INTRODUCTION

Lifestyle [1] and pharmacotherapy interventions [2,3] have been shown in randomised trials to be effective in achieving weight loss among individuals with overweight or obesity with high cardiovascular (CVD) risk because of type 2 diabetes, cardiovascular diseases or additional risk factors [3,4] In such high risk patients, there is evidence that weight loss is also beneficial for cardiovascular risk factors [4]. However, there are mixed findings on the effect of weight loss on CVD, as some studies found no effect of weight loss on fatal and non-fatal CVD [1,5,6], while a recent meta-analysis of trials reported moderate lower risk of CVD following weight loss [4]. In any case, there are no randomised controlled trials (RCTs) of any weight loss intervention assessing the effectiveness for primary prevention of cardiovascular diseases (CVDs) in otherwise healthy individuals with overweight or obesity. The prospect of performing such trials is low because of the very high number of participants required for reliable estimation of a primary preventive effect on CVD events. Therefore, it is not known whether weight loss reduces the risk of incident cardiovascular disease among people in the general population with overweight or obesity. This is particularly important as higher body mass index is associated with the onset of cardiovascular diseases [7] and the prevalence of obesity, already high, is predicted to risk further [8].

In such settings emulating target pragmatic trials using causal inference methods in large scale observational data may play a role in distinguishing effects of weight change in people with normal weight, overweight and obesity [9-12]. Observational studies of weight (or BMI) change are conflicting, some reporting increased risk of CVD [13-16], no association [17-20] or lower risk, especially after bariatric surgery in people with severe obesity [21]; weight gain has been associated with increased CVD risk in some studies[13-16], but not others[21]. Emulation of weight loss trials has been carried out in a consented cohort, the Nurses' Health Study, which found no relationship between weight loss and CHD [17,18].