Guidelines to assist General Practitioners in the Management of Type 2 Diabetes

April 2010

Foreword

The guidelines were devised by the Diabetes Day Centre in Beaumont Hospital in consultation with a number of primary care practices in the North Dublin area.
The guidelines have a number of objectives:

- To improve delivery and quality of care for patients with Type 2 diabetes attending both their primary care physician and the specialist diabetes team in Beaumont Hospital.

- To develop integration of care between primary care and the diabetes service in Beaumont Hospital for patients with Type 2 diabetes.

- As an educational resource for both primary care and Beaumont Hospital.

It is hoped that these guidelines are the start of a process to improve communication and consultation between the hospital and primary care and that further initiatives will follow which will continue to develop integrated care for patients with Type 2 diabetes.

Yours Sincerely

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Criteria for 2 Yearly Review

- **Type 2 Diabetes**
  - HBA1c < 7.0% (< 53 mmol/mol) either on diet or oral hypoglycaemic agents
  - No history of severe hypoglycaemia
  - Normal 12-lead ECG
  - No micro-vascular complications
    - No renal failure (Creatinine >135umol/L)
    - No retinopathy
    - No history of foot ulcer / Charcot foot / peripheral neuritis or severe peripheral arterial disease (PAD)

Criteria for Annual Review

- **Type 2 Diabetes**
  - HBA1c > 7.0% (>53 mmol/mol) either on diet or oral hypoglycaemic agents or GLP-1 injections
  - History of severe hypoglycaemia
  - Abnormal 12-lead ECG
  - Documented micro-vascular complications
    - Renal failure (Creatinine >135umol/L)
    - Microalbuminuria
    - Retinopathy
    - History of foot ulcer / Charcot foot / peripheral neuritis or severe PAD

Patients with Type 2 diabetes on insulin may need to be seen every 6 months in the clinic

Aim of the Guidelines

- Increase integration of care and improve communication between Beaumont Hospital diabetes service and primary care.

- Educational resource.

- Assist primary care in
  - Management of type 2 diabetes between annual or 2-yearly hospital clinic visits

- From July 2010, a new type of measurement is being introduced for measuring HbA1c. This will mean the HbA1c will be recorded in mmol/mol instead of %.

A guide to the new values expressed as mmol/mol

Current DCCT aligned HbA_{1c} (%)	New IFCC HbA_{1c} (mmol/mol)
4.0	20
5.0	31
6.0	42
6.5	48
7.0	53
7.5	58
8.0	64
9.0	75
10.0	86

Target HbA1c

- **On Hypoglycaemic Agents**
  - 6.5% (48 mmol/mol) – 7.0% (53 mmol/mol) with no severe hypoglycaemia
- **On Insulin therapy**
  - < 7.0% (<53 mmol/mol) with no severe hypoglycaemia
- This is a guide only, as patients individual circumstances need to be taken into consideration,
  - elderly, living alone, dementia, co-existing morbidities

Frequency of HbA1c testing

- Test HbA1c 3 months after change in dose or addition of new hypoglycaemic agent
- If patient is stable and HBA1c is in target then test every 6 months
- Do not test more than 3 monthly

Type 2 DM – BMI (**18.5 - 27 kg/m²**)

Asymptomatic new T2 patient,
no weight loss, no ketones

↓

Commence on Metformin 500mg bd

↓

Titrate Metformin to maximum dose (1g bd) if HbA1c > 7.0 % (> 53 mmol/mol)

↓

Add in Sulphonylurea once daily if HbA1c remains > 7.0 % (> 53 mmol/mol)
(Titrate dose to maximum dose, to achieve target)
For example: start Gliclazide MR 30mg once daily
max dose is 120mg once daily

↓

If HbA1c remains > 7.0 % (>53 mmol/mol) Contact Diabetes Centre

Type 2 DM –BMI (**18.5 - 27 kg/m²**)

Symptomatic, weight loss, ketones may be present

↓

Commence on Sulphonylurea once daily.
Titrate dose of Sulphonylurea to maximum dose if blood glucose remains elevated

↓

Refer to Diabetes Day Centre

↙

HbA1c > 7.0% (> 53 mmol/mol)
- Further weight loss or ketones present suggests need for insulin therapy

- Refer to Diabetes Day Centre urgently.

↘

HbA1c > 7.0% (> 53 mmol/mol)
- Weight stable, no ketones
- Commence Metformin and titrate to maximum dose.

↓

Contact Diabetes Day Centre if HbA1c remains > 7.0 %(> 53 mmol/mol) on maximum oral agents - will need to commence insulin therapy

Overweight T2 DM **BMI > 27 – 30 kg/m²**

Commence on Metformin 500mg bd

↓

Increase Metformin to to maximum dose (1g bd) if HbA1c > 7.0% (>53 mmol/mol)

↓

If HbA1c remains > 7.0 % (> 53 mmol/mol) will need a second glucose lowering agent

Option 1	Option 2
Sulphonylurea	DPP- 4 Inhibitor

The TZD Pioglitazone could also be used in this setting

Liaise with Diabetes Centre or Community Diabetes Nurse for advice

Overweight T2DM **BMI > 27 – 30 kg/m²**

Treatment Option 1 in combination with Metformin

↓

Add Sulphonylurea

↓

Titrate dose of Sulphonylurea to maximum dose if HbA1c remains > 7.0% (> 53 mmol/mol)

↓

Assess patient for signs and symptoms of hypoglycaemia

↓

Failure to achieve target Hba1c with Metformin in combination with Sulphonylurea – Contact Diabetes Centre

Overweight T2DM BMI > 27 – 30 kg/m²

Treatment Option 2 in combination with Metformin

↓

DPP-4 Inhibitor

Janumet (1gm/50mg bd – Metformin + Sitagliptin) or
Eucreas (1gm/50mg bd – Metformin + Vildagliptin) or
Onglyza (Saxagliptin 5mg once daily)

↓

Failure to achieve target Hba1c with Metformin in combination with DPP 4 Inhibitor – Add in Sulphonylurea

↓

Titrate dose of Sulphonylurea to maximum dose if HbA1c remains > 7.0 % (> 53 mmol/mol)

↓

Failure to achieve target Hba1c with Metformin + DPP-4 Inhibitor in combination with Sulphonylurea – Contact Diabetes Centre

Obese T2DM **BMI > 30 – 35kg/m²**

Commence on Metformin 500mg bd

↓

Increase Metformin to maximum dose (**1g bd**) if HbA1c > 7.0 % (> 53 mmol/mol)

↓

If HbA1c remains > 7.0 % (> 53 mmol/mol) will need a second glucose lowering agent

Option 1

Sulphonylurea

Option 2

DPP-4 Inhibitor

Option 3

GLP-1 injection

The TZD Pioglitazone could also be used in this setting

Obese T2DM **BMI > 30 - 35kg/m²**

Treatment Option 1 in combination with Metformin

↓

Add Sulphonylurea

↓

Titrate dose of Sulphonylurea to maximum dose if HbA1c > 7.0 % (> 53mmol/mol)

↓

Assess patient for signs and symptoms of hypoglycaemia

↓

Failure to achieve target Hba1c with Metformin in combination with Sulphonylurea

Contact Diabetes Centre or Community Diabetes Nurse for advice

Obese T2DM **BMI > 30 - 35 kg/m²**

Treatment Option 2 in combination with Metformin

↓

DPP-4 Inhibitor

Janumet (1gm/50mg bd – Metformin + Sitagliptin) or
Eucreas (1gm/50mg bd – Metformin + Vildagliptin) or
Onglyza (Saxagliptin 5mg once daily)

↓

Failure to achieve target Hba1c with Metformin in combination with DPP-4
- Add in Sulphonylurea (continue DPP-4) or GLP 1 injection (stop DPP 4).
Contact Diabetes Centre or Community Diabetes Nurse for advice

Obese T2DM **BMI > 30 - 35 kg/m²**

Treatment Option 3 in combination with Metformin

↓

GLP – 1 Injection

Exenatide BD Injection or Liraglutide OD Injection

↓

Failure to achieve target Hba1c with Metformin in combination with GLP-1 injection – Add in Sulphonylurea
Contact Diabetes Centre or Community Diabetes Nurse for advice

Obese T2DM **BMI > 35kg/m²**

Commence on Metformin 500mg bd

↓

Increase Metformin to maximum dose (**1g BD**) if HbA1c > 7.0 % (> 53 mmol/mol)

↓

If HbA1c remains > 7.0 % (> 53 mmol/mol) will need a second glucose lowering agent

Option 1
GLP-1 injection
(preferred option)

Option 2
DPP-4 Inhibitor

Option 3
Sulphonylurea

The TZD Pioglitazone could also be used in this setting

Obese T2DM **BMI > 35 kg/m²**

Treatment Option 1 in combination with Metformin

↓

GLP 1 agonist (injection)

↓

Exenatide BD Injection or Liraglutide OD Injection

Failure to achieve target Hba1c with Metformin in combination with GLP 1 agonist - Add in Sulphonylurea.

Contact Diabetes Centre or Community Diabetes Nurse for advice

Obese T2DM **BMI > 35 kg/m²**

Treatment Option 2 in combination with Metformin

↓

DPP-4 Inhibitor

Janumet (1g / 50mg bd – Metformin + Sitagliptin) or
Eucreas (1g / 50mg bd – Metformin + Vildagliptin) or
Onglyza (Saxagliptin - 5mg once daily)

↓

Failure to achieve target Hba1c with Metformin in combination with DPP-4
- Add in Sulphonylurea (continue DPP-4) or GLP 1 injection (stop DPP 4).
Contact Diabetes Centre or Community Diabetes Nurse for advice

Obese T2DM **BMI > 35kg/m²**

Treatment Option 3 in combination with Metformin

↓

Add Sulphonylurea

↓

Titrate dose of Sulphonylurea to maximum dose if HbA1c
> 7.0 % (> 53 mmol/mol)

↓

Assess patient for signs and symptoms of hypoglycaemia

↓

Failure to achieve target Hba1c with Metformin in combination with Sulphonylurea

Contact Diabetes Centre or Community Diabetes Nurse for advice

Metformin

Advantages

- Effective
- Promotes weight loss
- No hypoglycaemia
- Long term data

Disadvantages

- Nausea, flatulence, diarrhoea – titrate slowly
- Cannot be used in renal impairment (i.e. Creatinine ≥ 130 umol/L) – risk of Lactic Acidosis
- Can cause B12 deficiency

Maximum dose is typically 1gm twice daily
Give dose with food – breakfast and evening meal

Sulphonylurea

Advantages

- Effective
- Long term data

Disadvantages

- Hypoglycaemia
- Weight gain
- ? Accelerate beta cell failure
- Caution in patients with hepatic cirrhosis and renal impairment – increased risk of hypoglycaemia

Medications in this class include:
Gliclazide MR (preferred option)
Glimepiride

Patient must be educated on the risk and management of Hypoglycaemia

DPP 4 Inhibitors

Advantages

- Weight neutral
- No increased risk of hypoglycaemia
- May preserve pancreatic beta cell function (speculation currently)

Disadvantages

- Side effects nausea, abdominal bloating, diarrhoea
- No long-term safety data

Medications in this class include:

Sitagliptin 50mg bd (in combination with Metformin = Janumet)
Vildagliptin 50mg bd (in combination with Metformin = Eucreas)
Saxagliptin 5mg once daily

GLP 1 Agonist/Injection

Advantages

- Weight loss
- No hypoglycaemia when used on its own
- Reduces post-prandial hyperglycaemia
- Delays gastric emptying
- May preserve pancreatic beta cell function (speculation currently)

Disadvantages

- Nausea, bloating, diarrhoea
- Subcutaneous injection
- Pancreatitis (rare)
- No long-term safety data
- In combination with sulphonylurea, may need to reduce the dose of sulphonylurea to prevent hypoglycaemia

Medications in this class include:
Exenatide BD S/C injection
Liraglutide OD S/C injection

PIOGLITAZONE

(Thiazolidenedione or TZD)

Advantages

- No hypoglycaemia
- Insulin sensitizer
- Some data suggests cardiovascular benefit
- Preserve beta cell function

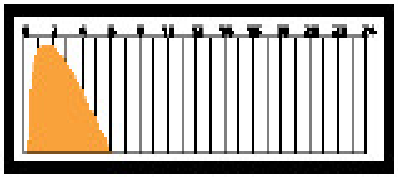
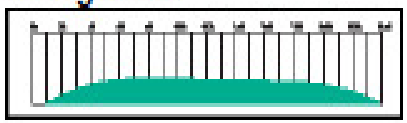
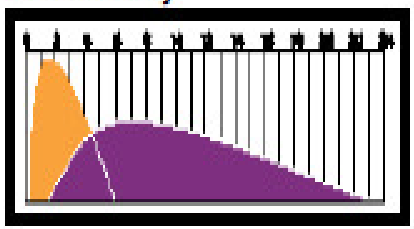
Disadvantages

- Weight gain
- Fluid overload
- NOT TO BE USED IN HEART FAILURE
- Increased risk of bone fracture – avoid in patients with metabolic bone disease
- Drop in haemoglobin

Starting dose is 15mg once daily, increased to 45mg a day

Can be used in combination with Metformin or sulphonylurea or insulin or DPP-4

Table of Insulin Therapy

Type of insulin		Insulin	Onset of action	Duration of action	Time of Administration	
Short acting pre-meal insulin		Actrapid	30 – 60 minutes	5 – 8 hours	20 minutes pre-meals	10 ml vial
		Insuman Rapid	30 – 60 minutes	5 – 9 hours	20 minutes pre-meals	3 ml cartridge Pre-filled pen (Optiset)
		Humulin S	30 – 60 minutes	5 – 8 hours	20 minutes pre-meals	3 ml cartridge 10 ml vial
Rapid acting pre-meal insulin analogue	Rapid Acting 	Aspart (Novorapid)	0 – 20 minutes	4 – 5 hours	Immediately as starting to eat	3 ml cartridge 10 ml vial Pre-filled disposable pen (Flexpen)
		Glulisine (Apidra)	0 – 20 minutes	4 – 5 hours	Immediately as starting to eat	3 ml cartridge 10 ml vial Pre-filled disposable pen (Optiset/ Solostar)
		Lispro (Humalog)	0 – 20 minutes	4 – 5 hours	Immediately as starting to eat	3 ml cartridge 10 ml vial Pre-filled disposable pen
Long acting insulin analogue	Background 	Glargine (Lantus)	1 – 2 hours	Up to 24 hours	Once daily (Typically with evening meal or bedtime)	3 ml cartridge 10 ml vial Pre-filled disposable pen (Optiset/ Solostar)
		Detemir (Levemir)	1 – 2 hours	14 – 20 hours	Once daily (as per Glargine) Twice daily (with breakfast and at evening meal/ bedtime)	3 ml cartridge Pre-filled disposable pen (Flexpen/ Innolet)
Intermediate Acting insulin	Background 	Insulatard	1½ – 2 hours	12 – 18 hours	Once or twice daily (as per Detemir)	3 ml cartridge 10 ml vial Pre-filled disposable pen (Innolet)
		Insuman Basal	45 – 60 minutes	12 – 18 hours	Once or twice daily (as per Detemir)	3 ml cartridge 5 ml vial Pre-filled disposable pen (Optiset)
		Humulin I	1½ – 2 hours	14– 18 hours	Once or twice daily (as per Detemir)	3 ml cartridge 10 ml vial Pre-filled disposable pen
Mixed insulin	Twice A Day 	Novomix 30 30% / 70%	0 – 20 minutes	12 – 16 hours	Twice day, pre breakfast & main evening meal	3 ml cartridge Pre-filled disposable pen (Flexpen)
		Mixtard 30 30% / 70%	30 – 60 minutes	12 – 16 hours	Twice day, pre breakfast & main evening meal	3 ml cartridge 10 ml vial Pre-filled disposable pen (Innolet)
		Humalog Mix 25% / 75%	0 - 20 minutes	12 – 16 hours	Twice day, pre breakfast & main evening meal	3 ml cartridge Pre-filled disposable pen
		Insuman Comb 25% / 75%	30 – 60 minutes	19 hours	Twice day, pre breakfast & main evening meal	3 ml cartridge 5 ml vial (Comb 25) Pre-filled disposable pen (Optiset)

ORAL HYPOGLYCAEMIC AGENTS

	Name of Drug	Dose	Max Dose	Time of Administration	Side Effects	Precaution
Biguanide	**Metformin** (Glucophage)	500 mg 850 mg 1000 mg	1g TDS Typical Dose is 1g BD	Once, twice or three times daily with food	GI upset B12 deficiency	Renal impairment Cirrhotic liver disease Acute CCF Metabolic acidosis Lactic acidosis Contrast studies*
Sulphonylureas	**Gliclazide MR** (Diamicron MR, Diaglyc)	30 mg	120 mg daily	Once daily - with breakfast	Hypoglycaemia GI upset	Renal impairment Liver impairment
	Gliclazide (Diaclide, Diabrazide)	80 mg	160 mg BD	Once or twice daily, with food - breakfast and evening meal		
	Glimepiride (Amaryl)	1 mg 2 mg 3 mg 4 mg	6 mg daily	Once daily - with breakfast		
	Glipizide (Glibenese)	5 mg	20 mg daily (Doses >15 mg should be taken in divided doses)	Once or twice daily, with food - breakfast and evening meal		
	Glibenclamide (Daonil) Avoid in patients > 65 years	2.5 mg 5 mg	15 mg daily	Once / twice daily with food - breakfast and evening meal		
Thiazolidinedione (TZD)	**Rosiglitazone** (Avandia) Avoid in patients with cardiac failure	4 mg 8 mg	8 mg daily	Once daily	Fluid retention Weight gain Anaemia	Hepatic impairment Renal impairment Macular oedema Osteoporosis Cardiovascular disorders
	Pioglitazone (Actos)	15 mg 30 mg 45 mg	45 mg daily	Once daily		
GLP-1 Analogue	**Exenatide** (Byetta)	5 mcg 10 mcg	10 mcg BD	Twice daily SC injection prior to breakfast & evening meal	Nausea Dizziness Pancreatitis	Liver failure Renal impairment, Severe GI disease Cachexia
	Liraglutide (Victoza)	0.6 mgs Increase after 1/52 to 1.2 mg	1.8 mg	Once daily SC injection		
DPP-4 Inhibitor	Sitagliptin (Januvia)-Caution with digoxin	100 mg	100 mg daily	Once daily	Nausea Dizziness Headache	Renal impairment Liver impairment
	Saxagliptin (Ongyza)	2.5 mg / 5 mg	5 mg daily			
	Vildagliptin (Galvus) with Metformin **Vildagliptin** (Galvus) with Sulphonylurea	50 mg 50 mg	50 mgs BD 50 mg daily	Twice daily Once daily - with breakfast		
Prandial glucose regulator	**Repaglinide** (Novonorm)	0.5 mg 1 mg 2 mg	16 mg daily	Before each meal	Hypoglycaemia GI upset	Renal impairment Liver impairment
	Nateglinide (Starlix)	60 mg 120 mg 180 mg	180 mg TDS			
Alpha-Glucosidase Inhibitor	**Acarbose** (Glucobay)	50 mg 100 mg	200 mg TDS	1 - 3 times daily with food	GI upset	Little effect on reducing blood glucose levels
Combination tablets	**Sitagliptin & Metformin** (Janumet)	50 mg / 850 mg 50 mg / 1000 mg	50 mg / 1000 mg BD	1 tablet twice daily with breakfast and evening meal	See individual agents above	See individual agents above
	Vildagliptin & Metformin (Eucreas)	50 mg / 850 mg 50 mg / 1000 mg	50 mg / 1000 mg BD			
	Pioglitazone & Metformin (Competact)	15 mg / 850 mg	15 mg / 850 mg BD			
	Rosiglitazone & Metformin (Avandamet) Avoid in patients with cardiac failure	1mg / 500 mg 2 mg / 500 mg 2 mg / 1000 mg 4 mg / 1000 mg	4 mg / 1000 mg BD			

* Contrast studies – Metformin should be stopped on day of contrast study if normal kidney function (48 hours before if abnormal kidney function ie Creatinine > 150 OR Egfr < 60ml/min) and only restarted 48 hours after study, if repeat U&E post contrast remains normal or unchanged.

Hypertension in T2DM

- Target Blood Pressure is <130/80 mmHg
- Blood Pressure should be checked every 3 months
- Patients often require 3 to 4 anti-hypertensive agents to reach their target blood pressure

Hypertension in T2DM (1)

Target Blood Pressure < 130/80 mmHg

FIRST LINE AGENT

ACE Inhibitor or ARB (first line agent)

(If creatinine >130umol/l check U&E 2-4 weeks after starting therapy)

↓

Fail to achieve target – Add in SECOND LINE AGENT

ACE Inhibitor or ARB

+ Calcium channel blocker (Amlodipine/Lercandipine/Diltiazem)

or

+ Diuretic: low dose Thiazide: 12.5 to 25mg Hydrochlorthiazide
or Indapamide: 1.5mg once daily
or Frusemide: 20 to 40mg once daily

Hypertension in T2DM (2)

Target Blood Pressure < 130/80 mmHg

Optimise combination of 1st and 2nd line agents
to achieve target BP
(*Thiazides/Indapamide should only be used in low dose)

↓

Fail to achieve target – Add in THIRD LINE AGENT

- If on ACE I or ARB + calcium channel blocker
  then add in diuretic (as before)

- If on ACE I or ARB + diuretic
  then add in calcium channel blocker

Hypertension in T2DM (3)

Add in beta-blocker or aldosterone anatagonist as 4th or 5th line agent

Rules of thumb

- Beta blocker should be used as **first line** if patient has **symptomatic angina**
- If serum creatinine > 130umol/l – **use** aldosterone antagonists with caution
- **Careful monitoring of U&E required when on aldosterone antagonists**
- If BP responds dramatically to **aldosterone antagonists consider renal artery stenosis**

↓

Add in alpha – blockers as 6th line agent
(Can be prescribed earlier if contraindications to other therapies)

Lipids in T2DM

- Check fasting lipids 3 months after starting therapy or after change in dose

- Once on stable dose check fasting lipid profile every 6 months

Lipid-Lowering (1)

no previous vascular event

Targets: LDL cholesterol < 2.6mmol/L
HDL > 1.0mmol/l in men, >1.1mmol/L in women
Triglycerides <1.7mmol/L

LDL cholesterol above target

Start statin: Atorvastatin 10mg* od **or**
Rosuvastatin 10mg* od **or**
Simvastatin 10mg* od **or**
Pravastatin 10mg od

Give at bed-time

Precaution: Renal failure
Liver failure (LFT > 3 times the upper limit of normal-caution)
Previous hx of myositis (avoid statins)
Previous reaction to statin therapy
Teratogenic
*Caution with Warfarin

Lipid Lowering (2)

no previous vascular event

Repeat fasting lipid profile 3 months after starting therapy.
Once stable check lipid profile 6 monthly
If patient has a history of renal or liver dysfunction monitor CK and LFT

LDL cholesterol remains above target

Increase statin dose: Atorvastatin to max dose of 80mg od
Rosuvastatin to max dose of 40mg od
Simvastatin to max dose of 80mg od
Pravastatin to max dose of 40mg od

Fail to achieve LDL cholesterol despite max dose

Try different statin agent (e.g. Atorvastatin more potent than Pravastatin)

Reaction to Statin therapy

Documented myositis: avoid statins
Acute deterioration in liver function: avoid statin
Non-specific symptoms: trial of another statin preparation

Lipid Lowering (3)

(no previous vascular event)

Baseline LDL cholesterol < 2.6 mmol/L on no treatment

↓

If more than one CV risk factor other than diabetes.
Start low dose statin

↓

Aim for reduction of > 30% from baseline LDL cholesterol

Lipid-Lowering

in patients who have had a previous vascular event.

All patients should be on a statin
no matter what their LDL cholesterol is

Target LDL cholesterol < 1.8mmol/L

Adjust therapy as per previous slide to achieve target LDL <1.8mmol/L

Anti-Platelet Agent

- Patients with a previous vascular event – should be on an anti-platelet agent
  Aspirin 75mg daily
  or
  Clopidogrel 75 mg daily

- Patients with no history of a previous vascular event but have one or more of the following – should be on an anti-platelet agent
  - Microalbuminuria
  - Smoker
  - Asymptomatic carotid artery disease (stenosis >30%)
  - Atrial fibrillation (consider Warfarin)
  - Peripheral arterial disease
  - Angina
  - Abnormal 12-lead ECG

Patients with no history of a previous vascular event – do not necessarily need to be on an anti-platelet agent

The usual contraindications to Aspirin and Clopidogrel therapy apply

Diabetes Centre

Telephone: (01) 809 2744 / 5
Fax: (01) 809 3370

Opening Hours

Monday to Friday: 8.00am to 4.00pm.

Urgent referrals

Please fax referral letter to Diabetes Centre

- These protocols are also available on http://www.beaumont.ie/diabetescentre

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