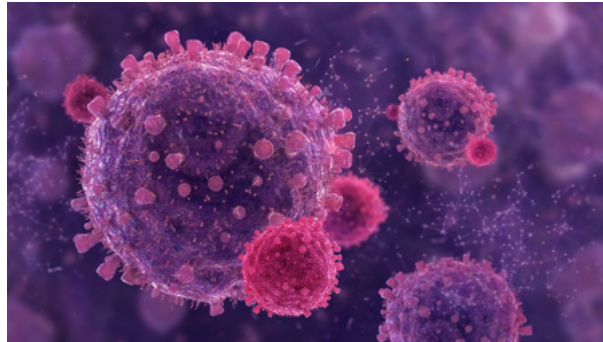


Physical Activity, Exercise and Nutritional Guidance for CLL



*David B. Bartlett, PhD
Lecturer of Exercise Immunology
University of Surrey
Guildford*

d.bartlett@surrey.ac.uk
@Bartlett_Lab

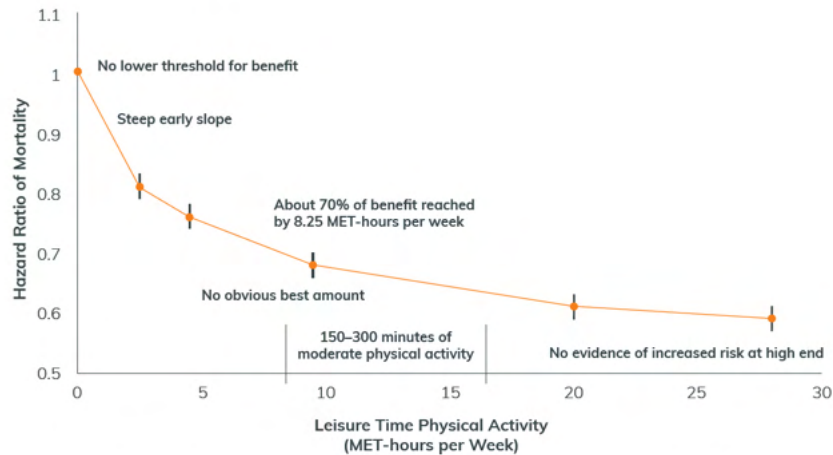
*Adjunct Assistant Professor
Duke University
Durham, North Carolina*

At the end of this Webinar you should be able to better understand:

- 1) The general and cancer recommendations for diet and physical activity
- 2) Why there are no haematological malignancies specific recommendations
- 3) The effects of higher physical fitness on CLL biology
- 4) The preliminary effects of exercise training in treatment naïve CLL
- 5) Where to go, who to speak to and how to improve your diet and physical activity levels

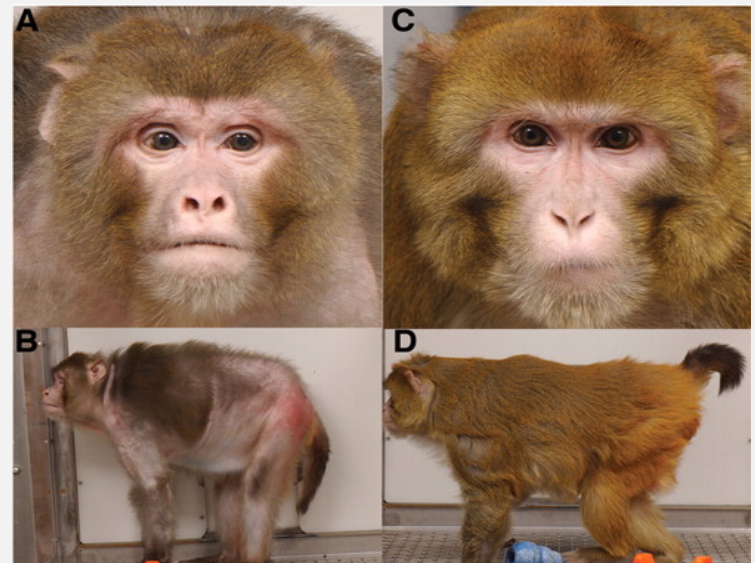
- Any kind of physical activity is better than nothing
- 150 – 300 minutes/week of moderate intensity physical activity

Figure 2-1. Relationship of Moderate-to-Vigorous Physical Activity to All-Cause Mortality



Source: Adapted from data found in Moore SC, Patel AV, Matthews CE. Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis. PLoS Med. 2012;9(11):e1001335. doi:10.1371/journal.pmed.1001335.

- Eating the correct balance of nutrients and caloric intake improves healthspan
- Calorie reduction should not induce malnutrition



What are the guidelines for adults

Physical activity for adults and older adults

Benefits health	Reduces your chance of	Type II Diabetes	-40%
Improves sleep		Cardiovascular disease	-35%
Maintains healthy weight		Falls, depression etc.	-30%
Manages stress		Joint and back pain	-25%
Improves quality of life		Cancers (colon and breast)	-20%

Some is good, more is better

Make a start today: it's never too late

Every minute counts

Be active

at least **150** minutes moderate intensity per week
increased breathing able to talk

OR

at least **75** minutes vigorous intensity per week
breathing fast difficulty talking

or a combination of both

Build strength
to keep muscles, bones and joints strong
on at least **2** days a week

Minimise sedentary time
Break up periods of inactivity

Improve balance
For older adults, to reduce the chance of frailty and falls
2 days a week

UK Chief Medical Officers' Physical Activity Guidelines 2019

Eatwell Guide

Use the Eatwell Guide to help you get a balance of healthier and more sustainable food. It shows how much of what you eat overall should come from each food group.

Check the label on packaged foods

Each serving (150g) contains	Energy 200kcal	Fat 3.0g	Saturated fat 1.3g	Sugar 34g	Salt 0.9g
	13%	6%	3%	68%	15%

of an adult's reference intake
Typical values (as sold per 100g: 697kcal/167kcal)

Choose foods lower in fat, salt and sugars

Eat at least 5 portions of a variety of fruit and vegetables every day

Choose wholegrain or higher fibre versions with less added fat, salt and sugar

Eat less often and in small amounts

Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

Choose lower fat and lower sugar options

Choose unsaturated oils and use in small amounts

6-8 a day

Water, lower fat milk, sugar-free drinks including tea and coffee all count.

Limit fruit juice and/or smoothies to a total of 150ml a day.

Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS

Source: Public Health England in association with the Welsh Government, Food Standards Scotland and the Food Standards Agency in Northern Ireland

© Crown copyright 2019

Recommendations if you have cancer

- 2018 WCRF Recommendations for Survivors is based on most common cancers
- Limited evidence persists



World Cancer Research Fund | American Institute for Cancer Research | CUP Continuous Update Project

Analysing research on cancer prevention and survival



DIET, NUTRITION, PHYSICAL ACTIVITY AND BREAST CANCER SURVIVAL – ALL CAUSE MORTALITY					
		DECREASES RISK		INCREASES RISK	
		Exposure	Time frame	Exposure	Time frame
STRONG EVIDENCE	Convincing				
	Probable				
LIMITED EVIDENCE	Limited – suggestive	Physical activity	Before diagnosis	Body fatness	Before diagnosis
			≥12 months after diagnosis		<12 months after diagnosis
		Foods containing fibre	Before diagnosis	Total fat	≥12 months after diagnosis
			≥12 months after diagnosis		Before diagnosis
Foods containing soy	≥12 months after diagnosis	Saturated fatty acids	Before diagnosis		
STRONG EVIDENCE	Substantial effect on risk unlikely				

STRONG: Evidence strong enough to support a judgement of a convincing or probable causal relationship and generally justify making recommendations

LIMITED: Evidence that is too limited to justify making specific recommendations

Survivors of breast and other cancers

2018

2019 American College of Sports Medicine Recommendations for Exercise and Health Related Outcomes

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 cancer-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

No Increased risk of hematologic cancer, including CLL with low physical activity or higher BMI

- No evidence for reduced mortality
- Physical exercise added to standard of care might improve fatigue and depression
- Inconclusive evidence for benefits to QoL, anxiety or SAEs

CLEARLY NOT ENOUGH EVIDENCE FOR PHYSICAL ACTIVITY/ NUTRITION TO BENEFIT CLL!

Anthropometric Characteristics, Physical Activity, and Lymphoma Subtypes and B-Cell Chronic Lymphocytic Leukemia Study

James R. Cerhan¹, Carol A. Janney¹, Celine M. Kay², John D. Potter³, Thomas A. Sellers¹, and

¹ Department of Health Sciences Research, Mayo Clinic
² Division of Hematology, Department of Medicine, Mayo Clinic
³ Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center
⁴ Division of Epidemiology, University of Minnesota School of Public Health

Received for publication January 9, 2002; accepted for publication February 14, 2002

Anthropometric characteristics of hematological malignancies: a meta-analysis of cohort studies

Theodora Psaltopoulou¹, Theodoros N. Sergentanis¹, Ioannis Ntanasis-Stathopoulos², Ioannis-Georgios Tzanninis¹, Elena Riza¹ and Meletios A. Dimopoulos²

¹Department of Hygiene, Epidemiology and Medical Statistics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

²Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

reviews

adult patients with haematological

ef I, Elter T, Skoetz N

hrane Review

- Of 1892 participants in 18 trials only 3.7% had CLL!
- 8 trials involved stem cell transplant
- Majority had ALL, AML and MM
- No inclusion of strength training only

What CLL mechanisms might we be able to change?

Metabolism

- CLL cells are lipid dependent
- LPL is a marker of disease progression

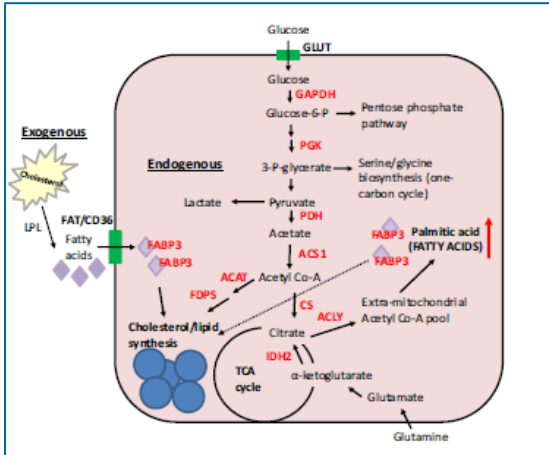
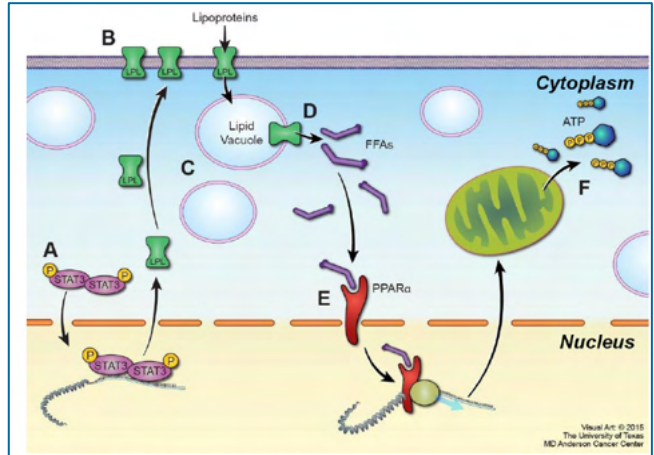
In healthy people, exercise & diet can alter cellular & tissue metabolism

Cell-to-Cell Communication

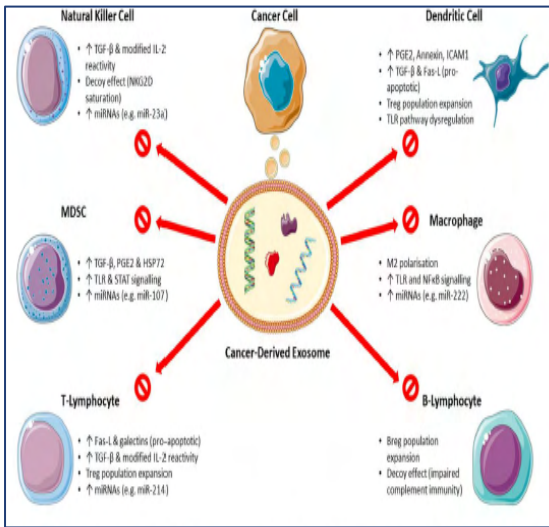
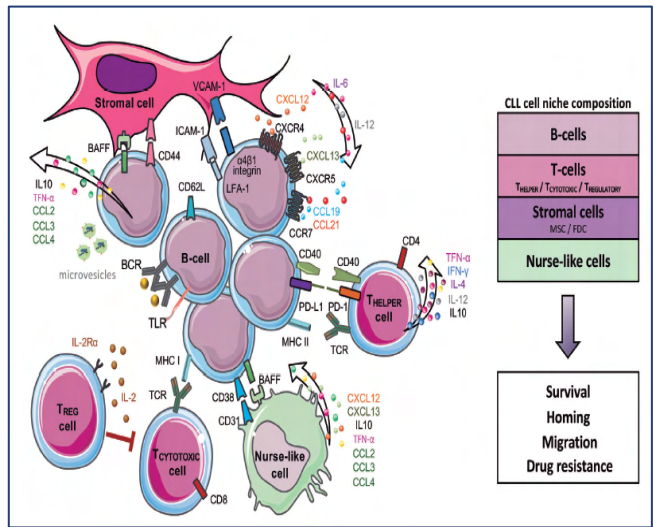
- CLL cells secrete extracellular vesicles that promote their survival
- The microenvironment then produces cytokines and chemokines to further enhance CLL cell survival
- The normal immune system is suppressed and unable to fully control the malignancy

In healthy people, exercise and diet adaptations are driven by working tissues/cells “talking” to other tissues/cells through a similar mechanism & drives improved normal immune functions

CLL Metabolism

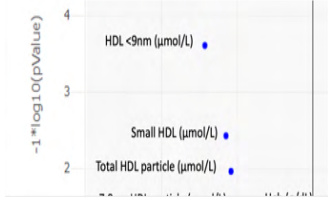
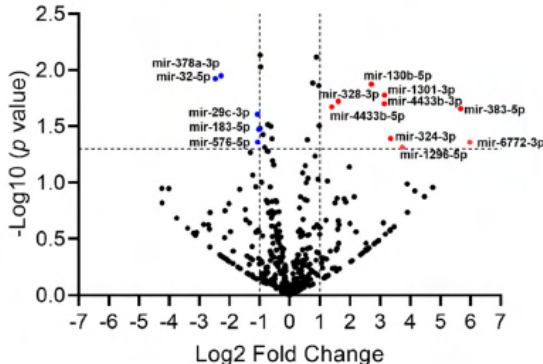


CLL Cell to Cell Communication



Higher aerobic fitness is associated with different levels of lipoproteins, exosomal miRNAs, and NK-cell phenotypes; all known to affect CLL cell survival

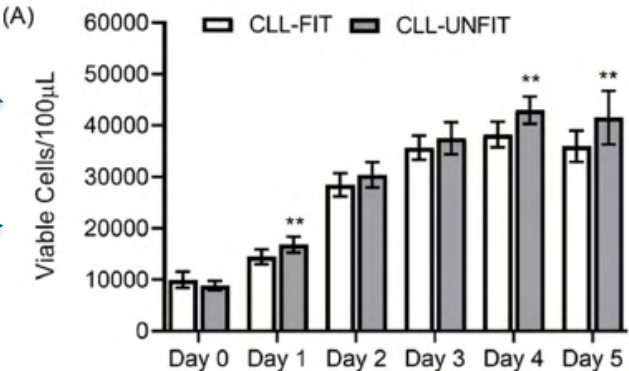
Serum from higher aerobic fitness blunts the growth of a CLL-like cell line



Article

Physiological Fitness and the Pathophysiology of Chronic Lymphocytic Leukemia (CLL)

Andrea Sitlinger¹, Michael A. Deal^{2,3}, Erwin Garcia⁴, Dana K. Thompson⁵, Tiffany Stewart⁵, Grace A. MacDonald^{2,3}, Nicolas Devos⁶, David Corcoran⁶, Janet S. Staats⁷, Jennifer Enzor⁷, Kent J. Weinhold⁷, Danielle M. Brander¹, J. Brice Weinberg⁵ and David B. Bartlett^{2,3,*}



Exercise training study

Population

- Sixteen treatment naïve CLL (65 ± 9 years old)
- Mean years since diagnosis was 6.3 years (range: 0.5 – 24 years).
- Rai stage 0 or 1 (81.2%),

Intervention

- 12 weeks of high-intensity interval training (HIIT)
 - 3 x 30-minute sessions/week
 - 80-90% of peak aerobic fitness (VO₂peak)
 - Plus 2 x 30 minute/sessions/week of resistance-based endurance training (70% max strength)

scientific reports

www.nature.com/scientificreports

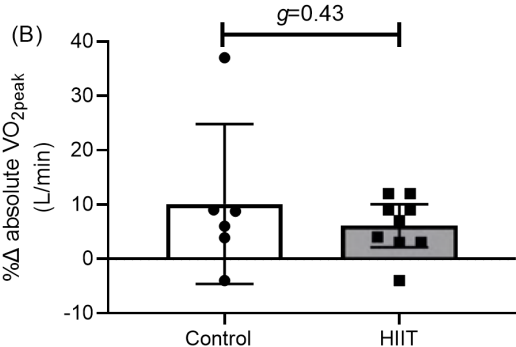
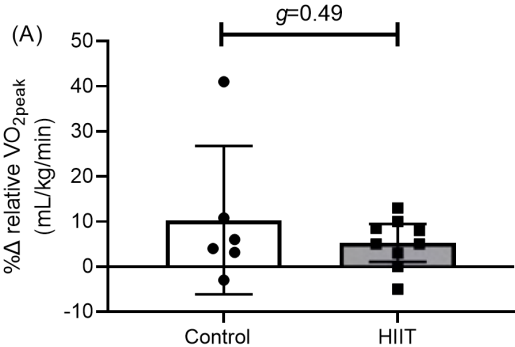
OPEN

A pilot study of high-intensity interval training in older adults with treatment naïve chronic lymphocytic leukemia

Grace MacDonald^{1,2}, Andrea Sitlinger³, Michael A. Deal^{1,2}, Erik D. Hanson⁴, Stephanie Ferraro⁴, Carl F. Pieper⁵, J. Brice Weinberg⁶, Danielle M. Brander³, David B. Bartlett^{1,2,7*}

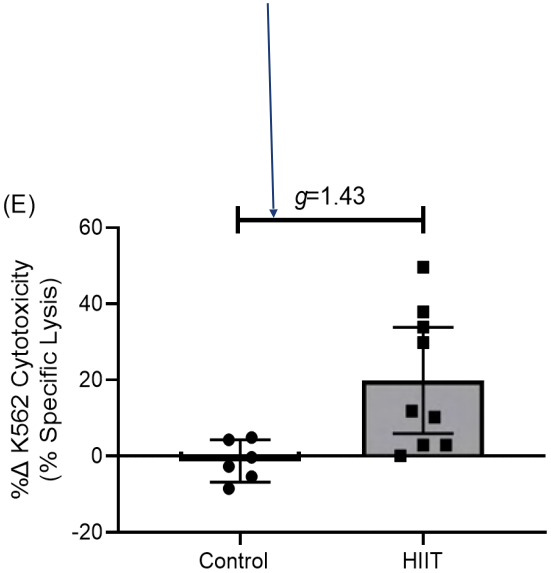
First exercise intervention specifically designed for CLL patients and to assess important biological effects.

Aerobic Fitness →

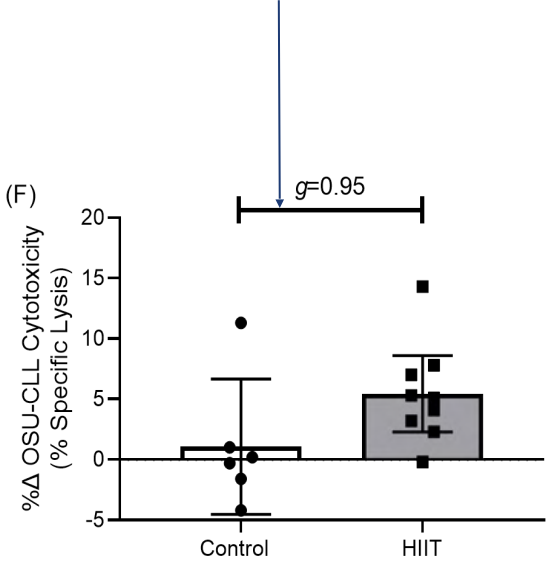


Muscle Strength →

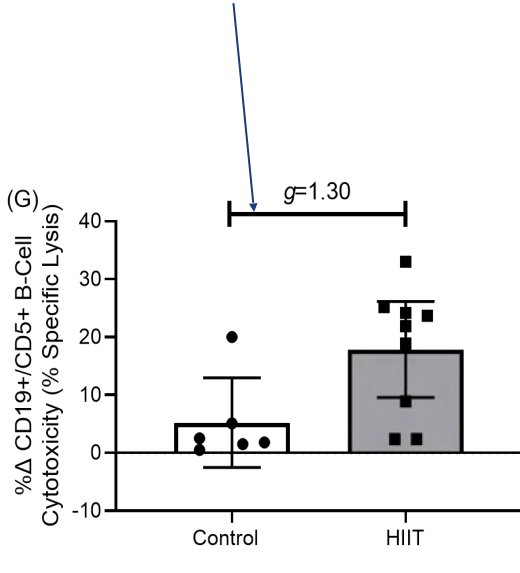
Secondary Cancer



CLL Cell Line



Patients own tumor cells

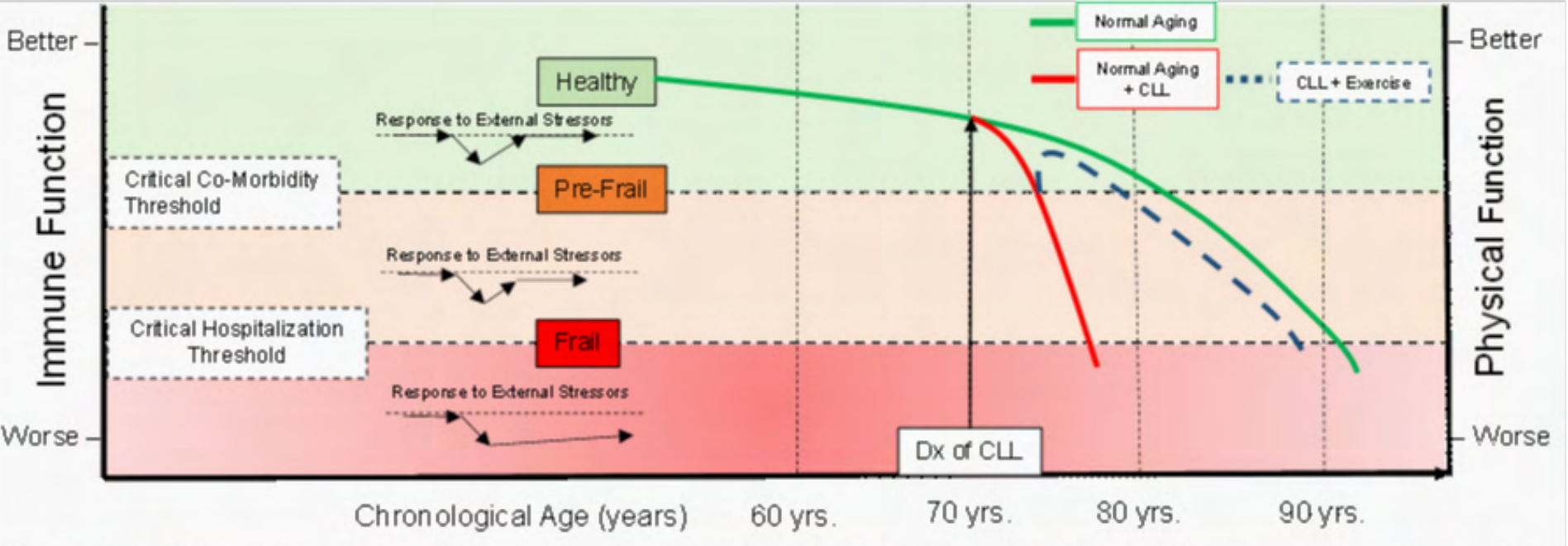


What do we think is happening

CLL causes a metabolic imbalance

Energy is redirected from healthy tissues to CLL cells

Exercise and diet can rebalance metabolism



Study 1: Effects of Exercise and Nutrition on Balancing Energy Demand in CLL (ENERGIZE-CLL)

Confirmed CLL & Partner (If suitable)
Watch & Wait
On-Treatment (not chemo)
Completed Treatment
Safe to Exercise

Must live close enough to Guildford to attend testing and training

12 – week intervention

Follow-Up Testing

~6 month Follow-Up

Supervised Exercise Training
3x 1 hour sessions/week aerobic + resistance

University of Surrey
Baseline Assessments (1-3 visits)

- Lipid Metabolism
- Peak Aerobic Fitness
- Maximum Strength
- Body Composition
- Blood Sample
- Functional Capacity
- Muscle Quality
- Dietary Intake
- Quality of Life
- Physical Activity Levels

Randomized

Nutritional Guidance
Weekly virtual consult to ensure a balanced healthy diet is achieved

Same as Baseline

Questionnaires

Supervised Exercise + Nutritional Guidance

Outcomes

1. Changes in physical health and risk factors for poor health
2. Changes in cell and tissue metabolism
3. # infections, hospitalizations, CLL specific medical needs

Study 2: Effects of remote exercise and nutritional guidance on CLL health (REMOTE-CLL)

Confirmed CLL & Partner (If suitable)

- Watch & Wait
- On-Treatment (not chemo)
- Completed Treatment
- Safe to Exercise

Willing to come to Guildford only for assessments

Continuous

Semi-Supervised Exercise Training
Goal of 150-300 mins moderate intensity aerobic exercise

- University of Surrey
Every 6-months Assessments (1 visits)
- Aerobic Fitness
 - Strength
 - Body Composition
 - Blood Sample
 - Functional Capacity
 - Muscle Quality
 - Dietary Intake
 - Quality of Life
 - Physical Activity Levels

University of Surrey

- Baseline Assessments (1 visits)
- Aerobic Fitness
 - Strength
 - Body Composition
 - Blood Sample
 - Functional Capacity
 - Muscle Quality
 - Dietary Intake
 - Quality of Life
 - Physical Activity Levels

Randomized

Nutritional Guidance
Monthly consult to ensure a balanced healthy diet is achieved

Semi-Supervised Exercise Training + Nutritional Guidance

Outcomes

1. Progression of disease or change in disease treatment
2. Changes in physical health and risk factors for poor health
3. Changes in cell and tissue metabolism
4. # infections, hospitalizations, CLL specific medical needs

Study 3: Effects of Virtual Physical Activity and Nutritional Guidance on CLL health (VIRTUAL-CLL)

Confirmed CLL & Partner (If suitable)

- Watch & Wait
- On-Treatment (not chemo)
- Completed Treatment
- Safe to Exercise

Virtual

- Baseline Assessments
- Dietary Intake
 - Quality of Life
 - Physical Activity Levels
 - Physical Function
 - Patient provided clinical records

Randomized

Physical Activity Guidance

Goal of 150-300 mins moderate intensity aerobic exercise

Nutritional Guidance

Monthly consult to ensure a balanced healthy diet is achieved

Physical Activity + Nutritional Guidance

Continuous

Virtual

- Every 6-month assessments
- Dietary Intake
 - Quality of Life
 - Physical Activity Levels
 - Physical Function
 - Patient provided clinical records

Outcomes

1. Progression of disease or change in disease treatment
2. Changes in physical health and risk factors for poor health
3. # infections, hospitalizations, CLL specific medical needs

What can you do now

1. To keep informed of when our studies will open you can email me at d.bartlett@surrey.ac.uk
2. If you want to start exercising more (<https://www.nhs.uk/live-well/exercise/>), we recommend contacting your GP. You may need tests done before starting. Don't rely on Google, contact an expert.
 - a. Level 1-4 requires least clinical input
 - b. >Level 4 will need clinical clearance
3. If you want to change your diet, speak to your GP and get expert advice (<https://www.nhs.uk/live-well/eat-well/>)
4. Start regularly recording your physical activity levels and diet. The more information we have the better we can understand their effects.



Adapted from the Marathon Handbook, by Thomas Watson