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Review

Producing high-oleic acid beef and the impact of ground beef consumption on risk factors for cardiovascular disease: A review

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ABSTRACT

This review summarizes the effects of high-oleic acid oil and high-oleic acid ground beef interventions on risk factors for cardiovascular disease (CVD) in human trials, and also summarizes studies designed to increase the amount of oleic acid (18:1n-9) in beef. In three human trials, high-oleic acid oils and high-oleic acid ground beef increased plasma high-density lipoprotein cholesterol – over baseline values or over high-carbohydrate diets. Neither low-oleic acid nor high-oleic acid ground beef increased risk factors for CVD, confirming earlier studies that used high-oleic acid oils. High-oleic acid beef can be obtained from cattle fed a corn-based finishing diet to USDA Grade of USDA Choice or greater; from beef from cattle with Japanese genetics; and from the brisket. Beef from grass-fed cattle contains more n-3 fatty acids than beef from conventionally-fed cattle, but also contains greater amounts of saturated and *trans*-fatty acids.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in the U.S., and risk factors include elevated plasma concentrations of low-density lipoprotein cholesterol (LDL-C) and depressed high-density lipoprotein cholesterol (HDL–C). For over five decades the general public has been cautioned to consume diets containing little or no red meat due to its inherent saturated fatty acid (SFA) content. Early research concluded that dietary SFA such as palmitic acid (16:0) elevated plasma LDL-C concentration; dietary polyunsaturated fatty acids (PUFA) such as linoleic acid (18:2n-6) reduced LDL-C concentrations (Hegsted, McGandy, Myers, & Stare, 1965; Keys, Anderson, & Grande, 1965). Monounsaturated fatty acids (MUFA) previously were reported to have little or no effect on cholesterol concentrations in humans. However, oleic acid (18:1n-9) later was found to lower plasma LDL-C concentrations and increase HDL-C concentrations in human studies (Bonanome & Grundy, 1988; Grundy, Florentin, Nix, & Whelan, 1988; Kris-Etherton et al., 1999). Paradoxically, palmitic acid also increases HDL-C concentrations in controlled, randomized crossover trials (RCT) (reviewed by Kris-Etherton & Yu, 1997). Relative to pork (the other primary red meat in the U.S. diet), beef is higher in palmitic acid and stearic acid (18:0) (St. John et al., 1987), but stearic acid has little effect on LDL-C or HDL-C concentrations (Kris-Etherton & Hu, 1997). Details of early human trials are presented in this review, as well as the results of four human studies that compared the effects low-oleic acid ground beef to high-oleic acid ground beef on risk factors for CVD (Adams, Walzem, Smith, Tseng, & Smith, 2010; Choi, Ghahramany, Walzem, Meade, & Smith, 2018; Gilmore et al., 2011; Gilmore et al., 2013). To our knowledge, these studies remain the only reports of the effects of an intact protein source containing naturally elevated oleic acid on risk factors for CVD. We conclude this review with a discussion of the management of cattle to increase oleic acid in beef, including a discussion of n-3 fatty acids in beef.

2. Animal fats and risk for cardiovascular disease

Reiser (1973) questioned the science responsible for the condemnation of animal fats in the diet. More current studies similarly have cast doubts on the potentially negative effects of red meat on risk factors for CVD and other causes of mortality. A report of meat consumption and mortality from the European Investigation into Cancer and Nutrition (Rohrmann et al., 2013) reported that a high level of unprocessed red meat intake (> 160 g/d, which included beef, pork, mutton/lamb, horse and goat) was associated with an RR of 1.07, i.e., there was no association of unprocessed red meat intake with mortality from CVD. Similarly, Feskens, Sluik, and van Woudenbergh (2013) reported RR factors for type II diabetes of 1.16 for red meat, indicating no association between unprocessed red meat and RR for type II

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diabetes. Kappeler, Eichholzer, and Rohrmann (2013) reported the associations between meat consumption, diet quality and mortality in the NHANES III population, and concluded that red meat, processed meat and white meat consumption were not consistently associated with all-cause or cause-specific mortality. Dehghan et al. (2017) concluded that high carbohydrate intake was associated with higher RR for total mortality and CVD, whereas intake of total fat, SFA and especially MUFA were related to lower RR for total mortality and CVD. Increasing the percent energy (%EN) to over 5% from SFA and MUFA decreased RR for total mortality and CVD, and increasing percent energy from MUFA to > 12% caused a further reduction in RR for CVD. In this respect, inclusion of high-fat ground beef in the diet, and especially high-oleic acid ground beef, may actually reduce the risk for CVD by elevating HDL-C concentration. Liu et al. (2019) reported that the provision of dairy foods (milk, cheese and yoghurt) and "meat" (which included beef, pork, lamb, game, poultry, seafood and eggs) increased HDL-C concentrations. The inclusion of such a variety of foods in their analyses makes it impossible to prescribe a single nutrient to their results, but would support current reports that the consumption of "meats" is relatively benign.

3. Plasma lipoprotein cholesterol concentrations in response to dietary fat interventions

3.1. Studies comparing dietary fats and oils

Reiser et al. (1985) documented the effects of supplementary beef fat, coconut oil and safflower oil in plasma lipoproteins of normo-lipidemic men. Nineteen men consumed centrally-prepared lunches and dinners containing 35%EN as fat, 60% of which was the test fat (supplemented in the form of meat dishes, bread spreads, ice cream, and cookies). Plasma HDL-C concentration was greater for men consuming the coconut oil-supplemented diet than for men consuming the beef fat-supplemented diet, but only for those men in the lower three quartiles for total cholesterol (127, 151, and 159 mg total cholesterol/dL). Men in highest quartile (199 mg total cholesterol/dL) did not respond to the dietary oil supplementations, and there was no difference in total, LDL or HDL-C concentrations between men fed diets supplemented with beef fat or soybean oil. The authors concluded that "The classification of dietary fats solely as saturated, unsaturated, or hypercholesterolemic is misleading, and may obscure a complex of significant metabolic effects." (Reiser et al., 1985).

To our knowledge, Grundy (1986) and Grundy et al. (1988) published the first reports of high-MUFA diets on plasma lipid levels in humans. Grundy (1986) compared a high-MUFA liquid diet to high-SFA and low-fat liquid diets. The high-MUFA diet (28%EN as fat) and the low-fat diet (20%EN as fat and 63%EN as carbohydrate) lowered LDL-C concentration, but the low-fat diet also decreased HDL-C concentration (Fig. 1A). Grundy et al. (1988) compared a high-MUFA diet to diets high in SFA plus cholesterol and a high-carbohydrate, low-fat diet. Compared with the high-SFA plus cholesterol diet, the high-MUFA and low-fat diet reduced plasma LDL-C concentration, and the low-fat diet reduced HDL-C concentration. Concentrations of the lipoprotein cholesterol fractions at entry were not reported. Bonanome and Grundy (1988) and Denke (1994) subsequently reported that, relative to a high-palmitic acid, liquid diet, liquid diets high in stearic acid or oleic acid reduced LDL-C but had no effect on HDL-C concentration (Fig. 1B). Again, concentration of the lipoprotein cholesterol fractions at entry was not reported, so it is not known if stearic acid or oleic acid reduced LDL-C concentration relative to entry into this study.

In a carefully controlled RCT, Wood, Kubena, O'Brien, Tseng, and Martin (1993) compared diets enriched with regular butter, MUFA- and PUFA-enriched butter, *trans*-fatty acid (TFA) margarine, and zero *trans*-fatty acid margarine (supplemented in the form of milk, bread spreads, ice cream, and cookies) on serum lipids in men. None of the dietary treatments affected plasma HDL-C concentration, but the regular butter diet (high in shorter-chain SFA) increased LDL-C and the zero TFA butter (high in PUFA) decreased LDL-C concentration relative to baseline. Kris-Etherton et al. (1999) reported that high-oleic acid diets (supplemented with olive oil, peanut oil or peanut butter) decreased plasma LDL-C concentration but did not affect HDL−C, relative to an average American diet (all diets contained 34% calories as fat and 50% calories as carbohydrate) (Fig. 1C). In a more recent crossover study (Kien et al., 2014), subjects consumed diets enriched with high-palmitic acid oil and high-oleic acid oil, and LDL-C concentration was greater after the high-palmitic acid diet than after the high-oleic acid diet. Plasma HDL-C concentration was not different between dietary treatments but, as entry LDL-C and HDL-C concentrations were not reported, it is unknown if the oil blends altered LDL-C or HDL-C relative to the habitual diets.

3.2. Studies studying whole meat protein sources

Chiu et al. (2016) tested the effect of a DASH diet (Dietary Approaches to Stop Hypertension) and a higher fat, lower carbohydrate DASH diet (DASH-HF) on blood pressure and lipoprotein cholesterol concentration. The DASH diet (27% energy as fat) decreased plasma concentrations of total cholesterol, LDL-C, HDL−C, as well as LDL peak diameter, relative to the control diet (38% energy as fat). Thus, although the DASH diet decreased total cholesterol, it also decreased HDL-C and LDL-peak diameter. Relative to the DASH diet, the DASH-HF diet (40% energy as fat) decreased plasma TAG concentration and increased LDL peak diameter.

(O'Dea, Traianedes, Chisholm, Leyden, & Sinclair, 1990) demonstrated that feeding a very-low fat (9%EN as fat), lean beef diet decreased total cholesterol from 236 mg/dL to 189 mg/dL, and subsequently adding beef fat (as beef drippings from beef from commercial cattle) increased total cholesterol to 218 mg/dL. The changes in total cholesterol were due almost entirely to changes in LDL-C concentration. Morgan, Sinclair, and O'Dea (1993) subsequently reported that LDL-C concentration was 13–14% lower and HDL-C concentration was 20–25% lower when participants consumed the very-low fat, lean beef diet compared with their usual diet and LDL-C and HDL-C concentrations remained low even after the addition of olive oil or safflower oil (to 30%EN) to the very low-fat diet.

Other studies compared lean beef to other protein sources (Beauchesne-Rondeau, Gascon, Bergeron, & Jacques, 2003; Davidson, Hunninghake, Maki, Kwiterovich Jr., & Kafonek, 1999; Hunninghake et al., 2000; Mahon et al., 2007; Mangravite et al., 2011; Melanson, Gootman, Myrdal, Kline, & Rippe, 2003; Scott et al., 1994). Increased lean beef consumption in older adults decreased HDL-C concentration (Asp, Richardson, Collene, Droll, & Belury, 2012; Roussell et al., 2012; Scott et al., 1994). In Roussell et al. (2012), male and female participants were fed lean beef in a Beef in an Optimal Lean Diet study (in which total fat consumption was decreased) and reported depressions in both HDL-C and LDL-C concentrations (Fig. 1D).

3.3. Controlled trials with men and women consuming high-fat ground beef

We have conducted one uncontrolled longitudinal study (Adams et al., 2010) and two controlled RCT (Gilmore et al., 2011; Gilmore et al., 2013) comparing the effects of low-oleic acid ground beef to high-oleic acid ground beef at the same fat level on risk factors for CVD (Trials 1–3). In addition, we compared the effects of lower-fat, high-oleic acid ground beef to a higher-fat, low-oleic acid ground beef in a subsequent RCT (Trial 4) (Choi et al., 2018). Due to the popularity of ground beef in the U.S. diet, and because the fat level between treatments can be carefully controlled when formulating ground beef, we have chosen to incorporate ground beef interventions in our human studies. Approximately 50% of total beef consumption in the U.S. is in the form of ground beef, especially in low socioeconomic groups (USDA, 2005). Approximately 41% of ground beef consumed in the U.S.

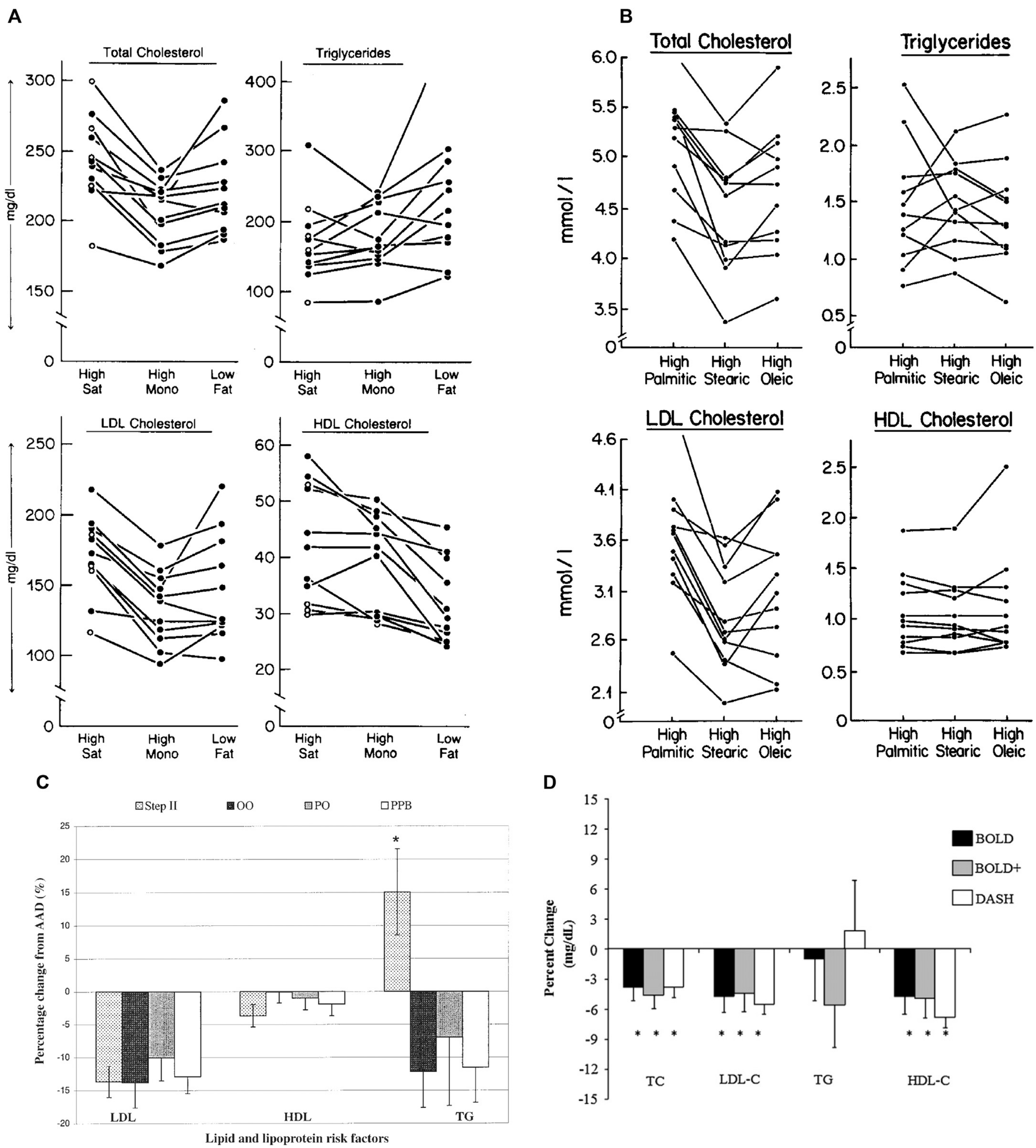

Fig. 1. A. Total, LDL, and HDL cholesterol and triglycerides in 11 patients during three dietary periods. Each diet consisted of a liquid formula supplemented with vitamins and minerals. High Sat, fat enriched with saturated fatty acids (40% calories as fat); High Mono, fat enriched with monosaturated fatty acids (40% calories as fat); Low Fat, 20% calories as fat, 63% calories as carbohydrate. Reprinted with permission from Grundy (1986). B. Plasma levels of total, LDL, and HDL cholesterol and triglycerides in 11 patients on High Palmitic, High Stearic, and High Oleic diets. All diets contained 40% calories as fat and cholesterol intake was less than 100 mg/d. Reprinted with permission from Bonanome and Grundy (1988). C. Effects of four cholesterol-lowering diets [Step II, olive oil diet (OO), peanut oil diet (PO), peanut butter diet (PPB), on LDL-C, HDL−C, and triglyceride (TG) concentration (n = 22) compared with the average American diet (AAD). *Significantly different from the other three diets. Reprinted with permission from Kris-Etherton et al. (1999). **D.** Mean percentage change (± SEM) for triglycerides (TG), total cholesterol (TC), LDL-cholesterol (LDL-C), and HDL-cholesterol (HDL-C) from the HAD (HAD: n = 33; DASH: n = 35; BOLD: n = 34; and BOLD+: n = 34). *Significantly different from the HAD, P < 0.05. BOLD, Beef in an Optimal Lean Diet; BOLD+, Beef in an Optimal Lean Diet plus additional protein; DASH, Dietary Approaches to Stop Hypertension; HAD, healthy American diet. Reprinted with permission from Roussell et al. (2012).

Table 1
Characteristics of low-oleic (Low) and high-oleic (High) ground beef used in four randomized, controlled trials[1].

Item[2]	Trial 1		Trial 2		Trial 3		Trial 4	
	Low	High	Low	High	Low	High	Low	High
Fatty acid, g/114 g patty								
Myristic, 14:0	1.00	1.08	0.99	0.66	0.74	0.58	0.86	0.55
Myristoleic, 14:1n-5	0.44	0.29	0.28	0.22	0.18	0.24	0.19	0.28
Palmitic, 16:0	9.67	9.28	8.78	7.89	6.06	5.32	6.46	4.53
Palmitoleic, 16:1n-7	1.24	1.76	0.85	0.97	0.64	1.00	0.91	0.90
Stearic, 18:0	6.14	4.01	5.57	4.31	4.46	2.67	4.05	2.15
Oleic, 18:1n-9	15.08	17.31	10.07	13.26	8.62	10.63	9.66	7.72
cis-Vaccenic, 18:1n-7	0.58	0.82	0.30	0.47	0.35	0.54	0.35	0.48
Linoleic, 18:2n-6	0.91	0.92	0.55	0.56	0.31	0.34	0.54	0.39
α-Linolenic, 18:3n-3	0.06	0.05	0.09	0.03	0.01	0.02	0.06	0.03
18:2*cis*-9, *trans*-11	0.17	0.17	0.18	0.14	0.17	0.18	0.15	0.19
18:2*trans*-10, *cis*-12	0.11	0.11	0.04	0.09	0.21	0.10	0.10	0.12
Total 18:1*trans*	1.73	1.25	1.07	0.69	1.59	1.09	1.59	0.83
Total SFA	17.3	14.8	15.3	12.9	11.3	8.6	11.9	7.6
Total MUFA	17.5	20.7	11.2	14.5	10.0	12.7	11.3	9.2
Total PUFA[2]	0.97	0.97	0.65	0.59	0.32	0.36	0.63	0.46
Total fat, g/114 g patty	40		29		24		25	18
MUFA:SFA[3]	0.95	1.31	0.71	1.10	0.86	1.43	0.96	1.24

[1] Data are means for at least n = 3 batches of ground beef for each trial. Ground beef was produced from: grass-fed (Low) or grain-fed (High) Wagyu and conventional cattle (Adams et al., 2010); plate and flank from grass-fed (Low) or grain-fed Angus steers (High) (Gilmore et al., 2011); chub pack ground beef (Low) or Akaushi ground beef patties (High (Gilmore et al., 2013); and from chub pack ground beef (Low) or Akaushi ground beef patties (High) (Choi et al., 2018).

[2] Sum of linoleic acid plus α-linolenic acid. Other, minor fatty acids are not listed in the table as they were not measured for every ground beef type. Eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3) were below levels of detection.

[3] 4MUFA:SFA = (14:1n-5 ± 16:1n-5 ± 18:1n-7 ± 18:1n-9) (14:0 + 16:0 + 17:0 + 18:0 + 20:0).

Table 2
Percent energy intake of specific fatty acids in which participants consumed low-oleic acid and high-oleic acid ground beef at the same fat levels (Trials 1–3)[1].

Item	Baseline[2]	Low-oleic	High-oleic
Energy, kcal/d	1987 ± 40	2029 ± 41	2029 ± 33
Percent energy			
Oleic acid, 18:1n-9	9.2 ± 0.2	11.1 ± 0.2***	11.4 ± 0.2***
Linoleic acid, 18:2n-6	3.5 ± 0.1	3.2 ± 0.1	3.2 ± 0.1
α-linolenic acid, 18:3n-3	0.42 ± 0.02	0.35 ± 0.01	0.33 ± 0.01
Eicosapentaenoic acid, 20:5n-3	0.05 ± 0.02	0.02 ± 0.01	0.01 ± 0.01*,**
Docosahexaenoic acid, 22:6n-3	0.09 ± 0.05	0.05 ± 0.02	0.01 ± 0.01*
Dietary n-6:n-3	9.79 ± 0.23	10.04 ± 0.23	10.34 ± 0.22
Dietary MUFA:SFA	0.90 ± 0.01	0.87 ± 0.01	0.97 ± 0.01*

Significantly different baseline concentrations, compared to their respective baseline values (entry or washout); paired *t*-test.

[1] Data are averaged across Trials 1–3.

[2] Baseline = average of entry and washout values. Entry and washout values were not different ($P > .10$).

* $P < .05$

** $P < .01$

*** $P < .005$

contains 23–30% fat, whereas 26% of ground beef consumed contains 15–22% fat (Beef Retail, 2010). Because of its relatively high fat content, ground beef comprises a primary source of SFA in the diet of U.S. consumers, and also contributes significantly to oleic acid intake (Nicklas, Hample, Taylor, Thompson, & Heird, 2004).

In all studies, ground beef was supplied to the participants in the form of 114-g (4-oz) frozen, vacuum-packaged ground beef patties for each entire diet period. The fatty acid composition of the ground beef patties for the four trials is listed in Table 1. All ground beef preparations had low amounts of α-linolenic acid (≤ 90 mg/patty) and the very-long-chain highly unsaturated n-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were below the level of detection (discussed below). For Trial 4, the lower-fat ground beef (from Akaushi cattle) had a higher MUFA:SFA than the higher-fat, commercial ground beef (1.24 vs 0.96, respectively), but it contained less oleic acid than the higher-fat ground beef due to its lower fat content.

For Trial 1 (Adams et al., 2010), ground beef patties were formulated from commercial lean trim and fat trim from grass-fed cattle (low-oleic acid) and from commercial lean trim and fat trim from grain-fed cattle (high-oleic acid). Men consumed low-oleic acid ground beef for 5 wk. and, following a 3-wk washout period, the men consumed the high-oleic acid ground beef for 5 wk. A two-period, controlled RCT design was used for Trials 2–4 (Fig. 2). Men of Trial 2 ($n = 27$) completed two ground beef interventions for 6 wk. each in a randomly assigned order with a 4-wk washout period between the ground beef interventions (Gilmore et al., 2011). Ground beef was produced from grass-fed steers that graded USDA Select (low-oleic acid) and from grain-fed steers that graded USDA Prime (high-oleic acid). The subjects for Trial 3 were postmenopausal women ($n = 17$), who completed two ground beef interventions for 5 wk. each in a randomly assigned order with a 4-wk washout period between the ground beef interventions (Gilmore et al., 2013). Ground patties were commercial chub pack ground beef (low-oleic acid) and ground beef produced from Akaushi cattle (high-oleic acid). Trial 4 compared lower-fat, high-oleic acid ground beef to high-fat, low-oleic acid ground beef. The subjects for Trial 4 were postmenopausal women ($n = 7$) and older men ($n = 5$), who completed two ground beef interventions for 5 wk. each in a randomly assigned order with a 4-wk washout period between the ground beef interventions. Ground patties were commercial chub pack ground beef (25% total fat; low-oleic acid) and ground beef produced from Akaushi cattle (18% total fat; high-oleic acid). The participants in all trials replaced one of their normal daily meat servings with a test ground beef patty.

Both ground beef types increased %EN from oleic acid but did not affect %EN from linoleic acid or α-linolenic acid. %EN from EPA and DHA was decreased in subjects consuming to high-oleic ground beef

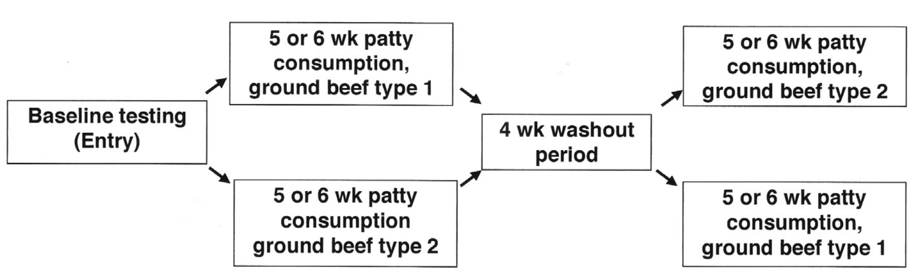

Fig. 2. Study design of Trials 2–4. From Gilmore et al. (2011, 2103) and Choi et al. (2018).

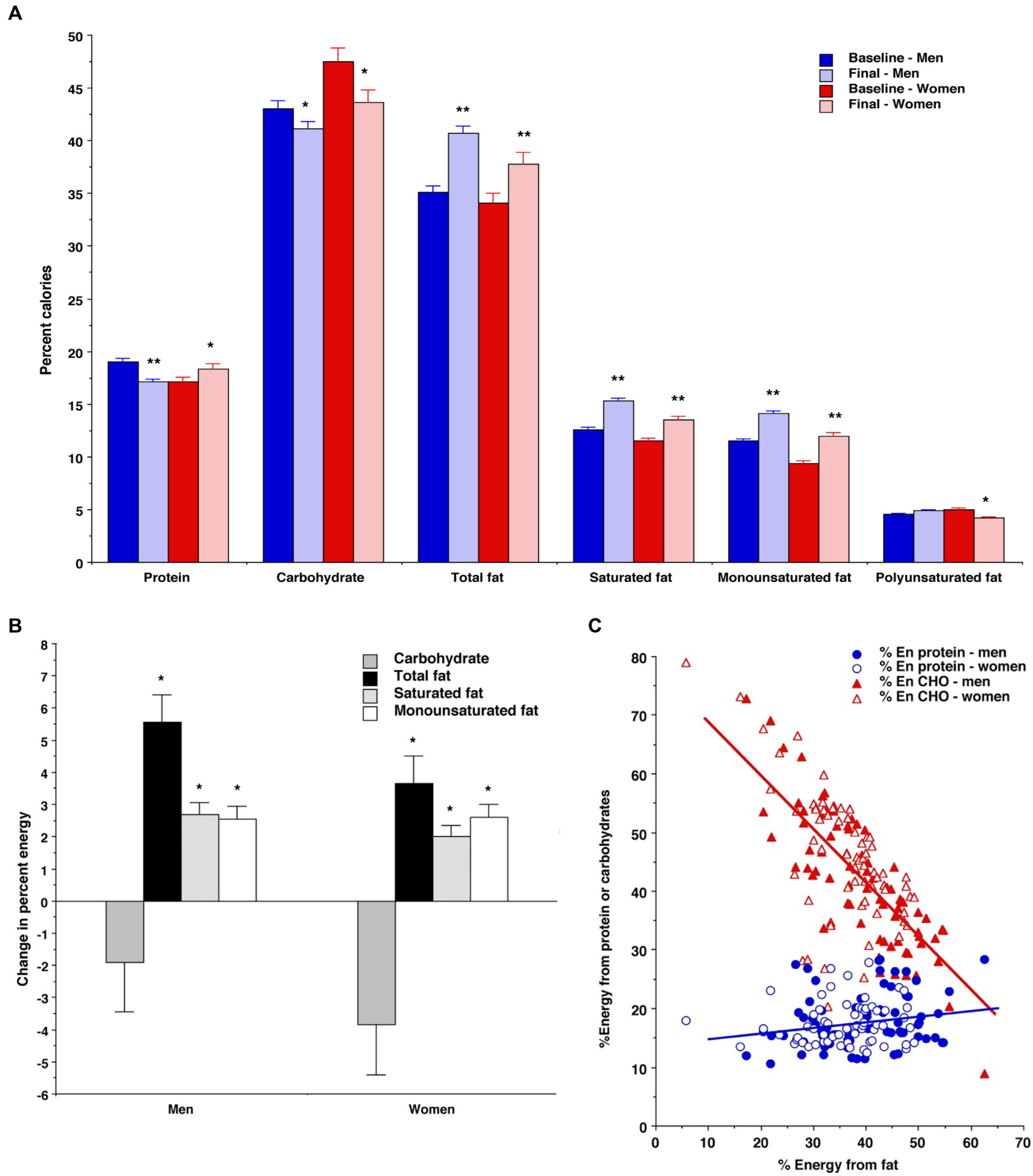

Fig. 3. A. Percent energy from baseline for carbohydrates, total fat, saturated fat, and monounsaturated fat for men ($n = 37$) and women ($n = 17$) for Trials 1–3. Data were pooled over ground beef type and are reported as the change in percent energy from baseline (entry and washout) during the ground interventions. Different from baseline $^{*}P < .05$, $^{**}P < .01$. B. Change in percent energy from baseline for carbohydrates, total fat, saturated fat, and monounsaturated fat for men and women for Trials 1–3. Data were pooled over ground beef type and are reported as the change in percent energy from baseline (entry and washout) during the ground interventions. Different from baseline $^{*}P < .05$. C. Percent energy from carbohydrates and protein as a function of percent energy from fat. Percent energy from carbohydrate was significantly, negatively correlated with percent energy from fat ($P = .001$). Percent energy from protein was significantly, positively correlated with percent energy from fat ($P = .006$). Data derived from diet records from Adams et al. (2010) and Gilmore et al. (2011, Gilmore et al., 2013); data include entry, washout, and values during ground beef interventions.

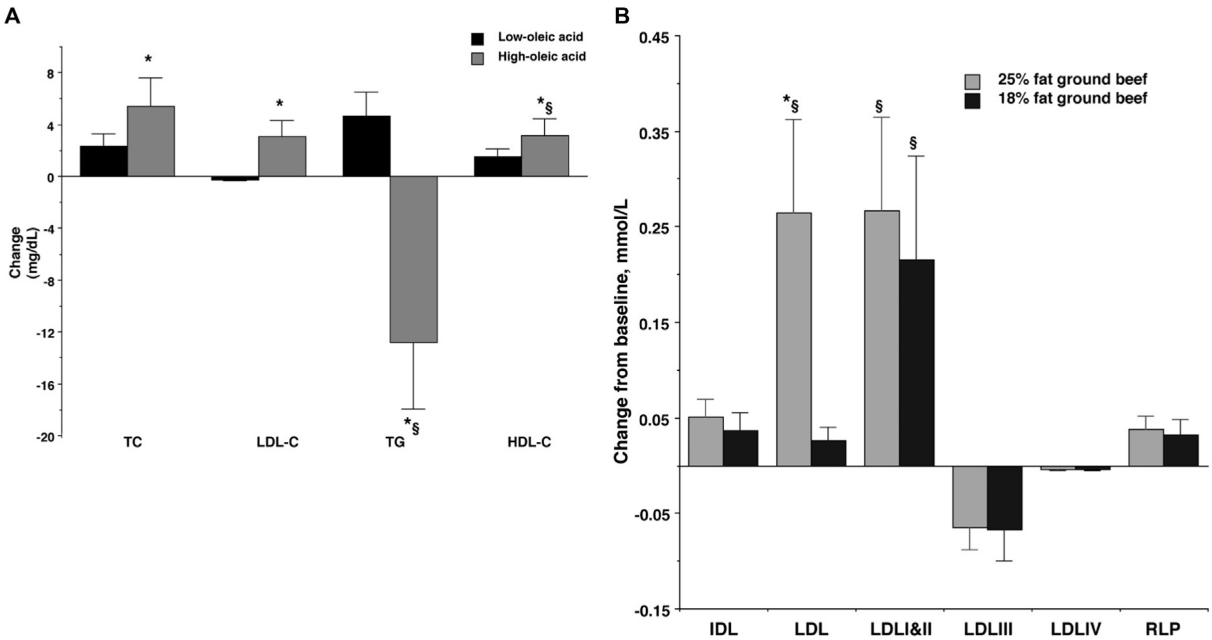

Fig. 4. A. Changes from baseline (entry and washout) for total cholesterol (TC), LDL-C, triglycerides (TG) and HDL-C for men (n = 42) and women (n = 24) would consumed low- and high-oleic acid ground (data pooled over ground beef type and gender). *Low-oleic acid ground beef significantly different from high-oleic acid ground beef; §Final values significantly different from baseline. Values were calculated from Adam et al. (2010), Gilmore et al. (2011, 2013), and Choi et al. (2018). B. −Changes from baseline (entry and washout) for intermediate-density lipoprotein-C (IDL), LDL-C, LDLI&II-C, LDLIII-C, LDLIV-C, and remnant lipoprotein-C (RLP). *Low-oleic acid ground beef significantly different from high-oleic acid ground beef; §Final values significantly different from baseline. Values were calculated from (Choi et al., 2018).

($P < .05$), but neither ground beef intervention affected the dietary n-6:n-3 (Table 2) ($P > .10$). Simopoulos (2002) reported that a dietary n-6:n-3 of 2–3:1 suppressed inflammation in patients with rheumatoid arthritis, an n-6:n-3 of 5:1 had a beneficial effect on patients with asthma, and an n-6:n-3 of 10:1 had adverse effects. Also, an n-6:n-3 of 4:1 was associated with a 70% decrease in total mortality. The overall baseline n-6:n-3 for our trials was approximately 10:1, which was not changed by the ground beef interventions. Thus, although scientific research supports decreasing the dietary n-6:n-3, this cannot be accomplished by changing the fatty acid composition of ground beef alone due to the low content of n-3 fatty acids in ground beef (discussed below).

Oleic acid accounted for most of the increase in %EN from MUFA during the ground beef interventions, and the overall dietary MUFA:SFA was greater ($P < .05$) during the high-oleic acid ground beef intervention. Current U.S. dietary guidelines recommend consuming less that 10% of total calories as SFA (Dietary Guidelines for Americans, 2015). During their entry/washout diets, the participants exceeded the recommended intakes of SFA (12.1%EN) and during consumption of the low-oleic acid ground beef, their intake of SFA increased further (to 14.8%EN) (Fig. 3A). Current dietary guidelines do not set limits for the intake of MUFA. However, the guidelines recommend that "saturated fats in the diet should be replaced with polyunsaturated and monounsaturated fats" (Dietary Guidelines for Americans, 2015), and consumption of all ground beef preparations in our trials increased oleic acid intake.

Nutrient intakes for the men and women of Trials 1–3 responded similarly to the ground beef interventions (data pooled across trials and ground beef types) (Fig. 3A). Subjects consumed less %EN as carbohydrate and more %EN as total fat, SFA and MUFA. Men consumed less %EN as protein during consumption of the test ground beef and women consumed more and women consumed less %EN as PUFA during consumption of the ground beef. The change in %EN from carbohydrate was not significant for men or women ($P > .10$) whereas change in %EN from total fat, SFA, and MUFA was significant ($P < .005$) for both genders (Fig. 3B). Based on diets records from Trials 1–3, %EN from carbohydrate was significantly, negatively correlated with %EN from fat ($P = .001$) (Fig. 3C). Percent energy from protein was significantly, positively correlated with percent energy from fat ($P = .006$). In general, subjects exchanged calories from carbohydrate for calories from fat. Percent energy from protein was significantly, positively correlated with percent energy from fat ($P = .006$), suggesting that fat intake increased as meat intake increased.

3.4. Plasma lipoprotein cholesterol

The change from baseline for total cholesterol, LDL-C, triglycerides, and HDL-C was calculated and averaged for Trials 1-3. In general, high-oleic acid ground beef increased total cholesterol, LDL-C and HDL-C, and decreased triglycerides from baseline (Fig. 4A). The very high-fat (35%), low-oleic acid ground beef produced from grass-fed cattle of Trial 1 numerically decreased plasma LDL-C (by 10 mg/dL) (Table 3). This could be considered a positive health benefit, but the low-oleic acid ground beef also decreased LDL particle size (from 19.7 to 18.1 nm), and rotating to the high-oleic ground beef diet only partially increased LDL particle size (to 18.4 nm). This suggests that the high-fat, low-oleic acid ground beef reduced the concentration of the more healthful, larger LDL particles (LDL-I and LDL-II), but this was not measured for Adams et al. (2010).

Neither ground beef type affected LDL-C concentration or LDL size in normocholesterolemic men (Trial 2) (Table 3). Women with larger LDL particles have lower RR for CVD than women with smaller LDL particles (Blake et al., 2002). Smaller, dense LDL particles (especially LDL-IV) have been identified as a predictor of CVD (Chaudhary et al., 2017). For this reason, we analyzed LDL-C sub-fractions in Trials 3 and 4. Sub-fractions LDL-III-C and LDL-IV-C were measured directly, and the concentration of LDL-I-C + LDL-II-C was calculated by difference: LDL-I-C + LDL-II-C = total LDL-C – (LDL-III-C + LDL-IV-C) (Choi et al., 2018). The concentration of LDL-I-C + LDL-II-C was not reported in Gilmore et al. (2013), but this information was calculated for this

Table 3
Plasma LDL and HDL cholesterol concentration and LDL diameter for four ground beef intervention trials in which participants consumed low-oleic ground beef and high-oleic ground beef in four randomized, controlled trials.

Item	Baseline[1]	Low-oleic	High-oleic
Lipoprotein cholesterol concentration, mg/dL			
Trial 1, n = 10			
LDL-C	142.8 ± 9.2	132.4 ± 13.2	144.0 ± 11.2
HDL-C	40.8 ± 2.4	35.2 ± 2.4*	42.4 ± 2.0*
Trial 2, n = 27			
LDL-C	121.6 ± 3.6	118.0 ± 6.4	120.4 ± 6.8
HDL-C	46.8 ± 0.8	48.0 ± 1.6	49.6 ± 2.0*
Trial 3, n = 17			
LDL-C	122.8 ± 6.0	127.6 ± 5.6	129.2 ± 6.4
LDL-I-C + LDL-II-C[2]	97.2 ± 5.6	99.7 ± 4.9	101.5 ± 5.2*
LDL-III-C	20.9 ± 1.3	21.9 ± 0.6	20.4 ± 0.8
LDL-IV-C	6.7 ± 0.2	6.9 ± 0.2	7.4 ± 0.3
HDL-C	60.4 ± 2.4	64.0 ± 2.4	64.8 ± 2.8*
HDL_{2a}-C	9.4 ± 0.3	9.1 ± 0.4	9.7 ± 0.4
HDL_{2b}-C	26.0 ± 1.0	26.9 ± 0.7	27.5 ± 0.9*
HDL_3-C	26.2 ± 0.4	27.8 ± 0.5	27.3 ± 0.5
Trial 4, n = 12			
LDL-C	124.5 ± 8.6	130.6 ± 8.5	132.3 ± 8.8
LDL-I-C + LDL-II-C[2]	92.9 ± 6.5	102.4 ± 7.4	102.7 ± 8.2§
LDL-III-C	23.3 ± 3.2	21.8 ± 1.3	20.3 ± 1.5
LDL-IV-C	8.3 ± 0.8	7.9 ± 0.9	8.5 ± 0.8
HDL-C	64.1 ± 5.6	61.1 ± 3.6	66.8 ± 4.6
HDL_{2a}-C	9.2 ± 1.9	7.6 ± 0.8	9.4 ± 1.5
HDL_{2b}-C	27.3 ± 4.1	24.6 ± 2.8	28.6 ± 3.5
HDL_3-C	27.6 ± 1.1	28.8 ± 1.2	28.8 ± 0.9
LDL diameter, nm			
Trial 1	19.7 ± 0.6	18.1 ± 0.7	18.4 ± 0.3§
Trial 2	26.0 ± 0.2	26.2 ± 0.2	26.3 ± 0.2
Trial 3	20.21 ± 0.01	20.17 ± 0.01	20.20 ± 0.01
Trial 4	20.11 ± 0.04	20.21 ± 0.04	20.17 ± 0.04§

[1] Baseline = average of entry and washout values. Entry and washout values were not different for any plasma lipoprotein cholesterol concentration (P > .35). 2Calculated total LDL-C – (LDL-III-C + LDL-IV-C).

* Significantly different baseline concentration (P < .05), compared to their respective baseline values (entry or washout); paired t-test.

§ Significantly different concentration (P < .05) from baseline, pooled across ground beef types.

review and is listed in Table 3. The sum of LDL-I-C + LDL-II-C was increased by the high-oleic ground beef in Trial 3, consistent with a numerical increase in LDL-C concentration (approximately 6 mg/dL). However, LDL size was unaffected by the ground beef interventions. For Trial 4, intake of both low-oleic acid and high-oleic acid ground beef numerically increased plasma LDL-C (by 6–8 mg/dL) and significantly increased LDL-I-C + LDL-II-C and LDL particle diameter (P < .05; data pooled across ground beef types) (Fig. 4B). These results suggest that increases in total LDL-C concentration may be considered healthful if LDL-I-C and/or LDL-II-C concentration is increased.

The low-oleic acid ground beef from grass-fed cattle in Trial 1 decreased HDL-C concentration and subsequent consumption of high-oleic acid ground beef increased HDL-C concentration (P < .05) (Table 3). In two of our three RCT (Trials 2 & 3), low-oleic acid ground beef had no effect on plasma HDL-C concentration whereas the high-oleic acid ground beef increased plasma HDL-C concentration. Furthermore, the high-oleic acid ground beef increased the concentration of the buoyant, more healthful HDL_{2b}-C in Trial 3. Trial 4 was unique among our RCT in that the high-oleic acid ground beef had no effect on HDL-C concentration, but the high-oleic acid ground beef of this trial contained only 7.72 g oleic acid/patty, versus 10.63–17.22 g oleic acid/patty for Trials 1–3 (Table 1). This suggests that there is a threshold level for ground beef oleic acid (and/or total dietary MUFA:SFA) to increase HDL-C concentration.

4. Production of beef enriched with oleic acid

4.1. Diet and time fed a high-concentrate diet

We and others have documented that feeding beef cattle a corn-based diet increases the amount of oleic acid and/or the MUFA:SFA in muscle and adipose tissue (Brooks, Choi, Lunt, Kawachi, & Smith, 2011; Chung et al., 2006; Duckett, Pratt, & Pavan, 2009; Huerta-Leidenz et al., 1996; Xie et al., 1996; Zembayashi, Nishimura, Lunt, & Smith, 1995). (Huerta-Leidenz et al., 1996) reported that the MUFA:SFA of subcutaneous (s.c.) adipose tissue in steers increases with time on a grain-based diet, and Duckett et al. (2009) reported that, relative to cattle fed pasture only, s.c. adipose tissue from concentrate-fed cattle had a greater MUFA:SFA and *stearoyl-CoA desaturase-1* (*SCD1*) gene expression. Similarly, Brooks et al. (2011) demonstrated that the MUFA:SFA and *SCD1* mRNA levels of intramuscular (i.m.) and s.c. adipose tissue were unchanged when Angus steers were fed pasture/hay and only increased when steers were transitioned to a corn-based finishing diet (Fig. 5A). The MUFA:SFA increased steadily for several adipose tissue depots with time fed a corn-based finishing diet (Fig. 5B) (Smith et al., 2012) and, in Chinese Yanbian Yellow cattle, the MUFA:SFA (Fig. 5C) and *SCD1* gene expression (Fig. 5D) in the chuck, round, and loin muscles increased with time fed a corn-based, concentrate diet (Li et al., 2018). Increased MUFA:SFA are associated with greater marbling scores (i.e., more i.m. lipid) and greater s.c. adipose tissue adipose tissue depth over the *M. longissimus dorsi* (Brooks et al., 2011; Li et al., 2018; Smith et al., 2012). Thus, in these studies, an elevated MUFA:SFA was indicative of a greater total amount of oleic acid in i.m. and s.c. adipose tissue. We and others have demonstrated that feeding corn-based finishing diets to beef cattle upregulates *SCD1* gene expression (Brooks et al., 2011; Chung, Lunt, Kawachi, Yano, & Smith, 2007; Duckett et al., 2009; Martin, Lunt, Britain, & Smith, 1999; Smith et al., 2012), which is responsible for the greater concentration of oleic acid in muscle and adipose tissue from corn-fed cattle.

4.2. n-3 fatty acids in beef

Grass-feeding and supplementing finishing diets with high-α-linolenic acid (18:3n-3) oils increases the amount of n-3 fatty acids in beef. Leheska et al. (2008) reported that strip steaks from the grain-fed cattle contained more i.m. lipid (%IML) than strip steaks from grass-fed cattle (4.4 vs 2.8% IML, respectively) confirming that grass feeding depresses marbling. Beef from grass-fed cattle contains elevated *trans*-fatty acid (TFA) and also contained greater amounts of SFA, the latter resulting in a lower MUFA:SFA (Adams et al., 2010; Brooks et al., 2011; Leheska et al., 2008; Turk & Smith, 2009). For our two studies that compared beef from grass-fed and grain-fed cattle, 114-g ground beef patties from grain-fed cattle contained 2–3 g more oleic acid and 0.1 to 0.8 g less TFA than ground beef from grass-fed cattle (Table 1). Conversely, beef from grass-fed cattle contains greater quantities of α-linolenic acid.

De Smet and Vossen (2016) summarized other research that reported n-3 fatty acids in livestock species and concluded that for ruminants, n-3 fatty acids were 47% higher in organic beef (likely due to grazing/forage-based diets) than in conventional beef. Ground beef produced from grass-fed and grain-fed cattle contained 676 and 207 mg α-linolenic acid/100 g total fatty acids, respectively (Leheska et al., 2008). Ground beef from grass-fed and grain-fed steers (Trial 2) contained 90 and 30 mg α-linolenic acid/114 g patty, respectively. These levels were similar those achieved by McAfee et al. (2011) in mince from grass-fed and concentrate-fed cattle (73 and 32 mg α-linolenic acid/100 g mince, respectively), and those authors reported significant increases in α-linolenic acid concentrations in plasma and platelets of men following consumption of beef from grass-fed cattle. The U.S. daily recommended intake of α-linolenic acid is 1.4 g/d for women and 1.6 g/d for men (Dietary Guidelines for Americans, 2015), so ground beef produced from grass-fed cattle contains less than 10% of the U.S.

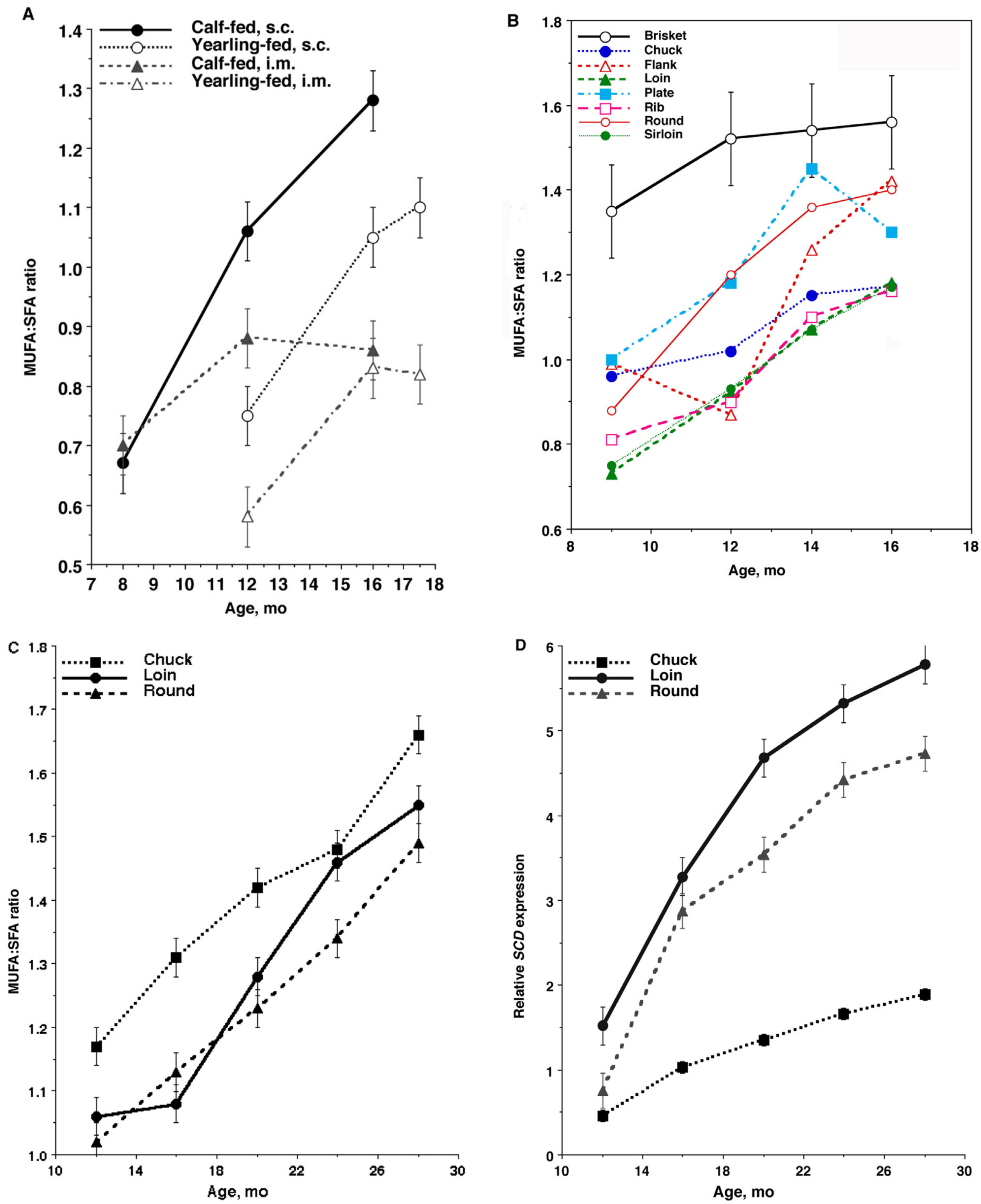

Fig. 5. A. Monounsaturated:saturated fatty acid (MUFA:SFA) of lipids from subcutaneous (s.c.) and intramuscular (i.m.) adipose tissues of steers adapted to a corn-based finishing diet as calves (calf-fed) or fed native pasture until 12 mo of age (yearling-fed). Samples were from s.c. adipose tissue overlying the 8th – 10th thoracic rib section of the LM and from i.m. adipose tissue dissected from the same thoracic rib section. Each data point is the mean of 4 or 5 steers. Data derived from Brooks et al., 2011. B. MUFA:SFA of lipids from eight subcutaneous adipose tissue depots of Angus steers sampled at 9, 12, 14, and 16 mo of age. Each data point is the mean for n = 4 steers. Data derived from Smith et al., 2012. C. MUFA:SFA and D. stearoyl-CoA desaturase (*SCD*) levels in chuck, loin, and round muscle of steers sampled at 12, 16, 20, 24, and 28 mo of age. Each data point is the mean for $n = 10$ steers. Data derived from Li et al. (2018). For all figures, pooled SEM is affixed to the symbols.

recommended daily intake of α-linolenic acid.

We previously fed steers with casein-formaldehye-protected canola oil (50% oleic acid, 7% α-linolenic acid), with the primary goal of increasing oleic acid in beef (Gilbert, Lunt, Miller, & Smith, 2003). Oleic acid was not increased relative to a corn-based, control diet, but α-linolenic acid increased from 0.10 to 0.99% total fatty acids in s.c. adipose tissue and from 0.10 to 0.93% in i.m. adipose tissue. Archibeque, Lunt, Gilbert, Tume, & Smith, (2005) fed flaxseed to steers, which increased α-linolenic acid from 0.12 to 0.79% total fatty acids in s.c. adipose tissue and increased α-linolenic acid from 0.13 to 0.78% total fatty acids in i.m. adipose tissue, relative to control steers. Similarly, the percentage α-linolenic acid increased from 0.07 to 0.15% total fatty acids in *M. longissimus dorsi* in steers fed 3% soybean oil, relative to control steers; however, soybean oil did not increase α-linolenic acid in s.c. or i.m adipose tissue (Choi et al., 2013, 2016).

Costa et al. (2020) fed soybean, sunflower and linseed oil (3.5% of the diet) to beef cattle. Only the linseed oil supplement increased α-linolenic acid in the *M. longissimus dorsi*; the content of EPA and DHA was not affected by the supplementary oils, relative to the control diet. Based on lipid content (1.89%IML) and percent α-linolenic acid/100 g total fatty acids (0.88%), *M. longissimus dorsi* from the linseed oil-supplemented cattle contained 16.6 mg α-linolenic acid per 100-g serving of beef. Similarly calculated, 100 g beef from the linseed oil-supplemented cattle contained 7.9 mg EPA plus DHA. The conversion of α-linolenic acid to EPA and subsequently to DHA is less than 5% in humans (Brenna, 2002), but to our knowledge the rate conversion of α-linolenic acid to EPA and DHA has not been established for ruminant species. The results of Costa et al. (2020) suggest that this rate of conversion is very low in beef cattle.

Previously, Leheska et al. (2008) reported that EPA was undetectable in ground beef from grain-fed cattle but there was 13 mg EPA/100 g total fatty acids in ground beef from grass-fed cattle; DHA in ground beef from grain-fed and grass-fed cattle was below their level of detection. McAfee et al. (2011) reported that mince from grass-fed and concentrate-fed cattle contained 15 and 6 mg EPA/100 g mince, respectively, and DHA was undetectable. However, beef steaks from grass-fed and concentrate-fed cattle contained 13 and 6 mg EPA/100 g steak, respectively, and 0.4 and 1.0 mg DHA/100 g steak, respectively (McAfee et al., 2011). Vahmani et al. (2015) reported that strip steaks from conventionally raised cattle contained 110 mg EPA/100 g fatty acids and 31 mg DHA/100 g fatty acids; a previous review by Wood et al. (2003) reported similar levels EPA and DHA for beef steaks. Total lipid content of the strip steaks was not reported by Vahmani et al. (2015) but if the strip steaks contained 5% fat, a 100-g portion of the strip steak would have contained 13 mg α-linolenic acid, 5 mg EPA and less than 2 mg DHA. Wood et al. (2008) previously demonstrated that EPA and DHA are concentrated in the phospholipid fraction of bovine muscle; neither EPA nor DHA was detected in the neutral lipid fraction of bovine muscle.

Concentrations of EPA and DHA in ground beef from our human trials were below detectable levels, even in ground beef from grass-fed cattle. In our laboratory, the lower limit of detection for fatty acids is 0.05% of total fatty acids. For a ground beef patty containing 25% fat, this would be equivalent to 0.25 mg fatty acid/patty. It is possible that trace amounts of DHA and/or EPA were present in the ground beef produced for our studies (at least for ground beef from grass-fed cattle) but, due to the high fat content (hence, high neutral lipid content) of the ground beef, we were unable to quantify amounts of these trace fatty acids. Dietary Guidelines for Americans (2015) recommends 227 g/d of a variety of seafood, which would provide approximately 250 mg/d of EPA plus DHA. A 114-g serving of salmon contains over 2 g of total n-3 fatty acids (primarily EPA and DHA) (Kris-Etherton, Harris, & Appel, 2002) and we conclude that ground beef from grass-fed cattle or high-α-linolenic acid oil would not be a significant dietary source of EPA or DHA.

4.3. Other sources of high-oleic acid beef

The early studies described above provided proof of concept the increasing %EN from oleic acid as an oil supplement depresses plasma LDL-C concentration and may increase HDL-C concentration in human studies. Consumption of SFA increases HDL-C concentration but also increases LDL-C concentration. Thus, human studies incorporating beef products cannot distinguish effects of %EN from SFA and MUFA on HDL-C concentration, except that the change in HDL-C concentration always was greater following a high-oleic acid ground beef intervention. As described above, beef from highly marbled, grain-fed cattle contains elevated amounts of oleic acid. In addition, beef from cattle with Japanese genetics (Black Wagyu and Akaushi [Red Wagyu]) contains greater amounts of oleic acid (Smith et al., 2006; Sturdivant, Lunt, K, & Smith, 1992; Xie et al., 1996). The brisket and ground beef produced from the brisket also are naturally enriched with oleic acid, such that the MUFA:SFA of the brisket approaches values seen in beef from American Black Wagyu or Akaushi cattle (Blackmon, Miller, Kerth, & Smith, 2015; Kerth, Harbison, Smith, & Miller, 2015; Smith et al., 2006; Smith et al., 2012; Turk & Smith, 2009). The availability of high-oleic acid beef in the marketplace provides consumers with an reasonable alternative for increasing oleic acid in the diet, in addition to consuming high-oleic acid oils.

5. Conclusion

Large-scale retrospective studies that have indicated no association between high-fat, unprocessed red meat intake and risk factors for CVD. Early human trials documented that supplementing diets with high-oleic acid oils decreased LDL-C concentration and frequently elevated HDL-C concentration, whereas our later trials demonstrated that high-oleic acid ground beef interventions consistently increased HDL-C concentration. The amount of oleic acid can be increased in beef realistically by feeding a corn-based diet, and beef from Black Wagyu or Akaushi cattle and the brisket contain naturally high concentrations of oleic acid.

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Declaration of Competing Interest

The authors declare that they have not conflict of interest.

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