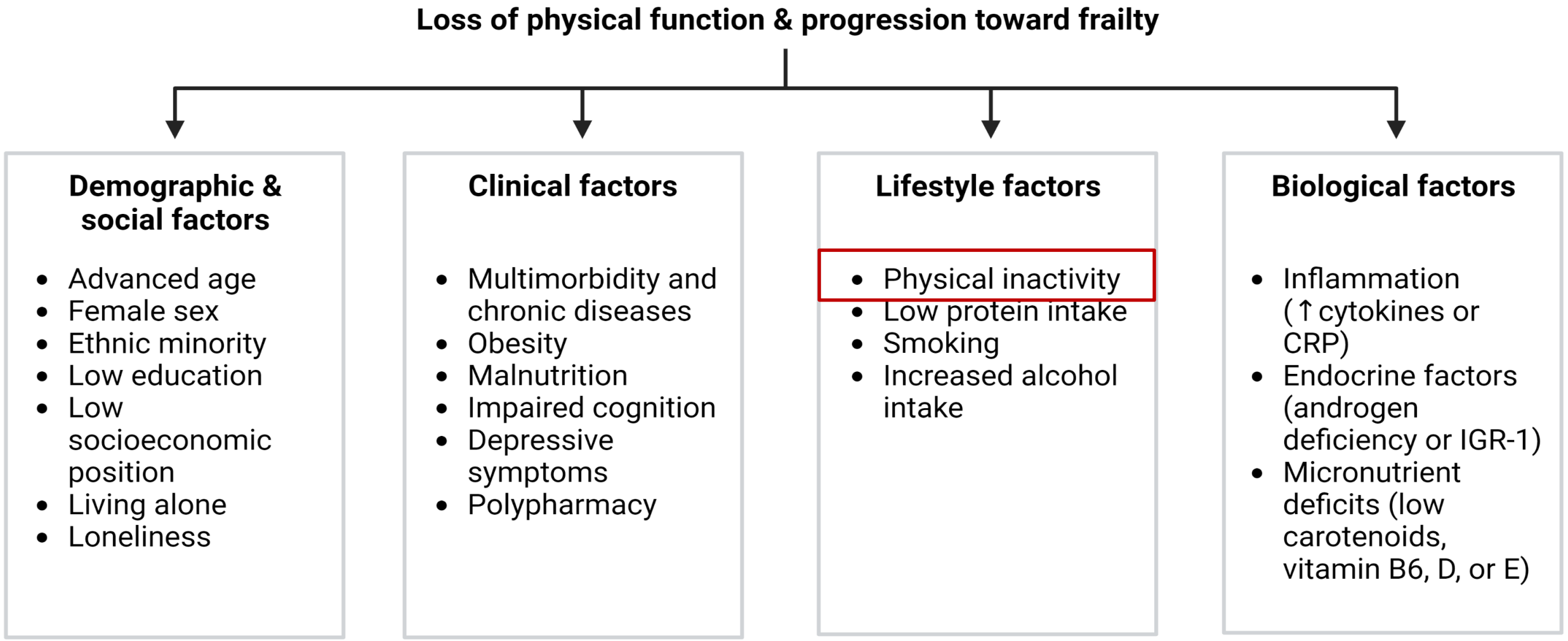


Figure 1. Risk factors for loss of physical function and progression toward frailty
Information derived and modified from Feng and colleagues (2017). CRP: C-reactive protein
IGF: Insulin-like growth factor

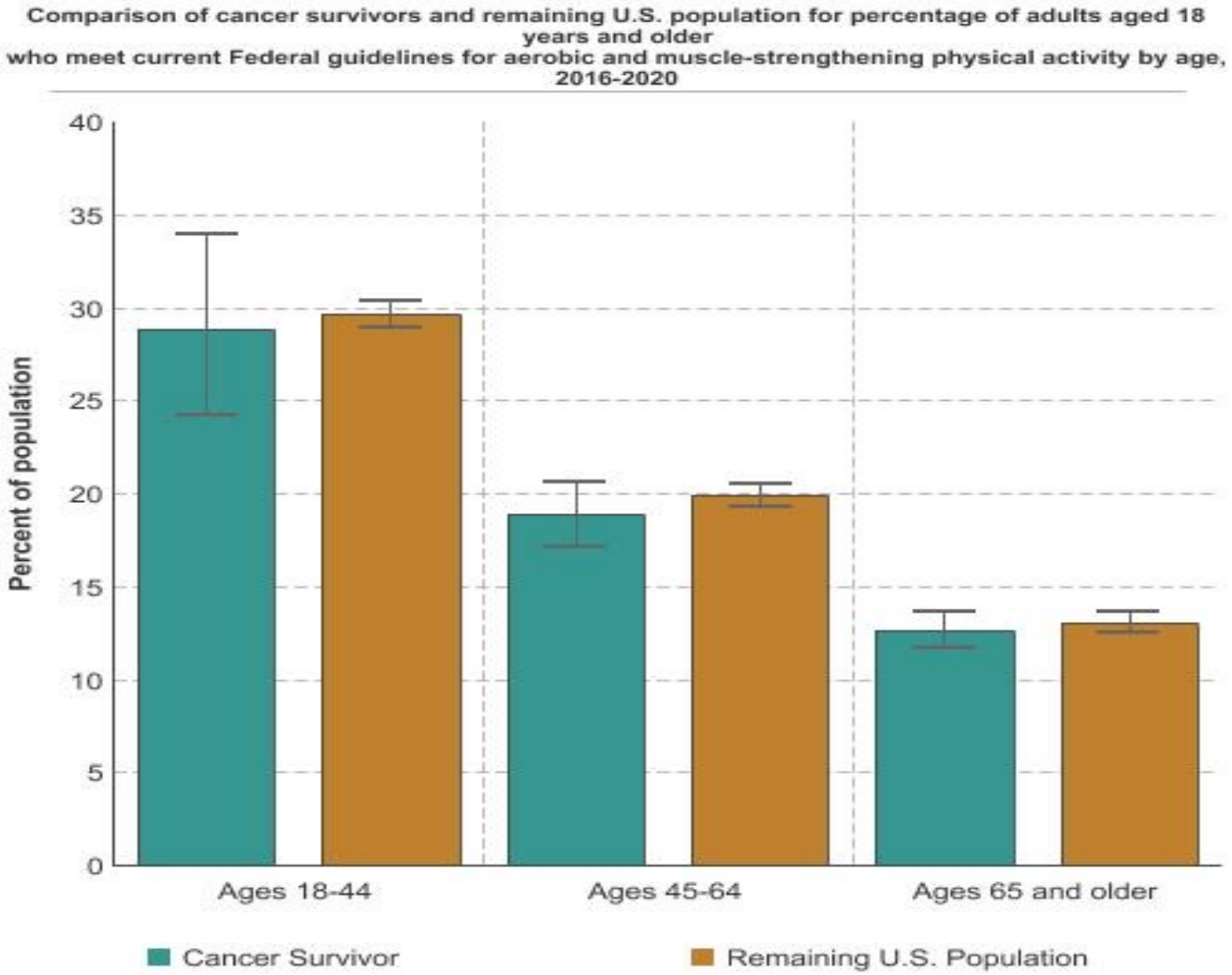
[1]Hoogendijk et al. (2019)

Effects of Exercise on Health-Related Outcomes[1]

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

[1]Campbell et al. (2019)

Meeting physical activity (PA) guidelines remains at suboptimal levels[1]

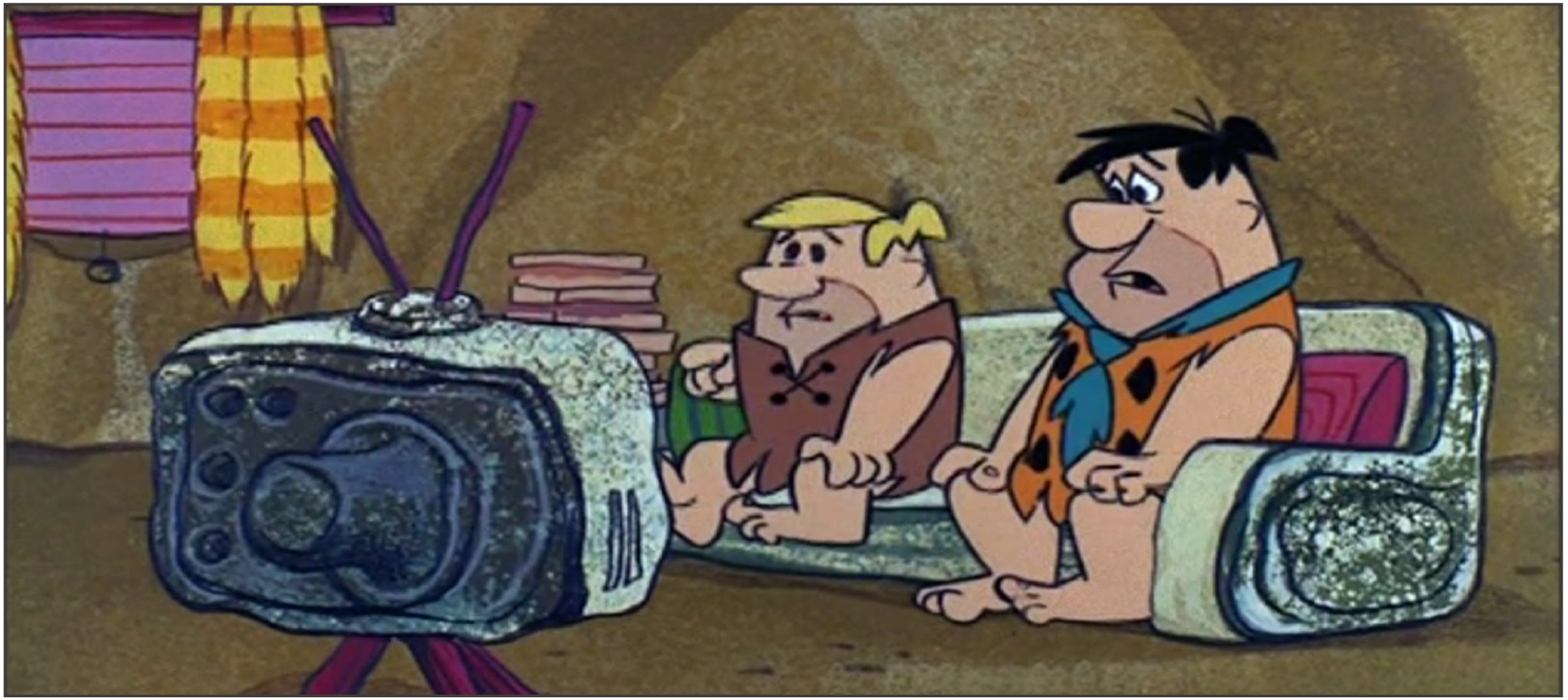


[1]Center for Disease Control and Prevention, NHIS Survey, 1997-2020

Perceived barriers to engage in PA

- **Common Barriers**
  - Competing demands for time
  - Weather
  - Access to places/programs to be physically active
  - Lack of motivation
  - Social support
  - Lack of belief in their ability to be active again
- **Additional barriers related to cancer diagnosis and treatment**
  - Cancer treatment-related fatigue
  - Pain
  - Physical function limitation
  - Fear of injury

[1]Hefferon et al. (2013); [2]Gomes et al. (2020); [3]Rogers et al. (2007); [4]Wurz et al. (2015); [5]Spiteri et al. (2019)



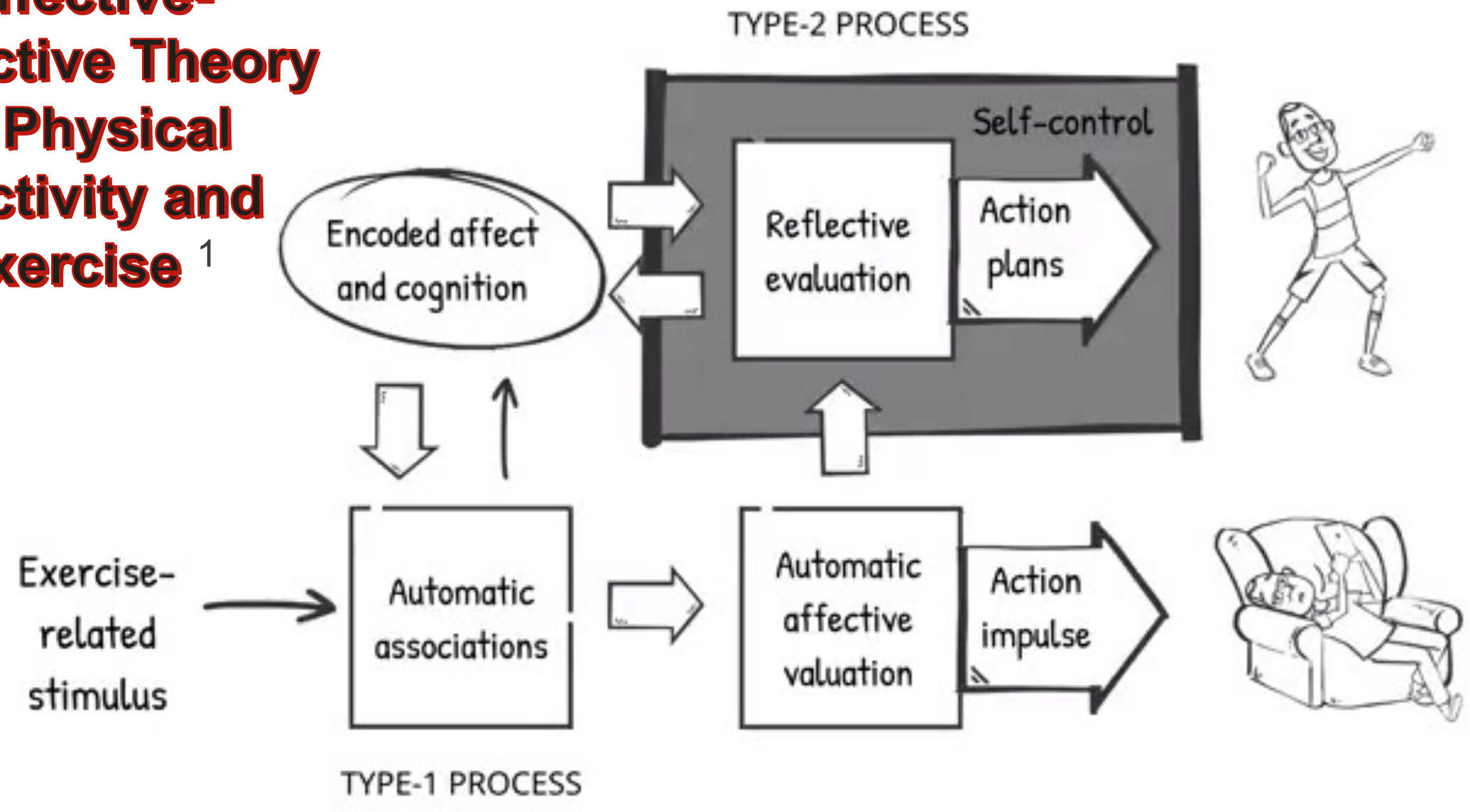
Our natural tendency is to conserve energy.[1]

[1]Liberman, DE (2015)

Run only for a purpose.[1] For example: Running from lions, tigers, and bears

[1]Liberman, DE (2015)

Affective-Reflective Theory of Physical Inactivity and Exercise [1]



Source: SportPsychologie Uni Potsdam; [1]Brand & Ekkekakis (2018)

Exergames: A potential solution

- Accumulating evidence suggests that targeting a person's motivation and reframing the internal reaction to PA may lead to a more effective intervention[1-5]
- Evidence-based behavior change techniques and allow for low-cost and flexible PA intervention[6,7]
- Encourage light to moderate PA and lead to better enjoyment to those activities[8,9]
- PA duration increases despite discomfort, and the intention to participate in non-exergame PA also increases[8,9]
- Gap: The use of exergames in combination with a group behavior-based PA intervention to improve function in breast cancer survivors has not been widely studied.

[1]Milne et al. (2008); [2]Teixeira et al. (2012); [3]Teixeira et al. (2020); [4]Steven et al. (2020); [5]Spiteri et al. (2019); [6]Tate et al. (2015); [7]Lyons et al. (2013); [8]Bock et al. (2020); [9]Peng et al. (2011)

Cancer Patients and Survivors

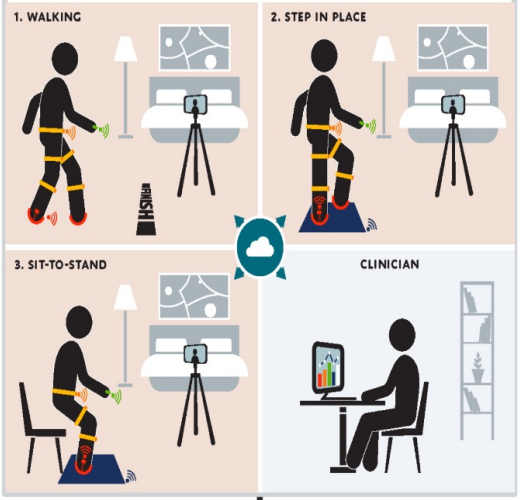
Comprehensive assessments

Patient-Reported (PRO)/Clinician-Reported Outcomes (ClinRO): Validated scales to reflect levels of reported physical function (e.g., PROMIS-29, ECOG PS)

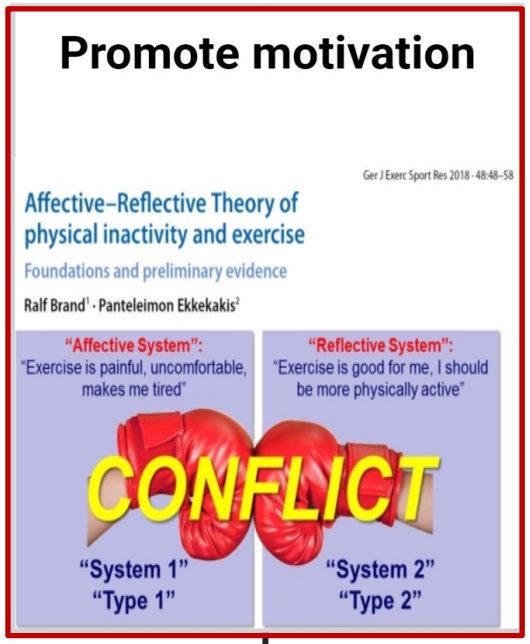
Performance Outcomes (PerfO): Maximum endurance, strength, balance, gait (e.g., 1-minute Sit-to-Stand)

Wearable Devices: Daily life activities (e.g., activity bouts, total distance, active minutes)

Remote assessments



Promote motivation



Remote Intervention

Social health

Mental health

Physical health

Inspiration: stage IV NSCLC, aged 83

Aim and Design for Pink Warrior 1

- **Aims:**[1]
  - Primary: To determine the feasibility and acceptability of a clinic-based multicomponent PA intervention (*Pink Warrior*) with a combination of exergame group play, group physical activity (PA) behavioral coaching and breast cancer support (i.e., survivorship navigation)[2,3]
  - Secondary: To determine the effect size of the intervention on PA and physical function in female survivors of breast cancer.
- **Design:**
  - A 13-week exergame-based and group-based PA intervention in female survivors of breast cancer 18 years and older (n=60)

Pink Warrior
Keep on Moving

[1]Swartz et al. (2022) doi: 10.2196/36889; [2]Basen-Engquist et al. (2006) doi: 10.1016/j.pec.2006.02.006; [3]Tami-Maury et al. (2022) doi: 10.1002/cncr.33904

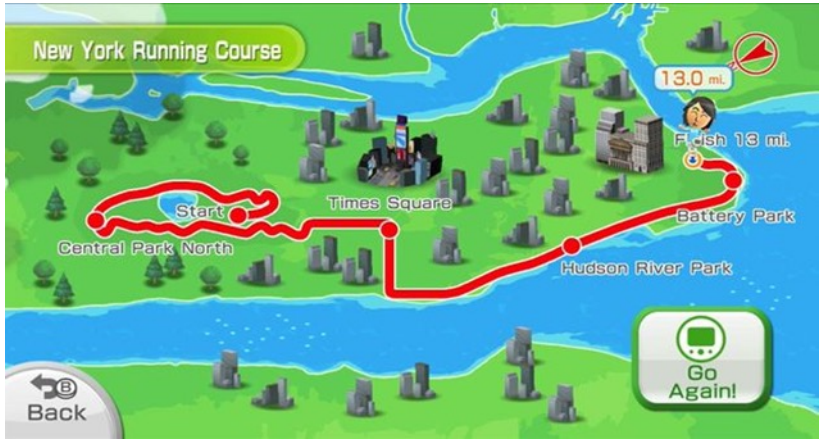
Methods (1): Intervention versus Control groups

Intervention:

- Received Wii Fit U (game-based) pedometer
- PA behavior coaching
- Weekly group exergame sessions
- Survivorship navigation discussions
- Manual with weekly reflection worksheets

Control:

- Conventional pedometers
- Participate in existing breast cancer support group



Methods (2): Primary outcomes

- **Feasibility Benchmarks**
  - ≥ 50% of approached eligible patients would consent
  - ≥ 80% retention rate
  - ≥ 75% of participants attended at least 9 sessions in the intervention group

- **Acceptability Benchmark**
  - Participants' attitudes (from strongly disagree=1 to strongly agree=5)
  - Mean rating of ≥4 for all 11 questions

Methods (3): Secondary Outcomes

- **PA changes**
  - Average daily steps
  - Average minutes of moderate to vigorous intensity physical activity (MVPA)
- **Physical function**
  - Short Physical Performance Battery (SPPB)
  - Grip strength
- **Health-related quality of life**
  - Functional Assessment of Cancer Therapy (FACT)-Breast
- **Fatigue**
  - PROMIS-Fatigue

Methods (4): Short Physical Performance Battery (Range: 0-12)

- **Balance:** Required side-by-side, semi-tandem, and full tandem stance for 30 seconds. Scores ranged from 0 to 4 (max)

- **Timed 3 meter walk:** Fastest time of two 3 meter usual-pace walk. Scores ranged from 1 to 4 (max)

- **Times chair stands:** Repeat five times of rising from a chair with arms folded across participants' chest. Scores ranged from 0 to 4 (max)

Methods(5): Statistical Methods

- Differences at baseline were investigated using Student's t test and chi-square test

- Differences between groups were estimated using ANCOVA controlling for baseline values of the dependent variable

- Analysis was performed according to Intent-to-treat (ITT) principal with missing data imputed using regression models

Results (1):

- Mean age 57.4 years old (SD 10.5), 70% Non-Hispanic White, and 58% off treatment
- **Feasibility:**
  - 55.9% (66/118 eligible participants provided consent)
  - 80% (48/60) retention rate
  - 78% of participants in the intervention group completed at least 9 intervention sessions
  - Acceptability:

Table 1. Acceptability of the Pink Warrior Intervention (time 2; N=26)

Item	Mean (SD)
Liked the Pink Warrior program	5.0 (0.2)
Appropriate activities	4.8 (0.4)
Program helped set reasonable goals	4.8 (0.5)
Contents were relevant	4.8 (0.4)
Program was worth my time & effort	5.0 (0.2)
Liked the contents presented (manual)	4.8 (0.5)
Liked the group setting	4.7 (0.6)
Liked the exergame portion	4.8 (0.5)
Liked the cancer survivorship topics	4.8 (0.4)
Liked the program length	4.4 (0.9)
I would continue to participate	4.6 (0.7)

Results (2): PA and Function

Table 2. Physiological effects of the intervention—mean differences between baseline and final assessment or the intervention and control groups

	Intervention (n=30) Δmean (SD)	Control (n=30) Δmean (SD)	Effect Size (between-group differences) Cohen's d (95% CI)
Average Moderate-Vigorous PA (min/day)	11.99±18.99	0.99±10.34	0.72 (0.19; 1.24)
Average Steps/day	1556.20±2614.8	-22.70±1639.3	0.72 (0.20; 1.24)
Total SPPB score	0.65 (0.86)	0.42 (1.01)	0.25 (-0.26; 0.75)
Gait speed (m/s)	0.11±0.19	0.03±0.13	0.48 (-0.03; 0.99)
FACT-B	12.97 (17.12)	7.18 (13.46)	0.38 (-0.14; 0.89)
Fatigue	-4.23 (7.71)	-1.77 (7.18)	0.33 (-0.18; 0.84)

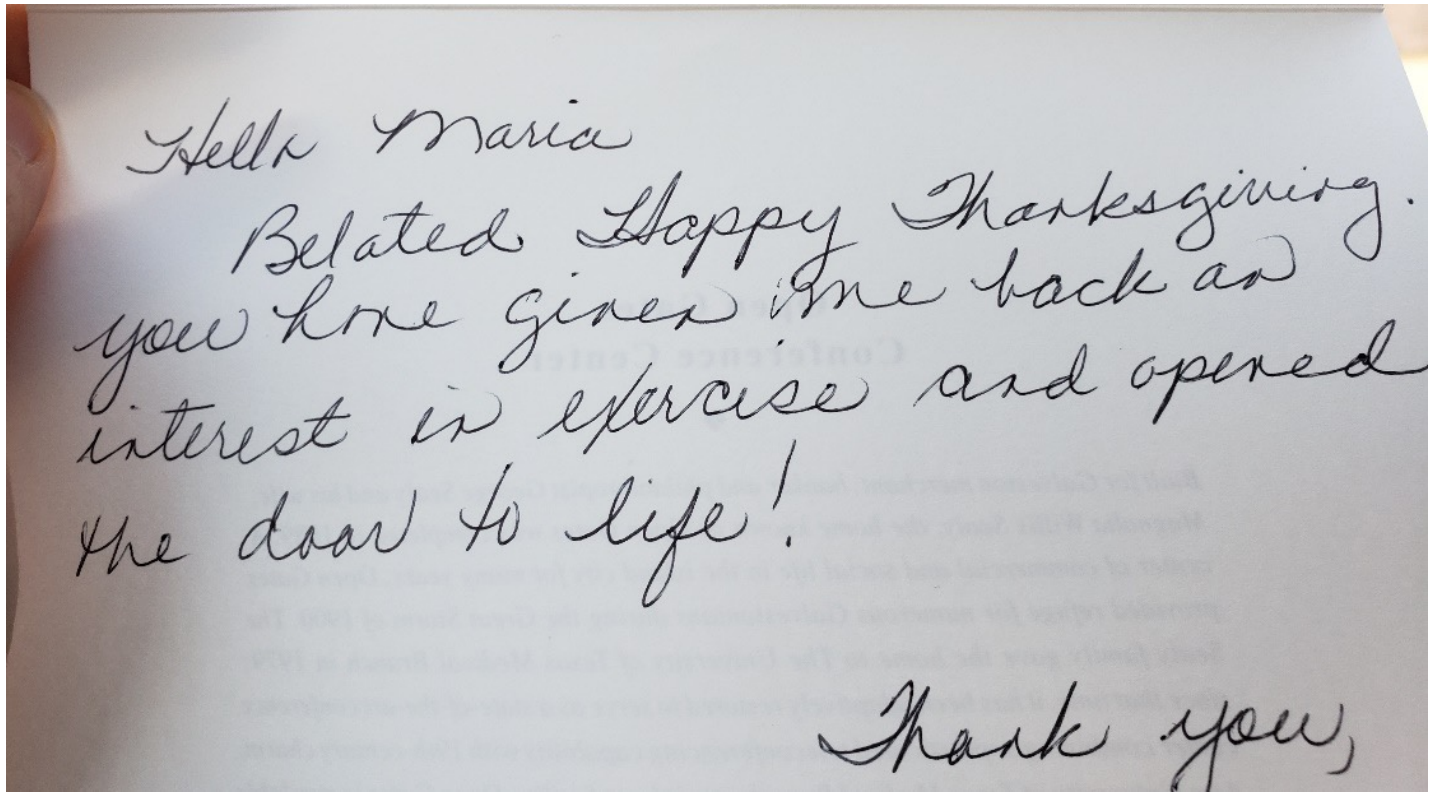
Post-intervention feedback

"The days that I drag myself to the group were the best group meetings ever. Made me feel better." (*PW6*)

"The support group was more important than I anticipated when I started." (*PW16*)

"The program motivated me to become more active. I am now running with my family. I have increased from running 0.5 to 1 mile." (*PW23*)

"I enjoyed our conversations, making new friends, setting goals, and tracking miles we walked, it was fun." (*PW52*)



The Wonder Woman costume kinda became my trade mark, I wore it to Walk a mile in her shoes a domestic violence awareness walk. I was on a walker at that time and my best friend [redacted] went with me, I was a fall risk at that time. I wore it for several Charity events. As sick as I was I always had the need to help others. Dr. Maria Swartz who was in charge of the Pink Warrior program was a God Send to me. She gave me strength when I wanted to give up. I owe the confidence I have gained to her and her assistant [redacted]

Conclusions (1)

- Results demonstrated that exergame-based and group-based PA intervention was feasible and acceptable in a sample of middle-aged survivors of breast cancer who were on and off treatment.

- Moderate effect sizes for PA metrics (e.g., 0.72 for steps and 0.72 for minutes of MVPA)
  - An increase of 1000 steps/day (mean age range 49.7-78.9) is associated with ↓ all-cause mortality[1]

- Small effect sizes for objective physical function outcomes (e.g., 0.48 for gait speed, and 0.25 for SPPB)
  - Despite the small effect size, clinically important change was found in the intervention group for gait speed[2]

- Small effect sizes for FACT-B and Fatigue.
  - Despite the small effect size, minimum important differences were also found in the intervention group[3,4]

[1]Hall et al. (2020); [2]Bohannon et al. (2014); [3]Yost et al. (2011); [4]Eton et al. (2004)

Conclusions (2)

- Our findings suggest a larger-scale implementation of the intervention has the potential to produce a small to moderate effect and also reach minimal important differences in PA, physical function, and quality of life metrics.

Limitations and future work:

- Pilot study with small sample size so we can only test the full multicomponent intervention
- Unknown regarding long-term maintenance PA behavior and physical function
- Limited to southeastern Texas community, so the results may not be nationally generalizable

Cancer Patients and Survivors

Comprehensive assessments

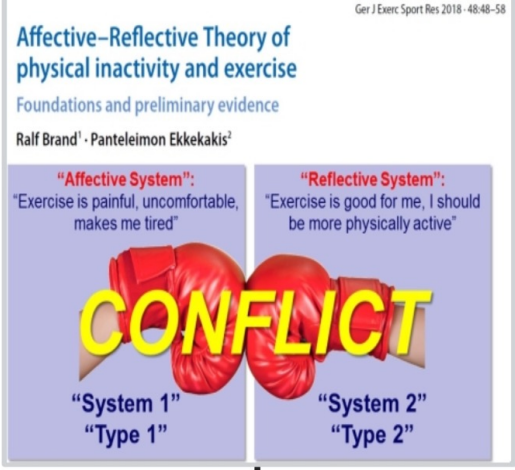
Patient-Reported (PRO)/Clinician-Reported Outcomes (ClinRO): Validated scales to reflect levels of reported physical function (e.g., PROMIS-29, ECOG PS)

Performance Outcomes (PerfO): Maximum endurance, strength, balance, gait (e.g., 1-minute Sit-to-Stand)

Wearable Devices: Daily life activities (e.g., activity bouts, total distance, active minutes)

Remote assessments

Promote motivation



Remote Intervention

Social health

Mental health

Physical health

August 2020 and October 2021

Aim and Design for Pink Warrior 2

- **Aims:**
  - Primary: To determine the feasibility of virtually delivering an exergame-and group-based PA intervention in a sample of older survivors of breast cancer
  - Secondary: To explore the potential influence of the intervention on physical function over 12 weeks
- **Design:**
  - A 13-week virtually delivered exergame-based and group-based PA intervention in female survivors of breast cancer 55 years and older (n=20)

Swartz et al. (2023) doi: 10.3390/life13020574

Methods (1): Intervention versus Control groups

Intervention:

- Received Fitbit
- PA behavior coaching (virtual)
- Weekly group exergame sessions (virtual)
- Survivorship navigation discussions (virtual)
- Manual with weekly reflection worksheets

Control:

- Xiaomi Mi Band
- Weekly group-based phone call
- Survivorship navigation discussions

SECUREVIDEO

Methods (2): Primary outcomes

- **Feasibility Benchmarks**
  - ≥ 0.92 participants/center/month recruitment rate
  - ≥ 80% retention rate
  - ≥ 75% of participants attended at least 10 sessions in the intervention group

- **Acceptability Benchmark**
  - Participants' attitudes (from strongly disagree=1 to strongly agree=5)
  - Mean rating of ≥4 for all 11 questions

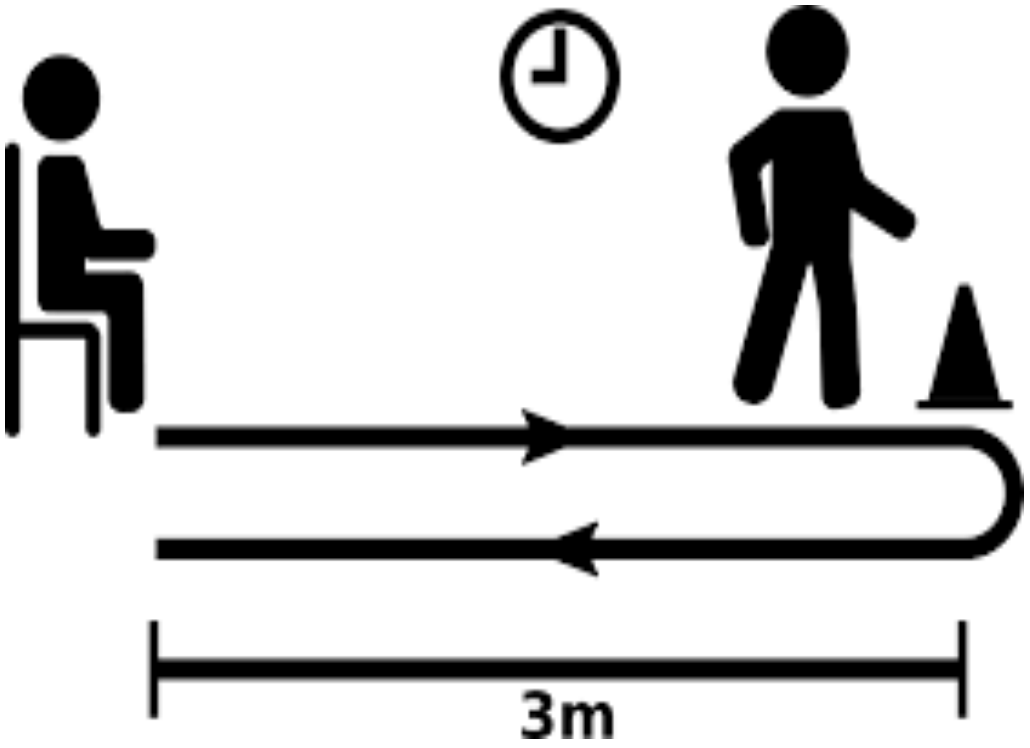
Methods (3): Secondary Outcomes

- **Physical function**
  - Short Physical Performance Battery (SPPB)
  - Timed Up & Go (TUG)
  - 2-minute step test

- **PA changes**
  - Average daily steps
  - Average minutes of moderate to vigorous intensity physical activity (MVPA)

Methods (4): TUG and 2-Minute Step Test

TUG test



2-Minute step test

Methods(5): Statistical Methods

- Differences at baseline were investigated using Student's t test and chi-square test
- We used means and standard deviations to compute Cohen's d effect size
- Analysis was performed according to Intent-to-treat (ITT) principal and used last-observation-carried forward for missing data

Results (1):

- Mean age 63.7 years old (SD 6.35), 80% Non-Hispanic White, and 89% off treatment
- **Feasibility:**
  - 1.93 participants/center/month
  - 90% (18/20) retention rate
  - 88% of participants in the intervention group completed at least 10 intervention sessions
  - Acceptability:

Table 1. Acceptability of the Pink Warrior 2 Intervention (time 2; N=10)

Item	Mean (SD)
Liked the Pink Warrior 2 program	4.8 (0.42)
Appropriate activities	4.7 (0.68)
Program helped set reasonable goals	4.3 (0.95)
Contents were relevant	4.9 (0.32)
Program was worth my time & effort	5.0 (0.0)
Liked the contents presented (manual)	5.0 (0.0)
Liked the group setting	4.8 (0.63)
Liked the exergame portion	4.4 (0.84)
Liked the cancer survivorship topics	4.7 (0.68)
Liked the program length	4.9 (0.32)
I would continue to participate	4.5 (1.27)

Results (2): PA and Function

Table 2. Differences between intervention and control groups

Variables	Intervention			Control			Effect Size
	Baseline Mean (SD)	Follow-Up Mean (SD)	Mean of Difference (SD)	Baseline Mean (SD)	Follow-Up Mean (SD)	Mean of Difference (SD)	Cohen's d
Gait speed (meter/seconds); n = 19	0.76 (0.24)	0.94 (0.17)	0.18 (0.17)	0.89 (0.18)	1.01 (0.15)	0.11 (0.13)	0.46
Total SPPB [a] score; n = 19	8.70 (1.57)	10.30 (1.34)	1.6 (1.17)	9.56 (1.59)	10 (1.12)	0.44 (1.01)	1.06
TUG [b] (seconds); n = 18	10.46 (3.52)	9.78 (3.11)	−0.69 (0.91)	9.12 (1.73)	8.93 (0.85)	−0.01 (2.06)	0.43
Two-minute step test (count); n = 18	62.89 (21.69)	75.0 (24.26)	12.11 (13.83)	75.89 (30.98)	76.11 (28.81)	0.22 (24.11)	0.61
Steps (average steps); n = 19	4652.60 (2659.88)	4423.09 (2016.41)	−229.52 (1905.94)	4268.52 (1721.36)	5838.69 (2767.52)	1570.17 (2355.59)	0.85
MVPA [c] (average minutes); n = 19	9.4689 (9.93)	10.00 (9.13)	0.54 (8.78)	12.07 (13.67)	17.34 (23.09)	5.28 (23.66)	0.27

[a] SPPB: Short Physical Performance Battery; [b] TUG: Timed Up & Go; [c] moderate-vigorous physical activity.

Post-intervention feedback

"The weekly meetings, I look forward to them." (*PW221*)

"Reminded me to put my health first." (*PW207*)

"Meeting with people and hearing different ideas." (*PW205*)

"Meeting with others who understood my diagnosis and side effects." (*PW213*)

Conclusions (1)

- Results demonstrated that the remotely delivered exergame-and group-based PA intervention was feasible and acceptable in a group of older survivors of breast cancer
- Both the Pink Warrior 2 intervention and attention control intervention appeared capable of producing increases in physical function and PA.
  - Both groups ↑ in speed by ≥0.11 meter/second[1]
  - Intervention group's SPPB ↑ by ≥1.0 point[2]
  - The intervention group participants started below the normative values (75-107) for 60-65 years old, but ↑ to meet the normative value by the end of the intervention[3]
- Surprisingly, the improvement in the objectively measured outcomes for the intervention group were not matched by the group's average step count and MVPA
  - Reasons: SARS-CoV2-related challenges[4] and the use of ActiGraph[5]

[1]Bohannon et al. (2014); [2]Brown et al. (2015); [3]Rikliet al. (1999); [4]Bu al. (2021); [5]Hergenroeder et al. (2018)

Conclusions (2)

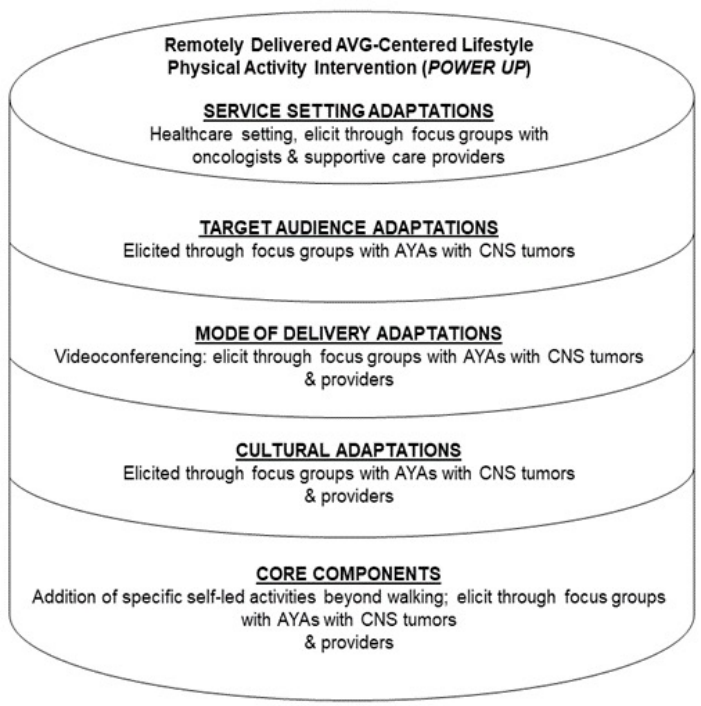
- Despite challenges, overall findings lend initial evidence that a virtually delivered multicomponent PA intervention is feasible and acceptable to older survivors of breast cancer

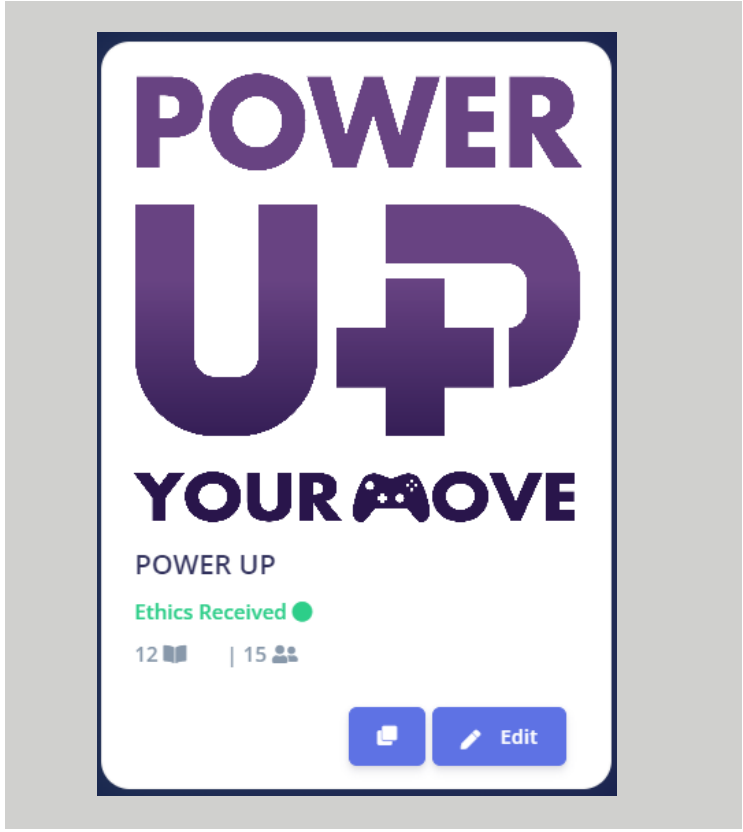
- Contributed to the evidence that it is possible to safely conduct objective mobility, aerobic endurance, and functional fitness assessments using a videoconferencing platform

- Exploratory findings indicate potential physical function benefits in survivors of breast cancer

- **Limitations and future work:**
  - Pilot study with very small sample size so we can only test the full multicomponent intervention
  - Need to verify in a larger pilot
  - Last observation carried forward may underestimate effect sizes
    - Only applied to 1 individual. W expect that underestimation, if any, would be minimal
  - Limited to Texas community, so the results may not be nationally generalizable

Adaptation: Participation Online While Exercising To Recover Using Play (POWER UP)





https://pathverse.ca/en/

- Adapted the intervention materials using the Adoptome Framework[1]
  - 32 Adolescent and Young Adult Brain Tumor Survivors and Providers
  - Converting the intervention materials from PDF/Print version to be delivered through an app (Powered by Pathverse)[2]

[1]Chambers et al. (2016); [2]Liu et al. (2022)

Summary

- **Important insights**
  - How to motivate patients to adopt physical activity to improve physical function
  - Potential to improve access to physical activity interventions for cancer survivors through virtual delivery of interventions
  - Potential for remote physical function assessments to be used as a way to systematically conduct physical function assessments in cancer patients and survivors

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Contact Information:

✉ mchang1@mdanderson.org

@MariaSwartzPhD

Q&A