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Safety of Low-Carbohydrate Diets

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Summary

Low-carbohydrate diets have re-emerged into the public spotlight and are enjoying a high degree of popularity as people search for a solution to the population’s ever-expanding waistline. The current evidence though indicates that low-carbohydrate diets present no significant advantage over more traditional energy-restricted diets on long-term weight loss and maintenance. Furthermore, a higher rate of adverse side-effects can be attributed to low-carbohydrate dieting approaches. Short-term efficacy of low-carbohydrate diets has been demonstrated for some lipid parameters of cardiovascular risk and measures of glucose control and insulin sensitivity, but no studies have ascertained if these effects represent a change in primary outcome measures. Low-carbohydrate diets are likely effective and not harmful in the short-term and may have therapeutic benefits for weight-related chronic diseases though weight loss on such a program should be undertaken under medical supervision. While new commercial incarnations of the low-carbohydrate diet are now addressing overall dietary adequacy by encouraging plenty of high-fibre vegetables, fruit, low glycaemic index carbohydrates and healthier fat sources, this is not the message that reaches the entire public nor is it the type of diet adopted by many people outside of the world of a well-designed clinical trial. Health effects of long-term ad hoc restriction of inherently beneficial food groups without a concomitant reduction in body weight remains unanswered.
Introduction

While the concept of low-carbohydrate diets have been with us for many decades, they appear to have had a resurgence in recent times and are currently generating a wide-degree of public interest and media attention; fuelled by the rising tide of obesity and insulin resistance in the general population. There are many variations on just what a ‘low-carbohydrate’ diet is. The most widely used low-carbohydrate diet is the one advocated by Robert C. Atkins, M.D. His 1972 book *Dr. Atkins’ Diet Revolution* sold millions of copies within the first two years (1). His 1998 update, *Dr. Atkins’ New Diet Revolution* has sold tens of millions of copies world wide (2). Many of the popular low-carbohydrate diets have common recommendations in that they advise consuming fat as the primary macronutrient for the body, with most of the remaining energy to be made up from protein. Ad hoc restriction of carbohydrate may also be done by using such simple rules as ‘no carbohydrates after 2 PM’, as a way of self-restricting dietary carbohydrate. The term ‘low-carbohydrate diet’ is a subjective term with different dieting approaches advocating variable quantities of carbohydrate to consume. For the purpose of this review, a ‘low-carbohydrate’ diet is considered to be a diet containing less than 60 g/d of carbohydrate with typical percentages by nutrient contribution to energy being 55-65% for fat, 25-35% for protein and less then 10% for carbohydrate.

While a low-carbohydrate diet does severely restrict carbohydrate; total protein and fat intake are only raised by a small degree at the cost of a decrease in the overall nutritional adequacy of the diet (3). The main premise of most popular low-carbohydrate diets is that a reduction in carbohydrates will result in a lowered basal insulin level and hence promote more triglyceride lipolysis into free fatty acids - leading to fat loss in overweight people. In reality, these diets work in the short term as they result in a reduction in total kilojoule intake which inherently leads to weight loss due to an energy deficit (4, 5). Factors that are thought to contribute to the greater weight loss that is consistently seen in the initial stages of a low-carbohydrate diet are hypothesised to be due to a combination of the satiating effect of protein, possible appetite suppression due to ketosis, reduced kilojoule intake due to restrictive food choices and great water and glycogen losses (6-8).

Studies on the health implications of low-carbohydrate diets are few in number while none have examined the effects of this type of dieting approach for greater than 12 months in a normal adult population; which is
not sufficient to assess whether dieters are at risk of chronic health problems. Most of the available data to do with long-term safety of low-carbohydrate diets has arisen from the application of ketogenic diets in the treatment of paediatric epilepsy (9). The diet used in this patient group is a high-fat, adequate protein, low-carbohydrate diet designed to mimic the biochemical changes that occur during starvation. Studies of children who have followed a ketogenic diet for management of epilepsy found that about 50% will continue on the diet for at least a year. Reasons for discontinuing the ketogenic diet were due to either a lack of efficacy or the restrictive nature of food choices. Common adverse events attributed to the diet include dehydration, gastrointestinal problems, hypoglycaemia, cognitive effects, constipation, hyperlipidaemia, impaired neutrophil function, amenorrhea, urolithiasis, optic neuropathy, osteoporosis and water-soluble vitamin deficiencies (10, 11). One study quantified adverse events in 129 paediatric patients following a low-carbohydrate diet and found the frequency of some common complications were: dehydration (46.5%); gastrointestinal discomfort such as nausea, vomiting, diarrhoea and constipation (38.7%); hyperuricaemia (26.4%); hypertriglyceridaemia (27.1%); hypercholesterolaemia (14.7%); osteopenia (14.7%); infectious disease (9.3%); symptomatic hypoglycaemia (26.4%); and iron-deficiency anaemia (1.6%) (12). The authors of this aforementioned study reported that many of these described symptoms were transient and could be improved with conservative management.

A systematic review published in 2003 examined the efficacy and safety of low-carbohydrate diets (5). Evaluation of 38 dietary intervention studies where intake of carbohydrate was ≤ 60 g/d concluded that there was insufficient evidence to make recommendations for or against this diet. The authors of the study also concluded that weight loss on low-carbohydrate diets is predicted by kilojoule intake, diet duration, and baseline weight, but not by carbohydrate content. Constraints of the review were the limited number of trials (n=5) that evaluated the efficacy of these diets for greater than 90 days. Lower-carbohydrate diets were not associated with adverse effects on serum lipids, fasting serum glucose or blood pressure although due to the small number of studies published at the time reporting on these outcomes, the systematic review lacked the power to detect small changes in these measures.

Subsequent studies to those reviewed by Bravata et al (5) have re-examined the efficacy of low-carbohydrate diets on metabolic risk factors over time periods of 6 to 12 months and while not showing a superior benefit
over low-fat diets in terms of weight loss after 1 year, greater improvements in certain metabolic risk factors including triglycerides, HDL-cholesterol and insulin response have been observed (13-17). Markers apart from the metabolic profile need to be examined when evaluating the efficacy and safety of low-carbohydrate diets. Such evaluations should include an assessment of known diet-disease links taking into account the nutrient composition of a low-carbohydrate diet and how these relationships may relate to the short- and long-term health of individuals who adhere to this type of diet over months to years; such aspects will be examined in this review.

**Nutritional Adequacy**

Low-carbohydrate diets are at greater risk of being nutritionally inadequate as they recommend restriction of food choices. Typically, low-carbohydrate diets are low in fibre, thiamin, folate, potassium, calcium, magnesium, iron, and vitamins A, E, and B₆ (4, 14, 17). Low-carbohydrate diets are also usually higher in saturated fat and cholesterol with protein mainly being derived from animal sources (4). Some popular low-carbohydrate diets recommend that participants take a daily multivitamin supplement and this advice would seem sensible to help protect against the risk of micronutrient deficiencies.

Comparison of a range of popular diets has revealed that low-carbohydrate diets (defined as less than 30% of energy from carbohydrate) fared worse in terms of dietary adequacy (as defined by the amount of inclusion of the five major foods groups and alignment with the U.S. Dietary Guidelines) (3). The study gave a rating, known as the Healthy Eating Index (HEI), to the different dietary types: high-carbohydrate diets received a HEI score of 82.9 (highest possible score is 100) which was the highest score recorded for the range of diets analysed while low-carbohydrate diets received a score of 44.6 (the lowest recorded score in the study).

An interesting finding from the aforementioned study was that people who followed a low-carbohydrate diet had the highest BMI. A consumer health and dieting survey also found that people who reported that they were on a carbohydrate-reduced diet were more likely to be obese, have diabetes, high blood pressure and have high cholesterol compared to those not following a low-carbohydrate diet (18). Such cross-sectional findings in no way provide evidence for a cause-and-effect relationship between dieting practices and BMI and health, but likely describe the type of person that may try a low-carbohydrate dieting approach. Further
characterisation of population groups that follow a low-carbohydrate diet, and their reasons for doings so, would be of great interest.

There is a paucity of longitudinal studies evaluating successful long-term weight loss with different dieting strategies. The U.S. National Weight Control Registry, which compiles details of individuals who have successfully lost more than 13 kg for a year or more, analysed the dieting strategies of 2,681 members since the registry was first established in 1994 (19). Entry into the database is voluntary and self-reported and requires the registrants to have already successfully lost the weight and kept it off before they can register. It was found that less than 1% of these successful people had followed a diet classified as ‘low carbohydrate’ (defined as 24% or less total daily kilojoules coming from carbohydrate) suggesting that this type of diet is not realistic for the achievement of long-term weight loss.

A low-carbohydrate is inherently one low in fibre-containing carbohydrate foods such as wholegrains, cereals and fruit. Several epidemiological studies have found that diets rich in wholegrains may protect against cardiovascular disease (CVD), stroke and type 2 diabetes (20). At present though, the long-term health effects of a low-carbohydrate diet of limited nutritional quality are unknown. Restrictive low-carbohydrate diets are unlikely to present any serious health problems related to the nutrient composition of the diet as dietary inadequacy can be tolerated in the short-term to achieve weight loss goals, but maintenance diets should include the correct balance of micronutrients to ensure optimal health.

**Cardiovascular Health**

The question of if low-carbohydrate diets increase the risk of CVD is the most raised issue by researchers and the general public alike. Numerous studies have been undertaken evaluating the efficacy of low-carbohydrate weight-loss diets in improving the CVD risk profile of individuals. One of the consistent findings reported in the literature is the ability of low-carbohydrate diets to significantly lower triglyceride levels (13-17, 21-24). The majority of these studies though have been of short duration (weeks to months) and only two have been of 12 months in duration (14, 15). In regards to cholesterol components, low-carbohydrate diets tend to result in increases in HDL-cholesterol while the effect on LDL-cholesterol is
variable with most studies showing no significant difference in changes when compared to a low-fat diet. (13-17, 21, 22).

In a randomised study evaluating a low-carbohydrate diet against a low-fat diet over 6 months in 132 severely obese subjects with a high prevalence of diabetes and the metabolic syndrome, Samaha et al (13) found greater weight loss and improvements in triglycerides and insulin sensitivity in the low-carbohydrate group. No adverse effects on other serum lipids were seen in either group. Of note, the study design involved regular group nutrition counselling sessions; weekly for the first 4 weeks then monthly after this. The overall amount of weight loss was small (5.8 kg versus 1.9 kg; low-carbohydrate diet and low-fat diet respectively; P = 0.002) with a high dropout rate for both groups (33% and 47%; low-carbohydrate diet and low-fat diet respectively; P = 0.10). The greater amount of weight loss in the low-carbohydrate group predicted some, but not all, of the metabolic improvements. In a follow-up study by the same research group, it was found that differences in weight loss with the same cohort of subjects did not differ significantly between the two groups after 12 months (5.1 kg versus 3.1 kg; low-carbohydrate diet and low-fat diet respectively) yet favourable HDL-cholesterol and triglyceride changes were maintained in the low-carbohydrate group (14).

A similar study evaluating low-carbohydrate versus low-fat dieting approaches followed 63 obese subjects over 12 months; however, professional contact over the course of the study was limited to replicate the approach used by most dieters in the ‘real world’ (15). Subjects on the low-carbohydrate diet lost more weight at 3 and 6 months, but the difference was not significant at 1 year (4.4% of initial body weight versus 2.5%; low-carbohydrate diet and low-fat diet respectively). No differences between the two groups were seen in total cholesterol, LDL-cholesterol, blood pressure or insulin sensitivity throughout most of the study while greater improvements in HDL-cholesterol and triglycerides were observed throughout most of the study in the low-carbohydrate group. Benefits of the low-carbohydrate diet on triglycerides and HDL-cholesterol appear greater than the benefit of weight loss alone and suggest a macronutrient-related effect of a low-carbohydrate diet. Attrition rates after 12 months for both diet groups were high (39% and 43%; low-carbohydrate diet and low-fat diet respectively). The low-carbohydrate diet produced greater weight loss at 6 months; however, the lack of positive benefit by one year, combined with the absence of significantly higher
levels of urinary ketones in this group after 3 months, suggests that long-term adherence to a low-carbohydrate diet may be difficult to maintain.

In a 24-week study involving 120 obese, relatively healthy hyperlipidaemic individuals, a low-carbohydrate diet resulted in greater weight loss than a low-fat diet (12.9% versus 6.7%) and improved outcomes in triglyceride and HDL-cholesterol levels while LDL-cholesterol levels remained stable (16). Both groups attended twice-monthly group meetings at which they received additional dietary counselling as well as exercise recommendations while the low-carbohydrate group received nutritional supplementation with multivitamins, essential oils (containing fish oil) and a herbal supplement. Dropout rates were 24% for the low-carbohydrate group and 43% for the low-fat group (P = 0.02). The major reason for the significant difference in dropout rates between the two groups was that 25% of those following the low-fat diet reported their reason for dropping out was because of difficulties in adhering to the meeting schedule compared with 7% from the low-carbohydrate group who dropped out for the same reason. Three participants in the low-carbohydrate group dropped out of the study because of adverse events related to either elevated LDL-cholesterol levels or feelings of shakiness and uneasiness. Symptomatic side-effects occurred significantly more frequently in the low-carbohydrate group and included: constipation, headache, halitosis, muscle cramps, diarrhoea, general weakness and rash. The nutritional supplements given to the group on the low-carbohydrate diet may have had some effect on the final study result as no attempt was made to correct for this. A study of a similar length involving 53 healthy, obese women found that a low-carbohydrate was superior for weight loss over 6 months compared to a low-fat diet (8.5 kg versus 3.9 kg); however, while improvements were seen, no significant differences were observed in blood pressure, lipids or fasting glucose between the groups (17).

While the previously described studies reported on various blood markers for CVD risk and insulin action, no evaluation was made of other important health markers such as exercise performance, bone health, renal function or quality of life. Importantly, all of the studies have been performed with obese people so the benefit of such dieting approaches in otherwise health overweight individuals is unknown. Furthermore, while there appears to be favourable macronutrient-related changes in some lipid parameters with a low-
carbohydrate diet, it is not possible to currently ascertain the exact contribution of macronutrient-specific effects due to confounding issues of greater short-term weight loss in some studies (13, 15).

The changes in triglyceride and HDL-cholesterol levels seen on a low-carbohydrate diet, while good, need to be put in the context of the high drop-out rates on this diet; albeit on a par with the drop-out rates on a low-fat dieting approach also. Some of the improvements in triglycerides can be explained by use of omega-3 fish oil supplements in several of the studies while further reduction in triglycerides in subjects following the low-carbohydrate diet may have been magnified due to the greater initial weight loss in this group (16, 21, 25). The clinical significance of carbohydrate-induced hypertriglyceridaemia in individuals who are otherwise healthy is an area of great debate and currently no firm conclusions can be made about long-term heart disease risk. Importantly, in many people the effect of carbohydrate feeding on triglyceride synthesis can be significantly diminished by weight loss, exercise and dietary restriction irrespective of the macronutrient composition of the diet (26, 27).

One question that has not been answered by weight-loss studies is what happens to CVD risk factors when weight loss ends and individuals maintain an isoenergetic diet of similar macronutrient ratios. One 6-week study involving 20 normal weight and lipidaemic men who switched from their habitual diet to a ketogenic diet (<50 g carbohydrate/day), found favourable improvements in fasting triglycerides (33% decrease), post-prandial lipaemia (28% decrease) and fasting serum insulin (34% decrease) with no significant changes in LDL- and HDL-cholesterol (24). Of note, in subjects with a predominance of the atherogenic small LDL particles, there was a significant increase in the less-atherogenic larger-diameter LDL particles. No lipid changes were seen in the control group and the authors suggest that the short-term application of a low-carbohydrate diet does not have a deleterious effect on CVD risk profile. One confounding factor in this study was a significant weight loss of 2.2 kg in the intervention group which would predict some of the favourable lipid changes. A similar study performed by the same research group failed to demonstrate a superior benefit of a hypoenergetic low-fat diet or a low-carbohydrate diet after 4 weeks on post-prandial lipaemia, total-cholesterol/HDL-cholesterol ratio, fasting triglycerides, oxidised LDL and LDL subclass distribution (28).
The only long-term studies evaluating markers of CVD risk have been in epileptic children maintained on a ketogenic diet for management of epilepsy for periods up to 2 years. Findings were significant increases in atherogenic apoB-containing lipoproteins and a decrease in antiatherogenic HDL-cholesterol; however, it was not possible to conclude if these changes affected atherogenic and inflammatory processes (29). A study by Best et al (30) investigating potential cardiac complications in 20 paediatric patients on a ketogenic diet for management of epilepsy found cardiac arrhythmias (as defined by changes in the QT interval of an ECG) in three of the patients on the diet. Prolongation of the QT interval is of clinical importance due to an increased risk for ventricular dysrhythmia and sudden death (30, 31). Such changes in the QT interval have also been observed in anorexia nervosa and very-low-calorie diets for obesity; both metabolic states where ketosis is very likely to occur and deaths have been reported due to cardiac arrhythmias (32-34). The safety of low- and very-low-carbohydrate ketogenic diets needs to be explored further, especially in light of the lack of information on electrolyte and physiologic changes during such dieting regimes.

Any diet that results in weight loss will elicit a favourable response on blood lipid parameters although macronutrient content (particularly saturated fat content) can have independent effects (35, 36). Low-carbohydrate diets appear to have favourable effects on some blood lipids in the short- to medium-term while the effect on LDL-cholesterol is variable with two studies showing no significant improvement of LDL-cholesterol after three months compared to a favourable lowering seen with a low-fat diet (15, 22). Studies conducted for longer periods of time though have failed to show significant differences in LDL-cholesterol changes when direct comparison is made against a low-fat diet (13-16). Low-carbohydrate dieters typically show increases in HDL-cholesterol which is the opposite to that observed on a low-fat diet; however, once weight stabilisation occurs on a low-fat diet, HDL-cholesterol levels usually increase (36). At least one study has shown that plasma homocysteine levels are raised on a low-carbohydrate weight-loss diet and lowered on a low-fat diet after 8 weeks although CRP levels fell on both diets (37). At present, the increase in HDL-cholesterol associated with low-carbohydrate diets is of unclear benefit.

The optimum diet for beneficial long-term reduction in CVD risk is currently unknown; however, the magnitude of weight loss, risk factor reduction and sustained long-term benefit should all be part of this. Published studies to date indicate that low-carbohydrate diets can be used safely for short-term weight loss
without adversely affecting CVD risk factors although issues of high dropout rates and non-compliance in studies evaluating low-carbohydrate versus low-fat diets confound a conclusive recommendation in favour of the safety of such a dieting approach. While risk factors such as weight and lipids are important to control, there are currently no long-term studies evaluating a low-carbohydrate-dieting approach in reducing primary measures of CVD. Larger study groups followed for periods of one year or greater are needed to further investigate the safety and efficacy of low-carbohydrate ad libitum diets on CVD risk factors while collection of data on primary CVD outcome measures are needed before definitive recommendation can be given.

**Diabetes**

Sustained weight loss of as little as 5% of initial body weight can have a significant impact on fasting blood glucose, insulin sensitivity, insulin levels, HbA1c concentrations and medication requirements of obese patients with type 2 diabetes. Furthermore, lifestyle changes aimed at a moderate weight loss through a hypoenergetic, low-fat diet plus physical activity have clearly shown the benefits of such approaches in reducing the progression to type 2 diabetes in obese adults at high-risk of developing the disease (38, 39). As yet, demonstrated efficacy of low-carbohydrate diets in achieving similar results has not been shown. While use of a low-carbohydrate diet has consistently shown benefits in improving insulin sensitivity both with and without weight loss (13, 15, 28, 40-43), the composition of dietary fat type (particularly saturated fat) in the diet can ameliorate some of these benefits. In one study, a 3-week isoenergetic high-fat diet (50% of energy fat; 35% carbohydrate) induced relative insulin resistance in healthy women compared with an isoenergetic low-fat diet with the detrimental finding attributed to a higher proportion of saturated fat in the high-fat diet (44). In controlled research studies, low-carbohydrate diets are usually higher in saturated fat content than habitual diets (17, 22-24, 28), but what effect this type of weight-loss approach has on diabetes control or development has not been investigated in well-controlled trials. Case study reports show efficacy in the short-term use of a low-carbohydrate diet in treating some of the metabolic consequences of type 2 diabetes; however, larger-scale studies are required to examine its efficacy against other weight loss approaches (41, 42).

Epidemiological data has linked high-fibre wholegrain foods and low glycemic index diets to less insulin resistance and a lower risk of the metabolic syndrome. In a cross-sectional study among 2,834 participants of
the Framingham Offspring Study, eating three-or-more servings of wholegrain foods a day was associated with lower insulin resistance and a reduced risk of the metabolic syndrome, with cereal fibre accounting for most of the wholegrain effect (45). While no direct evidence can be found linking a low-carbohydrate diet to greater risk of developing diabetes, the diet is one inherently low in fibre-containing carbohydrate foods such as wholegrains and cereals. While weight loss will undoubtedly reduce risk of diabetes, a sustained dietary approach that is deficient in ‘disease-preventing nutrients’ such as fibre, and does not have evidence for long-term adherence, may ameliorate some of the weight-loss benefits.

One of the central theories of a low-carbohydrate diet is that restricting carbohydrate intake will help modulate insulin levels. Investigations examining the insulin response to whole foods has shown though that protein foods such as meat and fish can elicit a greater peak insulin concentration than white pasta (46). Long-term adherence to a low-carbohydrate diet, coupled with elevated amounts of protein as a major macronutrient results in increased hepatic glucose production and decreased peripheral glucose utilisation, both indicative of an insulin resistant state (47, 48). Although more study in this area is needed, early findings suggest that higher fasting-glucose production, decreased suppression of hepatic glucose output and enhanced gluconeogenesis from a diet high in protein all potentially increase the demand on basal and post-prandial insulin release from the pancreas and may in fact hasten the onset of diabetes in susceptible individuals due to pancreatic beta cell failure (49, 50). In contrast, the use of high-protein, hypoenergetic weight-loss diets (as opposed to high-protein, isoenergetic diets) in the management of type 2 diabetes has shown comparable results to reduced-fat diets in terms of improvements in metabolic parameters such as blood glucose, lipids and insulin response as well as overall weight loss (13, 41, 42, 51). Although no reports exist in the literature of adverse events with the use of a low-carbohydrate diet for weight loss in type 2 diabetes, medical monitoring and medication review of insulin and oral hypoglycaemic agents would certainly be indicated to pre-empt hypoglycaemic episodes.

**Other Adverse Effects**

Little documented information has been reported in the scientific literature about adverse effects attributed to a low-carbohydrate diet although common short-term side-effects often cited include constipation, fatigue, halitosis, headache, thirst, polyuria and nausea (4, 16, 22, 52). One study evaluating adherence to a weight-
loss low-carbohydrate diet (<25 g/d) over 6 months found that of the 41 individuals who attended reviews: 63% reported bad breath, 51% reported headache, 10% noted hair loss, 1 woman reported increased menstrual bleeding and 1 subject had moderately severe headaches for 3 months (52). Direct comparison of side-effects of low-carbohydrate and low-fat dieters over 24 weeks found greater adverse events in the low-carbohydrate group such as constipation (68% vs 35%; P < 0.001), headache (60% vs 40%; P = 0.03), halitosis (38% vs 8%; P < 0.001), muscle cramps (35% vs 7%; P < 0.001), diarrhoea (23% vs 7%; P = 0.02), general weakness (25% vs 8%; P = 0.01) and rash (13% vs 0%; P = 0.01) (16).

An internet-based registry has documented health problems attributed to low-carbohydrate diets in 429 individuals (53). As of December 2003, prevalence of the most common problems reported by registrants were: constipation (44%); loss of energy (40%); bad breath (40%); difficulty concentrating (29%); kidney stones, kidney infections or reduced kidney function (19%); and heart-related and lipid problems (33%). Other problems of lower incidence reported in the survey included gout, gastrointestinal upsets, mood swings, fatigue and headaches. The data collected can not be considered a reliable estimate of true prevalence of adverse events of a low-carbohydrate diet in the general population as all side-effects were self-reported and were not subjected to verification through medical records or other methods. To provide a valid comparison, a similar method of data collection would need to be undertaken in individuals following a ‘low-fat’ or similar weight-loss diet.

Dropout rates from controlled studies would suggest that minor side-effects from a low-carbohydrate diet are not a major issue for participants when compared against similar dropout rates for a low-fat dietary approach (13, 15, 16). As there is a greater chance of adverse events occurring on a low-carbohydrate diet, caution should be exercised in recommending this style of dieting approach until it can be proven superior to other types of dietary interventions in maintaining weight loss and reducing primary metabolic syndrome outcomes. Large-scale controlled population surveys would prove invaluable in monitoring dietary adherence, weight loss and most importantly: side-effects and adverse events.

**Potential Long-Term Health Risks**
Following a dietary plan that is restrictive of certain food groups, and whose overall nutritional quality has been questioned, raises the issue of potential long-term health effects that could be encountered by following such a dietary lifestyle for many years.

**Cancer Risk**

The possibility that long-term adherence to a low-carbohydrate diet could modify an individual’s cancer risk is an important question to pose; yet also is one of the most difficult to provide direct evidence for. There is strong evidence for a protective effect of fruits and vegetables in almost all major cancers afflicting Western society today including colorectal, breast, pancreatic, lung, stomach, oesophageal and bladder cancer (54, 55). Fruits and vegetables contain a vast array of compounds that are implicated in providing protection against cancer. Substances such as antioxidants, fibre, isothiocyanates (in cruciferous vegetables), allyl sulphides (in onions and garlic), flavonoids, and phenols have all been linked to augmenting the body's protective mechanism against cancer promotion. The nature of a low-carbohydrate diet is one that is low in fruits, vegetables (if starchy vegetables aren’t adequately replaced with other types of low-carbohydrate-containing vegetables) and grains thus potentially placing an individual at an increased cancer risk if the diet is followed long term. Furthermore, the evidence strongly suggests that it is not the consumption of one or two varieties of vegetables and fruit that confer benefit, but rather the intake of a wide-variety of plant foods.

No studies have yet been conducted to see whether low-carbohydrate dieters have a greater risk of cancer though the time frame needed for this would require several decades of monitoring. One confounding issue is the relationship between obesity and cancer. Obesity likely has an independent effect on cancer risk with epidemiological evidence pointing to increased incidence of colon, breast (in postmenopausal women), endometrium, kidney, oesophagus, gastric, pancreas and gallbladder cancers in overweight and obese individuals (56). On the basis of findings from this study, it was estimated that 14% of all deaths from cancer in the United States in men and 20% of those in women can be linked to overweight and obesity. For any overweight person, losing and maintaining weight loss could be expected to have a positive impact on their individual long-term cancer risk regardless of what dieting approach was taken. Weight loss on a low-carbohydrate is not superior to that achieved on a low-fat diet after 12 months (14, 15) and there is limited
evidence that successful long-term weight loss and maintenance can be achieved through low-carbohydrate dieting (19).

The question that remains unanswered is what risk a person will experience in following a long-term isoenergetic eating plan that promotes the reduction in the overall intake of fruit, grains and some vegetables. While it certainly is correct to state that there is no evidence that a low-carbohydrate diet increases cancer risk, it is also correct to state that there is no evidence that a low-carbohydrate does not increase cancer risk. Promoting efficacious long-term weight loss methods and dietary variety messages would seem the wisest approach.

**Bone Health**

A potential effect of low-carbohydrate diets on bone health is an important consideration as these diets have been hypothesised to contribute to osteoporosis risk. Observational studies and controlled trials with children, young adults, and the elderly all support the important role for calcium intake in building and maintaining bone mass and reducing bone loss (57, 58). Low-carbohydrate diets promote the restriction of dairy products, particularly milk and yoghurt, which are the main sources of calcium in the diet (4). As peak bone mass is an important factor in determining long-term fracture and osteoporosis risk, adoption of dieting practices that restrict calcium intake (particularly in those under the age of 30) have the potential to compromise the attainment of peak bone mass. No studies of low-carbohydrate diets have yet been of sufficient duration to measure long-term bone loss.

Higher intakes of dietary protein on a low-carbohydrate diet have been postulated to have an impact on calcium and bone metabolism through increased calciuria (59, 60). Low-carbohydrate diets have the potential to generate a sub-clinical chronic metabolic acidosis (via the presence of ketone bodies in blood) which can then promote calcium mobilisation from bone (59-62). Barzel and Massey (59) proposed that diets with the potential to increase renal acid load lead to calciuria which can have adverse affects on bone unless buffered against the consumption of alkali-rich foods such as fruits and vegetables. Recent studies though appear to contradict this theory with a large-scale epidemiological study of over 900 adults showing no negative effect of consumption of animal protein on bone mineral density (63). Furthermore,
supplementation of protein intake to 1.55 g/kg/day (mostly from meat supplements) with a concomitant reduction in carbohydrate intake for 63 days in a healthy elderly population found no effect on urinary calcium excretion, but was associated with higher circulating IGF-1 (a bone growth factor) and lower levels of urinary N-telopeptide (a marker of bone resorption) (64).

The two aforementioned studies suggest a positive benefit for bone health with higher protein intakes as would typically be seen on a low-carbohydrate diet - at least in an elderly population. Conflicting reports on the effect of animal protein on bone health could be due in part to differences in participant ages, calculation of protein intakes, dietary data collection problems, and anatomical sites evaluated. Diets based mainly on plant proteins do not appear to augment calcium loss, an effect most likely attributed to a higher phosphate intake (dietary phosphate has the ability to increase renal tubular reabsorption of calcium) and a lower intake of sulfur-containing amino acids (65). The current evidence suggests that a low-carbohydrate diet does not have a detrimental direct impact on bone health though dietary restriction of calcium from a reduction in dairy product intake should be addressed by including additional calcium food sources or the use of calcium supplements.

Kidney Health

A low-carbohydrate diet is by its nature a diet higher in protein and fat than a typical habitual diet (4, 13, 16, 17, 23, 24). One question that has been raised is if a diet that is inherently higher in protein than usual dietary intake can affect kidney function. Previous studies of low-carbohydrate diets have not been of sufficient duration to evaluate their potential to affect kidney function. Recent observational data from 1,624 participants in the Nurses’ Health Study has linked diets high in protein with reduced kidney function over time (66). In this study, women who began the study with mildly decreased kidney function showed a worsening with increasing protein intake. Those women with healthy kidney function at the outset showed no signs of deterioration. The limitations of the study were that dietary protein intake was only assessed at two time points and participants were not randomised to follow specific diets so other dietary or lifestyle factors could be involved. If there is a link between higher protein intakes and kidney health, how significant could this issue be? One estimate puts the number of adults in the United States already having sub-clinical reduced kidney function at 25%, with the percentage considerably higher for those over forty or who have
hypertension (67). One prospective study conducted over 6 months found that moderate changes in dietary protein intake (25% of energy versus 12%) caused adaptive changes in renal size and function without any measurable adverse effects suggesting that individuals without pre-existing impaired renal function can likely tolerate a higher protein intake of a low-carbohydrate diet (68).

Most studies evaluating the efficacy and safety of low-carbohydrate diets have primarily focussed on markers of CVD and diabetes risk. Future studies involving low-carbohydrate diets need to assess kidney function to ascertain if population groups likely to follow low-carbohydrate diets for long-term weight loss and maintence are at risk of hastening kidney damage. For individuals with diagnosed pre-existing impaired kidney function, a low-carbohydrate would not be advised.

**What Message does the Public Receive?**

Most of the data to do with the efficacy and safety of low-carbohydrate diets has come from scientific trials using combinations of pre-determined diet types and counselling along with measuring defined parameters such as weight loss and blood markers of CVD risk. One question that has not been addressed in the scientific literature is how does the general public perceive these diets and what dieting approaches do they adopt? Investigating the efficacy and safety of diets in a controlled scientific study may be far removed from what the general population in fact is doing when they ‘go on a low-carbohydrate diet’.

Information on the public’s view of low-carbohydrate diets is scarce and has mostly been collected by private marketing firms, but the data does provide some interesting insights. Market research firm NPD Group (New York, USA) surveyed the eating habits of 11,000 adults in the United States from 2001 to 2003. NPD found that adults who stated that they were ‘cutting carbs’ to help lose weight were eating on average 128 g of digestible carbohydrate per day, which is much higher than what most common low-carbohydrate diets recommend (18). Only 25% of the respondents who were actively reducing carbohydrates in their diet were doing so at a level consistent with recommendations made by many popular low-carbohydrate diets. Based on the survey results it was estimated that at any one time, 4% of the American population are following a low-carbohydrate/high-protein diet. Findings from the same survey found that those people who
reported that they were on a carbohydrate-reduced diet were more likely to be obese, have diabetes, high blood pressure and have high cholesterol when compared to those not following a low-carbohydrate diet.

Another survey conducted by NPD Group found that the most popular type of diet was in fact a self-styled one where individuals modified several different types of diets to meet their own needs (69). Twenty-five percent of the population had tried a self-styled diet with 7% currently following one at the time of the survey. The Atkins’ Diet was the next most popular diet with 17% of the population having tried it at some stage and with 4% currently following it.

Supporting these findings was market research data collected by Opinion Research Corporation (New Jersey, USA) commissioned by the Partnership for Essential Nutrition who surveyed 1,017 adult Americans about their dieting habits (70). Of those trying to lose weight, 19% were doing so by primarily reducing carbohydrates, which equated to approximately 9% of the population following a low-carbohydrate diet at any one time. Many of the people surveyed showed a poor understanding of what the carbohydrate content of a variety of foods was and believed that low-carbohydrate diets could help them lose weight without the need to reduce the kilojoule content of the diet. Foods that people were increasing in their diet when following a low-carbohydrate diet were steak, bacon and ham while foods that were reduced included fruits, vegetables, wholegrains and many low-fat dairy foods. Other findings from this survey were that 36% of people believed that restricting carbohydrate consumption reduces the risk for cancer and 45% believed that low-carbohydrate diets were good for the heart.

Current popular commercial low-carbohydrate diets are now advocating including plenty of high-fibre vegetables, fruit, low glycaemic index carbohydrate sources and choosing healthier monounsaturated and polyunsaturated fats over foods high in saturated fats. Drinking plenty of water and taking a general vitamin and mineral supplement is also recommended on these diets. Such advice seems wise and provides for a healthier diet closer to general nutrition guidelines rather than a ‘meat, cheese and eggs’ diet that many people think is synonymous with a low-carbohydrate dieting approach. Results from consumer surveys though indicate that the low-carbohydrate diet message is being misconstrued by the general public. Many people are in fact following self-styled diets while there is a suggestion that many people are just receiving
the ‘carbohydrates are bad’ message and are cutting back on good carbohydrate sources such as wholegrain foods and fruits. Such trends across a large population raise the concern of a rise in the incidence of long-term health problems such as cancer, diabetes and heart disease – diseases where high intakes of wholegrain foods, fruit and fibre have shown to be protective (20, 45). Low-carbohydrate diets are low in fibre and even though some of these popular diets recommend the use of fibre supplements to counter this, the protective effect of foods high in fibre are related to not just their fibre content.

**Conclusion**

Low-carbohydrate diets are often promoted as being superior for weight loss yet the evidence demonstrates that weight loss on such a diet is not superior to traditional dieting practices after 6 months. Furthermore, limited evidence suggests that long-term adherence to such an eating plan for weight maintenance is difficult and comes at the cost of the overall nutritional adequacy of the diet unless strict attention to such issues are undertaken by the dieter. Low-carbohydrate diets are likely effective and not harmful in the short-term and may have therapeutic benefits for weight-related chronic diseases, but longer-term efficacy has not been tested. In individuals with obesity, insulin resistance, and elevated triglycerides, the short-term benefits of a low-carbohydrate diet may outweigh any risks. Conversely, in individuals with elevated LDL-cholesterol, nutritional deficiencies, or with renal disease, the risks may outweigh the benefits. Furthermore, even though a low-carbohydrate diet has shown efficacy in favourably modulating some blood markers of CVD risk, restriction of fruits, grains and fibre may have an independent effect on risk.

It remains to be determined if the positive metabolic changes that occur with low-carbohydrate diets translate into improved macro- and microvascular outcomes in those individuals ‘at risk’. The studies conducted so far show a higher rate of adverse side-effects from the diet hence long-term studies are needed to assess CVD risk factors and adverse events in both obese individuals exhibiting signs of the metabolic syndrome and otherwise healthy moderately overweight individuals. Such studies should also monitor other parameters such as kidney function, diabetes risk factors, exercise ability, dietary compliance and nutritional deficiencies. For those at risk of CVD or who have diabetes, embarking on a low-carbohydrate diet should be done under medical supervision where monitoring of lipids and hypoglycaemia risk (if the person is using insulin or oral hypoglycaemic agents) can be done.
Practical advice for those following a low-carbohydrate diet should promote the reduction of refined, ‘nutritionally deplete’ carbohydrate foods, but still encourage the inclusion of fruit and high-fibre carbohydrate sources. Replacing foods high in saturated fat with monounsaturated or polyunsaturated fat sources would also seem sensible. While new commercial incarnations of low-carbohydrate diets are now promoting these types of dietary changes, this is not the message that reaches the entire public hence the onus of promoting sensible health messages should be undertaken by the promoters of such diets as well as by doctors, nutritionists and also in public health education messages.
References