Michael Smith Health **Research BC**

Effects of Time Restricted Eating on Clinical & Metabolomic Outcomes in **People with Cancer: A Systematic Review**

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Background

Time Restricted Eating (TRE)

A rhythmic eating pattern that involves limiting ones eating hours to a set window (i.e., 6-12 hours) on a daily, or near daily basis often aligning with circadian rhythm (i.e., eating during active daytime hours)¹⁻⁴

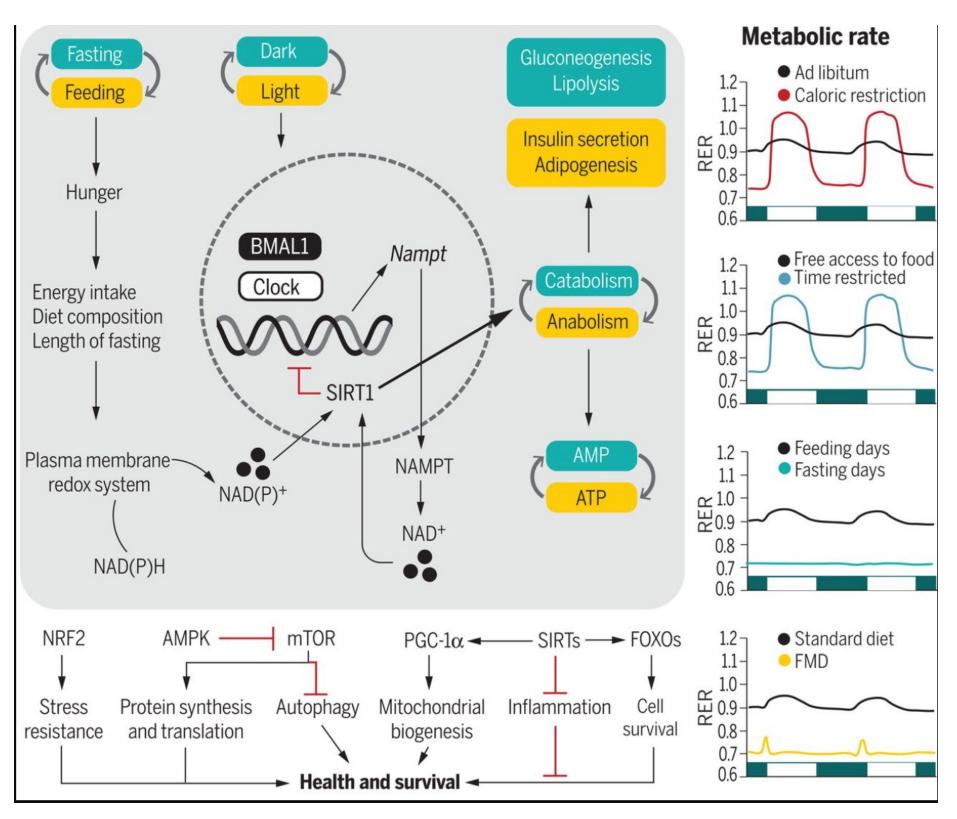


Figure 1. "Integration of the circadian rhythms and feeding-fasting cycles with metabolism"⁷

Metabolic Changes Resulting from TRE

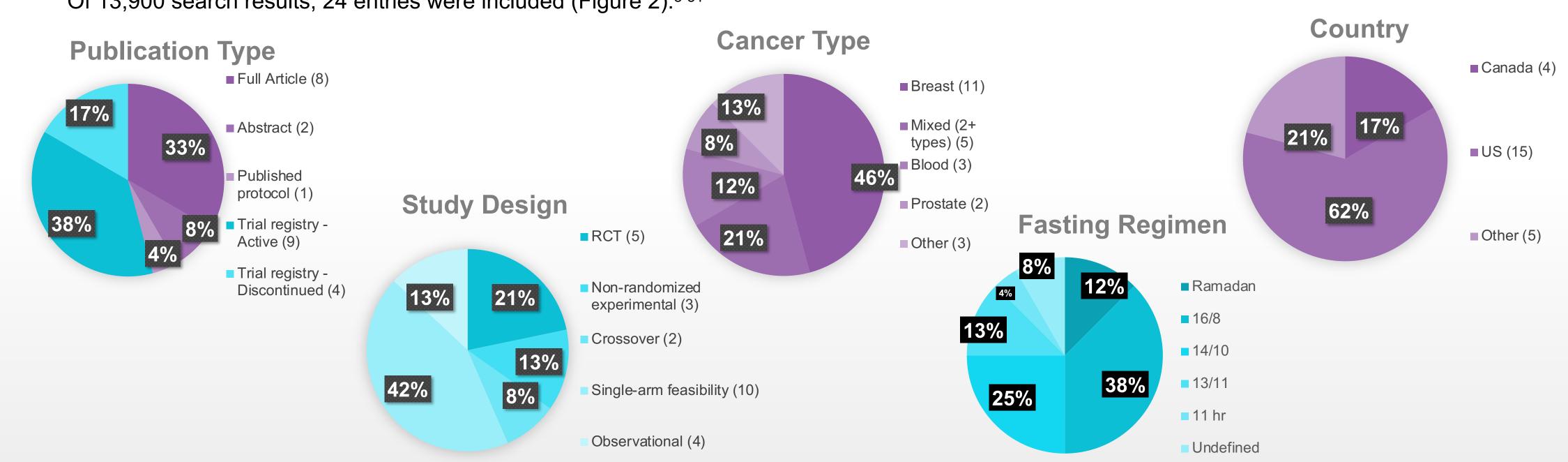
After 12 hours fasting: Hepatic glycogen depleted, serum glucose levels decrease by $20\%^{5,6} \rightarrow$ reliance on non-hepatic glucose, fatderived ketone bodies, and free fatty acids as energy sources⁷

Methods

(PROSPERO CRD42023386885)

- Objective: To systematically evaluate the clinical and/or metabolomic effects of TRE compared to ad libitum eating or alternative diets in people with cancer.
- Included: published original study designs, protocols, and clinical trial registries.
- •Six databases searched from inception to January 4, 2023.

Identification		Studies from databases/registers (n = 13900)			
				\rightarrow	Duplicates removed (n = 3056)
			/		
Screening	[Studies screened (n = 10844)			Studies excluded (n = 10722)
			/		
		Studies sought for retrieval (n = 122)			Studies not retrieved (n = 0)
		Studies assessed for eligibility (n = 122)			Studies excluded (n = 98) Not in human (3)
					Not in English (3) Pharmacokinetics (2) Procedural fasting (2) Short term fasting (28) Wrong study design (22) Extended water fast (2)
					Calorie restriction only (1) Fasting Mimic Diet (FMD) (31) Wrong patient population (4)
			,		
Included		Studies included in review	v (n = 24)		



Results

Of 13,900 search results, 24 entries were included (Figure 2):⁸⁻³¹

TRE May Reduce the Risk of Prostate and Breast Cancer Recurrence

1. Palomar-Cros et al. 2021 evaluated 607 prostate cancer (PCa) cases and 848 controls: Fasting \geq 11 hrs overnight \rightarrow lower odds of developing PCa (OR=0.77, 95% CI 0.54, 1.07). Breakfast after 8:30AM: increased odds of developing PCa compared to eating before 8:30AM(OR=1.30, 95% CI 0.92, 1.85) 2. Marinac et al. 2016 analyzed data from 2413 women with early stage, invasive breast cancer (Br Ca): Fasting <13 hrs/ night increased the risk for Br Ca recurrence compared to fasting \geq 13 hrs / night (hazard ratio, 1.36; 95% CI, 0.95 CI, 0.95 – 1.56) 3. Yassin et al. 2021 evaluated Ramadan fasting among CML patients receiving TKIs: Reduced (p > 0.05) mean values of WBC, neutrophils, BCR-ABL. Mean values for platelets, hemoglobin, basophils and eosinophils were maintained. 4. Alshammari et al. (2022) prospectively assessed 37 patients with colorectal cancer: CEA declined 40.9% when fasting >20days, compared to -12.4% in those who fasted <20days.





Mean adherence: **70-100%**^{8,9,17-19,,23,29,} Reduction in:^{23,29,18} - waist circumference - visceral adipose tissue



Improvement in:^{19,22,23}

- fatigue,
- chemotherapy side effects,
- physical/functional well-being,
- sleep.

Table 1. Summary	of TRE interventions

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Study	n	Description	Duration	Control/comparator
Alshammari et al., 2022	37	Ramadan: Fasting from dawn to sunset	≥20 d	<20 d
Badar et al., 2014	11	Ramadan: Fasting from dawn to sunset	Last 2 wks of Ramadan	2 wks during Shawwal (non-fasting)
Christensen et al., 2022	130	14-16 hr self-selected fast, start > 3 hrs before bedtime; ≥5 d /wk	12-18 wks	Standard of care
Kirkham et al., 2021	15	16 hr fast on weekdays, 8 pm – 12 pm	8 wks	N/A
Kirkham et al., 2022	22	16 hr fast on weekdays, 8 pm – 12 pm	8 wks	N/A
Kleckner et al., 2022	39	14 hr overnight fast, self-selected window	14 d	N/A
Marinac et al., 2016	2,413	≥13 hr overnight fast	Estimated at baseline,1 & 4yr	<13 hrs overnight
O'Donnell et al., 2022	40	13 hr overnight fast	12 wks	N/A
Palomar-Cros et al., 2021	1,455	11 hr fast per night	Not reported.	Control group fasting <11hrs overnight
Vega et al., 2022	16	≥16 hrs fast	12 wks	Caloric restriction of 25%
Yassin et al., 2021	49	Ramadan: Fasting from dawn to sunset	1 mo	N/A
NCT03523377, 2018*	40	≥14 hrs overnight fast	Daily x 6 mo	Cardiac diet & exercise ≥ 30 min 5d/wk
NCT04288336, 2020*	0	16 hr fast	1 y	N/A
NCT04560439, 2020*	0	Lifestyle modification intervention that utilizes IF. (No definition of IF)	16 sessions over 6 mo	N/A
NCT04626843, 2020*	15	16 hr fast	3 mo	N/A
NCT04691999, 2020*	0	16-18 hrs fast, 4 d/wk	6 mo	N/A
NCT04708860, 2021*	30	13 hrs overnight fast starting at 8pm, ≥6 d /wk	12 wks	N/A
NCT04783467, 2021*	15	14-16 hr fast	6 wks	4 wks, healthy meals, no time restriction
NCT05023967, 2020*	120	≥ 16 hr overnight fast for 4-6 wks.	4-6 wks	Usual dietary pattern
NCT05083416, 2021*	29	14 hr overnight fast	3 mo	Traditional eating pattern, no time restriction
NCT05259410,2022*	40	16 hr overnight fast with a Mediterranean style diet or usual diet, self-selected	12 wks	Standard care
NCT05312255, 2022*	150	16 hr overnight fast	1 mo	Exercise: strength training 2 x wk x 6 mo
NCT05327608, 2022*	55	14 hr fast	approx. 4 mo	N/A
NCT05722288, 2023*	60	Weekday fast - no fasting window provided	4 wks	Nutritional counseling
*Clinical trial registration year				



No results



Mean caloric deficit 450 kcals (22%)¹⁷ 202 kcals (10.5%)¹⁹



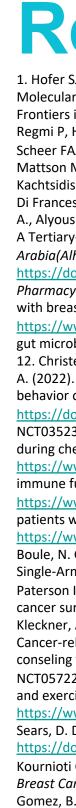
Decrease in absolute CVD risk¹⁸



The field of TRE in cancer is in its infancy. Of the completed studies, there was heterogeneity within the study populations, TRE regimens, and outcomes measures, so conclusions on the effect of TRE on cancer-related outcomes cannot yet be drawn. Despite this, these preliminary findings suggest that TRE is feasible in this population, may have clinical health benefits for people with cancer while also improving QOL.

Based on this review, it is premature to recommend the use of TRE for people with cancer. Due to the nutritional challenges that frequently accompany advanced stages of cancer and high-risk treatment protocols, TRE will not be appropriate for all patients. More studies are needed to elucidate the ideal fasting regimen that balances clinical and metabolic benefits with safety and the patient's perspective on acceptability.





https://www.clinicaltrials.gov/study/NCT0532760



Significance & Next Steps

Clinical Implications

Next Steps

Our team has completed 2 feasibility trials (NCT05708326, NCT04626843) on intermittent fasting in patients with chronic lymphocytic leukemia (CLL). With the generous support of Michael Smith Health Research BC and Lotte & John Hecht Memorial Foundation, we will be embarking on larger trial in fall of 2024.

Want to learn more?

This study has been accepted for publication in *Nutrition Reviews* Contact information (currently in-press).





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