Fatigue: What It Is, What It Is Not, Why It Happens and What Can We Do about It?

Celebrating a Second Chance at Life Survivorship Symposium

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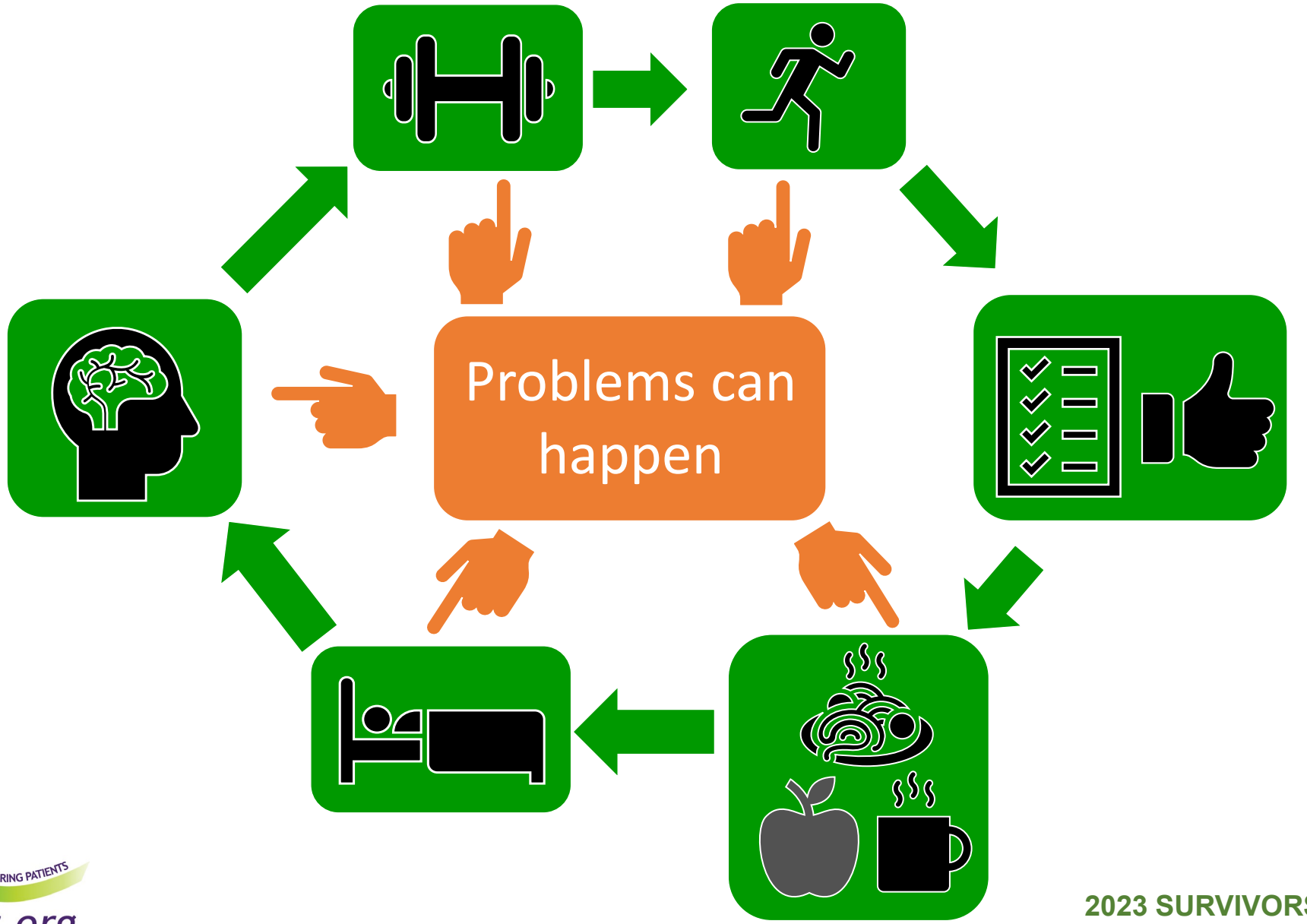
Learning Objectives

- What causes/contributes to fatigue in the short- and long-term after stem cell transplant
- The difference between normal fatigue and fatigue experienced by stem cell transplant recipients
- Strategies to conserve energy and plan a day to minimize the impact of fatigue on daily life
- Role of exercise, sleep and nutrition in managing fatigue
- Pharmacological and non-pharmacological options for managing fatigue

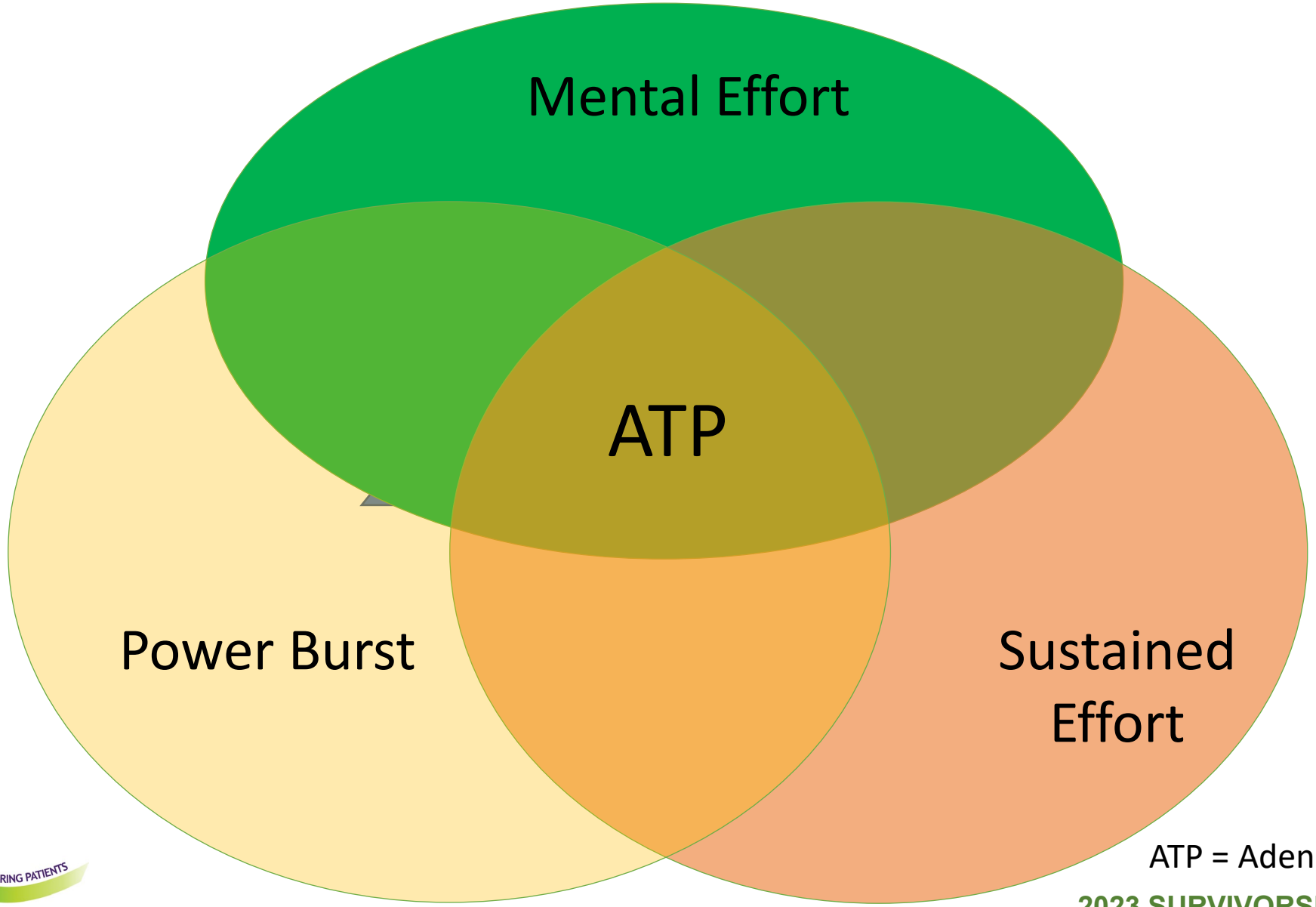
Cancer-Related Fatigue (CRF)

- Patient perspective:
  - “Rest does not make it go away, and just a little activity can be exhausting”
- Physician Perspective
  - Etiology “remains to be fully elucidated”
- Bottom line
  - Patients have trouble making things happen

Making Things Happen: the Bird's-Eye View

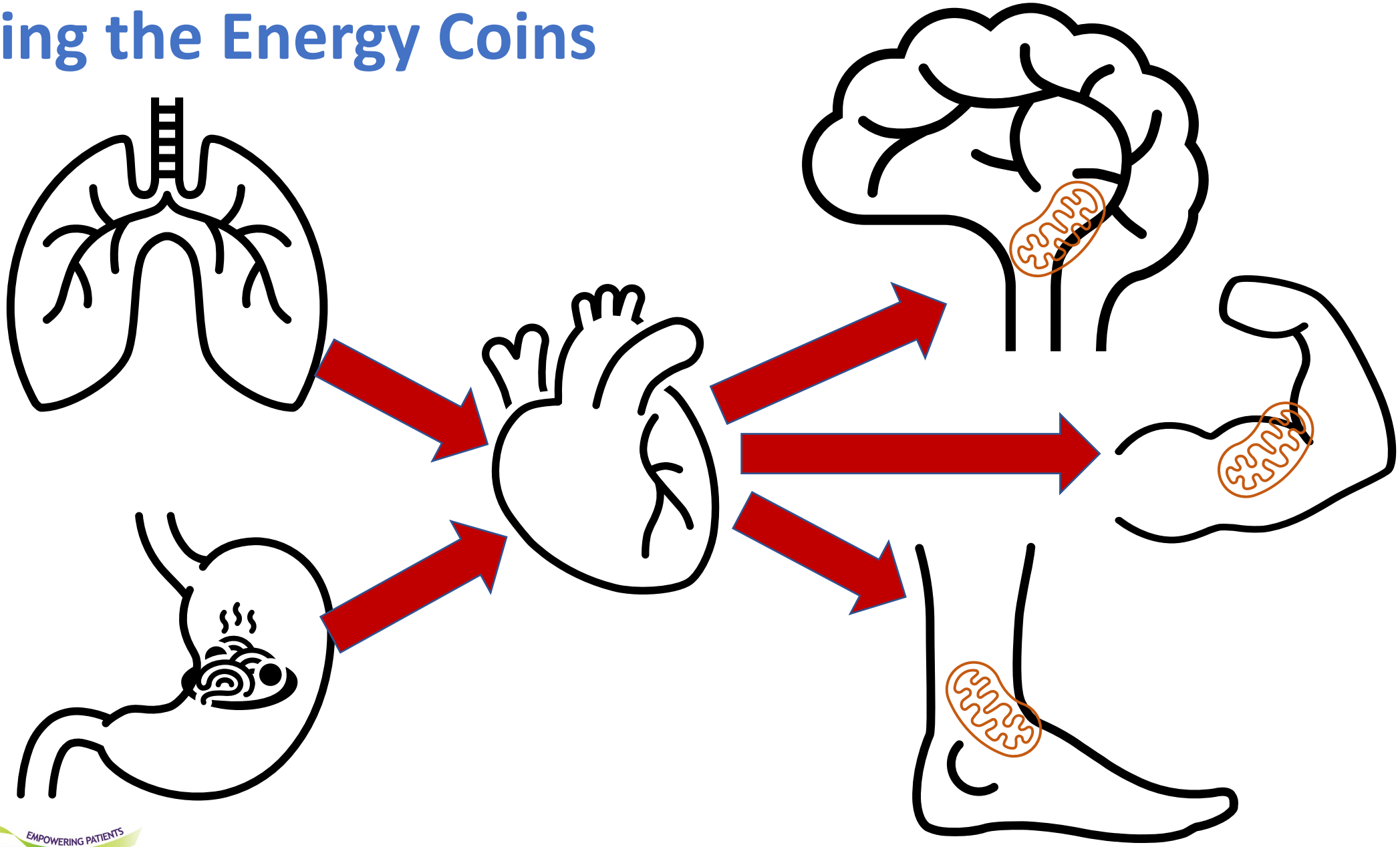


Making Things Happen: The Energy Coin



ATP = Adenosine Triphosphate

Minting the Energy Coins



What is the Cost of Daily Functions?

Activity	Energy Cost (METS)	Oxygen use VO_2 (ml/kg/min)
Doing nothing	0.7-1	3.5
Standing still	1.6	5.6
Making a bed	3	10.5
Walking ~ ½ normal speed	3.2	11.2
Walking briskly	4.28	15.0
Ascending stairs	4.77	16.7

15.4 ml/kg/min

Knaggs, 2011; Mansoubi 2015

Warburg Effect: Messing Up the Energy Coin Mint

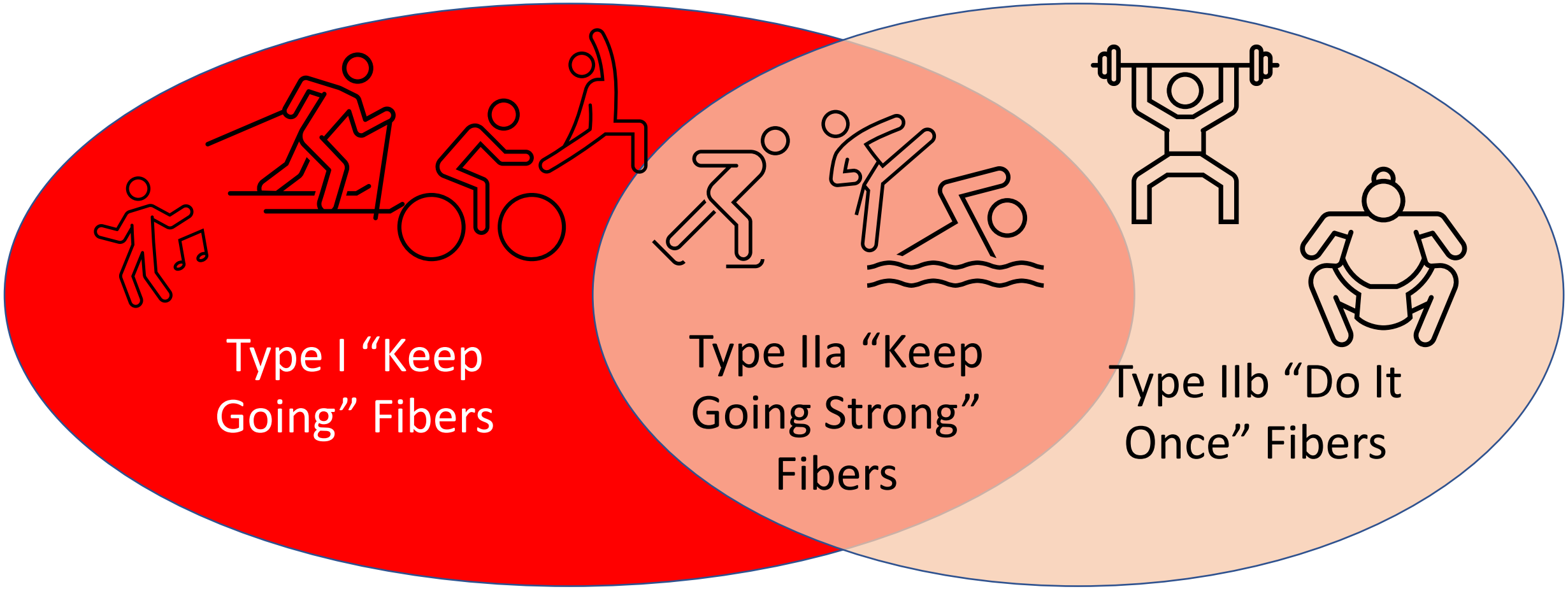
- Cancer cells prefer a very inefficient way of making ATP, using a lot of glucose
- Reason why PET scans work
- Cancer may shift the rest of the body into a less efficient mode
  - 2 ATP's from 1 glucose, instead of 36

O. Warburg
1931 Nobel Prize

ATP = Adenosine Triphosphate

SanMillan 2017

Where The Coins Are Used: Muscle Fibers



Chemotherapy Effects on Muscle

Direct Damage
Loss of "Power" Fibers
Secondary muscle loss due to neuropathy

Damage lasts longer when muscle is already injured

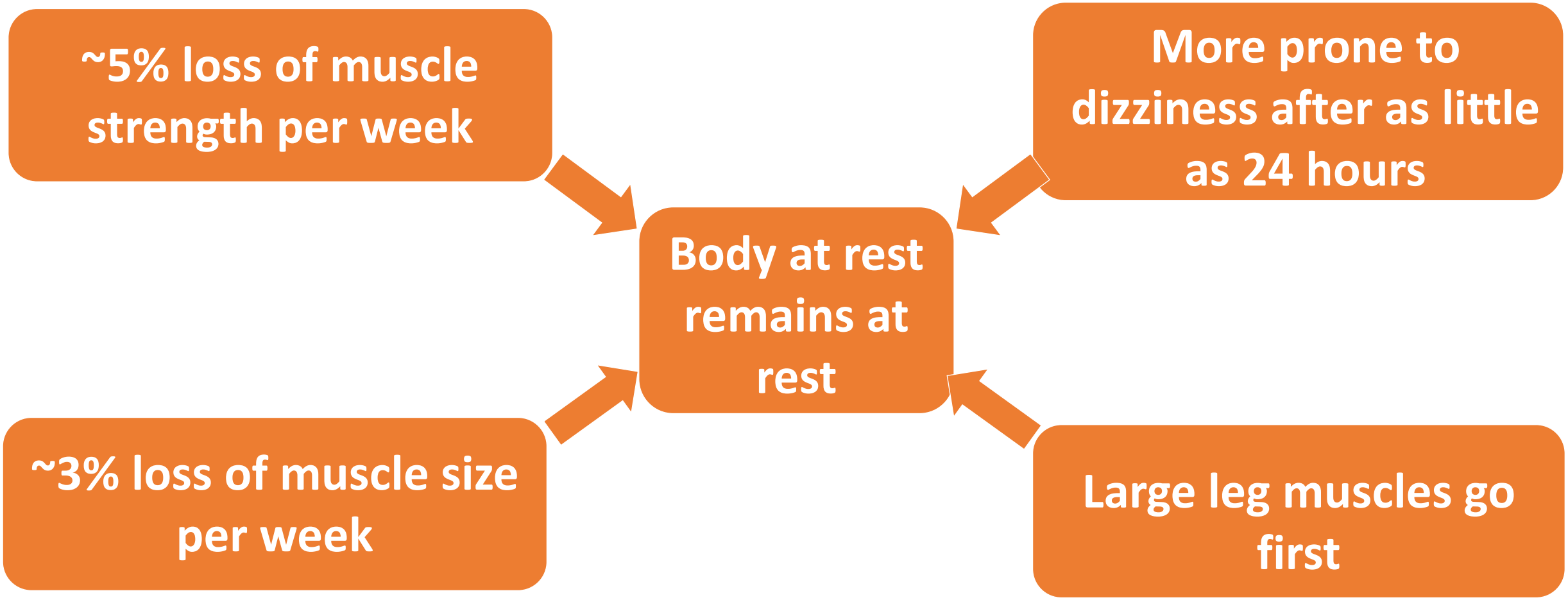
Muscle Weakness Fatigue

↓Muscle Fiber Strength
↓Muscle Fiber Endurance

↑ Inefficient work
↑ Muscle cell death
Mitochondrial damage
(↓ ATP/Energy Coins)

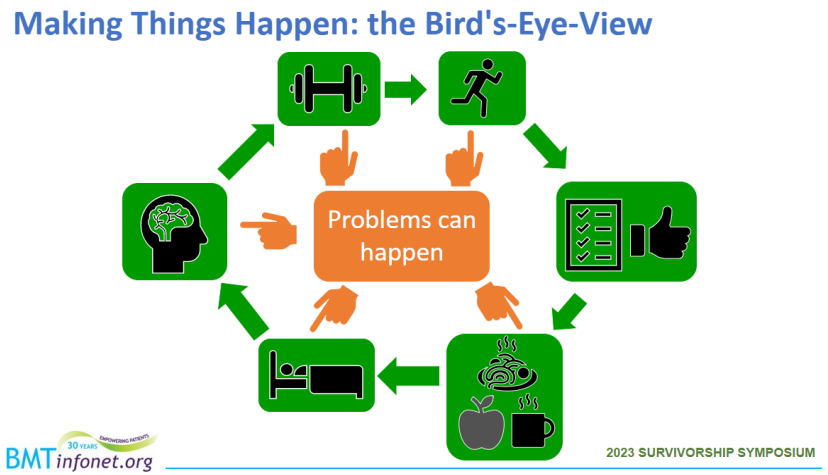
ATP = Adenosine Triphosphate

Bed = Bad (Even for Healthy Folks in Space Program)



Brown, 2009; Hortobágyi, 2000; Berg, 1985

What Cancer-Related Fatigue IS NOT

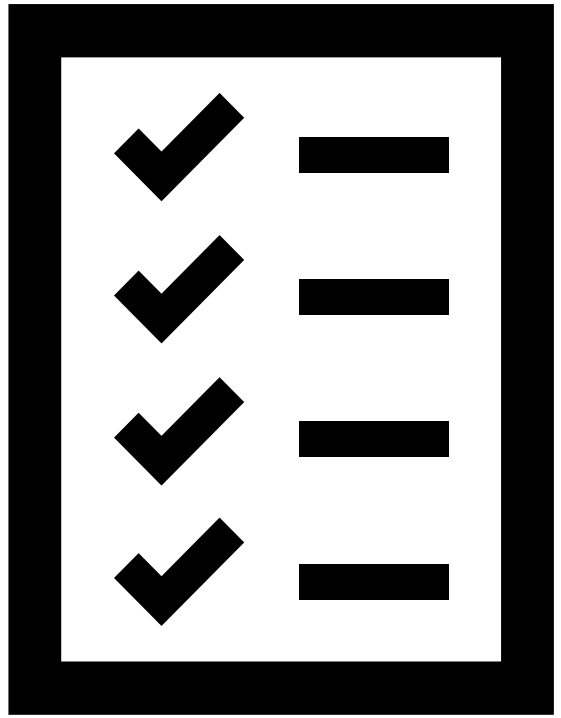


- Cancer-Related Fatigue IS NOT
  - Character flaw or personal weakness
- Stimulant medications have a very small effect (<10%)
- "Primary interventions should be exercise, psychological, or exercise plus psychological"

Mustian, 2017

Mindset

- Don't dwell on what you can't or didn't do
- Start low, go slow, try to stay consistent
- No task accomplished is too small to recognize, especially early in the journey
- Set sights on the future
- Track your progress



Amonoo, 2021

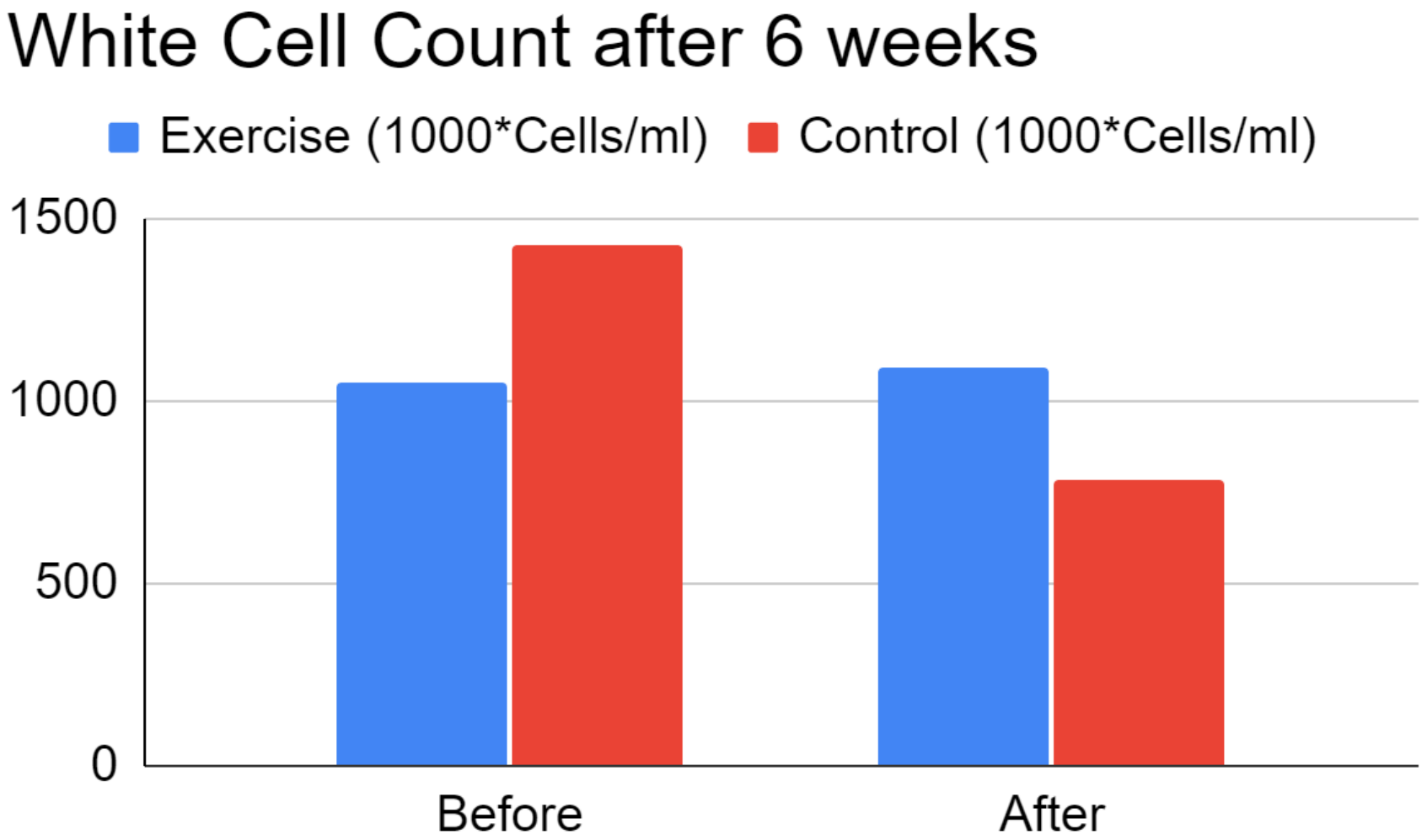
Mindfulness (Conscious Breathing)

- 10 minute preparation
  - Concentrate on lower abdomen 3 min
  - Place left ankle over right knee 2 min
  - Place right ankle over left knee 2 min
  - Bend both knees 2 min
- Relaxation breathing 10 minutes

- 10 minute finish exercises
  - Relax body and mind
  - Stroke face and hair
  - Rotate ankles
  - Stretch arm and legs
  - Stretch out on the bed

Kim, 2006

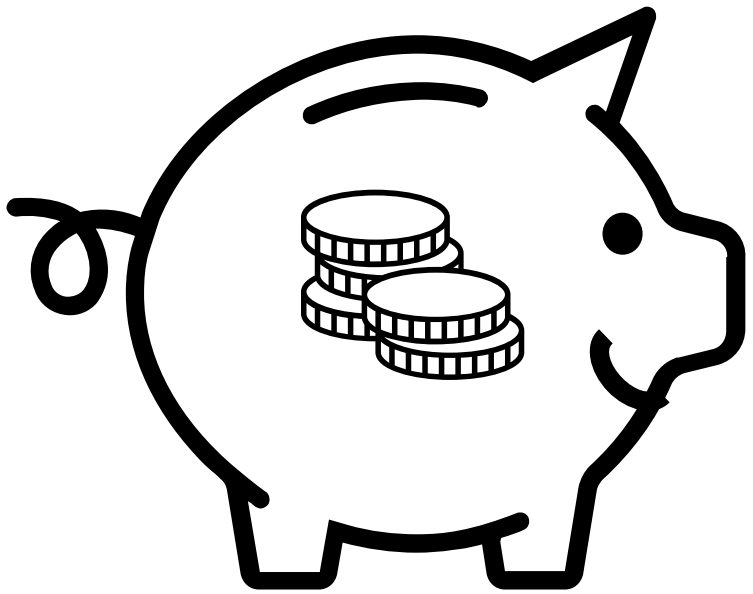
Mindfulness (Conscious Breathing)

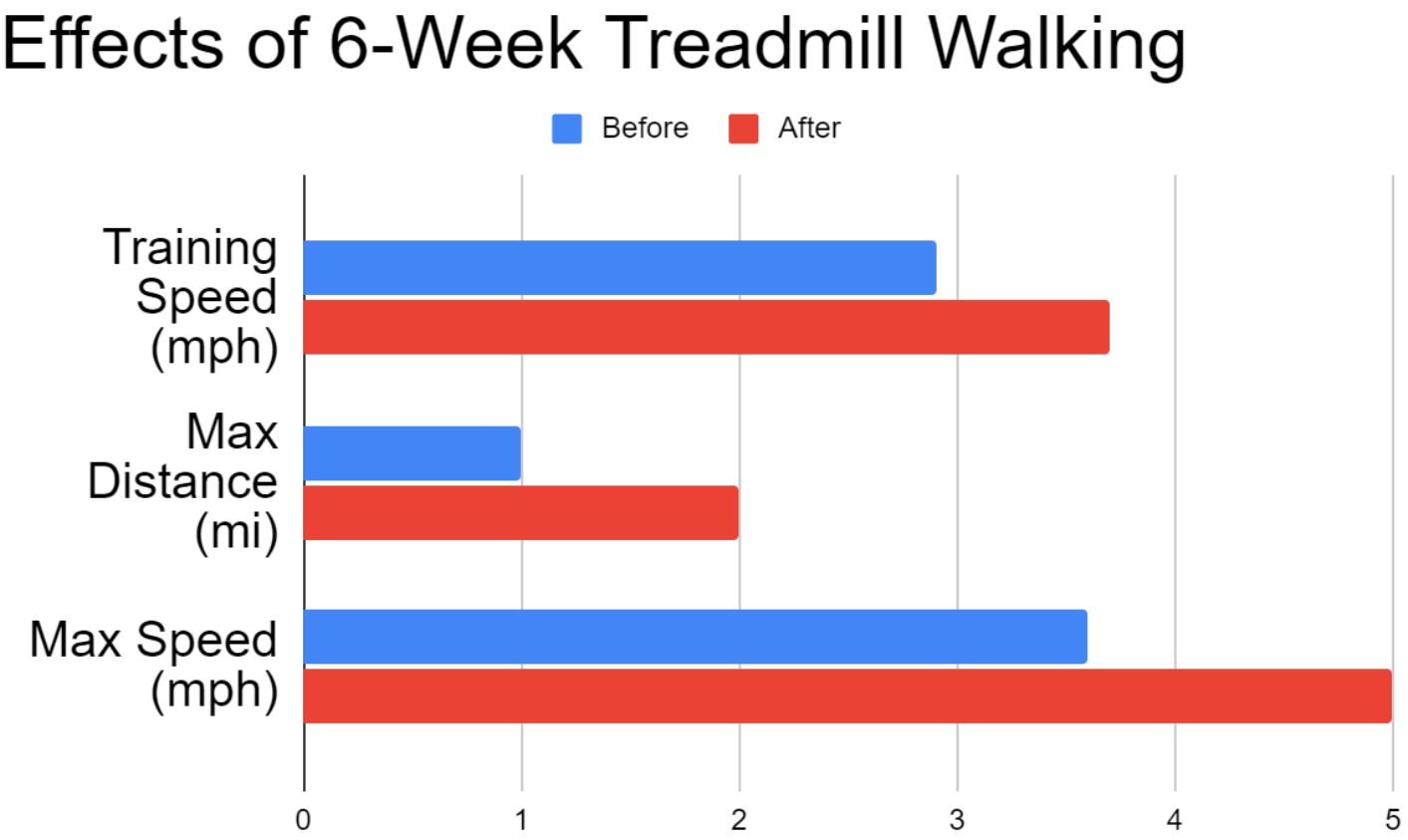


35 donor cell transplant recipients, ~ 33 yo, South Korea

Kim, 2006

Exercise: Why Spend More Coins If You Already Feel Short?

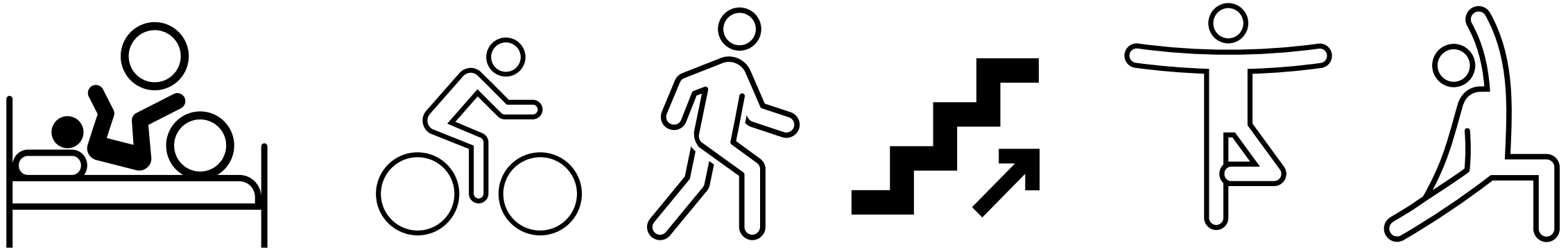




20 Transplant Patients (17 donor, 3 own)
36 yo, 18-42 days after transplant

Dimeo, 1996

Can Exercises Be Harmful During Treatment?



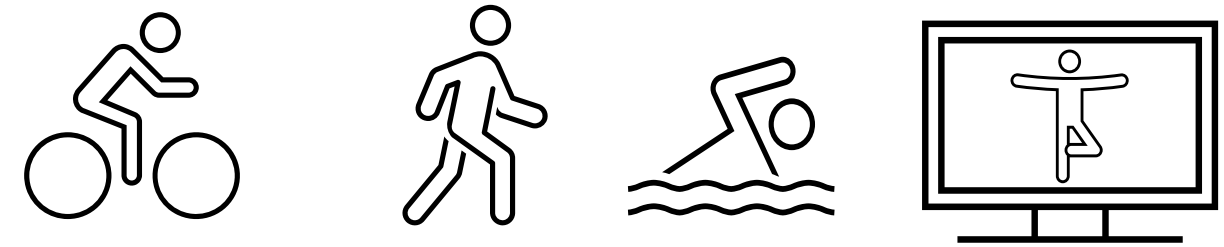
- **No side effects from exercise participation**
- Increased physical function score
- Increased endurance
- Decreased fatigue scores
- Fewer days with nausea

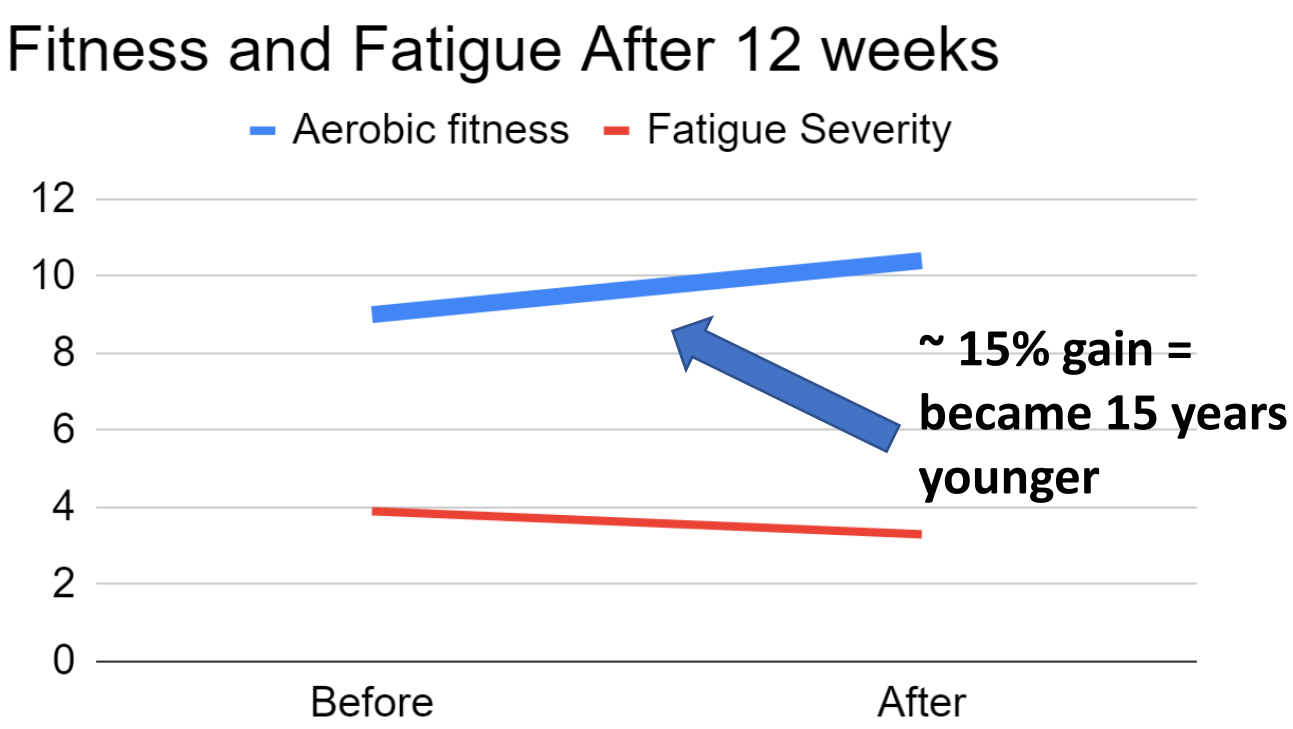
- 10-20 cycling
- 20 minutes resistance OR
- 20 minutes activities of living

Dimeo, 1999; Baumann, 2011; Oechsle 2014;

Can Unsupervised Exercise be Effective?

- 17 Floridians, ~ 49 yo
- ~16 months after transplant
- 13 own cells, 4 donor cells
- At least 3 times/week
- At least 20 minutes moderate intensity per heart rate monitor



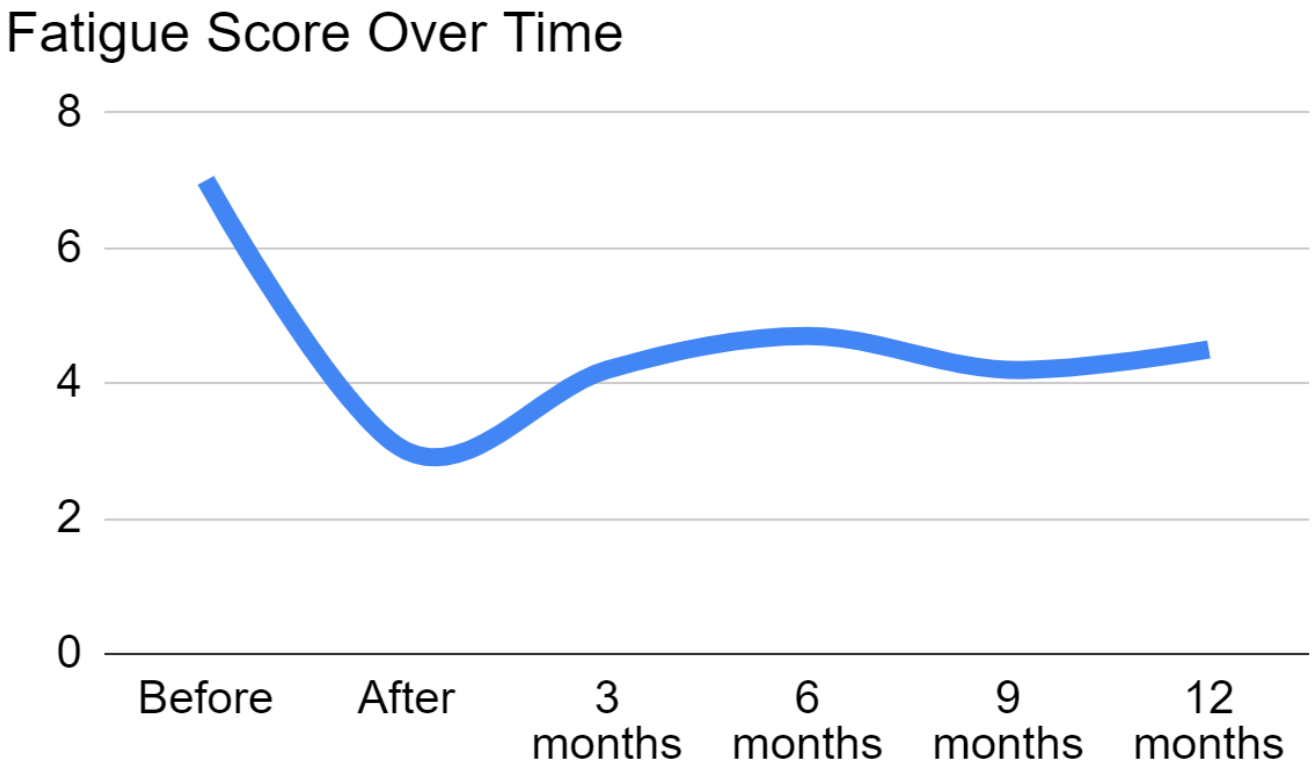


Wilson, 2005

Can Exercise Be Helpful if You're REALLY tired?

- 12 Canadian patients, ~49 yo
- ~ 39 months after donor cell transplant

- 20 minutes 2/10 effort
- 15 minutes 6/10 effort X 12 weeks
- 20 minutes 4/10 effort

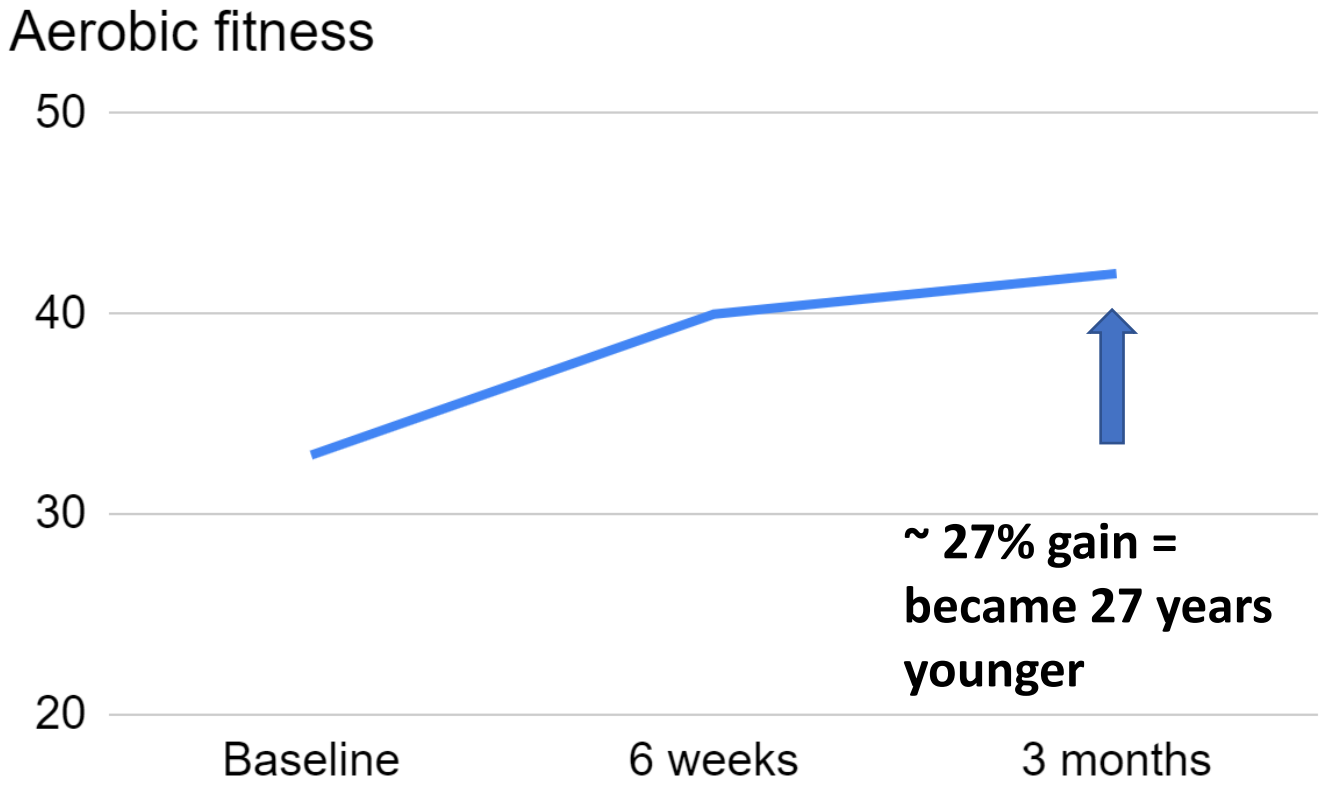


Bonus: Aerobic fitness improved 17%
(folks got ~ 17 years younger)

Carlson, 2006

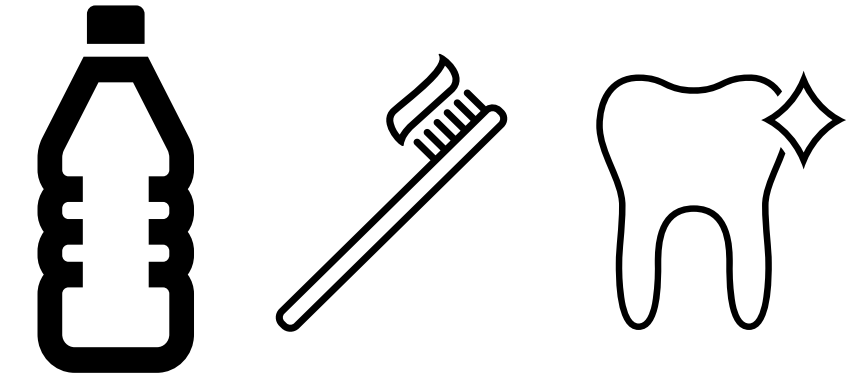
What About Both Physical Exercise and Mindfulness?

- 21 Australians, ~ 56 yo
- ~37 months after donor transplant
- 6 weeks of virtual coaching
  - 60 min physical
  - 60 min mindfulness
- 20-30 min aerobic exercise
- Resistance bands workout
- 3-5 times per week



Fueling Up

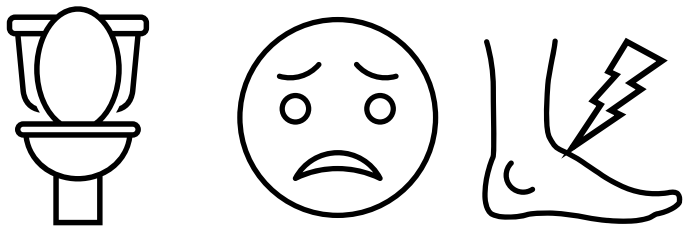
- Mouth can be sore
- Taste can be altered
- Nausea happens almost universally
- Food intolerances may develop
- Stomach and intestines can be affected by graft-versus-host disease (GI GvHD)
- Acupressure for nausea can be helpful

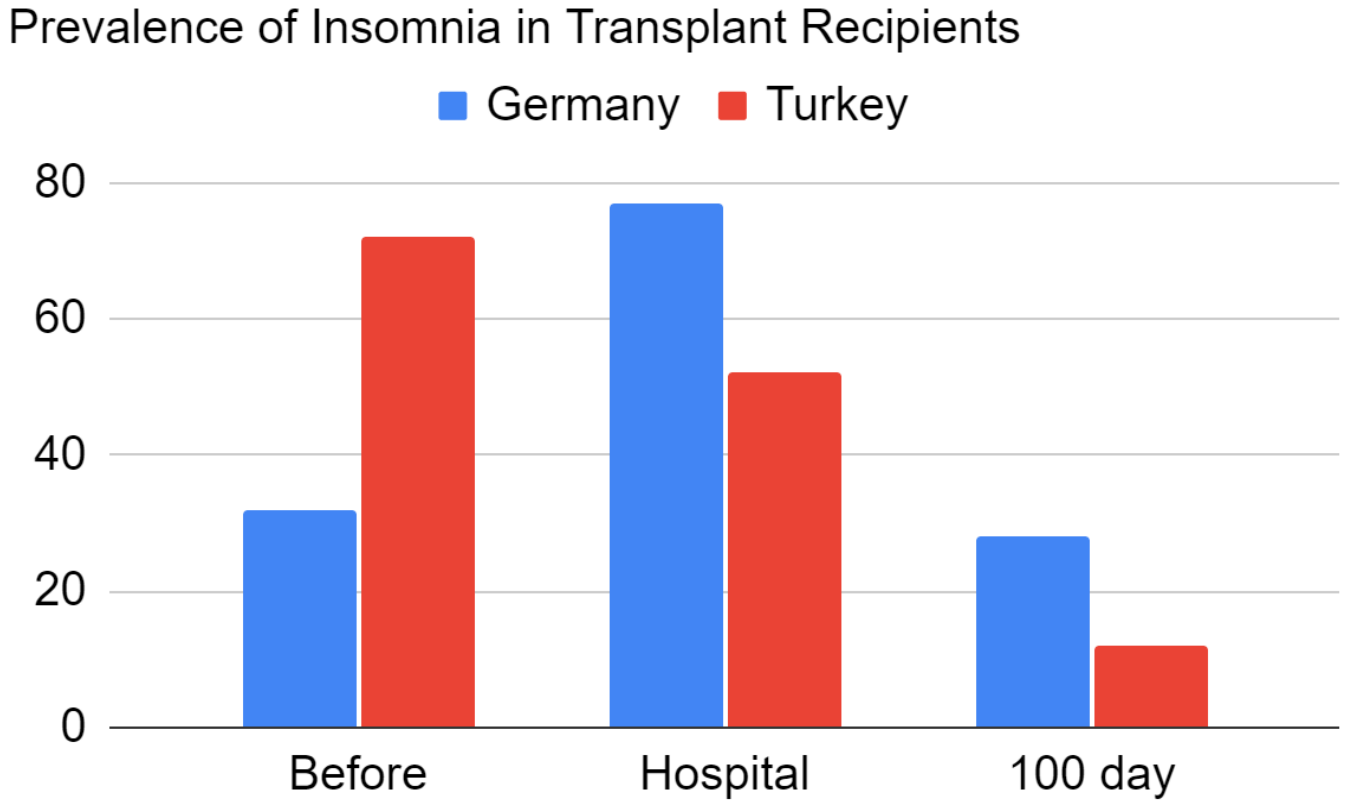


Scordo, 2018

Resting Up

- Biggest Problem: transplant admission
- Donor cell transplant recipients tend to fare worse
- ~1/3 of all remain affected



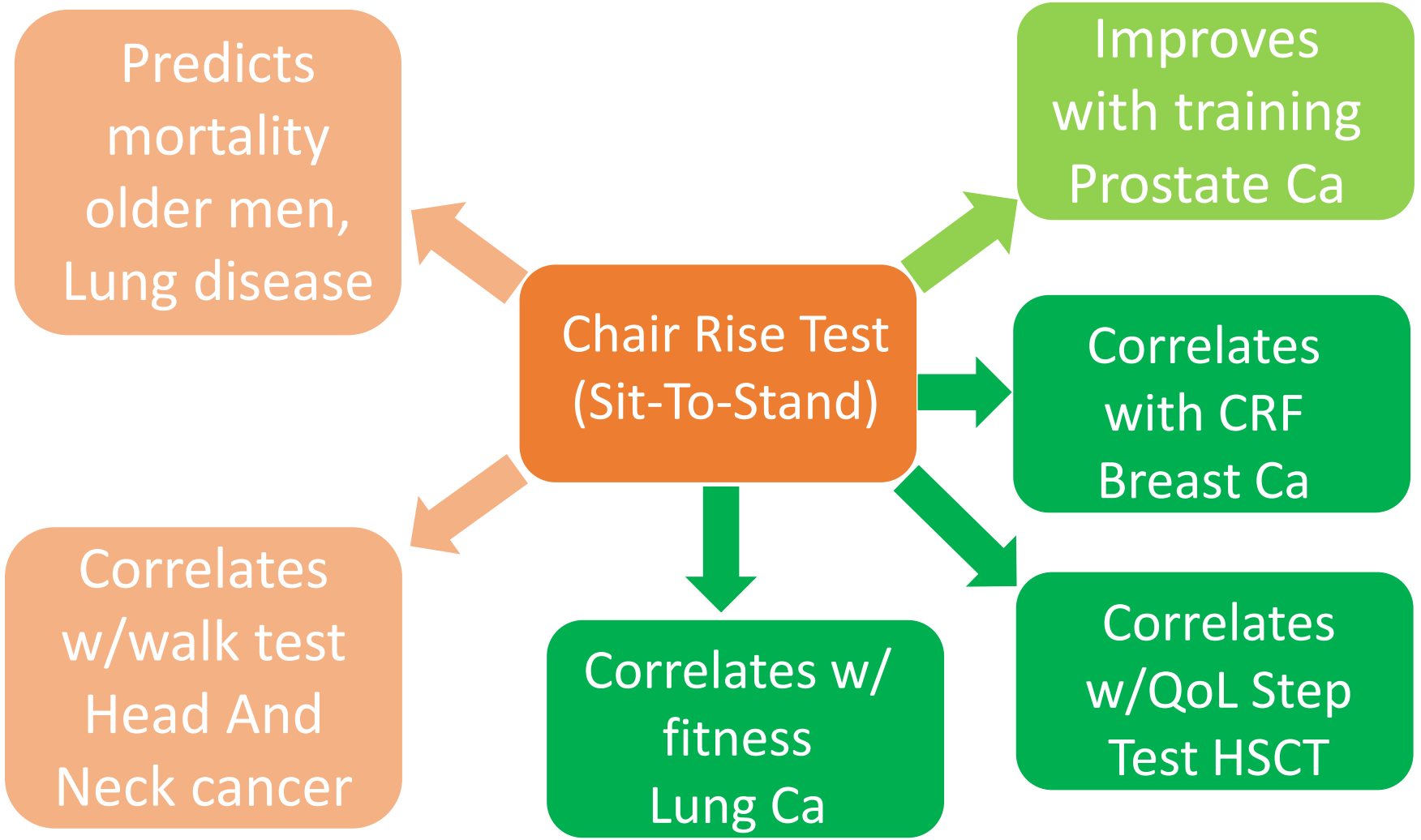


Sleep is a Habit that needs good maintenance

Rischer, 2009; Yavlal, 2022; Cancer.org

Our Approach: CHEAP-O Exercises Only (Sit-To-Stands for All)

- **C**ost nothing
- **H**ave meaning
- **E**asy and safe
- **A**daptable
- **P**ortable
- **O**utcome-friendly



De Buyser, 2013; Puhan, 2013; Eden, 2018; Gaskin 2016; Cuesta-Vargas, 2019; De Almeida 2019; Azzi 2021

Interval Training 101

High-Intensity Interval Training (HIIT)

Tabata Protocol
Go at 90% capacity
Work 20-30 sec, rest 10 sec
Repeat 16-12 times

The New York Times Scientific 7 Minute Workout

Meyer Protocol
Go at 85% capacity
Work 30 sec, rest 60 sec
Safe and Effective after heart surgery and in heart failure

Can Interval Training be safely applied to cancer patients?
YES!

Foster, 2015; NY Times, 2013; Meyer, 1990; Meyer, 1998; Dimeo, 1999

Non-negotiable Exercise Rules

1. If it hurts when you do it, don't do it (but mild discomfort is OK sometimes).
2. Don't work too hard – your effort or exertion level should almost never come up higher than 6 on a 0-10 scale (0 – no effort, 10 – absolute hardest, all-out effort). Exercise should not make it impossible to do other things later in the day.
3. Don't do things you regret. For example, if you've done something that leaves you sore or overly tired the next day, don't repeat it.

How To Get Started With Sit-To-Stand Training

1. Find a **comfortable seat height:** safely get up and sit down without arm help
2. Count how many times you can get up and sit down in 30 seconds, effort less than 6 out of 10 (0 – no effort, 10 – all-out effort).

Result: 5 repetitions or less
OR
The seat height is much greater than a normal chair

↓

Sunrise-Sunset

Results: 6-10 repetitions

↓

Breakfast-Lunch-Dinner

Results: 10 or more repetitions

↓

Interval Training
Every Minute
On the Minute
(EMOM)

Sunrise-Sunset Sit-To-Stand Training

- You are in the Sunrise-Sunset group if you need a seat much higher than a regular chair (similar in height to your bed) or did 5 or fewer repetitions during the test.
- You can practice sit-to-stands in the morning and at night, when you are next to the bed.
- For example, a person who did 3 sit-to-stands will start with just 1 repetition per workout and advance as per table to the right.
- Goal: 15 reps per set

	Sunrise	Sunset
Day 1	1	1
Day 2	1	2
Day 3	2	2
Day 4	2	3
Day 5	3	3
Day 6	3	4
Day 7	4	4
Day 8	4	5
Day 9	5	5
Day 10	5	6

Breakfast-Lunch-Dinner (BLD) Sit-To-Stand Training

- You are in the BLD group if you did between 6 and 10 repetitions during the test.
- You can practice sit-to-stands 3 times per day: breakfast, lunch, and dinner
- Take half of the test result and round it down. For example, a person who did 9 sit-to-stands will start with 4 repetitions per workout and advance as per table to the right.
- Goal: 15 reps per set

	Breakfast	Lunch	Dinner
Day 1	4	4	4
Day 2	4	4	5
Day 3	4	5	5
Day 4	5	5	5
Day 5	5	5	6
Day 6	5	6	6
Day 7	6	6	6
Day 8	6	6	7
Day 9	6	7	7
Day 10	7	7	7

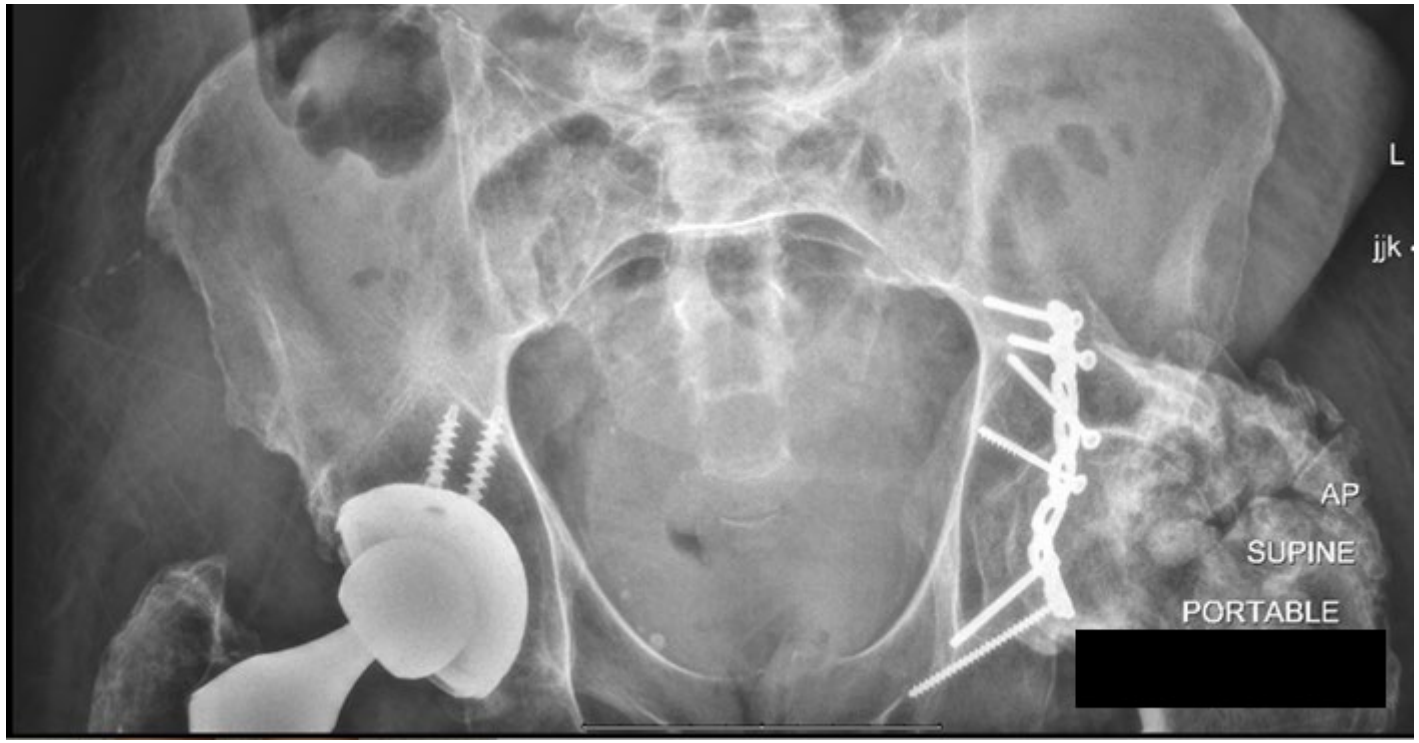
Every Minute on the Minute (EMOM) Sit-To-Stand Training

- You are in the EMOM group if you did more than 10 repetitions during the test.
- Take half of the test result and round it down. For example, a person who did 11 sit-to-stands during the test will start with 5 repetitions per set and advance as per table to the right.
- Warm-up then set a timer for 5 1-minute sets and do the prescribed number of sit-to-stands at the beginning of every minute.
- Goal: 15 reps per set

	Set 1	Set 2	Set 3	Set 4	Set 5
Day 1	5	5	5	5	5
Day 2	5	5	5	5	6
Day 3	5	5	5	6	6
Day 4	5	5	6	6	6
Day 5	5	6	6	6	6
Day 6	6	6	6	6	6
Day 7	6	6	6	6	7
Day 8	6	6	6	7	7
Day 9	6	6	7	7	7
Day 10	6	7	7	7	7

Case Study: Setting Goals and Keeping Track

- 61 yo readmitted with severe GI GvHD 1 month after donor cell transplant.
- 7 month stay, multiple infections, loses A LOT of muscle, suffers recurrent back pain.
- **Goal:** dance at a wedding in 3 months



Staying Accountable – "Not For Everybody"

THERE'S NO SUCH THING AS A BAD DAY! ZB

	Wedding	A	Uppers										Bed - Chair				30'	Chair - Table RT				30'	Chair-Kit-Chair			60'		
	Dance	B	Lowers										Bed - Chair w/B				40'	Chair - Bath RT				40'	Big Lap House			56		
	########	D	Legs										Office - Chair Lap				40'	Cen Island Lap				28'				Total	Stdup	Stdup
D	Date	7	8	9	9	930	10	1030	11	1130	12	12	1	2	3	4	4	5	6	7	8	8	9	10	Feet	Day	30sec
S	########	40	30			B		Back	Pain	#6	16			44	44	26				30				40	270	12	
S	########	30			16		30	40	Back	Pain	#6	36		B	30					30				30	242	16	
M	########	40	10	30	36			Back	Pain	#6	B			28	20	40					64		30		298	15	
T	########	64				64		Back	Pain	#7	B		64	40	20				32	40			30		354	15	
W	########	64					64	Back	Pain	#7	36		64	B	14				32	32			30		336	9	
TH	########	46	6AM	MSK	BackPain	#8										4pm		16	14	28	26			40	170	16	
F	########	40				Bacl	Pain	#7		B		64			Lisa	PT4		10	64	26				40	244	9	
S	########	30				64	20	Back	Pain	#7	B		C	44						64				30	252	14	
S	########	68				36	38	Back	Pain	#6	B			64					38	40	40	26		30	380	21	
M	########	68		64			BP#6	Lisa	PT	128		B		Kelly	OT	40				64				30	394	13	5
T	########	78					BP#6	85		B			Dr. S			67				103	26			30	389	21	
W	########	68		64		30		BP#5	Lisa	PT	64	26	B	Kelly	OT	A			64		64			30	410	19	5
TH	########	64	28	30	9AM	Hfd									3PM	58		BP#5		30	48	30		40	328	24	
F	########	32	86			54	BP#4	46	44	C	Lisa	PT	64	B	40	32		A	38					30	466	18	10
S	########	90	Sore	88			BP#4	86						B				102	A	C	26			30	422	22	X
S	########	106	Sore	wrst		BP#3	76					B				B		114						30	326	10	X
M	########	98	Sore	wrst		BP#3	88	Lisa	PT	B15	B15	84		58					C15	114		58		30	530	14	X
T	########	120	Sore	wrst	B15	BP#3	114	95				Kelly	OT	56	78				B25		26			30	519	16	X
W	########	24	160	32	56	30	Lisa	PT	B15	26	C15	175	14			BP#3					###	wst7	36	30	714	28	5
TH	########	5AM	MSK	60										58	4PM	BP#3			26		26	wst7		40	210	18	X

Staying Accountable – Pen and Paper

Sloan BLD Circuit Sit-To-Stand Rules:

1. Nothing should hurt in the process. Up and down movement is smooth - no bouncing or lur
2. Seat has to be high enough to perform sit-to-stand comfortably with as little assistance as
3. Keet the seat at the same height until you can do 3 sets of 30 reps with effort < 5.
4. At the end of each set, should not feel more than "pleasantly tired."
5. Don't advance until the last set feels no harder than the first set and effort is less than 5/10
6. Start writing down heart rate once you feel that it goes up after a set.

Date	Seat Height, In or Cm	Start Heart Rate	B'Fast	Lunch	Dinner	End Heart Rate	Effort (0/easy -> 10/about to pass out)
5-29-22	28"	116/67	121/80 3	104/70 3	125/75 3	121/87	1-1-2
5-30-22	24"	122/81	101/70 3	110/74 3	125/67 4	124/84	1-1-2
5-31-22	24"	120/76	118/76 3	119/73 4	123/80 4	127/83	1-1-1
6-1-22	24"	120/82	111/71 4	112/76 4	131/80 4	128/81	2-1-2
6-2-22	24"	122/75	123/71 4	118/74 4	118/72 5	112/74	1-1-2
6-3-22	24"	125/74	122/70 4	119/74 5	117/77 5	111/72	1-1-1
6-4-22	24"	119/71	109/70 5	122/74 5	120/76 5	110/70	1-1-2
6-5-22	24"	130/71	106/70 5	110/72 5	112/74 6	104/72	1-1-2
6-6-22	24"	128/70	124/72 5	116/73 6	116/77 6	108/70	1-1-1
6-7-22	24"	124/73	117/72 6	112/71 6	108/73 6	116/77	1-2-1
6-8-22			6	6	7		
6-9-22			6	7	7		
6-10-22			7	7	7		
6-11-22	24"	111/76	116/76 7	112/74 7	108/73 8	110/75	1-1-1
6-12-22	24"	130/76	106/76 7	111/79 8	118/70 8	116/73	1-1-1
—	—	—	— 8	— 8	— 8	—	—
—	—	—	— 8	— 8	— 9	—	—
—	—	—	— 8	— 9	— 9	—	—
—	—	—	— 9	— 9	— 9	—	—

—	—	—	— 9	— 9	— 10	—	—
7-11-22	24"	121/88	110/80 9	108/75 10	106/72 10	101/77	1-1-1
7-12-22	24"	120/80	114/86 10	119/76 10	107/70 10	105/70	1-1-1
7-13-22	24"	122/72	124/72 10	116/73 10	108/76 11	105/74	1-1-1
7-14-22	22"	132/77	114/80 10	112/75 11	111/70 11	119/79	2-2-2
7-15-22	22"	128/74	124/87 11	130/83 11	126/66 11	120/80	2-2-1
7-16-22	22"	118/78	118/76 11	132/82 11	126/72 12	121/88	1-1-1
7-17-22	22"	111/77	121/70 11	103/71 12	105/72 12	102/65	1-1-1
7-18-22	22"	116/77	123/68 12	119/71 12	108/71 12	124/79	2-2-2
7-19-22	22"	119/72	106/72 12	111/70 12	104/72 13	110/77	1-2-1
7-20-22	22"	105/72	107/70 12	121/74 13	106/77 13	108/76	1-1-1
7-21-22	22"	110/70	113/77 13	119/75 13	102/71 13	121/84	1-1-2
7-22-22	22"	126/74	121/70 13	126/70 13	103/72 14	110/70	1-1-1
7-23-22	22"	121/75	105/78 13	118/74 14	119/75 14	113/79	2-2-1
7-24-22	22"	108/70	107/70 14	105/71 14	111/78 14	106/74	2-2-3
7-25-22	22"	102/76					

60 days training sit-to-stands

28” seat became 22” seat

3 repetitions improved to 14

Take Home Points

- Difficulty getting things done after a stem cell transplant comes from the effects of disease and treatment
- Difficulty getting things done after a stem cell transplant is not a character flaw or a personal weakness
- Start low, go slow, stay consistent, track your progress and recognize your accomplishments
- Don't work too hard (keep effort less than 6 on a 0-10 scale) and don't work through pain (though minor discomfort is OK)
- Make your bed, brush your teeth, stay hydrated and talk to your team
- Sleep is a habit that may take time to build

MSKCC Exercise Videos

Breathing Video:

- https://www.mskcc.org/cancer-care/patient-education/breathing-exercises-01

Chair and bed exercise videos:

https://www.mskcc.org/cancer-care/patient-education/chair-exercises-01

- https://www.mskcc.org/cancer-care/patient-education/beginner-bed-exercises-01
- https://www.mskcc.org/cancer-care/patient-education/intermediate-bed-exercises-01
- https://www.mskcc.org/cancer-care/patient-education/advanced-bed-exercises-01

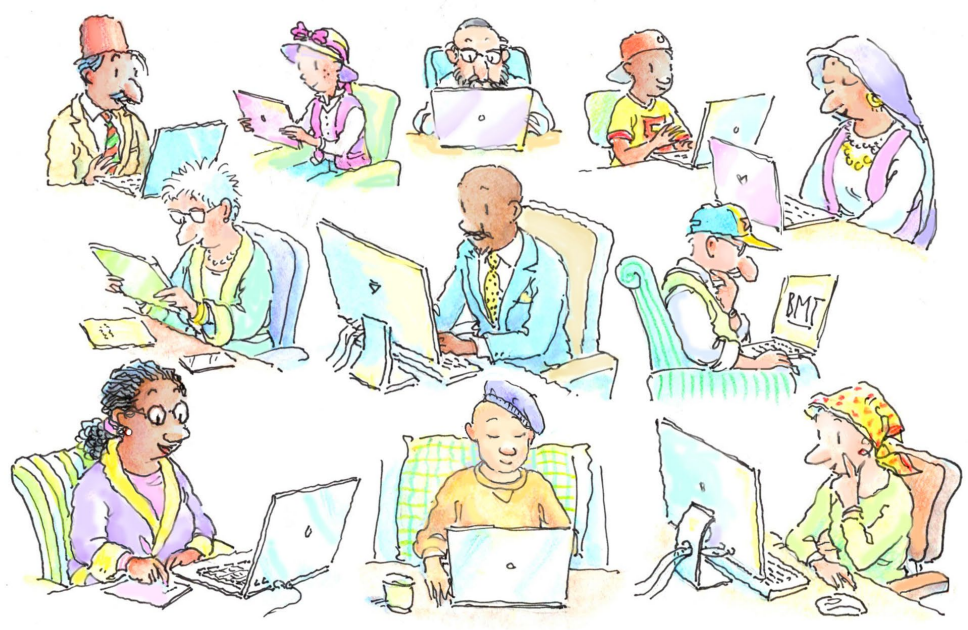
Thank you!

- Questions?
- Comments?
- Jokes?
- Tweet @RehabGrisha @CancerRehabDocs
- Visit: https://health.gov/our-work/nutrition-physical-activity/move-your-way-community-resources

QUESTIONS?

Grigory (Grisha) Syrkin MD
Memorial Sloan Kettering Cancer Center

LET US KNOW HOW WE CAN HELP YOU



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