

Divide and Conquer: The Multidisciplinary Approach to Achieving Significant Long-Term Weight Loss and Improved Glycemic Control in Obese Patients With Type 2 Diabetes

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Type 2 diabetes has become a worldwide epidemic, estimated to affect 1 in 14 adults, or 380 million people, globally by 2025.^{1,2} The problem is particularly acute in Australia, where the prevalence of diagnosed diabetes more than doubled between 1989 and 2005, amounting to 3 million people affected by the disease.^{3,4} Diabetes is the most common reason for renal dialysis, blindness in people < 60 years of age, nontraumatic lower-limb amputation, and cardiovascular disease and is the sixth-highest cause of death by disease in Australia.^{3,5}

First-line best-practice management includes brief counseling to promote lifestyle changes in diet, exercise, and education, with the aim to improve insulin resistance, reduce hypertension, correct dyslipidemia, and achieve weight reduction.⁶ Patients at high risk of developing type 2 diabetes and who are refractory to lifestyle intervention may be treated with pharmacological agents and insulin, many of which contribute to further weight gain.^{7,8}

According to several recent studies, a large proportion of newly diagnosed cases are potentially preventable or could at least be delayed through lifestyle and behavioral modification.^{9–11} Data from 20 longitudinal cohort studies illustrate consistently that regular physical

activity substantially reduces the risk of developing type 2 diabetes by 20–30%, with the greatest benefits obtained in obese patients with impaired glucose regulation undergoing moderate- or vigorous-intensity exercise.^{11,12} One recent study validated a rigorous lifestyle intervention program with counseling for physical activity, nutrition, and weight loss, resulting in a risk reduction of 40–60% in adults with impaired glucose tolerance.¹²

Recent research supports the potential benefit of significant weight loss leading to diabetes “remission” (i.e., consistent normalization of blood glucose levels and A1C). In a pivotal study by Dixon et al.,¹³ 73% of patients who were randomized to laparoscopic gastric banding achieved remission of their diabetes compared to 13% in the conventional therapy group, and the relative risk of remission for the surgical group was 5.5. The surgical group also had 20.0% body weight loss, representing 62.5% excess body weight (vs. 1.4% body weight loss or 4.3% excess body weight loss in standard group) at 2 years. Furthermore, remission was related to weight loss ($R^2 = 0.46$) and lower baseline A1C levels (combined $R^2 = 0.52$).

Nonsurgical metabolic rehabilitation poses several theoretical and logistical problems, and there

is no currently advocated model. Previously reported strategies have included telephone-derived interventions,² 1-day outpatient motivational workshops,¹⁴ general recommendation-based lifestyle programs,¹⁵ a supervised resistance training program,¹⁶ a supervised program of combined resistance and aerobic training,¹⁷ and a home-based walking and resistance program.¹⁸ These studies have all shown modest, short-term amelioration of cardiometabolic risk factors, but with various degrees of efficacy. In general, an absolute reduction of 0.4–0.5% in A1C can be achieved, with varying degrees of weight loss and modest improvement in lipid profiles. Nonetheless, these studies point to weight loss as the most important determinant in improving health outcomes in high-risk and diagnosed type 2 diabetes patients with cardiovascular risk factors.

With some exceptions,^{19–24} data are lacking with respect to ameliorating health risks in obese patients with established type 2 diabetes. We have established a multidisciplinary, nonsurgical metabolic rehabilitation program (MRP) with a mandatory exercise component and weight loss as the primary intervention. This study followed a small population of obese patients with type 2 diabetes presenting to the MRP, an

outpatient program established at a tertiary teaching hospital in Sydney, Australia. We hypothesized that an intensive exercise program with multidisciplinary support could achieve significant improvement in cardiometabolic risk factors and that these results could be sustained in the long term.

Methods

This was a retrospective study from 2004 to 2007 of patients enrolled in the MRP. Participants were required to fulfill three criteria: 1) have a BMI $> 30 \text{ kg/m}^2$, 2) have established type 2 diabetes, and 3) have a referral from their general practitioner or treating endocrinologist. Patients with cardiac or other conditions that precluded undertaking intensive exercise sessions or having a body weight $> 150 \text{ kg}$ were excluded. The minimum commitment was 1 year plus 80% attendance at all sessions. No exclusions were made related to duration of diabetes, primary or secondary causes of diabetes, or other comorbidities.

Design

The program consisted of clinical consultations and supervised exercise classes. It included 1) appointments with an endocrinologist specializing in obesity and diabetes management conducted monthly for the first 6 months and then every 2–3 months thereafter; 2) dietitian appointments, including an initial consultation, a follow-up visit at 6 weeks, an annual visit, and eight group sessions conducted throughout the duration of the program to help patients with a healthy eating plan and meal replacement (e.g., Optifast); 3) appointments with diabetes educators, including an initial visit and every 6 months thereafter if needed to provide monitoring of blood glucose levels and advice on administering medication; 4) psychologist appointments, including

an initial visit and four group sessions conducted throughout the duration of the program to detect and treat psychosocial barriers to healthy eating and exercise; 5) physiotherapists available on request to treat physical factors limiting patients' ability to exercise; and 6) exercise physiologists available daily for 6 days/week to help assess, prescribe, and supervise exercise.

The Bodylines program, a validated educational weight loss program developed at the Royal Prince Alfred Hospital in Sydney, New South Wales, Australia, was delivered in modules and integrated in the group sessions conducted by the dietitians and psychologists.

Exercise sessions were held in the early mornings and late afternoons each day to facilitate participation. The minimum level of participation was attendance at three exercise sessions per week, for a total of 180 minutes of supervised exercise in the hospital gymnasium. Patients were also prescribed 120 minutes (2×60 minutes) of exercise routines for off-clinic days to achieve an overall cumulative amount of 300 minutes/week of exercise, inclusive of the supervised exercise sessions. Off-clinic exercise routines could include walking, swimming, or whatever exercise was conducive to the patient's environment.

The supervised exercise sessions included a combination of resistance and aerobic exercises. The aerobic component lasted a total of 20–30 minutes using a variety of methods including treadmills, bikes, rowers, steppers, mini-trampolines, rebounders, step-up boxes, and lap-walking with light hand weights. Intensity levels were based on achievement of a heart rate (HR) response of 60–80% of predicted maximal HR (average range 110–140 beats per minute), taking into account age, fitness level, risk of injury, and cardiorespiratory

risk factors. For patients who were on negatively chronotropic medications (e.g., beta-blockers), rate of perceived exertion of the individual patient was used instead, aiming for 5–8 out of a maximum 10 as a subjective scale of exertion as a guide.

The resistance component usually consisted of 20–30 minutes, with the remaining 5–10 minutes for cooling down, stretches, and abdominal exercises. It included mostly pin-loaded machines and free weights (e.g., dumbbells), with patients given appropriate exercises taking into account their tolerance range and fitness, physical limitations, past injuries, age, medications, comorbidities, cardiac risk factors, and exercise history. Generally, the appropriate weight was a load that could be completed in 8–15 repetitions. This was repeated for up to three sets during the session, with the exercise routine designed to include a balance of opposing muscle groups (e.g., chest and upper back, quads and hamstring, etc.) with alternating upper-body and lower-body exercises to ensure maximum recovery between exercises. The emphasis was on resistance, not on body-building or heavy weight lifting, so as to minimize the risk of injury.

Physiological parameters were collected before enrollment and every 6 months for 30 months or until voluntary discharge from the program. The physical parameters collected included weight, waist circumference, BMI, A1C, systolic and diastolic blood pressure, and HDL cholesterol, LDL cholesterol, and triglyceride levels.

All contact and patient details were stored confidentially by the study coordinator in a private database file and de-identified. The local human research ethics committee approved the study.

All data are expressed as mean \pm standard error of mean (SEM). Percentage change was calculated as a percentage difference from baseline. Excess body weight (EBW) was defined as current weight (kg) minus $25 \times \text{height (m)}^2$. Statistical significance was determined using a repeated-measures, one-way analysis of variance. Pair-wise comparisons between different time points were calculated using the Holm-Sidak method. All statistical analyses were performed with SigmaStat (Systat Software Inc., Chicago, Ill.). Probability values < 0.05 were considered statistically significant.

Results

Of 62 participants enrolled, 15 were excluded from analysis because they participated for < 1 year. Forty-seven patients continued to 18 months; 44 participated for 24 months; and 41 participated for the full 30 months of the study period.

Baseline data are summarized in Table 1. There were approximately equal numbers of male (45%) and female (55%) participants. Ethnicity was divided as follows: 72% Caucasian, 21% Mediterranean, and the remainder divided among Hispanic, Asian, and Indian backgrounds (7%). Given the small cohort studied, subanalyses taking into account sex and ethnic differences were not analyzed.

The average age was 59.1 ± 9.4 years (range 33–72 years), and the mean weight was 104.7 ± 19.9 kg, representing a baseline EBW of 35.0 ± 16.6 kg. Baseline BMI (37.6 ± 5.7 kg/m²) fell within the World Health Organization obese class II.²⁵ Waist circumference at enrollment was 113.4 ± 12.6 cm, reflecting the substantially increased risk of cardiometabolic complications in this patient cohort.²⁵

Patients had suboptimal glyce-mic control, with an average A1C of

Table 1. Baseline Data of Participants in the MRP

Baseline Parameters	Mean \pm SEM
Sex (n [%])	
Male	21 (45)
Female	26 (55)
Duration of diagnosis (years)	10.5 ± 7.2 (range 1–34)
Weight (kg)	104.7 ± 19.9
Height (m)	1.67 ± 0.1
BMI (kg/m ²)	37.6 ± 5.7
Waist circumference (cm)	113.4 ± 12.6
EBW	35.0 ± 16.6
A1C (%)	8.2 ± 1.6
Systolic blood pressure (mmHg)	137.0 ± 18.6
Diastolic blood pressure (mmHg)	79 ± 9.1
HDL cholesterol (mg/dl)	48.7 ± 24.7
LDL cholesterol (mg/dl)	97.8 ± 34.8
Triglycerides (mg/dl)	183.2 ± 88.5
Patients taking anti-lipid medications (n [%])	31 (66)
Patients taking antihypertensive medications (n [%])	35 (74)
Patients taking oral hypoglycemic medications (n [%])	38 (81)
Patients taking insulin \pm oral agents (n [%])	12 (25)
Patients with metabolic syndrome	47 (100)

$8.2 \pm 1.6\%$, despite the fact that the majority were on conventional treatment with oral hypoglycemic agents (81%) or insulin plus oral agent therapy (25%). Although 74% were taking antihypertensive medications, patients were clinically defined as hypertensive (systolic blood pressure of 137.0 ± 18.6 mmHg and diastolic blood pressure of 79 ± 9.1 mmHg). Sixty-six percent of patients were taking anti-lipid therapy. Baseline HDL cholesterol (48.7 ± 24.7 mg/dl), LDL cholesterol (97.8 ± 34.8 mg/dl), and triglyceride levels (183.2 ± 88.5 mg/dl) were suboptimal according to

the recommended target ranges for adults with type 2 diabetes.²⁶

The average duration of diabetes was 10.5 ± 7.2 years (range 1–34 years). All patients were treated in a diabetes clinic or in a private practice by an endocrinologist, and 67% were referred to the MRP by their treating endocrinologist.

The average number of exercise sessions attended per week was 4.1 ± 0.9 , with 94% of patients attending an average of at least two sessions per week and 87% of patients attending an average of at least three sessions per week.

Significant reductions were achieved in all parameters (Figure 1A–H) as early as 6 months (6-month values vs. baseline, $P < 0.001$, are marked with α). Continued reductions were seen at 12 months (all values vs. 6-month values, $P < 0.001$, marked with asterisks) in weight (8.4 ± 0.9 kg), weight loss ($7.9 \pm 0.8\%$), EBW (26.8 ± 2.3 kg), EBW loss ($25.3 \pm 2.8\%$), reduction in BMI ($8.4 \pm 1.1\%$), reduction in waist circumference ($6.5 \pm 0.9\%$), percentage reduction in A1C ($11.4 \pm 2.1\%$), and absolute reduction in A1C (1.1 ± 0.2 percentage points).

All parameters were maintained for as long as 30 months: weight (10.8 ± 1.7 kg), weight loss $9.8 \pm 1.4\%$, EBW (25.2 ± 2.3 kg), BW loss ($29.5 \pm 4.1\%$), reduction of BMI ($10.0 \pm 1.5\%$), reduction of waist circumference ($6.3 \pm 1.3\%$), percentage of A1C reduction ($9.7 \pm 2.5\%$), and absolute reduction in A1C (0.9 ± 0.2 percentage points).

Significant reductions in systolic blood pressure ($6.4 \pm 1.99\%$, $P = 0.015$) and diastolic blood pressure ($6.6 \pm 2.0\%$, $P = 0.008$) were observed at 1 year. Insulin dosage was halved at 30 months (from 93.8 ± 6.3 IU to 46.0 ± 5.0 IU, $P < 0.01$).

A significant increase in HDL cholesterol was observed at 24 months ($10.6 \pm 4.3\%$, $P = 0.049$ [from 50.3 ± 31 mg/dl to 58.0 ± 15.5 mg/dl, $P = 0.018$]). Despite a general observable decrease at 30 months, LDL cholesterol and triglyceride levels (10.0 ± 7.3 and $12.9 \pm 6.6\%$, respectively) were not significantly different from baseline at 30 months.

Discussion

This study demonstrated that obese diabetes patients with suboptimal control of cardiometabolic risk factors despite standard best care can achieve significant improvements in weight, waist circumference, physical activity, and glycemic control in an

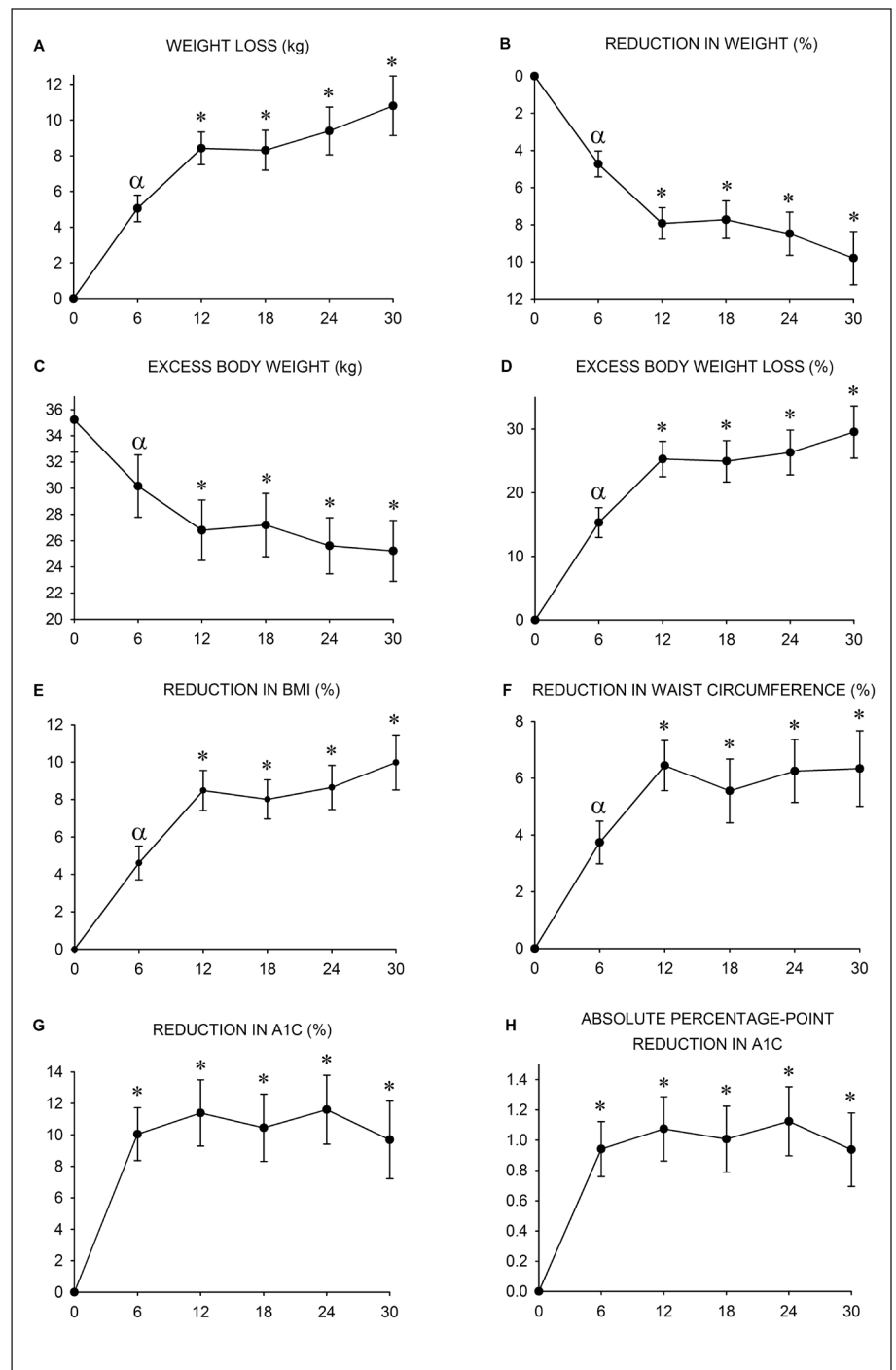


Figure 1. Significant reduction in cardiometabolic parameters maintained for 30 months in obese diabetes patients with multidisciplinary metabolic rehabilitation. A: Weight loss (kg); B: weight reduction (%); C: EBW (kg); D: reduction in EBW (%); E: reduction in BMI (%); F: reduction in waist circumference (%); G: reduction in A1C (%); and H: absolute reduction in A1C (%). Significant differences versus baseline are indicated with α ($P < 0.001$) and significant differences versus 6-month values are indicated with asterisks ($P < 0.001$). All data are expressed as mean \pm SEM.

intensive, nonsurgical interventional program focused on weight reduction, increased physical activity, dietary modification, and psychosocial support at 30 months.

Numerous randomized, controlled studies illustrate a beneficial effect on several metabolic parameters achieved through intensive interventional programs,^{15,27–31} but these programs often offer limited information because the time period is typically ≤ 1 year. Our program, which employed dietitians, clinical nurse educators in obesity and diabetes, physiotherapists, exercise physiologists, personal trainers, a psychologist, and an endocrinologist, achieved consistent long-term results.

Similarly, the Finnish Diabetes Prevention Study²⁰ showed favorable long-term results using multidisciplinary approaches in a randomized, controlled study involving patients with prediabetes (i.e., impaired glucose tolerance), in which patients were allocated to either a usual-care control group (dietary and exercise advice plus annual specialist visits) or an intensive lifestyle intervention group (dietary and exercise counseling plus circuit-type resistance training sessions). The intervention group lost 4.5 and 3.5 kg, whereas the control group lost 1.0 and 0.9 kg after 1 and 3 years, respectively. The gains, although modest, were sustained over the long term at 3 years' follow-up. This may reflect the necessity of a more intensive intervention to achieve meaningful outcomes in a high-risk population, whether for patients with prediabetes or established diabetes.

To date, the most comprehensive comparison between intensive lifestyle intervention and standard care is the Look AHEAD trial.^{21–23} Although baseline characteristics with respect to average age, BMI, weight, and waist circumference

were not significantly different in our study compared to the Look AHEAD trial, our participants were more complex at baseline, with a minimum BMI ≥ 30 kg/m² (vs. 25 kg/m²), poorer glycemic control (A1C 8.2 vs. 7.3%) and more hypertension (systolic blood pressure 137 vs. 128 mmHg, diastolic blood pressure 79 vs. 69 mmHg). Furthermore, 100% of our participants had a diagnosis of metabolic syndrome, and 24% were using insulin, versus 93 and 14.8%, respectively in the Look AHEAD trial.²² Our patients also had an appreciable mean time from diagnosis of type 2 diabetes of 10.5 years.

At 1 year, the Look AHEAD study achieved 8.6% weight loss in the intervention group versus 7.9% in our study.²¹ By 3 years, modest results were sustained for weight loss (5.5%), although our cohort lost more weight (9.8%), possibly because of the nearly doubled prescribed exercise requirement in our study (300 vs. 175 minutes per week), of which 180 minutes was supervised in our gymnasium. This finding substantiates the superiority of supervised exercise in achieving better outcomes.¹⁶

We also achieved a reduction in A1C of 11.4 versus 6.3% at 1 year and 9.7 versus 3.2% at 30 months.²³ This reflects the likely benefit of our increased exercise requirements and the favorable effects of a combination of aerobic and resistance training on glycemic control.^{17,24} The reduction in A1C in our study is significant considering that the U.K. Prospective Diabetes Study³² demonstrated that for each 1% reduction in A1C, there were reductions of 21% in deaths related to diabetes, 14% in the incidence of myocardial infarction, and 37% in microvascular complications.³²

Modest reductions in systolic blood pressure were reflected simi-

larly in the Look AHEAD trial and in our study (6.8 and 6.4%, respectively), although our study achieved a greater reduction in diastolic blood pressure at 1 year (6.6 vs. 3.0%) and increased HDL cholesterol at 2 years (10.6 vs. 9.6%). Blood pressure continued to decrease for 30 months, although this change was statistically nonsignificant.

Although there is a clear, short-term association between blood pressure reduction and weight loss and caloric restriction,³³ previous studies observed a rebound of blood pressure over the long term despite maintained weight loss.³⁴ A recent review by Aucott et al.³⁵ of nine clinical trials and eight cohort studies found that reductions in systolic blood pressure (but less reliably in diastolic blood pressure) of 1 mmHg to each 1 kg of weight loss may be expected, but only for short follow-up periods of 2–3 years, possibly because of the secondary effects of medications, diet, and pre-study blood pressure levels.

Studies have shown the rates of comorbid mental health problems to be substantially higher in diabetic patients than in the general population, with associated poorer functional status and clinical outcomes, more complications, and increased mortality.³⁶ Our program employed an onsite psychologist with inclusion of individual and group sessions to counsel patients about psychosocial barriers to achieving better emotional and psychological well-being, as well as to empower patients to become active participants in their own diabetes management. These strategies, which generally included assisting patients with decision-making and problem-solving skills, augmenting their confidence, supporting their goals, and promoting self-efficacy, have been shown to lead to better glycemic control and

encourage positive behavior change in type 2 diabetes patients.^{37–39} These approaches are also consistent with the recently revised American Diabetes Association standards of practice guidelines, which promote a more patient-centered model incorporating group sessions, ongoing support, and behavioral goal-setting as crucial aspects of diabetes self-management education.⁴⁰

Conclusion

In summary, cardiometabolic improvements were maintained over the long term in obese adults with complex type 2 diabetes using intensive multidisciplinary metabolic rehabilitation. Limitations of this study included its retrospective design and small number of subjects, which likely precluded reaching an appreciable statistical power to show long-term significant changes in lipid profiles and possibly blood pressure. The aim, however, was to establish improvements in health outcomes in high-risk obese patients with type 2 diabetes before larger-scale studies are implemented.

The effect of pharmacological unloading, particularly on lipid profiles and blood pressure, may also partially explain the lack of long-term significance in these parameters, as many patients reached clinical targets and ceased medications. Future studies involving larger numbers of patients with randomization to either usual “best-practice” clinics or the MRP are needed to evaluate long-term health outcomes.

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manuscript. J.Z. collected data from months 12–30. A.L. provided further review and editing of the manuscript. N.K. critiqued the data, manuscript, and access to the patient cohort for study. An abstract based on this study was accepted for presentation at the Australian Diabetes Society annual scientific meeting in 2011. The authors thank Professor Markus Seibel, head of the Department of Endocrinology and Metabolism, Concord Repatriation General Hospital, in Concord, New South Wales, Australia, for encouraging the organization of this study and Karen Evans for her assistance with the manuscript, particularly the exercise component.

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