

Mini Review

Reversal of Type 2 Diabetes in a 14 Year Old Post Pubertal Child using a Low Calorie Liquid Replacement Diet and a GLP1 agonist

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Submitted: 11 January 2023

Accepted: 27 February 2023

Published: 27 February 2023

ISSN: 2333-6706

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OPEN ACCESS

Abstract

Type 2 diabetes is an aggressive form of diabetes in children and young people with the risk of early onset micro and macrovascular complications. The intervention of a reduced calorie liquid diet and treatment with a GLP1 agonist to try to reverse type 2 diabetes in a 14-year-old patient is described.

BACKGROUND

Our patient was diagnosed with type 2 diabetes at the age of 10 years and has a strong family history of type 2 diabetes. She had an earlier puberty with menses at aged 10 years.

At the age of 14 years, she had poorly controlled Type 2 diabetes. Her BMI was high, greater than 30kg/m² (Figure 2) and her glycaemic control was poor with high HbA1c levels (Figure 3). Her treatment regimen comprised Metformin 1000mg twice daily, Degludec insulin 16 units daily and Novorapid insulin with all meals (total daily insulin dose approximately 0.6 Units/kg/day). She was not taking her insulin reliably which made it difficult for the diabetes team to make changes to her treatment regimen and she was not carbohydrate counting thus the doses of Novorapid were determined based on previous experience only.

The intervention of a reduced calorie liquid diet and treatment with a GLP1 agonist to try to reverse her type 2 diabetes was proposed and discussed with our patient and her family. It was agreed that it would be safest for this intervention to be carried out as a hospital admission. This decision was based on our previous experience of a liquid diet intervention causing frequent hypoglycaemic episodes and it was also felt that our patient could be better supported as an inpatient to follow the plan. Both our patient and her parents were keen and committed to try this intervention.

Dietary intervention

A liquid dietary plan was created by the paediatric dietitian.

Due to our patient's young age a calorie restriction of 1200kcal/day proposed; this is not as low as adult based interventions (typically 800kcal/day).

The dietary plan consisted of 2 phases (appendix 1-adapted from Portsmouth hospitals version):

Phase 1 (weeks 1 and 2) - liquid shakes (supermarket own brand) + multivitamin supplements (over the counter)

Total 1200kcal/day

Phase 2 (weeks 3 to 6) - meal reintroduction + multivitamin supplements

- Week 3- introduce lunch (back at school)
- Week 4- introduce breakfast
- Week 5- introduce evening meal + snack
- Week 6- introduce 1 more snack

Total 1400kcal/day

The family purchased the required liquid replacement shakes and the multivitamin tablets prior to the admission. A range of options for the shakes were provided by the dietitian and choices were made based on our patient's preferred brand and flavouring.

GLP 1 Semaglutide intervention

The Semaglutide regimen was prescribed as per BNF guidelines

-Semaglutide 0.25mg subcutaneous injection once weekly for 4 weeks

-Semaglutide 0.5mg subcutaneous injection once weekly for 4 weeks

-Semaglutide increased to 1mg once weekly if required

Management during hospital admission

Our patient was admitted to the paediatric ward during the school summer holiday period to avoid missing time at school.

At admission her treatment regimen comprised Metformin 1000mg twice daily, Levemir insulin 16 units and Novorapid insulin 7 units with each meal. Her basal insulin had been changed just prior to admission to Levemir insulin from Degludec insulin to enable more responsive dose adjustments. She was commenced on a liquid diet from admission. Novorapid doses were calculated based on a 1:10g carbohydrate ratio (2 units per shake).

A libre 2 subcutaneous glucose sensor was used by our patient to help monitor glucose levels as well as intermittent finger prick blood glucose measurements.

During her admission our patient was reviewed by a diabetes specialist dietitian regularly, to monitor progress and support motivation. The diabetes consultant, specialist nurse and ward nursing staff also provided intensive support.

A daily exercise programme was devised by the paediatric physiotherapy team for our patient which she adhered to throughout the admission.

The ward play team provided activities and emotional support.

Progress during the admission and following discharge home

On day 4 of the admission our patient reported that she was struggling with the meal replacement shakes and was not managing the prescribed volume. Encouragement by the ward nursing staff and diabetes team was essential to support her to continue with the dietary plan. Insulin doses had been reduced to Levemir 10 units and Novorapid 2 units with each shake by this stage and blood glucose levels were stable at 4-8mmol/L with no hypoglycaemic episodes.

By day 10 of the admission insulin had been stopped completely and our patient was only taking Metformin 1000mg BD to maintain blood sugars in a 4-8mmol/l range. She had achieved a weight loss of 2kg.

The GLP1 agonist, Semaglutide was started on day 10 of admission. Semaglutide is currently licenced for young people aged 18 years and over but is used in younger children for obesity management by the local tertiary obesity service in Southampton. The use of Semaglutide in our patient was recommended by the tertiary obesity specialist team due to its effectiveness in weight reduction and appetite suppression and for the advantage that it only needs to be administered on a once weekly basis.

Appetite suppression on the lower dose of Semaglutide 0.5mg weekly was achieved for our patient.

Our patient continued to struggle to tolerate the meal replacement shakes and on day 15 of admission it was agreed that she could reduce the volume of the milk added to the powder and her lunch time shake was replaced with a normal meal (300kcal).

On day 16 our patient was discharged home to continue the treatment plan. She had lost 2.2kg in weight during this admission.

A home visit by the dietitian to review progress was carried out at 12 days following discharge from hospital. Our patient had remained fully compliant with the dietary plan and was delighted that the intervention had been successful.

Her dose of Metformin was reduced by half and stopped by 4 weeks following discharge.

She continues on weekly Semaglutide 0.5mg and has not required insulin (4 months post discharge from hospital). Blood sugars have remained in a normal range.

At 11 weeks following the intervention our patient's weight and BMI have reduced: weight 72.6kg to 61.9kg, BMI 30.9 kg/m² to 26.3kg/m² (Figure 1 and 2) and her HbA1c has also reduced from 70mmol/mol to 43mmol/mol (non-diabetic range) (Figure 3).

We have also facilitated a reduced gym membership fee to a local gym for our patient and have encouraged her to take advantage of this.

SUMMARY

We have demonstrated that the intervention of a reduced calorie liquid diet can reverse type 2 diabetes and eliminate the need for insulin. Maintaining a low-calorie diet in the longer term can be very difficult but this has been achieved successfully in our patient with the use of the GLP1 agonist Semaglutide.

The success for our patient has been achieved in a secondary care setting by a 2-week hospital admission and an intensive multidisciplinary team effort. Our patient and her family were committed to and fully engaged with the treatment plan at the outset. Our patient has reported that although the initial hospital admission was very hard for her at times, she is very happy with the intervention and that her life is much better now that she doesn't have to have 4 insulin injections per day. She will require long term regular follow up and we are hopeful that she will continue to maintain normal glycaemic control and thus significantly reduce her risks of long-term complications associated with type 2 diabetes.

We hope that this case report will encourage others to consider treatment of type 2 diabetes in children and young people with a low calorie diet intervention and become familiar and confident with the use of the newer anti-obesity drugs available.

Appendix 1 – dietary plan

Patient/carer information leaflet

A Low Calorie Diet

Leading studies has shown that for some people, type 2 diabetes can be put into remission by a substantial weight loss.

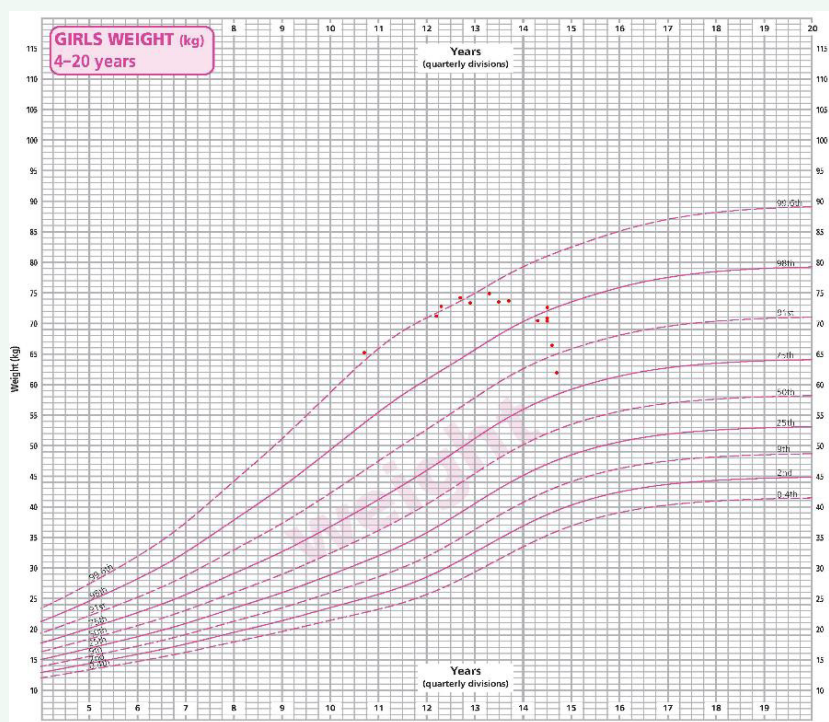


Figure 1 Weight history chart from outpatient appointments with the diabetes team Nov 2018-Sept 2022.

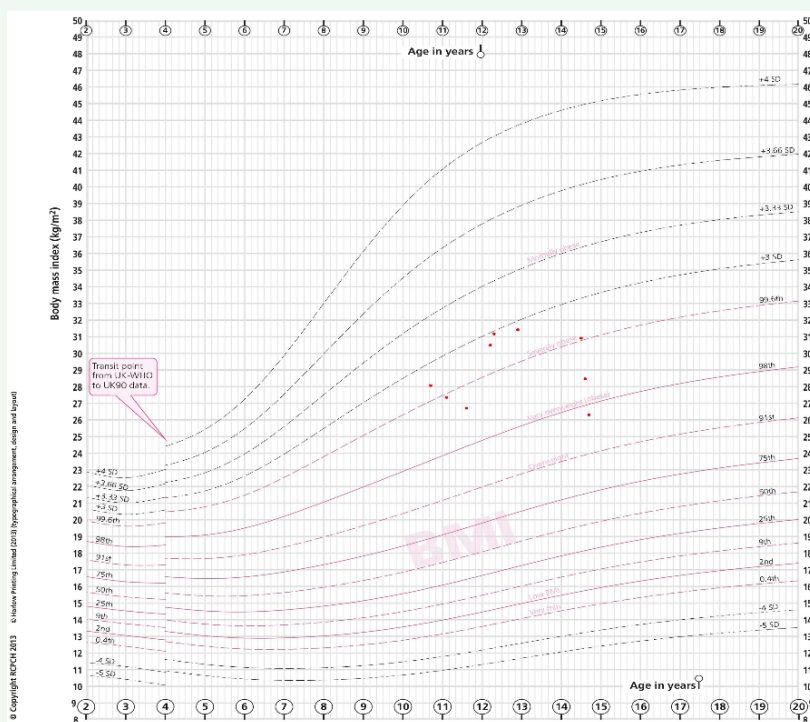


Figure 2 BMI history chart from outpatient appointments with the diabetes team Nov 2018-Sept 2022.

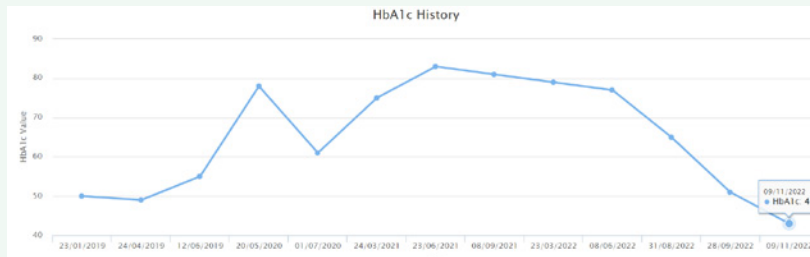


Figure 3 HbA1c history chart from outpatient appointments with the diabetes team Nov 2018-Sept 2022.

How much you need to lose depends on your starting body mass index (BMI). The weight loss diet is a 5 week low calorie diet (LCD, 1200kcal per day). It is important to bear in mind that the diet is only a few weeks long, it is followed by a return to normal eating but with reduced calorie intake than previously. You will not be missing out on things for too long! For this diet to be successful, it is important to stick to 1200kcal a day for a period of 4 weeks. It isn't easy and is not right for everyone.

The liquid diet involves 2 phases:

Phase 1 - NO SOLID FOOD is eaten for 2 weeks, liquid replacement only.

Phase 2 - food is gradually reintroduced over a further 4 weeks to achieve a 1200-1400kcal diet of solid foods. After this phase you can discuss increasing your calorie intake with your dietitian back to estimated requirements of 2000kcal per day.

To follow this diet effectively you need to be committed for 6 weeks.

Your dietitian is: xxxxxxxx

If you have any queries or concerns contact them on: xxxxxxxxxxxxxxxxxxxxxx

A Low Calorie Diet

PHASE 1 Liquids only – NO FOOD

Advantages	Disadvantages
Doesn't involve any food planning or cooking, which therefore removes some of the temptations. They are also easy to have 'on the go'.	Initially you may experience symptoms like headache, dizziness, tiredness and hunger but these are expected to wear off after a few days once your body adjusts.
A complete break from old eating habits and behaviours so at the end of 8 weeks you can begin creating new eating habits when you begin to reintroduce foods.	Increased risk of constipation, although this can be managed and prevented by ensuring an adequate fluid intake and taking a fibre supplement if required.
The shakes are quick and easy to prepare, come in a variety of flavours, and are nutritionally complete when taken with a multivitamin.	Some people may experience hair loss/thinning but this is usually only temporary, and hair will re-grow.
Weight loss is expected due to the calorie deficit created and it can be very motivating to see results quickly, especially if it allows you to come off some of your medications too.	You may experience an increased sensitivity to the cold, so are advised to wrap up warmly and include warm fluids. The soup sachets in the colder months can be useful.
It can be cost effective as it works out cheaper than doing a weekly food shop, especially if using a supermarket own brand (see our suggestions below).	It can be socially isolating. You may need a lot of support from your friends and family.

How to do it

Use a meal replacement product: shakes, 4 individual sachets, each providing approximately 250-300 calories. This provides a total of 1000-1200kcal per day when prepared correctly, plus 1 additional serving of whole milk if required. You must have all the shakes to ensure you are getting all the essential vitamins and minerals required to prevent nutritional deficiencies. Have these instead of your usual meals/snacks. The only equipment you need is a shake mixer cup.

Weeks 1 and 2	
Week 1 start date: _____	During phase 1 you should have the following every day : <ul style="list-style-type: none"> • 4 meal replacements per day (Approximately 1000-1200kcal) • 1400ml of other sugar free fluid (see page 2 for examples) • +/- 200-300ml whole skimmed milk
Week 2 start date: _____	

Example daily plan, depending on which shake is chosen

8am:	Meal replacement (250ml)
9am:	Sugar free drink (200ml)
11am:	Sugar free drink (200ml)
12 noon:	Meal replacement (250ml)
1pm:	Sugar free drink (200ml)
3pm:	Whole milk (200ml)
5pm:	Meal replacement (250ml)
6pm:	Sugar free drink (200ml)
8pm:	Meal replacement (250ml)
9pm:	Sugar free drink (200ml)

The volume of the shake will depend on which one is chosen; see the table at the end of this document.

Steps to take before starting the diet

- As far as possible, remove all tempting foods from the house
- Discuss the diet with your family and close friends
- It would also be helpful not to eat meals away from home all the time. You may wish to have your drink with your family so you can still share in meal times.
- Think about how you might manage any social occasions. If you are invited out for a meal, you should explain the diet to them so they are aware you will not be eating any solid foods

- When reintroducing foods you should plan your meals in advance
- Write a shopping list and buy everything you will need before you start

e.g.

- your meal replacements
- milk to make up meal replacement if required (see instructions on pack)
- your sugar free fluid e.g. diet soft drinks, herbal teas, sugar-free squash

Frequently Asked Questions

Which meal replacements can I use?

<p>Choose a product that matches the criteria below (all values are calculated after the shake or soup has been made with either milk or water as per the manufacturer's guidance):</p> <ul style="list-style-type: none"> • At least 15g of protein per serving • At least 2.5g of fibre per serving • Less than 20g of sugar per serving (including any natural sugars found in milk) • No corn syrup or hydrogenated vegetable oils • At least 33% of the Daily Value for vitamins and minerals 	<p>Suggested examples: **</p> <ul style="list-style-type: none"> • Asda Great Shape shakes-make up with skimmed milk • Tesco Ultralim shakes- make up with skimmed milk • Optifast soups and shakes- make up with water • Cambridge soups and shakes- make up with water • Exante - soups and shakes - make up with water
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**If you have any dietary intolerances/preferences please check with a dietitian as there are some products which may not be suitable and they can recommend alternatives.

Please note that none of these products are funded by the NHS in Hampshire.

Prices will vary depending on special offers and it is best to shop around. Buying a tub of powder and making them up yourself often works out cheaper.

Do I need additional supplements?

Yes, you will need to take an additional vitamin supplement. If iron deficiency anaemia is suspected prior to starting then your iron status should be assessed by your GP.

What sugar-free drinks can I have?

You must drink sugar free fluids in addition to your meal replacements. You can have:

- plain water
- carbonated water
- soda water (check the label to ensure it has no added sugar)
- flavoured water (check the label to ensure it has no added sugar)
- herbal teas (e.g. mint, lemon & ginger)
- diet or zero fizzy drinks

- no added sugar squash
- sugar free squash
- tea/coffee (you can use milk from your daily allowance of 100ml & add sweetener but not sugar)

Why not add a slice of lemon or lime to your water to make it more refreshing?

Will I have any side effects?

A small number of patients may experience mild side effects whilst on this diet. The most common side effect is constipation.

Please contact your Dietitian if you suffer any extreme side effects from this diet.

What should I do if I get constipated?

If after 1-2 days you find this is becoming a problem then we recommend that you take Optifibre to relieve these symptoms.

Do I need to monitor my blood glucose levels?

Yes, you will need to check on waking, before each shake, 2 hours after each shake and before bed.

Please contact your diabetes health care professional if:

- Your blood glucose levels are above 14mmol/l on waking or before meals
- Your blood glucose levels are below 4mmol/l (hypo) or you are having any hypo symptoms.

Do any of my medications need adjusting?

Your health care professionals will interpret and help you manage your diabetes and any related complications in light of your individual circumstances and adjust your medication accordingly.

Other diabetes medication:

All other oral medications can be decreased or stopped in agreement with your health care professional dependent on how well your diabetes control improves.

Meal replacement shakes are not a long-term solution for weight management. Long-term weight loss requires a significant change in lifestyle, including altering the composition of the diet. This is when phase 2 begins, the re-introduction of food and healthy eating behaviours with which you can also be supported.

Leslie WS, Ford I, Sattar N, Hollingsworth KG, Adamson A, Sniehotta FF, McCombie L, Brosnahan N, Ross H, Mathers JC, Peters C, Thom G, Barnes A, Kean S, McIlvenna Y, Rodrigues A, Rehackova L, Zhyzhneuskaya S, Taylor R, Lean ME. The Diabetes Remission Clinical Trial (DiRECT): protocol for a cluster randomised trial. BMC Fam Pract. 2016 Feb 16;17:20.

PHASE 2 (weeks 3-6)

Food Reintroduction

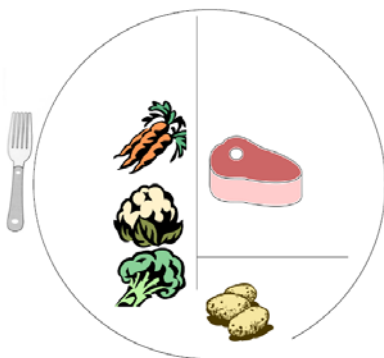
During phase 2 you will start to introduce food whilst reducing your milk intake. As a general guide when re-introducing meals have $\frac{3}{4}$ of what you used to eat. In summary each week you will re-introduce a meal or snacks.

Week 3 INTRODUCE LUNCH Start date:	Have the following every day: <ul style="list-style-type: none"> • One LUNCH - see overleaf • 3 meal replacements per day • 1.5 litres of other sugar free fluid
Week 4 INTRODUCE EVENING MEAL Start date:	Have the following every day: <ul style="list-style-type: none"> • One LUNCH - see overleaf • One EVENING MEAL - see overleaf • 2 meal replacements per day • 1.8 litres of other sugar free fluid
Week 5 INTRODUCE BREAKFAST + 1 x SNACK Start date:	Have the following every day: <ul style="list-style-type: none"> • One LUNCH - see overleaf • One BREAKFAST - see overleaf • One EVENING MEAL - see overleaf • One SNACK - see overleaf • 2 litres of other sugar free fluid
Week 6 INTRODUCE 1 MORE SNACK	Have the following every day: <ul style="list-style-type: none"> • One LUNCH - see overleaf • One BREAKFAST - see overleaf • One EVENING MEAL - see overleaf • Two SNACK - see overleaf • 2 litres of other sugar free fluid

EVENING MEAL (400 kcal)

This meal must include:

- 100g (4oz) lean meat *or* 125g (5oz) plain white fish/ tinned tuna *or* 150g (6oz) plain prawns *or* 2 boiled eggs *or* 150g (6oz) Quorn mince
- 4 egg size potatoes (185g/7.5oz cooked) *or* 4 tbsp cooked plain rice/cous cous (50g/2oz/2tbsp uncooked) *or* 6 tbsp cooked plain pasta (50g/2oz uncooked)
- ½ plate of salad or vegetables
- One piece of fruit
- Optional - gravy (instant – with no added meat juices!) *or* one dessertspoon of low fat salad dressing/ketchup/ pickle



Tips

- Do not add fats when cooking - prepare foods by dry-frying, dry-roasting, stewing, grilling, boiling, steaming
- Add extra flavour without adding calories e.g. use garlic, chilli, lemon juice, pepper, curry powder, herbs, spices
- Add flavour to salads with lemon juice or balsamic vinegar
- Have the fruit as a dessert – why not chop and add to one of your yoghurts?

Meal ideas

Roast - roast or grill 100g/4oz meat - ½ plate of vegetables
Fish - 125g/5oz grilled fish (sprinkle with lemon juice & herbs for extra flavour) - ½ plate salad or vegetables
Chilli - in water cook ½ onion, ½ pepper, 1 courgette, 1 carrot - add lean mince (100g/4oz), Quorn mince (125g) or chopped chicken (100g/4oz) - add 1 tin of tomatoes/passata, 2 tsp tomato paste, 1tsp chilli, 1tsp cumin, chopped garlic - serve with 4 tbsp rice or 1 jacket potato
Fish pasta - in water cook ½ onion, ½ pepper, 1 courgette, 1 carrot - add 1 tin of tomatoes/passata, 2 tsp tomato paste 1tsp mixed herbs & 1 clove of garlic - add 125g/5oz tinned fish or chopped fresh fish
Curry - in water cook ½ onion, ½ pepper, 1 courgette, 1 carrot - add 1 tsp curry powder & 1 tin of tomatoes/passata - add lean meat (100g/4oz), Quorn chunks (150g/6oz) or 2 halved boiled eggs
Spicy chicken - marinade chopped chicken (100g/4oz) with chilli or curry powder, then grill - ½ plate salad or vegetables - 4 new potatoes or 4 tbsp rice/couscous

BREAKFAST (300Kcal)

Choose one of the following for breakfast:

Breakfast cereal 6tbsp cereal (40g) (e.g. branflakes, cornflakes, All Bran) <i>or</i> 2 weetabix/shredded wheat <i>or</i> 4tbsp plain oats/muesli (no added sugar varieties) Serve with 1/3 pint (200ml) semi-skimmed milk
or
Toast 2 slices of toast (medium cut) topped with <i>one</i> of the following: - 1 tsp low fat spread and 1 level tsp jam on each slice - 1 tin of tomatoes and a handful of mushrooms - 1 egg (dry scrambled, poached, boiled) - ¼ tin baked beans - low fat cheese spread (60g)
or
Crackers 4 oatcakes <i>or</i> 5 Ryvita (original) <i>or</i> 5 plain rice cakes Top with low fat cheese spread (60g), <i>or</i> a scraping of low fat spread, marmite or jam

LUNCH (300Kcal)

Choose one of the following for lunch:

Sandwich 2 slices of bread (medium cut) <i>or</i> 1 pitta <i>or</i> 1 small roll filled one of the following: - 2 sliced boiled eggs - 3 slices of cold meat - 10 slices of wafer-thin ham, chicken or turkey - 125g fat-free cottage cheese - 75g low fat cottage cheese - 25g (1oz) chunk of cheese (matchbox size) - 2 grilled fish fingers 2 grilled slices of lean bacon
Toast toppers 2 slices of toast (medium cut) topped with one of the following: - 2 eggs - scrambled or poached - ½ tin of baked beans - 25g of cheese (matchbox size) 100g (4oz) tinned sardines, mackerel or pilchards (in tomato or mustard sauce)
Omelette 2 egg omelette cooked with onions, mushrooms, peppers and tomatoes. Serve with 2 slices bread (medium cut) <i>or</i> 4 egg sized boiled potatoes

Crackers

4 oatcakes or 5 Ryvita/plain rice cakes with one of the following:

- 2 sliced **boiled eggs**
- 3 slices of **cold meat**
- 125g **fat-free cottage cheese**
- 75g **low fat cottage cheese**
- 25g chunk of **cheese** (matchbox size)
- 75g reduced fat **hummus**
- Low fat **cheese spread** (60g)

Jacket potato

One potato (the size of your fist) with one of the following toppings:

- 125g **fat-free cottage cheese**
- 75g **low fat cottage cheese**
- 25g chunk of **cheese** (matchbox size)
- ½ tin of **baked beans**
- 125g **tuna** (in brine/water)
- 150g **plain prawns**
- 4tbsp **mixed beans in spicy sauce**
- 100g **tinned sardines** or **pilchards** in tomato sauce

Tips

- Add plenty of salad or veg to your lunch e.g. salad leaves, radish, cucumber, celery, beetroot, mushrooms, pepper, grated carrot, spring onion, pickled onions, fresh or tinned tomatoes – aim for ½ plate
- Watch your added fats – do not add fats when cooking and do not add more than 2 tsp low fat spread *or* 2 tsp low fat mayo/salad cream *or* 1 dessert spoon of low fat salad dressing/ketchup/pickle/brown sauce
- Dress salads with lemon juice or balsamic vinegar for no extra calories

SNACKS - Choose **ONE** of the following snacks each day (Total 200kcal):

Sweet	Savoury
1 sugar free jelly	1 slice of toast (medium cut - no spread) with 2 tinned tomatoes
2 pieces of fruit	1 slice of bread (medium cut - no spread) with marmite or scraping of low fat cheese spread
1 tablespoon of raisins/sultanas	2 original Ryvita/plain rice cakes topped with scraping of marmite or low fat cheese spread & tomatoes/cucumber or 100g tomato salsa
6 dried apricots	1 original Ryvita/rice cake with 100g fat free cottage cheese/50g low fat cottage cheese & 7 cherry tomatoes
1 small slice of malt loaf (no butter!) or finger of cake	1 original Ryvita/rice cake topped with a sliced boiled egg
1 Muller lite or Shape/Activia 0%	1 mini pitta/½ standard pitta filled with lots of salad or scraping of low fat cheese spread or marmite
2 Rich Tea, Ginger Nuts biscuits or Jaffa Cakes	2 oat cakes & 7 cherry tomatoes
1 hob nob or chocolate digestive	1 small packet of Quavers, Skips, Twiglets or reduced fat crisps
2 finger KitKat	
1 bite-size Brownie or mini chocolate roll	
1 small meringue nest with a handful of berries	
2 low calorie hot chocolate drinks	
½ mini apple pie or bakewell tart	
1 crumpet with a scraping of jam (no butter!)	
1 weetabix or 1 shredded wheat with semi-skimmed milk	
3 tablespoons of cereal with semi-skimmed milk	

Tip: Plan your snacks when you most likely feel the need to eat e.g. evening time, mid-afternoon

Meal Replacements

	Kcal/shake	Shakes	No per day	Fluid		Approx cost per day
Slim fast Powder	300	Y	4	250	Add 250ml whole milk	£3.00
Slimfast (ready to drink)	204	Y	5 + 300ml milk	325	Pre made	£9.50
Ultra slim (Tesco)	250	Y	4 + 200ml milk	200	Add 215ml whole milk	£2.00
Shake that weight	292	Y	4	250	250ml whole milk	£6-7
Asda Great Shape Shakes	250	Y	4 + 200ml milk	250	Add 215ml whole milk	£2.00