

18 December 2018

Ms Louise Adams, MAPS
Clinical Psychologist & Founder
UNTRAPPED and Treat Yourself Well Sydney
Via email: louise@untrapped.com.au

Dear Ms Adams,

Re: HREC/17/SCHN/164 - Fast Track to Health: The alternate day fasting diet in adolescents with obesity: a randomised controlled trial

The Sydney Children's Hospitals Network Human Research Ethics Committee (SCHN HREC) refers to your complaint received on 5 November 2018 regarding the abovementioned clinical trial.

The SCHN HREC conducted a review of your concerns in accordance with the National Statement on Ethical Conduct in Human Research 2007 (updated 2018) (the National Statement), the Australian Code for the Responsible Conduct of Research 2018 (the Code), and local HREC and institutional policies. This review included a response from the investigators to this complaint and advice from an independent, advisory expert panel. The expert panel comprised of highly experienced experts who are nationally and internationally recognised for their expertise in the areas of eating disorders and mental health, chronic disease and weight management and research ethics. As per HREC standard practices, panel members' identities cannot be disclosed to respect their privacy and confidentiality. The panel members are not affiliated with the SCHN and do not have any conflicts of interest in providing advice to the SCHN HREC on this matter. The SCHN HREC assesses and manages conflicts of interest as per the National Statement ([Chapter 5.4](#)).

Please refer to the following for an outcome report for each of the concerns raised in your complaint letter.

1. Integrity of the Research Justifications and Assumptions

The HREC noted that this trial was reviewed, approved and funded by the National Health and Medical Research Council (NHMRC). Applications funded by the NHMRC are rigorously peer-reviewed in a transparent and fair manner by the NHMRC Grant Review Panels. Please click on this [link](#) for more details on the NHMRC peer review system. This trial was also reviewed and approved by the SCHN HREC's Scientific Advisory Committee. The Fast Track trial has therefore been considered by these review bodies to comply with the National Statement ([paragraphs 1.1 – 1.3](#)) which outlines the criteria for research merit and integrity.

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The HREC understands that the prevalence of severe obesity in Australia has significantly increased over the past three decades [1]. Adolescents with obesity are not just at risk of future health problems, but increasingly are being diagnosed with conditions such as type 2 diabetes, insulin resistance, orthopaedic disorders, fatty liver disease, high blood cholesterol, high blood pressure, and obstructive sleep apnoea [2, 3]. Although there are various approaches to weight management, there is currently no gold standard weight management intervention and there are differing views on the effectiveness of diet-based interventions. It is also noted that different interventions may work for different individuals highlighting the important need for scientific investigations of various weight management approaches to ensure the provision of a range of effective, evidence-based and safe options.

Study documentation and the response from the investigators revealed that although the investigators state there is evidence that MADF achieved weight loss in adults, they do not claim the losses are long term. The complaint raises further concerns that the absence of a non-diet control group or no treatment group impacts on the trial's merit and integrity as it will not be possible to measure the impact of the interventions compared to typically developing adolescents who do not receive treatment. A request was therefore made by the complainant for the study to remove the MADF arm and replace it with a non-diet arm.

The Committee noted however that the Fast Track trial's aim is to determine if MADF is effective, safe and acceptable to adolescents compared to a standard weight control diet. The current study design was considered to be scientifically valid in answering this research question, as also demonstrated by approvals from the NHMRC's Grant Review Panels and the SCHN HREC's Scientific Advisory Committee. Including a non-diet control group will essentially result in a separate and unrelated research question. Please also note that as per the National Statement ([chapter 3.1.5](#)), inclusion of 'non-treatment' groups in research projects is not ethical when there are current and available treatments available.

2. Risk of Harm

The HREC reassessed the trial's risk-benefit profile in light of this complaint, the response from the investigators, the expert panel's advice and in accordance with the National Statement, [paragraphs 1.6 – 1.7](#) and [chapter 2.1](#). The HREC notes that the National Statement does not require for risks to be eliminated, rather for the design of the project to minimise the risks of harm or discomfort to participants (National Statement, [paragraph 1.7 \(a\)](#)).

The HREC recognises that there is a risk for a young person to develop an eating disorder with exposure to restrictive diets, and in particular very restrictive diets [4]. Although these risks appear to be lower in medically supervised dieting programs, they will still be present. The SCHN HREC was advised by the expert panel that these risks can be justified by the likely benefits of the trial provided that the trial is adequately monitored with an appropriate risk management plan to minimise and communicate the risks associated with eating disorders.

The current study protocol acknowledges these risks and provides a risk management plan. The HREC has requested that the risk management plan be strengthened in consultation with eating disorder experts and as per the following:

- Ensuring the appropriate level of involvement of trained and supervised mental health professionals in the conduct and supervision of the trial;

- Increasing the frequency of the eating disorder related monitoring assessments together with a more detailed process for management and referral of emerging eating disorder patterns and behaviours;
- Formulating an appropriate strategy to further follow up participants following completion of the trial;
- Improving communication with participants and their families regarding the risks associated with eating disorders and the trial's risk management plan;
- Undertaking an interim analysis by an independent data management board on data from existing participants to ensure participants' safety and well-being to date.

The HREC, has determined that study recruitment can resume when the investigators have addressed the above issues, and these have been ethically reviewed and approved.

The HREC further noted the complainants' concern regarding the raised LDL cholesterol being seen in a trial of modified alternate day fasting by Trepanowski et al 2017. This was however not considered as clinically significant as the raised LDL cholesterol was in the region of 0.3 mmol/L.

3. Weight Bias

The HREC and the expert panel considered that the outcomes measures adopted in the trial include both psycho-social assessment as well as weight reduction. The HREC further noted that this trial is being conducted in compliance with the American Academy of Pediatrics' recommendations to decrease weight stigma in health service delivery which include the following:

- i) Role modelling of supportive and non-biased behaviour by clinical staff;
- ii) Use of non-stigmatising spoken and written language;
- iii) Use of patient-centred, empathetic behaviour change approaches;
- iv) Provision of safe, welcoming and non-stigmatising clinical environments; and
- v) Incorporation of broad behavioural health screening in clinical assessment.

The HREC also acknowledged the study team's commitment to reducing weight stigma and assisting other health professionals to have appropriate and patient-centred helpful conversations about body weight. Therefore, the HREC determined that the complaint of weight bias in this clinical trial is not supported.

Thank you for your patience and assistance throughout the HREC investigation of these concerns. Please note that the HREC's determination regarding this complaint is final. If you are not satisfied with the outcome of this investigation, you can refer your complaint to the SCHN Chief Executive as per the SCHN HREC's Standard Operating Procedures.

Yours Sincerely,



Ms Asra Gholami
Executive Officer, Research Ethics
Sydney Children's Hospitals Network

References:

1. Xu J., H.L., Guo CZ., Garnett SP, The trends and prevalence of obesity and morbid obesity among Australian school-aged children, 1985-2014. *Journal of Paediatrics and Child Health*, 2018. 54(8): p. 907-912.
2. Garnett, S.P., et al., Body mass index and waist circumference in midchildhood and adverse cardiovascular disease risk clustering in adolescence^{1,2,3}. *The American Journal of Clinical Nutrition*, 2007. 86(3): p. 549.
3. Skinner, A.C., et al., Cardiometabolic Risks and Severity of Obesity in Children and Young Adults. *New England Journal of Medicine*, 2015. 373(14): p. 1307-1317.
4. Patton et al., Onset of adolescent eating disorders: population based cohort study over 3 years *BMJ* 1999 Mar 20; 318(7186): 765–768.