Effect of a high-egg diet on cardiometabolic risk factors in people with type 2 diabetes: the Diabetes and Egg (DIABEGG) Study—randomized weight-loss and follow-up phase

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ABSTRACT

Background: Some country guidelines recommend that people with type 2 diabetes (T2D) limit their consumption of eggs and cholesterol. Our previously published 3-mo weight-maintenance study showed that a high-egg (≥12 eggs/wk) diet compared with a low-egg diet (<2 eggs/wk) did not have adverse effects on cardiometabolic risk factors in adults with T2D.

Objective: The current study follows the previously published 3-mo weight-maintenance study and assessed the effects of the high-egg compared with the low-egg diets as part of a 3-mo weight-loss period, followed by a 6-mo follow-up period for a total duration of 12 mo.

Design: Participants with prediabetes or T2D ($n = 128$) were prescribed a 3-mo daily energy restriction of 2.1 MJ and a macronutrient-matched diet and instructed on specific types and quantities of foods to be consumed, with an emphasis on replacing saturated fats with monounsaturated and polyunsaturated fats. Participants were followed up at the 9- and 12-mo visits.

Results: From 3 to 12 mo the weight loss was similar (high-egg compared with low-egg diets: -3.1 ± 6.3 compared with -3.1 ± 5.2 kg; $P = 0.48$). There were no differences between groups in glycemia (plasma glucose, glycated hemoglobin, 1,5-anhydroglucitol), traditional serum lipids, markers of inflammation [high-sensitivity C-reactive protein, interleukin 6, soluble E-selectin (sE-Selectin)], oxidative stress (F2-isoprostanes), or adiponectin from 3 to 12 mo or from 0 to 12 mo.

Conclusions: People with prediabetes or T2D who consumed a 3-mo high-egg weight-loss diet with a 6-mo follow-up exhibited no adverse changes in cardiometabolic markers compared with those who consumed a low-egg weight-loss diet. A healthy diet based on population guidelines and including more eggs than currently recommended by some countries may be safely consumed. This trial is registered at http://www.anzctr.org.au/ as ACTRN12612001266853. *Am J Clin Nutr* 2018;107:1–11.

Keywords: diabetes, nutrition, obesity, overweight, prediabetes

INTRODUCTION

Epidemiologic studies show little association between high egg intake and cardiovascular disease (CVD) or mortality in the general population (1–8) but not in people with type 2 diabetes (T2D) (3, 9, 10), in whom a positive association between a higher egg intake and the relative risk of CVD and all-cause mortality has been reported (8, 10–15). However, controlled studies in those with prediabetes or T2D have shown predominantly favorable effects of higher egg intakes on cardiovascular and metabolic risk factors (16–20) or no adverse effect on cardiovascular risk factors or glycemic control (21–24). This includes our findings from the Diabetes and Egg (DIABEGG) Study, which showed that, in people with prediabetes or T2D, a high-egg diet (≥12 eggs/wk) did not have any adverse effect on cardiometabolic risk factors compared with a low-egg diet (<2 eggs/wk) during weight maintenance over 3 mo (24). This disparity in findings between epidemiologic and controlled studies measuring risk factors may explain the differing guidelines for dietary cholesterol and egg intakes between countries and for specific population groups within a country. For example, the British Heart Foundation and Diabetes UK do not recommend limiting

Supported by a research grant from the Australian Egg Corporation. AS was supported by a research fellowship from the National Health and Medical Research Council (NHMRC) of Australia (1042555). AJJ has received an NHMRC Practitioner Fellowship and a fellowship from the Sydney Medical School Foundation.

Supplemental Tables 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: apo, apolipoprotein; CVD, cardiovascular disease; FAQ, Food Acceptability Questionnaire; HbA1c, glycated hemoglobin; hs-CRP, high-sensitivity C-reactive protein; sE-selectin, soluble E-selectin; T2D, type 2 diabetes; VAS, visual analog scale; 1,5AG, 1,5-anhydroglucitol.

Received December 5, 2017. Accepted for publication February 23, 2018.
First published online 0, 2018; doi: https://doi.org/10.1093/ajcn/nqy048.

cholesterol or egg consumption (25). The American Diabetes Association until recently recommended a limit on total cholesterol consumption (300 mg/d) (26), but there is now no longer any such limit (27). However, another US group, the National Lipid Association, revised their guidelines for those with dyslipidemia and currently recommends <200 mg dietary cholesterol/d (28–30). In Australia, the National Heart Foundation recommends a maximum of 6 eggs/wk for persons with T2D (31).

The primary aim of the current study was to determine the effects of a high- compared with low-egg diet, as part of a weight-loss program, on cardiometabolic risk factors in persons with prediabetes or T2D. To our knowledge, there has been only 1 other weight-loss diet study comparing high- with low-egg intake in a similar cohort but only over 3 mo (19). Our current study expands the indexes of cardiometabolic health previously analyzed (19) to include novel vascular risk factors. These include measures of systemic and vascular inflammation [high sensitivity C-reactive protein (hs-CRP), IL-6, soluble E-selectin (sE-selectin)], oxidative stress (F2-isoprostanes), the adipokine adiponectin (which also modulates insulin resistance), and glycemia [fasting plasma glucose, glycated hemoglobin (HbA1c), and a medium-term measure of glycemia, 1,5-anhydroglucitol (1,5AG)]. These detailed biochemical analyses in a study conducted over a longer time frame (12 mo) provide a more comprehensive assessment of cardiometabolic health.

The present study followed the 3-mo weight-maintenance period of our DIABEGG study (24). It involved a 3-mo weight-loss intervention period (month 3 to month 6) with a 6-mo follow-up period (month 6 to month 12) with the use of a large panel of cardiovascular markers of disease to give a more definitive insight into whether or not persons with T2D should limit their egg intake.

METHODS

Study design and participants

This prospective, randomized, controlled, parallel-arm study was conducted in accordance with guidelines from the International Conference on Harmonization–Good Clinical Practice. A total of 128 participants diagnosed with prediabetes or T2D [as defined by the American Diabetes Association guidelines at the time of study conduct (32)], aged ≥18 y, and with a BMI (in kg/m^2) ≥25 commenced the 3-mo weight-loss study. Participants taking any class of antidiabetic (glucose-control) medication including insulin for T2D were included. A full list of inclusion and exclusion criteria, as well as a description of the 2 intervention groups, has been published with results of the 3-mo weight-maintenance study (24), which preceded the 3-mo weight-loss study.

All of the procedures were approved by the University of Sydney Human Ethics Review Committee, and all participants provided written informed consent. All clinic visits took place at the Boden Institute of Obesity, Nutrition, Exercise, and Eating Disorders at the University of Sydney. This trial is registered at http://www.anzctr.org.au/ as ACTRN12612001266853.

Dietary interventions

At the 3-mo visit, participants met the study dietitian where they were prescribed a diet for weight loss that was either high or low in eggs. Participants who had been consuming the high-egg diet during the preceding 3-mo weight-maintenance phase continued consumption of a high-egg diet for the 3-mo weight-loss phase and for the follow-up phase. Similarly, those consuming the low-egg diet were instructed to continue consumption of a low-egg diet for all phases of the study. Throughout all study phases, including the 3-mo weight-loss phase, participants consuming the high-egg diet were instructed to eat 2 eggs/d at breakfast for 6 d/wk (12 eggs/wk). Those in the low-egg group were directed to consume <2 eggs/wk, and to match the protein intake that the high-egg group had consumed at breakfast with 10 g lean animal protein (meat, chicken, or fish) or other protein-rich alternatives, such as legumes and reduced-fat dairy products (also consumed at breakfast). Recommended egg-cooking methods were boiled or poached, but they could also be fried if a polyunsaturated cooking oil, such as olive oil, was used. The prescribed diets were energy and macronutrient matched, as reported previously (24).

Participants were provided with a goal for energy intake, based on the Harris-Benedict equation, which was 2.1 MJ (500 kcal)/d less than their estimated energy requirements for weight maintenance. The study dietitian provided a written guide as to the specific types of foods and the quantities to be consumed. At the start of the weight-loss phase, participants were provided with a pedometer and encouraged to increase their activity level to 10,000 steps/d. During the weight-loss phase, participants attended the clinic and met with the study dietitian every month (3 times over 3 mo). As in the earlier 3-mo weight-maintenance study, to aid adherence, participants consuming the high-egg diet were given the prescribed quota of eggs at every monthly visit and participants consuming the low-egg diet were given a grocery voucher of equivalent value (5 Australian dollars/wk, 20 Australian dollars/mo). After the 3-mo weight-loss phase, all participants were reviewed at 9 and 12 mo at the clinic. Participants were advised to continue with their high- or low-egg prescription during this follow-up period and were given the option to attend the clinic for egg collection during this time. For those participants who wished to attend the clinic for their egg quota (high-egg), they were advised to come to the clinic to collect them on a monthly basis. No dietary advice was given at any of the egg collection times during the follow-up period and the eggs were picked up from a reception collection point.

Outcome measures

All of the outcome assessments were conducted at 3 (beginning of weight-loss phase), 6 (end of weight-loss phase), and 12 (end of follow-up period) mo. These included blood collection for pathology testing, anthropometric measures, blood pressure and pulse, nutritional analysis of food diaries, and completion of questionnaires, as described below. Monthly review visits also took place at months 4 and 5 for anthropometric measures and a nutritional review with the dietitian. Anthropometric measures were also collected at month 9. Monitoring for adverse events and medication changes took place at every visit.

Pathology

Blood samples were collected between 0730 and 1030 after an overnight fast (from 2200 the previous night) for the measurement of total serum cholesterol, serum HDL cholesterol,

serum LDL cholesterol (calculated by Friedewald), serum hs-CRP, serum apolipoprotein (apo) B, fasting plasma glucose, and whole-blood HbA1c. Samples were collected and centrifuged (Thermo Megafuge 16R at 3200 RPM for 10 min at 4°C) at the clinic and then sent to a commercial pathology service for analysis (Douglass Hanly Moir, Sydney, Australia). Plasma samples were also collected and stored at −80°C for future analysis of IL-6, sE-selectin, F2-isoprostanes, total adiponectin, and 1,5-AG, as well as an objective marker of dietary compliance (homocysteine). These analyses were completed at the National Health and Medical Research Council Clinical Trials Center, University of Sydney. The detailed biochemical analyses were carefully selected, as explained in **Supplemental Table 1**.

Change in anthropometric measures and vital signs

Body weight was measured by using a calibrated scale (to the nearest 0.1 kg); waist circumference was measured at the midpoint between the highest point of the iliac crest and the lowest part of the costal margin in the mid-axillary line (to the nearest 0.5 cm); total body fat and fat-free mass were measured by bioelectrical impedance analysis (calibrated to the nearest 0.1 kg; Tanita Analyzer BC-418); mean systolic and diastolic blood pressures were measured twice in the same arm and the average of the 2 recordings reported (if a difference of >10 mm Hg was found between the 2 readings, a third reading was taken; each measure was taken with the use of the same digital sphygmomanometer and after the participant had been sitting quietly for 10 min); and heart rate was measured at the radial pulse (for 1 min).

Nutritional analysis

Participants were instructed by the dietitian to complete a weighed 5-d (self-reported) food diary (4 working days and 1 weekend day) at 3, 6, and 12 mo. The food diaries were analyzed by the dietitian with the use of Food Works Professional, version 7, software (Xyris Software 2012), based on Australian food-composition tables and food manufacturers' data. The quantity of eggs consumed, reported in the 5-d food diaries, was analyzed for both groups throughout the study. Plasma homocysteine concentrations were measured as a surrogate marker of dietary adherence (33). In the current study, we hypothesized that excess choline from the egg-enriched diet would result in an increase in betaine production, which, in turn, should lower homocysteine concentrations (34).

Questionnaires

The following questionnaires were completed by participants at the time points described above:

1. The Three-Factor Eating Questionnaire–21 item (35).
2. The International Physical Activity Questionnaire–short version (36).
3. The Impact of Weight on Quality of Life Questionnaire–Lite Version (37).
4. The Food Acceptability Questionnaire (FAQ) (38, 39). The FAQ is composed of 10 questions that are scored on a 7-point linear scale, with 1 being "dislike" and 7 being "total acceptance." The exception is for question 4, where the reverse applies, as described previously (24).
5. A visual analog scale (VAS) for assessment of appetite (40). The VAS for appetite is composed of 10 questions that are scored on a 10-point linear scale, with 0 being "not at all" and 10 being "very," as described previously (24). Participants were required to answer the questions at 30 min before and 30 min after breakfast at their home.

Statistical analysis

Sample size

Allowing for a 10% drop-out rate at 3 mo, a total of 140 participants were recruited. Assuming a detectable difference in HDL cholesterol of 0.12 mmol/L between the 2 groups, and an SD of 0.24 mmol/L, 126 participants were required to achieve 80% power of detecting a treatment effect on HDL cholesterol (2-sided significance level of 5%), which has been reported previously (24). The current study followed up the initial findings. The number of study participants ($n = 72$ and $n = 68$ randomly assigned to the high- and low-egg groups, respectively) allowed the detection of differences between measurements of 15% (of the mean) with 80% power (2-sided $P = 0.05$), assuming a SD of 25% (of the mean) or a difference of 18% (of the mean), assuming a SD of 35% with the same power and in either case allowing for a 5% non compliance rate. With the number of participants in the high- and low-egg groups presented in this article, the sample size was sufficient to detect differences between measurements of ≥13% (of the mean) with 80% power (2-sided $P = 0.05$), assuming a SD of 25% of the mean or a difference of ≥18% (of the mean), assuming a SD of 35% with the same power.

Randomization

The treatment groups were stratified during randomization according to age, sex, cholesterol-lowering medication treatment, and diabetes status (prediabetes or T2D). Once stratified, participants were randomly allocated to either the high-egg or low-egg diet groups.

Data analysis

Statistical analysis was performed by using SPSS 19.0 software. All of the participants who completed an initial assessment were included in the final results by an intention-to-treat analysis. For this study, the month 3 visit was the start of the weight-loss intervention and hence was considered the baseline observation, as shown in **Figure 1**. Multiple imputations with the use of linear regression were used to impute missing values from study commencement to 12 mo and were based on the assumption that data were missing at random. Five imputed data sets were created for each variable. An ANCOVA was used to compare treatment groups. Analyses were adjusted for the pre–weight-loss (month 3) observation. A 2-sided $P < 0.05$ was considered significant. Values are presented as means ± SDs. Between-group differences are presented as means with 95% CIs in parentheses, and represent the Δ change between 3 and 12 mo for the 2 groups. Differences in pre–weight-loss characteristics were analyzed by independent-sample *t* tests.

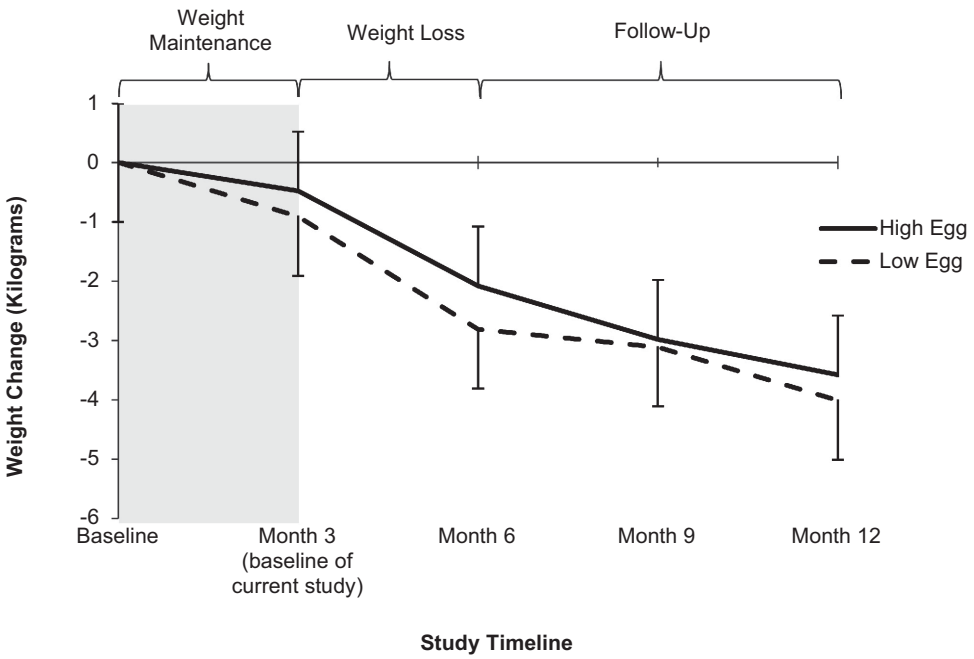

FIGURE 1 Weight loss for participants ($n = 128$) who consumed the high-egg ($n = 66$) or the low-egg ($n = 62$) diets throughout the study. An ANCOVA was used to compare treatment groups. Analyses were adjusted for the month 3 observation (before the start of the weight-loss intervention).

An analysis was also performed for all participants who were randomly assigned into the trial (at the screening visit). This was done for all of the outcomes (excluding nutrition and questionnaire data). An ANCOVA was used to compare treatment groups. In this instance, analyses were adjusted for start of study (screening) measurements.

RESULTS

Trial disposition

A flowchart detailing participant disposition is provided in **Figure 2**. The complete 12-mo study was conducted between January 2013 and July 2014. There was an overall drop-out rate of 20.7% (29 participants: 16 from the high-egg group and 13 from the low-egg group) between the start of the study (month 0) until the end of the 12-mo intervention. Of those who started the weight-loss phase (month 3) and who completed the 12-mo study, 1 participant was considered to be noncompliant with the high-egg diet, although all were compliant with the low-egg diet (Figure 2).

Pre–weight-loss characteristics

Pre–weight-loss characteristics of the participants are detailed in **Table 1**. Demographic and clinical characteristics were well matched across the 2 groups, albeit there were significant differences at baseline in fasting serum HDL-cholesterol concentrations, with the higher values being found in the high-egg group (Table 1). There were significant differences in baseline dietary intake between groups with respect to carbohydrate, total fat, fiber, and cholesterol, but all other aspects of dietary intake before weight loss were similar between groups (**Table 2**). These differences are due to the study design because participants had been consuming a high- or low-egg maintenance diet for 3 mo immediately before collection of these data, as previously described (24).

Medication changes

There were no significant differences in medication changes between groups during this study. The medication changes during the study (**Supplemental Table 2**) did not influence the primary or secondary outcome results (except for systolic blood pressure), because the findings were identical regardless of whether or not data from those participants who had a change in medication were included in the intention-to-treat statistical analyses (results not shown).

Primary outcome

There was no significant difference in the change in HDL-cholesterol concentrations over the 3-mo weight-loss intervention period (months 3 to 6) between the 2 groups (**Table 3**). This was consistent when the change from the start of the weight-loss intervention (3 mo) to 12 mo was analyzed (Table 3). Similarly, no differences were evident between groups when the change from screening to 6 or 12 mo was assessed (results not shown).

Secondary outcomes

Changes in LDL cholesterol, total cholesterol, apoB, triglycerides, hs-CRP, IL-6, sE-selectin, and F2-isoprostanes

There were no significant differences in fasting serum concentrations of LDL cholesterol, total cholesterol, apoB,

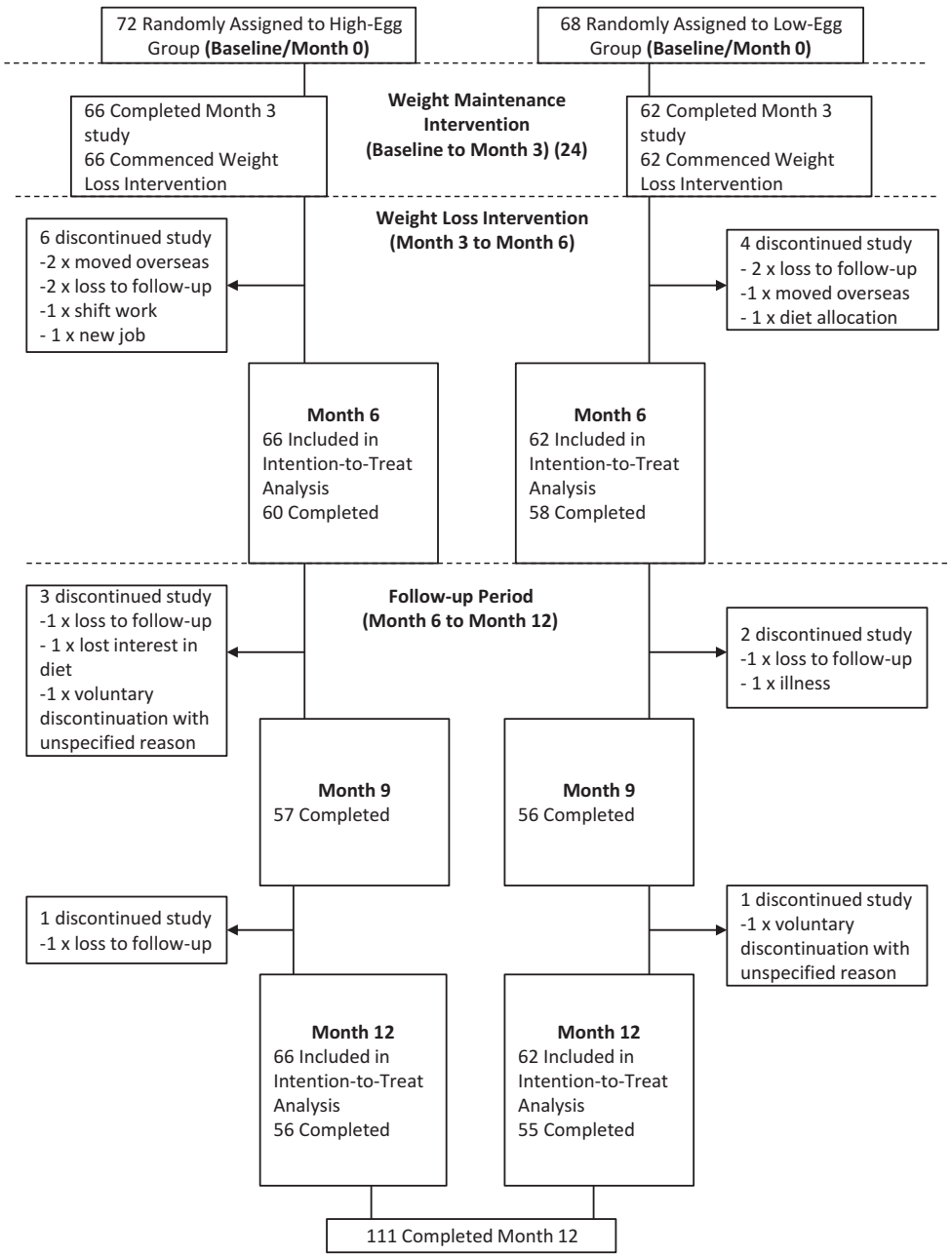

FIGURE 2 Participant disposition throughout the study.

triglycerides, IL-6, sE-selectin, or F2-isoprostanes between the 2 groups from start of the weight-loss intervention (3 mo) to 6 or 12 mo (Table 3). There was a significant difference from the start to the end of the weight-loss intervention (i.e., 3–6 mo) for hs-CRP, with the concentrations in the low-egg group decreasing more in this time frame (Table 3). However, when one participant in the high-egg group, who reported having had removal of a squamous cell carcinoma and an upper respiratory tract infection at the time of the month 6 visit, was removed from the analysis this finding was no longer significant. Similarly, no differences in hs-CRP concentrations were evident between groups when assessing the change from screening to 6 or 12 mo (results not shown).

Change in glycemic control

There were no significant differences in markers of glycemic control from the start of the weight-loss intervention (3 mo) to 6 or 12 mo between the 2 groups (Table 3). Similarly, no significant differences were evident between groups when assessing the change in these variables from screening to 6 or 12 mo (results not shown).

Change in anthropometric measures and vital signs

The energy-reduced diet resulted in a weight loss of ∼2 kg, with no difference between groups (Table 3, Figure 1). However,

TABLE 1
Pre–weight-loss (month 3) characteristics of study participants[1]

Characteristic	High-egg group ($n = 66$)	Low-egg group ($n = 62$)
Female sex, *n* (%)	33 (50)	36 (58)
Prediabetic, *n* (%)	19 (29)	15 (24)
Type 2 diabetic, *n* (%)	47 (71)	47 (76)
Years diagnosed with T2D	7.3 ± 7.8	5.9 ± 4.9
Age, y	59.7 ± 9.9	61.1 ± 10.8
Age >45 y, *n* (%)	61 (92)	57 (92)
Weight, kg	96.7 ± 19.3	91.2 ± 16.5
BMI, kg/m^2	34.9 ± 5.5	33.2 ± 5.8
Waist circumference, cm	111.8 ± 13.7	108.5 ± 13.4
Total body fat, %	29.7 ± 10.9	30.0 ± 11.3
Fat-free mass, kg	68.2 ± 19.7	63.7 ± 17.2
Systolic blood pressure, mm Hg	134.7 ± 16.8	131.4 ± 13.2
Diastolic blood pressure, mm Hg	79.2 ± 7.6	78.3 ± 7.5
Radial pulse rate, bpm	70.1 ± 10.1	73.7 ± 9.8
Taking cholesterol-lowering medication, *n* (%)	38 (58)	35 (57)
Serum cholesterol, mmol/L		
HDL	1.3 ± 0.3	1.2 ± 0.2[2]
LDL	2.9 ± 0.9	2.6 ± 1.0
Total	5.0 ± 1.1	4.6 ± 1.1
Serum apoB, g/L	1.0 ± 0.3	0.9 ± 0.3
Serum triglycerides, mmol/L	1.6 ± 0.8	1.7 ± 0.6
Serum C-reactive protein, mg/L	4.8 ± 4.3	4.4 ± 8.3
IL-6,[3] pg/mL	3.4 ± 2.1	2.9 ± 1.6
sE-selectin,[3] ng/mL	47.8 ± 20.7	47.7 ± 26.0
F2-isoprostanes,[3] pg/mL	13,677 ± 7724	13,713 ± 6766
Plasma glucose, mmol/L	6.6 ± 2.1	6.8 ± 1.6
HbA1c		
%	6.5 ± 1.1	6.5 ± 0.9
mmol/mol	47.3 ± 12.1	47.5 ± 10.2
1,5AG,[3] μg/mL	14.3 ± 7.6	13.0 ± 7.2
Adiponectin,[3] ng/mL	5960 ± 3229	5802 ± 3525
Homocysteine,[3] μmol/L	12.4 ± 3.5	12.7 ± 3.8

[1] Values are means ± SDs unless otherwise indicated; $n = 128$. Circulating factors were measured after an overnight fast. *P* values represent pre–weight-loss (month 3) differences between groups; *t* tests were used for comparison of means between groups. bpm, beats per minute; HbA1c, glycated hemoglobin; sE-selectin; soluble E-selectin; T2D, type 2 diabetes; 1,5AG, 1,5-anhydroglucitol.

[2] $P = 0.03$.

[3] $n = 110$ for the analyses (high-egg = 58, low-egg = 52).

the weight loss continued in both groups after the end of the intervention from 6 to 12 mo, to reach ~3 kg (Table 3, Figure 1). When assessing the change in weight from the initial contact with participants (the screening visit), the total weight loss over the 12-mo period was −3.6 and −4.0 kg for the high- and low-egg groups, respectively, with no significant difference between groups (Figure 1). This was equivalent to ~4% of initial body weight loss for both groups.

Similar to the results for body weight, no significant differences in waist circumference, total body fat, fat-free mass, or radial pulse rate were identified between the groups (Table 3). A significant decrease in systolic blood pressure favoring the high-egg group was evident at 6 mo, but this was no longer evident when the change between groups from the start of the weight-loss intervention (3 mo) to 12 mo was analyzed (Table 3). This significant difference was also not evident when adjusting for the changes in antihypertensive medications for both groups (data not shown).

Dietary changes

On the basis of self-report, the adherence to the allocated diet (12 eggs/wk or <2 eggs/wk, respectively) was satisfactory. At 6 and 12 mo, the high-egg group reported consuming a mean ± SD of 12.2 ± 3.8 and 10.5 ± 4.9 eggs/wk, respectively (a significant decrease in egg consumption from 6 to 12 mo; $P < 0.0001$), although the low-egg group reported consuming 1.0 ± 2.2 and 1.1 ± 2.0 eggs/wk, respectively (no significant difference in egg consumption from 6 to 12 mo; $P = 0.56$). Surrogate measures of egg adherence (homocysteine) suggested that the high-egg group followed their prescribed diet; however, this was not evident throughout the entire study. A significant difference in homocysteine concentrations was evident between groups at month 12 (Table 3); however, this was not evident at month 6.

The groups were well matched for nutritional intake during the study period (**Table 4**). As expected, on the basis of the dietary prescription, there was a significant difference between groups from the start of the weight-loss intervention (3 mo) to 6 and

TABLE 2
Pre–weight-loss (month 3) dietary intake of study participants[1]

Characteristic	High-egg group ($n = 61$)	Low-egg group ($n = 62$)
Energy, kJ	7160 ± 1631	7389 ± 1913
Protein, % of energy	22.5 ± 4.0	21.6 ± 4.0
Carbohydrates, % of energy	36.6 ± 7.4	40.2 ± 7.9[2]
Total fat, % of energy	35.1 ± 5.5	31.9 ± 7.1[3]
Alcohol, % of energy	2.5 ± 4.8	2.2 ± 3.9
Saturated fat, % of total fat	37.4 ± 5.3	36.0 ± 7.3
Polyunsaturated fat, % of total fat	19.7 ± 4.5	21.0 ± 5.2
Monounsaturated fat, % of total fat	42.8 ± 3.6	43.1 ± 4.9
Dietary fiber, g	21.2 ± 7.2	24.7 ± 8.0[2]
Cholesterol, mg	585.7 ± 146.7	247.0 ± 164.7[4]

[1] Values are means ± SDs; $n = 123$. Dietary intakes are percentages of total energy intake unless otherwise indicated. *t* Tests were used for comparison of means between groups. Five participants did not complete a month 3 food diary in the high-egg group.
[2] $P = 0.01$.
[3] $P < 0.01$.
[4] $P < 0.001$ for the differences between groups pre–weight loss.

12 mo for dietary cholesterol, with a higher intake in the high-egg group (Table 4).

Food acceptability

The FAQ was completed by 124 of the 128 participants who commenced this current study (63 from the high-egg group, 61 from the low-egg group). There were no significant differences in the acceptability of the 2 diets at 6 and 12 mo and both diets were well liked and accepted over the course of the study, implying that both the high- and low-egg diets were enjoyed and adhered to over the 12-mo study. For question 1 ("How well do you like the food that you have been eating in the past 2 weeks?"), the mean difference for the high-egg compared with the low-egg group at 6 mo was +0.2 (95% CI: −0.1, 0.5; $P = 0.1$) and at 12 mo the mean difference between groups was +0.0 (95% CI: −0.3, 0.3; $P = 0.9$). Similarly, for question 10 ("Overall, how satisfied or dissatisfied are you with this diet?"), the mean difference for the high-egg compared with the low-egg group at 6 mo was +0.1 (95% CI: −0.3, 0.4; $P = 0.8$), which, again, was consistent at 12 mo (+0.1; 95% CI: −0.3, 0.5; $P = 0.7$).

TABLE 3
Change from pre–weight loss (month 3) at 6 and 12 mo in chemical pathology results, anthropometric variables, and vital signs[1]

	Month 6				Month 12			
	High-egg ($n = 66$)	Low-egg ($n = 62$)	Between-group comparison (high-egg vs. low-egg)	Between-group comparison (high-egg vs. low-egg), *P*	High-egg group ($n = 66$)	Low-egg group ($n = 62$)	Between-group comparison (high-egg vs. low-egg)	Between-group comparison (high-egg vs. low-egg), *P*
Serum cholesterol, mmol/L								
HDL	0.01 ± 0.13	0.00 ± 0.14	0.01 (−0.04, 0.06)	0.60	0.01 ± 0.16	0.05 ± 0.22	−0.02 (−0.09, 0.05)	0.54
LDL	−0.01 ± 0.72	0.02 ± 0.71	0.06 (−0.18, 0.30)	0.61	−0.04 ± 0.78	−0.01 ± 0.90	0.04 (−0.24, 0.32)	0.77
Total	−0.05 ± 0.82	0.05 ± 0.74	−0.02 (−0.29, 0.24)	0.86	−0.07 ± 0.91	0.14 ± 0.88	−0.11 (−0.40, 0.19)	0.47
Serum apoB, g/L	−0.09 ± 0.29	−0.03 ± 0.18	−0.04 (−0.12, 0.04)	0.34	−0.11 ± 0.22	−0.06 ± 0.21	−0.02 (−0.09, 0.05)	0.57
Serum triglycerides, mmol/L	−0.15 ± 0.54	−0.02 ± 0.54	−0.15 (−0.33, 0.02)	0.09	−0.07 ± 0.71	0.04 ± 0.67	−0.14 (−0.36, 0.08)	0.21
Serum hs-CRP, mg/L	1.51 ± 5.80	−0.66 ± 6.71	2.32 (0.40, 4.24)	0.02	0.58 ± 6.33	−0.31 ± 12.77	1.07 (−2.21, 4.35)	0.52
IL-6,[2] pg/mL	0.31 ± 2.94	0.43 ± 2.36	0.22 (−0.71, 1.15)	0.64	0.33 ± 2.88	0.74 ± 2.34	−0.21 (−1.19, 0.77)	0.67
sE-selectin,[2] ng/mL	−2.46 ± 11.05	−0.54 ± 11.82	−1.90 (−5.97, 2.17)	0.36	−2.68 ± 8.68	0.94 ± 10.17	−3.61 (−7.18, 0.05)	0.05
F2-isoprostanes,[2] pg/mL	3016.3 ± 11,688.8	3495.9 ± 10,428.6	−485.0 (−4666.3, 3696.2)	0.82	4051.0 ± 9579.2	3568.2 ± 9405.4	475.6 (−3021.8, 3972.9)	0.79
Plasma glucose, mmol/L	−0.03 ± 1.56	−0.05 ± 1.20	−0.05 (−0.48, 0.38)	0.83	−0.21 ± 1.85	−0.11 ± 2.29	−0.42 (−1.06, 0.23)	0.20
Whole-blood HbA1c								
%	−0.24 ± 0.44	−0.23 ± 0.62	−0.01 (−0.18, 0.16)	0.90	−0.28 ± 0.66	−0.15 ± 0.86	−0.14 (−0.39, 0.11)	0.27
mmol/mol	−2.64 ± 4.82	−2.37 ± 6.64	−0.29 (−2.08, 1.50)	0.75	−3.07 ± 7.20	−1.53 ± 9.34	−1.57 (−4.25, 1.12)	0.25
1,5AG,[2] μg/mL	0.63 ± 3.00	0.61 ± 2.73	0.21 (−0.80, 1.22)	0.68	0.02 ± 4.24	−0.03 ± 3.79	0.32 (−1.11, 1.75)	0.66
Adiponectin,[2] ng/mL	162.23 ± 1477.02	426.00 ± 2154.92	−252.88 (−947.09, 441.34)	0.47	655.74 ± 2994.89	198.94 ± 2817.64	487.69 (−595.97, 1571.35)	0.37
Homocysteine,[2] μmol/L	0.81 ± 2.07	0.59 ± 2.09	0.17 (−0.60, 0.95)	0.66	0.09 ± 2.20	1.00 ± 2.51	−0.94 (−1.83, −0.05)	0.04
Weight, kg	−1.59 ± 2.46	−1.89 ± 2.35	0.43 (−0.41, 1.28)	0.31	−3.11 ± 6.34	−3.08 ± 5.23	0.69 (−1.22, 2.60)	0.48
Waist circumference, cm	−1.62 ± 3.02	−2.52 ± 3.53	1.03 (−0.11, 2.17)	0.08	−3.22 ± 5.96	−3.99 ± 5.02	1.18 (−0.66, 3.03)	0.21
Total body fat, %	−0.48 ± 3.62	−0.48 ± 4.77	−0.04 (−1.44, 1.37)	0.96	−1.42 ± 3.42	−1.42 ± 4.13	−1.44 (−1.26, 1.18)	0.95
Fat-free mass, kg	−1.27 ± 5.26	−1.88 ± 8.85	0.97 (−1.53, 3.47)	0.44	−0.15 ± 5.39	−2.05 ± 9.17	2.44 (−0.07, 4.95)	0.06
Systolic blood pressure, mm Hg	−4.94 ± 14.04	0.83 ± 12.32	−4.32 (−8.34, −0.30)	0.04	−6.18 ± 16.05	−1.98 ± 14.49	−2.34 (−6.80, 2.12)	0.30
Diastolic blood pressure, mm Hg	−1.72 ± 7.10	0.23 ± 6.99	−1.64 (−3.96, 0.67)	0.16	−2.48 ± 7.91	−0.47 ± 7.86	−1.54 (−3.93, 0.86)	0.21
Radial pulse rate, bpm	1.23 ± 8.07	−1.29 ± 7.27	1.74 (−0.88, 4.37)	0.19	0.46 ± 7.96	−0.99 ± 8.82	0.61 (−2.25, 3.47)	0.68

[1] Values are means ± SDs or mean differences (95% CIs); $n = 128$. Circulating factors were measured after an overnight fast. An ANCOVA was used to compare treatment groups. Analyses were adjusted for pre–weight-loss (month 3) observations. *P* values represent between-group differences from the start of the weight-loss time point (month 3) to 6 or 12 mo, after adjustment for the pre–weight-loss value (month 3). apo, apolipoprotein; bpm, beats per minute; HbA1c, glycated hemoglobin; hs-CRP, high-sensitivity C-reactive protein; sE-selectin; soluble E-selectin; 1,5AG, 1,5-anhydroglucitol.
[2] $n = 110$ for the analyses (high-egg = 58, low-egg = 52).

TABLE 4
Change from pre–weight loss (month 3) in mean dietary intake at 6 and 12 mo[1]

	Month 6				Month 12			
	High-egg group ($n = 61$)[2]	Low-egg group ($n = 62$)	Between-group comparison (high-egg vs. low-egg)	Between-group comparison (high-egg vs. low-egg), P	High-egg group ($n = 61$)[2]	Low-egg group ($n = 62$)	Between-group comparison (high-egg vs. low-egg)	Between-group comparison (high-egg vs. low-egg), P
Energy,[3] kJ	−148.5 ± 1686.5	−636.7 ± 1766.1	360.9 (−191.7, 913.7)	0.20	−253.1 ± 1735.3	−855.2 ± 1936.5	534.8 (16.7, 1052.9)	0.04
Protein, % of energy	3.3 ± 11.2	2.0 ± 4.7	2.3 (−0.8, 5.4)	0.15	0.6 ± 4.6	−0.4 ± 5.8	1.7 (−0.0, 3.3)	0.05
Carbohydrates, % of energy	0.5 ± 14.4	0.4 ± 6.8	−2.2 (−6.3, 1.8)	0.27	−0.4 ± 7.1	0.5 ± 8.5	−2.5 (−5.3, 0.4)	0.09
Total fat, % of energy	0.4 ± 10.0	−2.4 ± 6.9	4.4 (1.2, 7.5)	0.01	−0.3 ± 5.9	−0.0 ± 8.1	1.9 (−0.5, 4.2)	0.13
Alcohol, % of energy	−0.3 ± 3.1	−0.3 ± 2.9	0.1 (−0.9, 1.1)	0.85	−0.2 ± 2.8	−0.3 ± 2.4	0.2 (−0.8, 1.1)	0.72
Saturated fat, % of total fat	−1.1 ± 6.4	−0.2 ± 10.0	0.1 (−2.6, 2.8)	0.94	1.3 ± 7.7	1.5 ± 7.4	0.8 (−1.8, 3.3)	0.55
Polyunsaturated fat, % of total fat	−0.8 ± 4.7	0.1 ± 6.9	−1.7 (−3.5, 0.2)	0.08	−0.5 ± 6.1	−0.7 ± 5.7	−0.5 (−2.5, 1.5)	0.61
Monounsaturated fat, % of total fat	0.9 ± 4.2	−0.4 ± 5.6	1.2 (−0.4, 2.7)	0.13	−0.8 ± 5.1	−0.8 ± 5.6	−0.3 (−2.0, 1.5)	0.74
Dietary fiber, g	−0.3 ± 7.9	−0.5 ± 8.2	−1.7 (−4.5, 1.0)	0.21	1.0 ± 8.3	−2.7 ± 8.3	2.0 (−0.8, 4.9)	0.17
Cholesterol, mg	7.7 ± 189.9	19.0 ± 226.3	245.5 (160.2, 330.9)	< 0.0001	−66.5 ± 183.6	−26.4 ± 161.4	167.9 (95.9, 239.8)	<0.0001

[1] Values are means ± SDs or mean differences (95% CIs); $n = 123$. Each dietary variable is a percentage of total energy intake unless otherwise indicated. An ANCOVA was used to compare treatment groups. Analyses were adjusted for pre–weight-loss (month 3) observations. P values represent between-group differences from the start of the weight-loss time point (month 3) to 6 or 12 mo, after adjustment for the pre–weight-loss value (month 3).

[2] Five participants in the high-egg group did not return baseline food diaries.

[3] 1 kJ = 0.239 kcal.

Appetite

VAS responses were collected from 101 of the 128 participants who commenced this study (79%; 50 from the high-egg group, 51 from the low-egg group). The high-egg group reported less satiety (question 4: "How much food do you think you can eat?") than the low-egg group with respect to the change in satiety from baseline: the mean difference for the high-egg compared with the low-egg group from the start of the weight-loss intervention (3 mo) to 6 mo was +1.0 (95% CI: 0.2, 1.7; $P = 0.02$). However, this effect was no longer evident when analyzing the change from the start of the weight-loss intervention (3 mo) to 12 mo. There were no other differences between groups in changes from baseline in any of the other questions from the VAS appetite questionnaire.

Eating behavior, physical activity, and quality of life

There were no significant differences between groups when assessing the change from baseline in eating behavior (as determined by the Three-Factor Eating Questionnaire–R21) over the study period (data not shown). Nor were there any significant differences between groups when assessing the change from baseline in the total time spent engaging in physical activity per week or quality of life (data not shown).

Subgroup analyses

The findings for the primary and secondary outcomes were consistent when comparing treatment effects in subgroups, by prediabetes and T2D status, and by those taking and not taking lipid-lowering medications (data not shown).

DISCUSSION

In this 12-mo study, a high-egg diet produced no detrimental outcomes in cardiovascular risk factors, including lipids (circulating concentrations of HDL cholesterol, LDL cholesterol, total cholesterol, triglycerides, and apoB), inflammatory markers (hs-CRP, IL-6, and sE-selectin), oxidative stress (plasma F2-isoprostanes), or measures of glycemia (fasting glucose, HbA1c, adiponectin, and 1,5AG) for persons with overweight or obesity and prediabetes or T2D. This extends our previous finding that a high-egg compared with a low-egg diet has no detrimental effect on CVD risk factors in persons with prediabetes or T2D during 3 mo of weight maintenance (24) by showing that the same is true during weight loss and for a 12-month period. Importantly, this was with the inclusion of a more comprehensive battery of traditional and novel cardiometabolic risk markers. These findings do not align with the health recommendations of some countries that specifically recommend a low-egg diet for people with T2D (29–31). Our findings suggest that a high-egg diet is safe for those with T2D—just as for the general population—without adverse consequences for cardiovascular risk factors.

Participants in both (high- and low-egg) groups reported enjoying the foods they were eating throughout the study period. Adherence to the high-egg diet during the 3-mo weight-loss intervention was high and similar to that observed in the 3-mo weight-maintenance study (24), indicating that a high-egg diet was well accepted. Thus, a diet with a higher egg intake not only appears to be not detrimental from a cardiometabolic perspective but is likely to be acceptable to persons with T2D in whom compliance with nutritional management is very important. Participants were advised to continue with their high- or low-egg diet during the follow-up period (6–12 mo) and adherence was measured by participant food diary egg counts and a surrogate dietary marker (homocysteine). A trend was evident at 12 mo of a lower homocysteine concentration in those in the high-egg group. It is hypothesized that excess choline from an egg-enriched diet results in an increase in betaine production, which lowers homocysteine concentrations (41, 42). Apart from protecting cells from osmotic stress, betaine serves as a methyl group donor to facilitate remethylation of homocysteine into methionine (43). A high homocysteine concentration is a risk factor for CVD (44), pregnancy complications (45), and cognitive decline in the elderly (46–48). In observational studies, plasma betaine concentrations were inversely associated with fasting homocysteine concentrations (49). In studies in healthy volunteers, high doses of betaine

(3 or 6 g/d) over 12 wk was related to a 10–20% decrease in homocysteine concentrations in a dose-dependent manner (50, 51). An egg contains ∼0.20 mg betaine and 0.24 mg choline (42). Over time, consumption of these amounts may produce a decrease in homocysteine, as was observed in our study at 12 mo.

The weight loss achieved was small and similar for both groups (high- and low-egg) at the end of the study (∼4 kg). Interestingly, the participants did not gain weight during the follow-up period (6–12 mo) but instead continued to lose weight during this time with no evidence of reaching a plateau. This contrasts with many clinical weight-loss interventions that showed that weight is regained after the end of an intervention. The weight regain reported by Dansinger et al. (52) was, on average, 0.01 BMI kg/m^2 between 6 and 12 mo, 0.02–0.03 BMI kg/m^2 between 12 and 18 mo, and 0.04 BMI kg/m^2 between 24 and 30 mo. Participants in our study were taught weight-maintenance skills and were requested to maintain their weight for 3 mo before being coached to lose weight. Although clinical weight-loss trials usually investigate a weight-maintenance period after the weight-loss phase, we chose to investigate a weight-maintenance phase before the weight-loss phase for 2 reasons: first, to study the effects of a high- compared with a low-egg diet independently from the effects of weight loss as per our initial study (24), and second, because recent research indicated that teaching weight-maintenance skills before losing weight improved long-term weight-management outcomes. This weight-maintenance-first approach implemented by Kiernan et al. (53) showed a weight loss of 7 kg at 12 mo. Our weight-maintenance intervention differed from their work (53) in that our focus was on teaching nutritional changes on a monthly basis. Participants were given a booklet to guide the specific types of foods and quantities to be consumed, with an emphasis on replacing foods containing saturated fats with foods containing monounsaturated and polyunsaturated fats to improve diet quality; yet, they were to maintain energy intake over the 3 mo (24). The study by Kiernan et al. (53) included weekly sessions, was based on 5 stability skills informed by psychological theories, and was conducted in persons with overweight or obesity who were otherwise healthy. Individuals with T2D have been shown to lose less weight and to regain more weight after weight-loss interventions than those with normoglycemia (54–56). The findings from the current study provide support for teaching participants how to maintain a consistent body weight before a weight-loss intervention.

This study has several strengths and limitations. The strengths of this study include that it is the first prospective, randomized, controlled trial, to our knowledge, to measure the effects of a high-egg intake in a group with prediabetes or T2D over a 12-mo period on cardiometabolic risk factors. Other strengths include the high rates of participant retention and detailed measures of body composition and multiple biochemical markers, including traditional and novel vascular risk factors, and of dietary quality and adherence. It builds upon previous controlled studies in this field of research by including a broad range of systemic and vascular inflammatory markers and cardiovascular and glycemic risk factors.

A limitation of the current study is that it assesses risk factors of cardiovascular disease, which are relatively weak predictors of risk, when compared with the actual risk of cardiovascular events and of actual cardiovascular outcomes. Moreover, it has been shown that postprandial circulating lipid concentrations and markers of oxidative stress and endothelial function (57) are adversely affected by a high cholesterol intake (58) and that this may be a limitation of this study because any such potential change was not assessed or measured. In a previous study (59), an acute high dietary cholesterol load (1000 mg) resulted in an increase in postprandial VLDL apoB-48 concentrations. However, the authors of that study (59) also suggested that long-term dietary changes may not have the same effect on postprandial lipid concentrations as found in their acute studies. Indeed, in studies in which participants followed a high-cholesterol diet for 6–8 wk (60–62), there were no adverse effects on postprandial lipids and, in particular, no effect on chylomicron metabolism, even in participants with hypercholesterolemia or combined hyperlipidemia (62). Other study limitations include the combination of participants with prediabetes and T2D, the lack of a comparator group with normal glucose tolerance, and the combination of participants taking and not taking lipid-lowering drugs.

In conclusion, individuals with prediabetes or T2D who followed a high-egg diet for 12 mo, which included a 3-mo weight-loss phase, had no adverse changes in cardiovascular risk factors, inflammatory or oxidative stress markers, or measures of glycemia. These findings suggest that it is safe for persons at high risk of T2D and those with T2D to include eggs, an acceptable and convenient food source, in their diet regularly.

The authors' responsibilities were as follows—NRF: designed and conducted the research, analyzed the data, wrote the manuscript, and had primary responsibility for final content; TPM and AS: designed the research and wrote the manuscript; KHW, NSL, IDC, and GD: designed the research and were involved in the writing of the manuscript; ASJ and AJJ: designed and conducted the biochemical analyses, assisted with data analyses, and were involved in writing the manuscript; CL, MF, and JG: conducted the research; and all authors: read and approved the final manuscript. The Australian Egg Corporation had no role in the protocol design, the study conduct, the analysis of the data, or the writing of the manuscript. NRF, IDC, NSL, and TPM have received research grants for other clinical trials funded by Sanofi-Aventis, Novo Nordisk, Allergan, Roche Products, MSD, and GlaxoSmithKline. NRF is the author of *Interval Weight Loss* (Penguin Random House; 2017). IDC has received payment for lectures from iNova Pharmaceuticals, Ache Pharmaceuticals, Pfizer Australia, and Servier Laboratories (Australia). TPM acts as an advisory member to the Egg Nutrition Council and Nestlé Nutrition and has received payments for lectures from Novo Nordisk and Astra Zeneca. AS has received research and fellowship funding from the National Health and Medical Research Council and the University of Sydney; she has received honoraria from Eli Lilly, the Pharmacy Guild of Australia, Novo Nordisk, the Dietitians Association of Australia, Shoalhaven Family Medical Centers, and the Pharmaceutical Society of Australia for seminar presentation at conferences; and has served on the Nestlé Health Science Optifast VLCD Advisory Board since 2016. She is also the author of *The Don't Go Hungry Diet* (Bantam, Australia and New Zealand; 2007) and *Don't Go Hungry For Life* (Bantam, Australia and New Zealand; 2011). None of the other authors declared any conflict of interest.

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