Ms Asra Gholami
Executive Officer, Research Ethics
Human Research Ethics Committee
Sydney Children's Hospital Network

21 February 2019

Dear Ms Gholami

I am writing to lodge a formal complaint to the Sydney Children's Hospital Network Human Research Ethics Committee (SCHN HREC) regarding the "Fast Track to Health" trial (approval number HREC/17/SCHN/164). The complaint is endorsed by the undersigned health professionals, representing a diverse group of specialties, all of whom have significant clinical experience; parents and guardians caring for children or young people with eating disorders; and individuals who have recovered from eating disorders.

It is our belief that this trial places the health and well-being of every participant both at immediate risk and also long-term risk. The complaint focuses on three areas of concern:

1. failure to disclose extent of risks when gaining informed consent;
2. risks associated with extreme calorie restriction; and
3. inefficacy and unsustainability of weight loss interventions.

Each of these is elaborated below.

1 Failure to Disclose Extent of Risks when Gaining Informed Consent

The primary issue of concern is that participants and parents or guardians involved in the consent process have not been provided with the opportunity to provide informed consent as to the extensive risks associated with exposing a teenager to clinical starvation. In the original information sheet supplied to parents and participants, the only mention of risk is regarding radiation from the DXA scan. The information sheet claimed outright that no other "side effects or risks" are expected: "We do not expect any side effects or risks associated with this study. If the study makes your child feel upset, you or your child may stop the study at any time. You will be provided with information and contacts your child can talk to, if that is what they want to do."

A complaint was made to the Sydney Children's Hospital Network Human Research Ethics Committee last year by a group of 29 eating disorder professionals, asking for

an urgent review of the study. An independent ethics review was undertaken at this time and the ethical review requested additional safeguards [1]. The researchers updated the participant and parent information sheet to indicate that there may be a *minimal* risk of increased eating disorders from engagement in restrictive dieting. However, the researchers have not acknowledged the risks as mentioned within the registered study protocol (https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373225) itself, wherein a number of undisclosed harms are listed as "Secondary Outcomes". The first is "Secondary Bulimic Episodes". The second is not specifically outlined, but reference is made to "Depression and Emotional Wellbeing," using the Centre for Epidemiologic Studies Depression Scale Revised (CESDR-10), implying that impact on the participants' emotional and psychological status is anticipated.

Given that the adolescent population in Australia comprises a particularly vulnerable demographic [2], it is essential that *any* clinical trials receive ethical clearance *only* if they are designed and managed so as to protect this group.

1.1 Secondary Outcomes as Likely Outcomes

There is ample evidence identifying the "secondary outcomes" as *likely* outcomes; as well, in contrast to the claim made in the statement regarding risk, these outcomes also carry a number of serious risks both in the short term and in the long term.

1.1.1. Risks Associated with Secondary Bulimic Episodes

Because the trial places participants in a prolonged state of calorie restriction, the risk of bulimic episodes is considerably heightened. Calorie restriction is a known primary trigger for hyperphagia (often termed binge eating) [3, 4], and is often accompanied by purging. The "Fast Track" trial induces participants to behave in a way that mimics Anorexia Nervosa (AN) [5] (severe restriction of calories), placing them in considerable risk of going on to *develop* AN, Bulimia Nervosa (hyperphagia with or without purging), or Binge Eating Disorder (hyperphagia). Given that eating disorders are defined in very general terms as "disturbance in eating habits that may be either excessive or insufficient food intake" – and that "currently well-known risk factors for eating disorders are *concurrent symptoms* (italics mine) of eating disorders" [6], the participants in this study are being placed in a position of extraordinary risk because of being in a state of induced clinical starvation. The potential for immediate iatrogenic psychological and physiological harm from the "treatment" that forms the basis of this study is significant, especially when considering the body of research that has already established the inefficacy of weight loss interventions (as will be discussed in a later section), which heightens the existing ethical concerns.

There is abundant evidence that bulimic episodes carry with them an immediate risk of death due to electrolyte imbalance and its impact on a variety of bodily systems if left untreated. Other risks associated with bulimic episodes include refeeding syndrome, cardiac failure, kidney failure, haemorrhage, dental erosion, hernia, compromised pulmonary function, impaired reproduction [7, 8].

Although the research proposal suggests that the risk of bulimic episodes is secondary, and not warranting disclosure of risk to participants and their guardians, there has been no consideration given to the increase in the likelihood of such episodes stemming from both the premise of the study itself, and also the deliberate placement of the participants in a calorie deficit that falls within the category of "clinical starvation".

One aspect of the study that places all participants at immediate risk of bulimic episodes, before even commencing, is that it will reinforce the perception of themselves as "overweight" [9]. Given the underlying premise of the study within the field of "obesity prevention and or treatment" it is inevitable that the participants will see themselves as fitting within that category, and that it will also likely drive their likelihood of signing up for the trial in the first place. There is also firm evidence that body image concern alone (operationalized in a variety of ways in different studies) contributes to increased risk for eating disorder symptoms [9].

1.1.2. Risks Associated with Depression and Mood Disturbances

The second potential for "secondary outcomes" alluded to but not explicitly specified in the research protocol involves the need for participants to be assessed on the CESDR-10. There is no doubt that severe calorie restriction can have a marked effect on a person's psychological state [10]. Being in a short-term calorie deprived state causes a rise in corticosterone, an indicator of physiological stress, in response to lowered blood glucose levels [11]. Chronic levels of corticosterone have been linked to more long-term disruption of circadian rhythms and a corresponding negative impact on mood [12]. This recent research bears out the findings of the Ancel Keys-led Minnesota Starvation Experiment [13], that stress associated with moderate caloric restriction promotes *long-term* (italics mine) alterations in genes critical in feeding and reward circuitry that influence food intake and stress-related behaviours. The participants selected for the Minnesota Starvation Experiment were healthy, average weighted adult men, men selected because they were seen to be the most "psychologically and physically robust". The psychobiologic "stamina" of the subjects was unquestionably superior to that likely to be found in any random or more generally representative sample of the population. Even so, the psychological and physical impact of starvation on these men has been well documented. "Most experienced significant emotional deterioration as a result of semistarvation. Most subjects experienced periods during which their emotional distress was quite severe; almost 20 percent had extreme emotional deterioration that markedly interfered with

their functioning. Depression became more severe during the course of the experiment" [13].

If such robust, fully grown men experienced extreme emotional deterioration on an average intake of 1500 KCAL per day; adolescents (whose calorie requirements are higher than those of a sedentary adult male) in the "Fast Track" trial will spend one month at less than half that intake a day, and the same for three days of every week thereafter for a full year, are being placed at immediate and immense risk of prolonged psychological distress *during* the trial, and prolonged and complex distress long after the trial is completed.

Depression and emotional distress are linked inextricably with self-harm and suicide, something that is at its highest level historically in Australia [14]. It is unethical to deliberately expose adolescents to behaviours that are known to exponentially increase the risk of suicide or self-harm.

2. Risks Associated with Extreme Calorie Restriction

The risks associated with prolonged calorie restriction are not limited to the psychological. Of primary and immediate concern is the risk of refeeding syndrome which is potentially, and not rarely, fatal [15]. As discussed previously, extreme calorie restriction heightens the risk of hyperphagia, particularly ingesting a large amount of carbohydrates, forcing a shift in electrolytes, and the onset of refeeding syndrome. This risk is heightened as already discussed, given the propensity to bulimic behaviour in young people who perceive themselves as overweight. The risk may persist not only during the trial, but also for a prolonged period after the trial, given research indicating that adolescents pressured to diet are more likely to have food and eating pathologies in young adulthood. Acquiring an extreme behaviour such as placing themselves in a state of clinical starvation that is supported by clinicians and presented to them as a no-risk behaviour heightens the possibility that at any time in their life they may revisit this behaviour and be at immediate risk of hyperphagia and refeeding syndrome [16]. Importantly, the onset of dieting behaviour in adolescence is identified as a significant risk factor for its continued use ten years later [17].

2.1 Diabetes

As discussed above, calorie restriction increases the level of corticosteroids; prolonged exposure to corticosteroids disrupts the hypothalamus pituitary adrenal system, leading to continuous high levels of glucocorticoids and insulin resistance (IR), increasing the likelihood of contracting Type 2 Diabetes (T2D) and a range of stress induced health disorders [18]. Given that one aim of the "Fast Track to Health Trial" is to "decrease risk factors for heart disease and diabetes," once again the ethical implications are clear. To expose adolescents to known and robustly

evidenced risk factors for these two health conditions, as a means of avoiding them both, cannot be justified.

2.2 Eating Disorders

Dieting at any level has been termed the “most important predictor of eating disorders” [15]. It has also been identified as “a risk factor for *both* obesity and eating disorders.” It has been clearly linked to an increase in binge eating and greater weight gain. Children who are not in the “obese” range who diet are *more likely to have a BMI over 25* some years later than non-dieters. Just *talking* about weight loss has been found to contribute to adolescents gaining weight [19].

Eating disorders have the highest mortality rate among young people in Australia. In comparison to the general population, mortality rates are almost twice as high for people with eating disorders. This rises to 5.86 times higher for people with (AN) [20]. Clinical starvation mimics AN. It also places a vulnerable person at immediate risk of acquiring AN because of the precise relationship between calorie restriction and AN onset. Placing a vulnerable group of adolescents in a situation where their risk of both physical and psychological disease is considerably heightened is unethical; failing to inform the participants of this risk is even more so.

The American Academy of Pediatrics identified a number of high-risk eating and activity behaviours, including severe dietary restriction (at a slightly lower intake than that suggested in the “Fast Track” trial), skipping of meals to lose weight, profound fear of gaining weight, body image distortion and, among other things, rapid weight loss and falling off percentiles for weight and BMI as of clinical concern [19]. The question must be asked that if these behaviours are seen as dangerous, and clinically significant, why are the risks being ignored and/or not being fully disclosed to participants in the trial?

2.3 Bone Density

Extreme calorie restriction causes bone density loss, with many studies of starvation and the bone metabolism in laboratory animal models and humans finding evidence of either developmental delays, stunted bone growth, decreased bone mineral density or decreased cortical strength. Both the reduction of the basal metabolic rate as well as the commonly present vitamin and nutrient deficiencies have been hypothesized to contribute to stunted growth, bad bone quality, and an earlier onset of osteoporosis in later life. Starvation may occur for either limited periods of time followed by a return to a regular food intake or subsist over extended periods of time, thereby leading to a chronic adaptation to the low caloric intake or absorption [21]. Given that there is evidence that dieting in adolescence is a pathway to cyclic and repeated dieting, the “Fast Track to Health” trial places the bone density of the participants at risk.

2.4 Weight Gain

While dieting, or restriction/reduction of calorie intake is a widespread means of inducing weight loss, it is only in recent years that studies have emerged showing that weight cycling, repeated periods of weight loss/weight gain increases health risks normally associated with, and attributed, to having a BMI in the obese or overweight range, even in people not termed overweight [22]. These include fluctuations in cardiovascular risk factors, such as blood pressure, heart rate, sympathetic activity, and circulating levels of glucose, lipids and insulin. These, along with repeated overshoots above normal values during periods of weight regain put additional stress on the cardiovascular system. The stress induced by repeated overshoot of these risk variables during food excess periods may not be compensated for by a reduction in risk factors during weight loss periods. As a consequence, the fluctuations in risk factors put an extra load on the heart and may lead to vascular injury [23].

Cortisol is a central mechanism that promotes eating behavior and fat deposition. Elevated cortisol also mediates known stress-related health conditions, including hypertension, T2D, and cardiovascular disease which notably are the same conditions found most often in individuals with a BMI over 30 [24]. This overlap observed between health conditions activated by stressors on the one hand and having a BMI over 30on the other suggests that weight stigma may even be “salt in the wound” contributing to the pathophysiology associated with obesity [25]. In other words, it may be that a portion of the negative health consequences of living in a larger body can be attributed to stigma rather than simply weight *per se*.

Add to this, recent findings re metabolic adaptation after weight loss in teens. The implications are that teens who lose a significant amount of weight after bariatric surgery are forced to stay in a state of calorie restriction, less than the intake predicted for their current body weight if they are to maintain the lower weight. If they took in a total calorie intake at the ‘predicted’ resting energy expenditure, weight gain would occur at approximate a rate of 7 lb per year, based on the fact that 1 lb is approximately 3,500 kcal. The researchers admitted that the underlying mechanisms contributing to metabolic adaptation are not well-understood. Potential mechanisms include decreased circulating leptin levels after surgery, decreased thyroid hormones linked to blunted sympathetic nervous system activity or decreased catecholamines associated with weight loss. This adaptation is already evident 12 months past surgery; there is no known mechanism to ensure and sustain weight loss [26]. Of greater concern, the reduction in Resting Energy Expenditure (REE) is identical to that seen in subjects with AN and begs the question of how ethical can it be to induce a state of clinical starvation in teenagers that mimics the mental illness with the highest mortality rate [27]? As already mentioned, **the risks associated with weight gain that is a direct product of medical weight loss interventions are**

many and varied, and in the view of the signatories to this complaint, untenable in the Fast Track to Health Trial.

2.5 Weight Stigma

Weight stigma is defined as the social devaluation and denigration of people perceived to carry excess weight and leads to prejudice, negative stereotyping and discrimination toward those people. This model characterizes weight stigma not as a static construct but rather a “vicious cycle” – a positive feedback loop wherein weight stigma begets weight gain through increased eating and other biobehavioral mechanisms. As previously mentioned, prolonged or acute exposure to stressors is most likely to engage the stress-responsive hypothalamic–pituitary–adrenocortical (HPA) axis. Social-evaluative threat and HPA activation ultimately result in elevated secretion of the endocrine stress hormone cortisol. Prolonged exposure to elevated levels of cortisol, in turn, mediates a number of health conditions such as hypertension and cardiovascular disease of the myriad stressors; individual encounters, social situations containing the potential for negative judgment from others are counted among the most significant of these stressors [28].

Stice and Rysin’s (2018) eight-year study on the “temporal sequencing of the emergence of risk factors” for eating disorders in young adolescent girls identified the *primary* risk as having a “perceived pressure to be thin”, followed by internalized weight stigma (which the authors describe as body dissatisfaction), followed by dieting, followed by ED development. However, of grave concern in the light of these findings is that ED does not emerge for 27 months post dieting behavior [29]. There is absolutely no provision made in the study itself for longitudinal follow up, either of participants who complete the trial, or those who drop out.

There is no doubt that the participants currently enrolled in the study have *already* crossed the disorder-predictive cutpoint for the primary risk factor, “perceived pressure to be thin”, as identified by Stice and Rysin. Fast Track Trial participants are self-referred, with the callout targeting parents with the words: “Do you think your child might be above a healthy weight? Are they between the age of 13–17 years? … The Children’s Hospital at Westmead is conducting a study for young people who are above a healthy weight” [30].

They are also likely to have already crossed the disorder-predictive cutpoint for the secondary and tertiary risk factors Stice and Rysin identify, “body dissatisfaction” (weight stigma), and “dieting behaviour”. Given that these three factors comprise a clear pathway to the development of eating disorders, these participants have been placed on that track and are risking direct iatrogenic harm.

Every adolescent in this study is experiencing the impact of the stigma associated with living in an above average sized body. Being referred to a weight loss program

by their parents, or asking their parents to allow them to join the trial is evidence of that. They are living with “pressure to be thin”. The **potential harm associated with weight stigma is on its own compelling reason to question the ethical foundations of the “Fast Track” trial**. The evidence of the range of harms associated with intentional weight loss and weight cycling suggests that it is a serious public health issue for people across the entire weight spectrum.

3. Inefficacy and Unsustainability of Weight Loss Interventions

The final area of concern to be raised within this complaint stems from a survey of the burgeoning body of research around deliberately induced weight loss, either as a means of simply reducing body mass, or of improving health outcomes in the participants, with one of the justifications for the study is that it is intended to test a relatively new form of low calorie dieting as a means of “reducing weight and improving risk factors for heart disease and diabetes.”

A number of two-to-three-year studies have outlined the inefficacy of various weight loss interventions in young people. Two of these included a “school and family based healthy lifestyle programme” incorporating “healthy eating and movement” initiatives with no marked improvement in weight across the participants [31]; a similar program found “found no substantive difference between intervention and control children on anthropometric or dietary measures or on physical activity” [32]. In a randomized controlled cognitive behavioural trial with three-year follow-up involving 150 women with obesity, the great majority regained almost all the weight they had lost with the new treatment being no better than the behaviour treatment in preventing weight regain [33].

A wider view was taken in the “Pathways from Dieting to Weight Regain, to Obesity and to the Metabolic Syndrome: An overview,” which outlined the proceedings of the 7th Fribourg Obesity Research Conference (2015), showing that studies of the long-term outcomes of diets show that at least one-third of dieters regain more weight than they lost, together with prospective studies indicating that dieting during childhood and adolescence predicts future weight gain and obesity [34]. This last finding is borne out by the National Health and Medical Research Council of Australia, stating that “weight loss following lifestyle interventions is maximal at 6-12 months. Regardless of the degree of initial weight loss, most weight is regained within a 2-year period and by 5 years the majority of people are at their pre-intervention bodyweight” [35]. The evidence for this last finding is classed by the NHMRC as Level A, the *same level* as the evidence linking smoking with cancer [34]. These findings are not unusual, with many reviews of long-term outcomes of dieting concluding that sustainable weight loss *is not, on average, a common outcome of dieting*. The authors of one such review state pragmatically that between one third to two thirds of dieters regain more weight that lost on their diets,

reinforcing the findings of the NHMRC, with methodological problems that often bias the studies toward showing successful weight loss maintenance.

Given that weight loss is generally maximal at 6-12 months, the results of the “Fast Track to Health” trial run the risk of being skewed, because the subjects would not be followed for the length of time necessary to ascertain long term sustainable change. The study cited previously regarding bariatric surgery in teens supports this notion, because of the major metabolic adaptations observed as already in place 12 months post-surgery [26]. To see such a major adaptation at the moment that weight loss is maximal suggests that the young people in the “Fast Track to Health” trial are being exposed to the full range of risk-laden metabolic adaptations and regain of weight above their starting as already discussed with reference to related research.

Of specific concern in relation to the “Fast Track Trial to Health” are the findings of the Dianne Neumark-Sztainer Project EAT (Eating and Activity in Teens and Young Adults), a 15-year population-based, longitudinal study, which examined patterns of weight control behaviors beyond young adulthood using data from 1,455 males and females. The findings from this study alone call into question the appropriateness and ethical standards being applied in the “Fast Track to Health” trial.

> *Between Waves 3 and 4 in adulthood, dieting increased for both genders (Women: $p < .001$; Men: $p = .004$) and high-frequency dieting ($p < .001$) and unhealthy weight control behaviors ($p = .011$) increased for men.* ***For both genders, dieting and unhealthy weight control patterns initiated in prior to young adulthood were more likely to persist than cease in adulthood*** *(ps < .001)* [36].

Of paramount concern in the context of this complaint, no extant longitudinal study provides consistent evidence that calorie restriction and weight loss in adolescence results in significant health improvements, regardless of weight change. The title of the “Fast Track to Health” trial implies otherwise. The body of current peer reviewed evidence does not support the notion that calorie restriction leading to weight loss leads either to lasting weight loss or health benefits [37].

4. Conclusion

There is compelling evidence that the “Fast Track to Health’ trial is incapable of achieving its express goal of “reducing weight and improving risk factors for heart disease and diabetes”, given that weight loss is not sustainable, with a 97% rate of regain. Calorie restriction can cause prolonged psychological distress, which in itself has been identified as a contributing factor to a number of physiological conditions, including cardiovascular disease, T2D, and metabolic syndrome because of the mechanisms involved in cyclic loss and gain.

Scholarly literature starkly outlines the critical risks inherent in subjecting adolescents to prolonged periods of clinical and subclinical starvation. Extreme calorie restriction is implicated in the short term with **potentially fatal bulimic episodes and refeeding syndrome;** it is also implicated in causing **debilitating psychological distress**, which is in turn a **contributor to self-harm and suicide**. Subjecting an adolescent to such treatment places them at immediate risk of the above.

Added to this established evidence that **dieting in adolescence can trigger the onset of an eating disorder, including AN, BN, BED and OSFED**. Even if the person does not acquire an eating disorder, they are at a considerably heightened risk of entering into cyclic weight loss and gain, which carries already mentioned health risks, **including bone density loss**. Ironically, the connection between cyclic dieting and weight gain is inarguable, with a wealth of current scholarly literature mapping out the cyclic relationship between dieting/calorie restriction and weight gain, and highlighting the significant role that weight stigma plays in perpetuating and restarting this cycle.

The protocols of the “Fast Track to Health” study could be renamed the “Pathways from dieting to weight regain, to obesity and to the metabolic syndrome” [32] given that it mimics precisely the starting point that sees many people living in increasingly larger bodies as a result of that cycle. Before embarking on the study, the young people involved have already “crossed the disorder-predictive cutpoint for a primary risk factor” for developing an eating disorder, “which is perceived pressure to be thin [29]”.

The evidence that induced weight loss is inefficacious is difficult to misinterpret; simply said, it has *never* been effective long term and there is no evidence that it is sustainable. The findings of the NHMRC bear this out. Current studies further outline the failure of weight loss interventions to bring about the health benefits promised. This ever-growing body of evidence reminds us time and again that weight loss interventions contribute directly to the incidence of ‘obesity’ across the population.

Where then should we look for ethical support for the “Fast Track to Health” trial? **It is certainly not to be found in scholarly literature on the topic.** It has been **clearly established that that severe calorie restriction is ineffective in bringing about sustainable health outcomes.** It is undisputed that 97% of dieters end up at the same weight or heavier than when they started. It has been shown, time and again, that repeated weight loss by calorie restriction corresponds with increasing levels of weight overshoot each time, and contributing directly to worsening health outcomes.

By way of illustration: one cannot imagine, given the Level A evidence that smoking is linked with cancer, the NHMRC funding a trial that would see participants engage

in smoking as a means of “improving health”, behavior that places them at inarguable risk [38]. And yet here, the *same* body is funding a weight loss trial, even though by their own admission, the evidence linking weight loss interventions with regaining all of the weigh lost within five years, [35], is *also* classed by NHMRS as Level A evidence. On what basis has ethical approval been given for a study whose premise has been so roundly debunked, and which carries such potential for grave harm to its participants?

No long term, sustainable outcomes as borne out by a substantial body of scholarly evidence can be used to support this trial proceeding. **It is inaccurate and unethical to explicitly claim that being in a state of subclinical to clinical starvation will allow a person to achieve a sustainable state of improved “health”, especially in the face of compelling and repeated studies that show that this is simply not achievable.**

There can be no ethical reason that this trial is allowed to continue, given its immediate and long-term risks. While recognising the goodwill inherent in the researchers updating the information provided to parents and caregivers, the actual risks have not been adequately considered. **We collectively urge the SCHN HREC to stand down the “Fast Track to Health” trial immediately in light of the information discussed here.**

Yours sincerely

Ruth Leach BA MPhil: Eating Disorder Researcher and Advocate

[co-signed by 37 other individuals, including parents with experience in caring for children and adolescents with EDs, individuals with an ED history, clinicians with experience in treating people with: EDs, disordered eating because of dieting in adolescence, and a variety of psychological and psychiatric issues related to a history of restrictive eating. Names removed to preserve privacy.]

Endorsed by:

HAES Australia is a professional association that brings together the highest quality information, training, and specialists in Australia for the Health at Every Size® (HAES®) approach.

Eating Disorders Families Australia is a registered charity whose mission is to facilitate and advocate for families and carers to ensure they are supported, equipped and acknowledged as a central part of optimising the recovery process for the person with the eating disorder.

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