

# Evaluation of metabolic changes in clinic attendees with therapeutic carbohydrate restriction

**Authors:**

Kirsty Woods<sup>1,2</sup>   
Hilmi S. Rathomi<sup>3,4</sup>   
Thomas L. Smith<sup>1</sup>   
Nahal Mavaddat<sup>5</sup>   
Judith Katzenellenbogen<sup>3</sup> 

**Affiliations:**

<sup>1</sup>Metabolic Health Solutions, Perth, Australia

<sup>2</sup>School of Medical and Health Sciences, Ralph and Patricia Sarich Neuroscience Research Institute, Edith Cowan University, Perth, Australia

<sup>3</sup>School of Population and Global Health, Faculty of Health and Medical Science, University of Western Australia, Perth, Australia

<sup>4</sup>Department of Public Health, Faculty of Medicine, Universitas Islam Bandung, Bandung, Indonesia

<sup>5</sup>Medical School, Faculty of Health and Medical Science, University of Western Australia, Perth, Australia

**Corresponding author:**

Kirsty Woods,  
kirsty.woods@metabolicealthsolutions.org

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**Background:** Obesity and related metabolic health disorders are major clinical problems that have become increasingly prevalent worldwide.

**Aim:** This before-after study examined the impact of therapeutic carbohydrate restriction (TCR) in managing metabolic health and promoting weight loss in a clinical setting using indirect calorimetry (IC).

**Setting:** Data were collected from medical records obtained from a specialised allied health clinic focusing on metabolic health.

**Methods:** The study analysed retrospective data from 202 overweight or obese participants (77% female, mean age 47.3) who received TCR as part of a behavioural modification programme involving multiple visits where their lifestyle, body composition and respiratory quotient (RQ), a key indicator of fat oxidation were recorded.

**Results:** The study found that TCR improved fat oxidation in 84% of participants at short term visit (around 2 weeks), with an average weight loss of 1.8 kg. At medium term visit (around 12 weeks), 82% of participants maintained an increase in fat oxidation rate, with an average weight loss of 3.9 kg. In addition, among those with recorded body composition and waist circumference, 71% of weight lost was from fat, with an average reduction of 4.9 cm in waist measurements.

**Conclusion:** This real-world study suggests that personalised TCR guided by IC can be an effective strategy for improving metabolic flexibility to help manage excess weight and related co-morbidities in a free-living population. Further research is needed to examine the long-term effects of TCR using this approach.

**Contribution:** The utilisation of IC allows for the examination of individual shifts and improvements in metabolism among patients undergoing TCR.

**Keywords:** carbohydrate restriction; fat oxidation; indirect calorimetry; obesity; weight loss; metabolic flexibility; lifestyle.

## Introduction

Obesity and related metabolic health disorders are major clinical problems that have become increasingly prevalent worldwide and are associated with numerous health risks and costs.<sup>1,2,3,4</sup> Current approaches to assessing and managing these conditions appear inadequate, with innovative interventions to prevent and reduce their prevalence and complications continuing to be sought.

One crucial aspect of metabolic health is metabolic flexibility, which refers to the ability to efficiently adapt metabolism to varying metabolic demands.<sup>5</sup> Impairments in metabolic flexibility are associated with reduced fat oxidation and development of conditions such as obesity, diabetes and metabolic syndrome.<sup>6,7</sup> Understanding these impairments can help to explain individual fat loss from diet and exercise.<sup>8,9</sup>

Indirect calorimetry (IC) is regularly used to assess metabolic flexibility in individuals in intervention studies and can provide the basis for individualised care.<sup>10,11</sup> It is a non-invasive method that measures oxygen consumption and carbon dioxide production in the breath to determine the body's energy expenditure and fuel utilisation.<sup>10</sup> One valuable output from IC is the respiratory quotient (RQ), a metabolic ratio indicating the cellular level metabolism of substrates

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at rest, specifically fat versus glucose. Importantly, fasting RQ can provide insights into the metabolic characteristics that differentiate individuals, ultimately influencing their unique responses to dietary interventions.

However, IC has faced limitations in widespread adoption within clinical settings because of the associated costs and technological complexity. These challenges have hindered the utilisation of this gold standard approach in real-world clinical practice, despite a growing interest in its application.<sup>8,10</sup> Notably, most studies using RQ have had relatively short durations, spanning from 24 hours to 4 weeks and long-term information regarding different individuals is lacking.<sup>9</sup>

One lifestyle management strategy that has gained popularity in recent years is therapeutic carbohydrate restriction (TCR).<sup>12</sup> Emerging evidence suggests that TCR can result in a significant reduction in fat mass and improvement in disease management outcomes. For example, a systematic review that assessed the effects of carbohydrate-restricted diets found that carbohydrate-restricted diets could be offered to people living with diabetes as part of an individualised management plan.<sup>13</sup> It can also help to reduce body weight and help manage heart disease risk factors such as cholesterol and raised blood pressure.<sup>14</sup> For weight loss and body composition, TCR with adequate protein has been shown to be at least as effective or even more effective than low-fat diets in the short term with additional metabolic benefits in terms of hunger and metabolic risk factors.<sup>9,15,16,17</sup>

Given the promising outcomes of TCR, it is important to explore opportunities for its broader adoption. According to a review conducted by Rathomi and colleagues, many General Practitioners (GP's) globally find what messages to give their patients around the most effective ways to lose weight confusing.<sup>18</sup> The review also highlights that some GPs already prescribe TCR or low carbohydrate diets in practice, despite these not frequently being advised in dietary guidelines, as a result of their own personal or family experiences of success with these methods. Therapeutic carbohydrate restriction could therefore be a valuable option to be offered to patients seeking weight loss advice were it to be found to be effective in the real world.

Indeed, while most human studies on TCR have tended to follow ketogenic dietary patterns and been conducted in research settings, there is limited evidence from individuals who have applied this strategy in their daily lives.<sup>9</sup> There also appears to be little research evaluating the degree of carbohydrate restriction necessary for beneficial outcomes and a lack of clinical tools for enhancing motivation, education and evaluating the effectiveness of these regimes at an individual level. Hence, it is necessary to explore technologies such as IC to help measure physiological mechanisms such as fat oxidation and enhance personalisation of such strategies in real-world settings. This can add to the growing evidence regarding the effectiveness of TCR.

In this article, we aim to investigate the short- and medium-term impact of TCR on the metabolic health status of individuals who were overweight or obese that attended a community-based clinic, specifically in relation to weight loss and fat oxidation. We used IC to measure RQ as a marker of metabolic flexibility<sup>8,19</sup> and study the clinical benefits of integrating TCR into a lifestyle management strategy within a clinical setting.

## Research methods and design

### Study design and setting

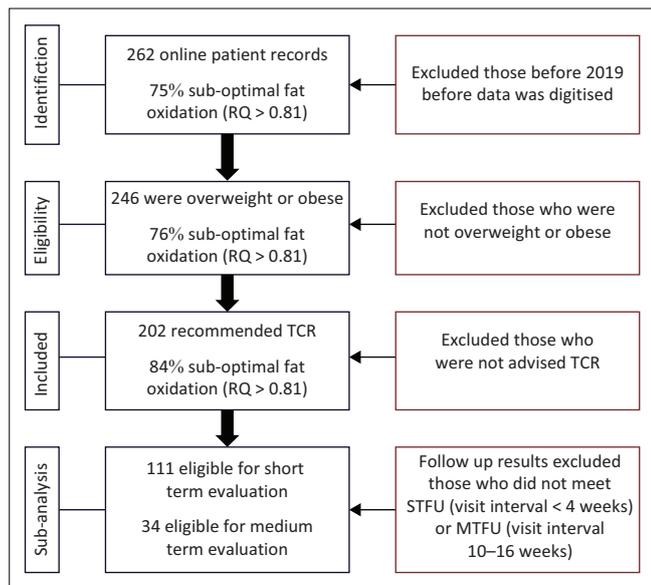
This study followed a single-arm, before-after design, involving a retrospective chart review. Data were collected from medical records obtained from a specialised allied health clinic, Metabolic Health Solutions Pty Ltd (MHS), based in Perth, Western Australia. This clinic concentrates on addressing metabolic health concerns and specialised testing to assist individuals dealing with weight and metabolic health disorders. Their approach includes lifestyle-based interventions, including TCR.

Services are delivered face-to-face by qualified allied health professionals (Dietitian or Exercise Physiologist) using standardised clinical care models. Patients who present with a higher than expected RQ for that of a standard Western diet  $\geq 0.81$  corresponding to a fuel utilisation ratio of 62% Fat and 38% CHO<sup>20</sup> or with a metabolic condition that could benefit such as fatty liver, T2DM, or PCOS, were prescribed TCR. This nutritional strategy focuses on whole foods to reduce the insulin response of the participants diet to help to improve metabolic flexibility and fat oxidation, weight loss and health. Many participants continue with subsequent testing and long-term support. Patients who attend the clinic (with or without a GP referral) are required to pay an out-of-pocket expense. In 2019, the MHS clinic moved to online collection of clinical data, facilitating ongoing analysis of data.

### Participants

The study included self-selected individuals with excess weight (body mass index [BMI]  $\geq 25$  kg/m<sup>2</sup>) who received care at the clinic from 2019 to 2022 and were recommended TCR. Study patients were adults ( $\geq 18$  years old) who had signed consent and agreed to their data being used for audit and/or research purposes. Participants with incomplete key data points were excluded. The participant selection process is illustrated in Figure 1.

Out of the 202 patients included in the initial visit, 144 attended further follow-up visits. As a result of the variation in follow-up intervals, we have defined specific timeframes for inclusion in both short-term and medium-term analysis. Short-term analysis criteria include those who came for a second visit within a 4-week period, while medium-term analysis includes patients who attended additional follow-up visits within a 10–16 week timeframe from the initial visit. With these criteria, 111 patients were eligible for short-term follow-up (STFU) evaluation, and 34 patients were eligible



STFU, short-term follow-up; MTFU, medium-term follow-up; TCR, therapeutic carbohydrate restriction; RQ, respiratory quotient.

**FIGURE 1:** Flow chart of patients on the database included in the study.

for medium-term follow-up (MTFU) evaluation. In the case of medium-term evaluation, the data points utilised were derived from the latest visit that occurred during the 10–16 week timeframe.

## Intervention

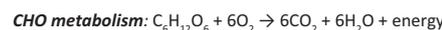
All participants received personalised counselling and were prescribed TCR based on their medical history and test results. The TCR consisted of advice to limit carbohydrates and emphasised the consumption of whole foods, healthy fats and non-starchy vegetables. A general prescription methodology was used in line with MHS' protocols to ensure interventions were appropriate, safe and personalised. Those recommended TCR may have also had changes in exercise, time of feeding and other correctional prescriptions such as sleep if indicated, but were generally not instructed to reduce or restrict calories. Where appropriate, protein consumption and ensuring adequate essential fatty acids (EFAs) with TCR were discussed during consultation.

A review consultation was provided at the end of each visit, which also included motivational intervening techniques to assist in the adoption of appropriate lifestyle change adoption. The time periods between visits and interventions were not rigid but individualised for each patient based on results, practitioner insight and scheduling.

## Baseline measures

Before their initial visits, patients completed an online questionnaire and received pre-test instructions advising them to observe a minimum of 4 hours of fasting before their visit following a protocol developed for using IC in clinical practice.<sup>10</sup> During their initial visit, patients provided a detailed case history focusing on key areas of their pre-test questionnaire as determined by the practitioners. This, in

Calculating substrate oxidation (RER):



Source: Katch M. Exercise physiology: Nutrition, energy, and human performance. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2009; 1136 p.

**FIGURE 2:** Calculating substrate oxidation (RER).

conjunction with the results from metabolic health testing – IC (ECAL by Metabolic Health Solutions Pty Ltd) and anthropometric measurements (weight [scales], waist [measuring tape] and body composition [bio-electrical impedance]) were used to develop personalised dietary and exercise advice, including TCR.

Respiratory exchange ratio (RER) was measured with IC at rest, and in this state is equivalent to RQ and fuel utilisation at a cellular level<sup>8,20</sup> and as such may be referred to as RQ in previous sections for simplicity – see Figure 2.<sup>19</sup> A modified Weir equation was used in calculations, as measuring nitrogen in ambulant patients is generally not necessary.<sup>21</sup>

## Outcome measures

Calorimetry and weight were measured at every visit. In addition, body composition and anthropometry measurements were performed based on clinicians' judgement. All data points for the short-term analysis come from patients' second visit, while data for the medium-term analysis were derived from the latest follow-up visit within the defined time frame (10–16 weeks). According to this criterion, 18% of data points were from patients' third visits, 47% from the fourth visit and 35% from the fifth visit. The median duration of short-term follow-up is 14 days (range: 6–28 days), while for MTFU, it is 85 days (range: 70–112 days).

## Statistical analysis

Descriptive statistics, including means, medians, percentages and their confidence intervals were used to characterise the study population and examine changes in outcomes over time. Paired t-tests were used to compare changes in RQ, weight and body composition from baseline to the defined follow-up period. To address multiple testing, we applied a Bonferroni correction, setting the level of statistical significance at 0.008 (0.05/6 tests). In the secondary analysis, we used multivariable linear regression to examine factors associated with changes in primary outcomes (weight and RQ) among patients with TCR. Covariates included age, gender and medical conditions such as diabetes and cardiovascular problems. All statistical analyses were performed using STATA 13 (StataCorp, LP).

## Ethical considerations

This study was approved by the Institutional Review Board of the University of Western Australia (Project number 2021/ET000993). Metabolic Health Solutions is an evidence-based metabolic testing and management programme. Patients are informed of intentions to publish data collected during

testing procedures, to further extend the evidence base. Thus, all participants provided written informed consent prior to participation. These data were anonymised and used in accordance with our privacy policy and accepted clinical practice.

## Results

The vast majority of patients providing baseline measures were females (77%) and predominantly identified as Caucasian (92%). The age distribution indicated that over half of patients were between 45 and 65 years old (54%), with over a third under 45 years (38%) and relatively few over 65 years (8%), mean  $\pm$  standard deviation (s.d.) of age is  $47.3 \pm 12.4$ .

On initial presentation, a significant portion of the patients were categorised as obese (76%) with 24% falling into the overweight category. The majority (70%) of patients reported gaining weight over the previous year. At least one medical condition was self-reported in 83% of patients highlighting the potential influence of underlying health issues on weight-related challenges. Moreover, two thirds (67%) were on multiple medications.

Regarding metabolic health, 84% of the patients had a sub-optimal fat oxidation, represented by a RQ  $> 0.81$ . High blood pressure, diabetes and sleep apnoea were among the most

prevalent conditions. In addition, 13% of patients had polycystic ovary syndrome (PCOS), which may have implications for weight management. Notably, the mean waist circumference was higher in the older age group, suggesting age-related influences on weight and metabolic health (Table 1).

Overall, 202 of the participants were prescribed TCR as a part of a behavioural modification programme. Among the 111 patients who had complete data records in the short-term follow-up visit, 84.1% showed improved fat oxidation. On average, there was a 63% relative increase in fat oxidation from baseline. Moreover, the participants exhibited an average weight loss of 1.8 kg (95% confidence interval [CI] = 1.6 kg – 2.1 kg) during the same period, representing a 2% relative change. Data for body fat analysis were not available at this follow-up period (Table 2).

At the MTFU period ( $n = 34$ ), approximately 80% of the patients maintained an increase in fat oxidation rates, with a mean relative change of 70% from baseline. This improvement was accompanied by an average weight loss of 3.9 kg (95% CI = 2.6 kg – 5.3 kg). Among those with waist measurements recorded at this visit, there was an average reduction of 4.9 cm (95% CI = 2.9 cm – 5.8 cm), as well as a significant reduction of 2.7 kg

**TABLE 1:** Patients' characteristics.

Characteristics	Age group											
	< 45 years (N = 78)			45–65 years (N = 108)			> 65 years (N = 16)			Total (N = 202)		
	n	%	mean $\pm$ s.d.	n	%	mean $\pm$ s.d.	n	%	mean $\pm$ s.d.	n	%	mean $\pm$ s.d.
<b>Gender</b>												
Female	67	89	-	78	72	-	10	63	-	155	77	-
<b>Ethnicity</b>												
Caucasian	70	90	-	100	93	-	16	100	-	186	92	-
Other	8	10	-	8	7	-	-	0	-	16	8	-
<b>Medical problems</b>												
Has at least 1 problem	56	75	-	96	89	-	15	94	-	167	83	-
High blood pressure	10	13	-	23	21	-	10	63	-	43	21	-
Diabetes	19	25	-	24	22	-	6	38	-	49	24	-
Heart condition	7	9	-	8	7	-	5	31	-	20	10	-
Sleep apnoea	7	9	-	22	20	-	5	31	-	34	17	-
Fatty liver	10	13	-	23	21	-	4	25	-	37	18	-
Polycystic ovary syndrome (PCOS)	15	22	-	5	6	-	-	0	-	20	13	-
Bariatric surgery	5	7	-	3	3	-	-	0	-	8	4	-
<b>Weight change over past year</b>												
Decreased	8	11	-	7	6	-	-	0	-	15	7	-
Stable	16	21	-	24	22	-	8	50	-	48	24	-
Increased	54	72	-	77	71	-	8	50	-	139	69	-
<b>BMI category</b>												
Overweight	18	24	-	27	25	-	3	19	-	48	24	-
Obese	60	80	-	81	75	-	13	81	-	154	76	-
<b>RQ level (cutoff 0.81)</b>												
Optimal RQ (< 0.81)	10	13	-	18	17	-	5	31	-	33	16	-
Weight	-	-	96.8 $\pm$ 22.5	-	-	99.5 $\pm$ 20.1	-	-	98.7 $\pm$ 20.8	-	-	98.4 $\pm$ 21.1
Waist circumference ( $n = 201$ )	-	-	100.9 $\pm$ 15.4	-	-	108.8 $\pm$ 18.0	-	-	111.8 $\pm$ 15.3	-	-	105.9 $\pm$ 17.3
BMI	-	-	34.7 $\pm$ 6.7	-	-	34.9 $\pm$ 6.7	-	-	34.4 $\pm$ 4.9	-	-	34.8 $\pm$ 6.5
Body fat in kg ( $n = 193$ )	-	-	38.9 $\pm$ 13.1	-	-	38.7 $\pm$ 12.9	-	-	38.1 $\pm$ 10.5	-	-	38.7 $\pm$ 12.7
RQ	-	-	0.92 $\pm$ 0.11	-	-	0.89 $\pm$ 0.09	-	-	0.88 $\pm$ 0.11	-	-	0.91 $\pm$ 0.10
Fat oxidation	-	-	30.7 $\pm$ 25.9	-	-	35.9 $\pm$ 24.5	-	-	43.9 $\pm$ 24.3	-	-	34.5 $\pm$ 25.2

s.d., standard deviation; BMI, body mass index; RQ, respiratory quotient.

**TABLE 2:** Short term (< 4 weeks) outcome changes ( $N = 111$ ).

Measurement	Mean at baseline		Mean at STFU		Mean difference	95% CI	% relative changes	<i>p</i>
	Mean	s.d.	Mean	s.d.				
Respiratory quotient	0.91	0.89–0.93	0.83	0.82–0.85	0.07	0.06–0.09	8	0.0000*
Fat oxidation (%)	32.7	28.2–37.1	53.2	48.8–57.6	20.5	16.1–24.9	63	0.0000*
Weight (kg)	100.4	96.2–104.6	98.6	94.5–102.8	1.8	1.5–2.2	2	0.0000*
Waist circumference (cm) ( $n = 11$ )	111.8	101.2–122.3	108.5	98.3–118.7	3.2	1.8–4.7	3	0.0003*
BMI	35.3	34.0–36.6	34.7	33.4–35.9	0.6	0.5–0.7	2	0.0000*
Body fat (kg) ( $n = 0$ )	-	-	-	-	-	-	-	-

STFU, Short term follow up (2 weeks on average, ranging from 6 to 28 days); CI, confidence interval.

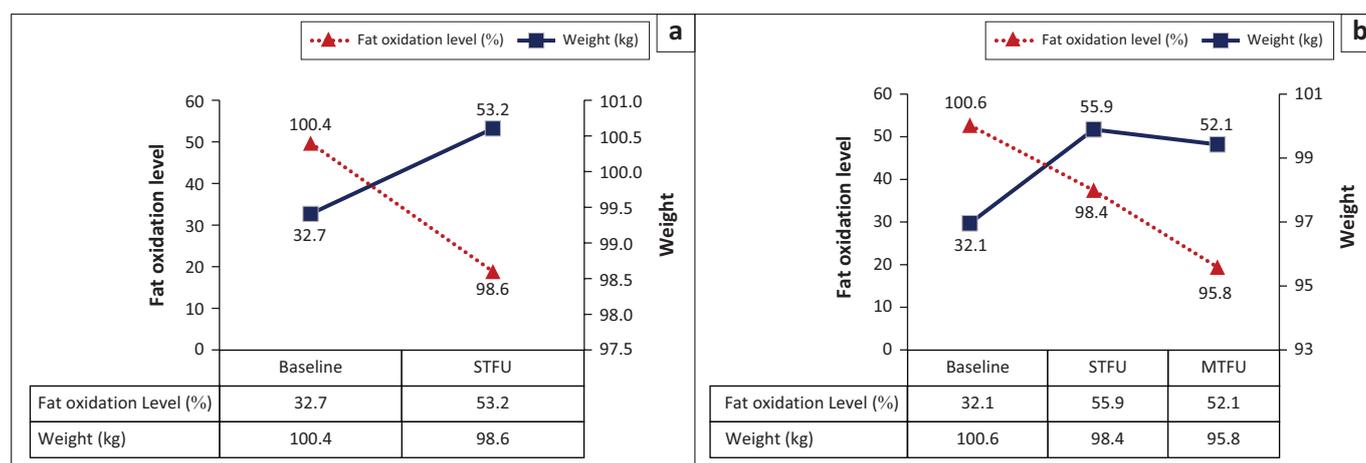
\*, statistically significant difference using the *t*-test.

**TABLE 3:** Medium-term (10–16 weeks) outcome changes ( $N = 34$ ).

Measurement	Mean at baseline		Mean at MTFU		Mean difference	95% CI	% relative changes	<i>p</i>
	Mean	s.d.	Mean	s.d.				
Respiratory quotient	0.92	0.88–0.96	0.84	0.81–0.87	0.08	0.04–0.11	9	0.0000*
Fat oxidation (%)	32.1	22.8–41.4	52.1	43.1–61.2	20.0	11.0–29.0	62	0.0000*
Weight (kg)	100.4	92.2–108.5	96.4	87.9–104.8	3.9	2.6–5.3	4	0.0000*
Waist circumference (cm) ( $n = 14$ )	115.0	103.3–126.8	110.0	98.0–122.1	4.9	2.3–7.7	4	0.0001*
BMI	35.5	33.1–37.9	34.1	31.6–36.5	1.4	0.9–1.9	4	0.0000*
Body fat (kg) ( $n = 14$ )	35.0	26.9–43.0	32.4	24.8–39.9	2.7	1.2–4.1	8	0.0000*

MTFU, Medium term follow-up (12 weeks on average, ranging from 10 to 16 weeks); CI, confidence interval; BMI, body mass index.

\*, statistically significant difference using the *t*-test.



STFU, short-term follow-up; MTFU, medium-term follow-up.

**FIGURE 3:** Comparison of changes in weight and fat oxidation levels from baseline to the follow-up period: (a) Among patients eligible for short-term analysis ( $N = 111$ ). (b) Among patients eligible for medium-term analysis ( $N = 34$ ).

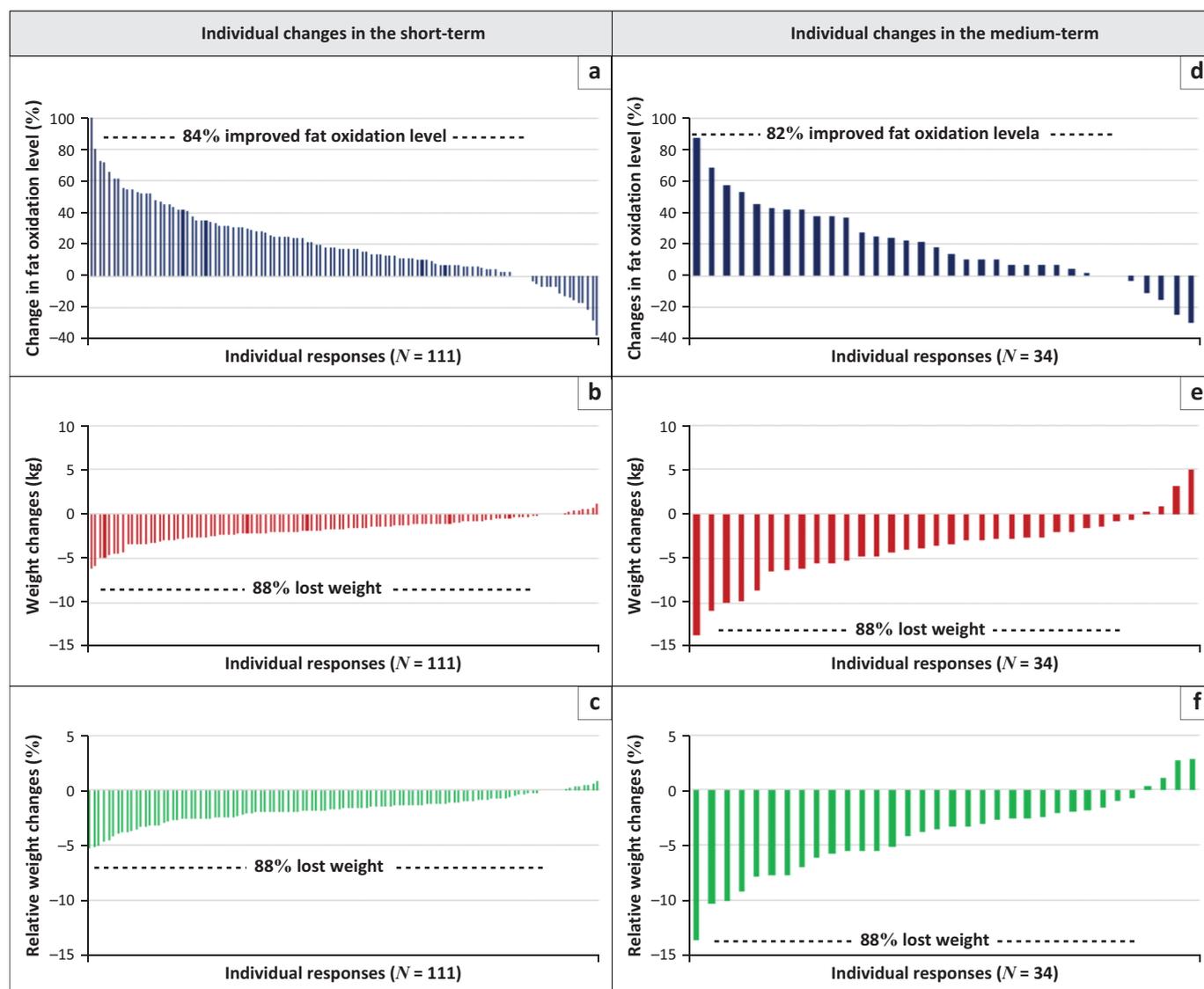
(95% CI = 2.4–5.1) in fat mass (equivalent to 8%). There was still a significant improvement fat oxidation from the baseline, resulting in a 4% decrease in body weight and BMI (Table 3).

In both the short and medium term, patients experienced an increase in fat oxidation levels and a decrease in weight. Improved fat oxidation is maintained in the medium term, and despite having similar fat oxidation levels between the STFU and MTFU, patients continued to experience ongoing weight loss (see Figure 3).

On an individual level, there was considerable variation observed in both fat oxidation level and weight changes. The prevalence of improvements in fat oxidation levels was similar in both the short term (84%) and medium term (82%), with the highest observed change being 100% in the short term and 87% in the medium term. Regarding weight

changes, 88% experienced a reduction in weight in both the short and medium terms, with the highest reductions being 6.1 kg or 5% of body weight in the short term and 13.6 kg or 14% of body weight in the medium term. Individual changes in fat oxidation and weight among patients are illustrated in Figure 4.

Among potential covariates in the multivariable linear regression analysis, including age, gender, diabetes and cardiovascular problem, gender was the only factor associated with short-term weight changes, with weight loss being higher in male patients ( $\beta = -1.11$ , 95% CI [-1.84, -0.39],  $p = 0.003$ ). However, for the MTFU, this difference disappeared, as there was no significant difference of weight changes between genders after adjusting for age, diabetes and cardiovascular problems ( $\beta = 0.63$ , 95% CI [-3.93, 5.19],  $p = 0.779$ ). In addition, no covariates were associated with either short- or medium-term changes of RQ.



**FIGURE 4:** Short- and medium-term changes in fat oxidation levels (a, d), absolute weight (b, e) and relative weight changes (c, f) among individual patients who underwent therapeutic carbohydrate restriction.

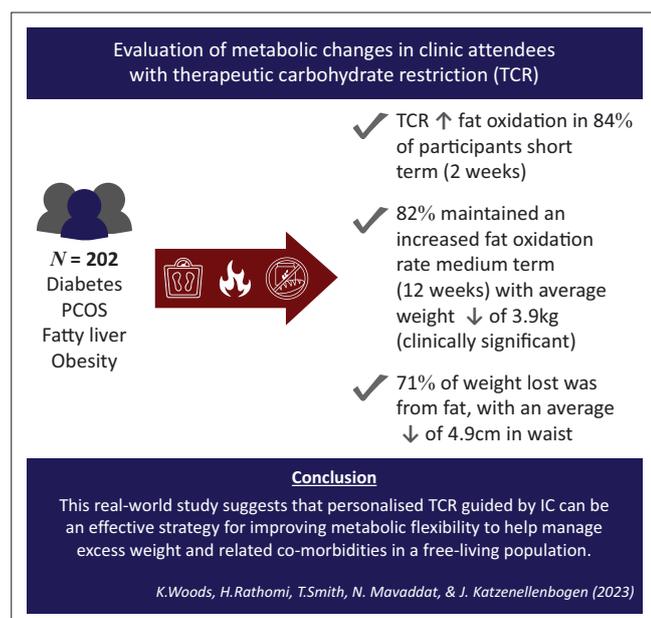
## Discussion

The results of this clinical analysis suggest that TCR, when combined with a behavioural modification programme and metabolism testing, can lead to significant improvements in metabolic flexibility, health and weight. These findings are consistent with previous studies that have shown TCR to be an effective dietary approach for promoting weight loss and improving metabolic health.<sup>9,13,15,16,17,21,22</sup>

Specifically, we observed that the majority of participants experienced improvements in fat oxidation levels during the short-term follow-up (84%), and this improvement was sustained in the medium term (82%). Regarding weight loss, our study found that 88% of patients experienced weight loss, with an average reduction of 1.8 kg (2% of body weight) in the short term and 3.9 kg (4%) in the medium term. Individual variation in these changes was also evident, suggesting a personalised response influenced by multiple factors. Weight loss of around 5% results in significant improvements in cardiometabolic risk factors associated

with obesity; this degree of weight loss is also required for the approval of novel antiobesity medications by the US Food and Drug Administration.<sup>23</sup> These changes may also have the potential to help to enhance adherence to physical activity and improve the ease of daily tasks. It may also be important to observe that the health benefits of diet-induced weight loss are thought to be compromised by loss of lean body mass, which could increase the risk of sarcopenia (low muscle mass and impaired muscle function). In this data set, it was shown that 71% of weight loss was from fat mass, which is congruent with previous research highlighting an expected 20% – 30% loss from fat-free mass.<sup>24</sup>

The improvement in fat oxidation levels observed in this study is particularly noteworthy, as it suggests that TCR may help to improve metabolic flexibility in non-research setting and helps to contribute the understanding of the physiological changes that can occur by implementing TCR. Other studies have explored the impact on anthropometric data of such diets in those with chronic disease, without looking at these



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PCOS, polycystic ovary syndrome.

**FIGURE 5:** Visual abstract.

metabolic parameters.<sup>17</sup> Our results of 3.9 kg weight loss in medium term are at least comparable to those found by purely measuring anthropometrics and meet the minimal clinically important difference (MCID) threshold for cardiovascular risk factors in patients with type 2 diabetes<sup>23</sup> and the threshold of clinically relevant weight loss for health outcomes reported by the Obesity Medicine Association.<sup>25</sup> Another TCR lifestyle programme in primary care for a free-living population resulted in a 5% weight change and a 2% change in waist circumference over an average follow-up of period 15 months.<sup>26</sup> In our study, we observed a similar outcome in a shorter follow-up period, highlighting the potential role for measuring metabolism in a clinical setting.

Given no intentional calorie restriction was generally observed in our cohort, the weight loss can likely be attributed to these changes in fat oxidation. The improvements in fat oxidation levels were accompanied by expected weight loss and reductions in waist circumference. It is reasonable (although not measured in this group) to presume that endogenous insulin levels would have reduced in our patients as observed in other TCR-focused research<sup>9,12,27</sup> and is likely a contributing mechanism to these changes.

Notably, despite having a similar fat oxidation level between short term and medium term follow-up visit, the patients continued to experience ongoing weight loss. This finding suggests that continued increases in fat oxidation are not required for weight loss to persist, likely because of an upper physiological limit. The results reinforce the significance of maintaining fat oxidation in the weight loss process.

Data provided by this study and others<sup>28,29</sup> show that integrating IC into practice (and the data it provides) can be

successful for weight loss and chronic disease management; however, further feasibility studies are required to explore the direct impact on the quality of life (i.e. sleep, pain, energy) and the role of IC in adoption, motivation and adherence, specifically in regard to TCR. There is potential for using this metabolic approach to provide a new, innovative approach to obesity and related conditions, which may have implications for standard practice and reducing healthcare costs and disease burden. In clinical care, IC could be used to measure the impact of carbohydrate restriction on metabolism and identify personalised dietary recommendations that are individually beneficial.

While the results of this study are promising, there are some limitations that should be considered. Firstly, this was a single-arm, before-and-after study with a relatively small sample size. As such, it is possible that the improvements observed were because of factors other than the TCR intervention, such as exercise, meal timings and sleep. Moreover, the small samples may have precluded statistical significance when investigating factors associated with improvements. Additionally, the lack of a control group limits our ability to draw conclusions about the efficacy of TCR compared to other dietary approaches. Baseline and follow-up pathology were not readily available for many participants and visit time frames varied for each participant. The retrospective nature of the data collection meant that the study relied on data not designed for statistical analysis, with missing data limiting the number of people that could be included. Furthermore, there may be a potential for selection bias given that participants were self-selected to receive care at the specialised clinic who could afford to fund out-of-pocket expenses for the service. The incomplete follow-up of the cohort means that those for whom we have follow-up measurements may have differed from those who were excluded from the before-after analysis, introducing a potential bias. The findings of this study also do not apply to long-term outcomes. Finally, the personalised nature of the TCR diet limits the generalisability of these findings to other dietary approaches, particularly given adherence was not strictly monitored. Despite these limitations, this cohort represents the real-world clinical constraints in allied health situations and may provide insight into the multifactorial challenges in this setting, which clinical trials may miss.

Further research, including randomised controlled trials with larger sample sizes, is needed to confirm the findings of this study and explore the potential benefits of TCR in more detail. Measurement of patient engagement, having supervised exercise sessions with compulsory baseline and follow-up pathology at regular intervals would also be beneficial. Exploration of the potential of medication as an adjunct therapy using IC is also warranted. Importantly, improvements in data quality and completeness have the potential to increase the utility of the routinely collected data, thereby allowing ongoing real-world reporting on outcomes.

## Conclusion

In conclusion, our study provides evidence to support the use of TCR as a viable dietary approach and treatment option for promoting weight loss and improving metabolic health in those with excess weight and accompanying chronic disease in a clinical setting, particularly when paired with IC.

Future research should aim to replicate these findings in larger, more diverse populations and explore the mechanisms underlying the observed improvements in metabolic flexibility and weight loss, including the role of metabolism-specific data for enhancing motivation and improving outcomes.

We hope to provide insight into the effectiveness and applicability of using this metabolic approach combining TCR and IC to improve weight loss and metabolic health outcomes in patients to help bridge the gap between research and practice.

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### Competing interests

K.W. and T.L.S. work with the company that owns the technology mentioned in the article.

### Authors' contributions

K.W. initiated the project and conducted testing with interventions for this analysis and authored the first draft, subsequently revising and reviewing the article. H.S.R. co-initiated the study, developed the methodology, conducted data curation and statistical analysis, authored the initial draft and contributed in article review. K.W. and H.S.R. contributed equally to this work. T.L.S. contributed to data acquisition and/or curation and reviewed the article. N.M. provided guidance on conceptualisation and methodology and reviewed the article. J.K. provided guidance in conceptualisation, methodology and data analysis and contributed to the article review. All authors participated in result discussions and approved the final article.

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### Data availability

The data that support the findings of this study are available on request from the corresponding author, K.W.

### Disclaimer

The views and opinions expressed in this article are those of the authors and are the product of professional research. It does not necessarily reflect the official policy or position of any affiliated institution, agency or that of the publisher. The authors are responsible for this article's results, findings and content.

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