1-year outcomes of REVISE-Diabesity clinical trial

Randomisation to EndobARRIER alone Versus with Incretin analogue in Sustained Diabesity

Dr Bob Ryder, Birmingham City
Dr Barbara McGowan, Guys, London
Dr Piya Sen Gupta, Kings, London and Birmingham City
Dr Russell Drummond, Glasgow Royal
Prof Stephanie Amiel, Kings, London

ABCD Meeting, Manchester, Spring 2016
Introduction – Bob Ryder

- Prologue
- Concept
- Aims
- Methods
Prologue
Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol


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Abstract

Aims/Hypothesis Type 2 diabetes is regarded as inevitably progressive, with irreversible beta cell failure. The hypothesis was tested that both beta cell failure and insulin resistance can be reversed by dietary restriction of energy intake.

Methods Eleven people with type 2 diabetes (49.5±2.5 years, BMI 31.6±1.2 kg/m², nine male and two females) were studied before and after 1, 4 and 8 weeks of a 2.5 MJ (600 kcal/day) diet. Basal hepatic glucose output, hepatic and peripheral insulin sensitivity and beta cell function were measured. Pancreas and liver triacylglycerol content was measured using three-point Dixon magnetic resonance imaging. An age-, sex- and weight-matched group of eight non-diabetic participants was studied.

Results After 1 week of restricted energy intake, fasting plasma glucose normalised in the diabetic group (from 9.2±0.4 to 5.9±0.4 mmol/l, p=0.003). Insulin suppression of hepatic glucose output improved from 43±4% to 74±5% (p=0.003 vs baseline; controls 68±5%). Hepatic triacylglycerol content fell from 12.8±2.4% in the diabetic group to 2.9±0.2% by week 8 (p=0.003). The first-phase insulin response increased during the study period (0.19±0.02 to 0.46±0.07 mmol min⁻¹ m⁻², p<0.001) and approached control values (0.62±0.15 mmol min⁻¹ m⁻², p=0.42). Maximal insulin response became supranormal at 8 weeks (1.37±0.27 vs controls 1.15±0.18 mmol min⁻¹ m⁻²). Pancreatic triacylglycerol decreased from 8.0±1.6% to 6.2±1.1% (p=0.03).

Conclusions/Interpretation Normalisation of both beta cell function and hepatic insulin sensitivity in type 2 diabetes was achieved by dietary energy restriction alone. This was associated with decreased pancreatic and liver triacylglycerol stores. The abnormalities underlying type 2 diabetes are reversible by reducing dietary energy intake.

Keywords Insulin secretion - Liver fat - Low energy diet - Pancreatic fat - Type 2 diabetes

Introduction

Type 2 diabetes has long been regarded as a chronic progressive condition, capable of amelioration but not cure. A steady rise in plasma glucose occurs irrespective of the degree of control or type of treatment [1]. Beta cell function declines linearly with time, and after 10 years more than 50% of individuals require insulin therapy [2]. The underlying changes in beta cell function have been well described [3, 4], and betacell mass depreciation rapidly.
11 patients diabetes <4 years duration
600 kcal diet/day diet for 8 weeks:

- Decreased liver fat
- Decreased pancreatic fat
- Normalisation of beta cell function
- Normalisation hepatic insulin sensitivity
- Normalisation glucose metabolism

ie “Cure” of type 2 diabetes!

Lim EL, et al Diabetologia 2011; 54: 2506-2514
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Lim EL, et al Diabetologia 2011; 54: 2506-2514
11 patients diabetes <4 years duration
600 kcal diet/day diet for 8 weeks:

• Decreased liver fat
• Decreased pancreatic fat
• Decreased coronary artery fat
• Decreased carotid artery fat
The Treat-to-Target Trial

Randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients

Matthew C. Riddle, MD
Julio Rosenstock, MD
Matthew Riddle, MD

OBJECTIVE — To compare the effectiveness and associated hypoglycemic risks of adding glargine and human NPH insulin added to oral therapy of type 2 diabetes to achieve 7% HbA1c.

RESEARCH DESIGN AND METHODS — In a randomized, open-label, parallel 24-week multicenter trial, 756 overweight men and women with inadequately controlled type 2 diabetes were randomized to receive either glargine or NPH insulin once daily, starting using a simple algorithm selecting a target fasting plasma glucose (FPG) of 7.8 mmol/L (140 mg/dL). Once target FPG was reached, HbA1c, hypoglycemia, and percentage of patients reaching HbA1c <7% without documented nocturnal hypoglycemia were assessed.

RESULTS — Mean FPG at end point was similar between glargine and NPH (117 ± 120 mg/dL vs 117 ± 123 mg/dL, P = 0.823). A majority of patients c (79%) reported a mean HbA1c of 6.6% ± 0.7% with each insulin type. However, mean HbA1c was similar (7.0% ± 0.7% vs 7.1% ± 0.7%, respectively, P = 0.102). The incidence of nocturnal hypoglycemia (≥3 discrete episodes) was 14% with glargine and 15% with NPH, respectively (P = 0.448). The incidence of hypoglycemia was similar between the two treatments (8% vs 9%, respectively, P = 0.102). Mean FPG was similar between the two treatments (7.8 ± 2.0 mg/dL vs 7.7 ± 2.0 mg/dL, P = 0.05).

CONCLUSIONS — Systematically treating bedtime basal insulin added to oral therapy can safely achieve 7% HbA1c in a majority of overweight patients with type 2 diabetes with HbA1c between 7.5 and 10.0% on oral agents alone. In doing so, glargine causes significantly less nocturnal hypoglycemia than NPH, thus reducing a leading barrier to initiating insulin. This simple regimen may facilitate earlier and effective insulin use in routine medical practice, improving achievement of recommended standards of diabetes care.

Diabetes Care 26:3080-3086, 2003

Hannele Yki-Jarvinen

Yki-Jarvinen et al, Diabetologia 2006; 49: 442-451
Type 2 diabetes is a progressive disorder of β-cell dysfunction. Patients receiving oral therapy for it seldom achieve and maintain the recommended 7% HbA1c goal (13 mmol/mol) for glycemic control and are exposed to increasing risks of diabetic complications as central women over time (2-5). The U.K. Prospective Diabetes Study (UKPDS) (6) showed that keeping increasing the insulin to drive down the HbA1c helps. The Treat-to-Target Trial (7) showed that adding insulin to oral therapy in type 2 diabetic patients with HbA1c > 7% (53 mmol/mol) improved glucose control and reduced excess β-cell dysfunction and β-cell death. The insulin analogues glargine and lispro are more effective and better tolerated than Lente insulin at achieving target HbA1c levels (8, 9). The U.K. Prospective Diabetes Study (UKPDS) (6) showed that adding insulin to oral therapy in type 2 diabetic patients with HbA1c > 7% (53 mmol/mol) improved glucose control and reduced excess β-cell dysfunction and β-cell death. The insulin analogues glargine and lispro are more effective and better tolerated than Lente insulin at achieving target HbA1c levels (8, 9).
Treating to Target

Type 2 diabetes is a progressive disorder of β-cell dysfunction. Patients receiving oral therapy for it seldom achieve and maintain the recommended 7% HbA1c goal.2,3)4)5)6)7)

HbA1c was <7% in only 30% of patients treated with glargine at a mean follow-up of 2.6 years. In addition, 75% of patients had HbA1c levels >8% at the end of the study. This suggests that long-term treatment with glargine is not effective in achieving target HbA1c levels.

In conclusion, the use of glargine in combination with metformin is an effective treatment option for type 2 diabetes. However, further studies are needed to evaluate the long-term efficacy and safety of this treatment regimen.

Keywords: Glargine - metformin - type 2 diabetes

References:
1. Riddle et al, Diabetes Care 2003; 26: 3080-3086

Julio Rosenstock
Matthew Riddle
Hannele Yki-Jarvinen

Keep increasing the insulin to drive down the HbA1c
But ....
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**Keep increasing the insulin to drive down the HbA1c**

But ....

**increasing the insulin increases the weight**
A patient in Dr Ryder’s clinic who followed the treat to target approach

- May 2006
- Wt = 160 kg
- BMI = 53
- 325 units insulin daily with pioglitazone
- HbA1c = 6.7%
Roux-en-Y stomach gastric bypass surgery
Roux-en-Y gastric bypass surgery

- May 2006
  - Wt = 160 kg
  - BMI = 53
  - Trouser size = 54 inch
  - 325 units insulin daily with pioglitazone etc
  - HbA1c = 6.7%
  - BP 162/75 on 3-4 antihypertensive agents

- April 2008
  - Wt = 83 kg
  - BMI = 27
  - Trouser size = 32 inch
  - No insulin; no OHAs
  - HbA1c = 7%
  - BP 112/70 - no anti-hypertensives
Roux-en-Y gastric bypass surgery

- May 2006
- April 2008
Roux-en-Y gastric bypass surgery

- Spent 1 month in intensive care unit post op because of post op complications
  - 325 units insulin daily with pioglitazone etc
  - HbA1c = 6.7%
  - BP 162/75 on 3-4 antihypertensive agents
  - No insulin; no OHAs
  - HbA1c = 7%
  - BP 112/70 - no anti-hypertensives
Wouldn’t it be great if there was a less invasive procedure?

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Wouldn’t it be great if there was a less invasive procedure?
EASD Lisbon, 2011
EndoBarrier® Duodenal-Jejunal Bypass Liner rapidly improves diabetes parameters paralleled by increased postprandial GLP-1 and PYY levels in obese type 2 diabetic patients

Charlotte de Jonge
Department of Surgery, Maastricht University Medical Centre
Endobarrier – implantable duodenal-jejunal liner

- 60 cm impermeable sleeve
- Minimally invasive
Weight loss and diabetic improvement

**Weight:**

- Weight:
  - D0: 120 kg
  - W24: 110 kg
  - P < 0.001

- Excess weight:
  - D0: 100%
  - W24: 75%
  - P < 0.001

**Diabetes:**

- HbA1c:
  - D0: 9%
  - W24: 6%
  - P < 0.001

Reduction of anti-diabetic medication in 16/17 patients

---

de Jonge et al. EASD Lisbon, 2011
REVISE- Diabetes study came into existence during this presentation with its outline as notes “on the back of an envelope” completed before the presentation was finished!
2 year endobarcare

ABC thesis audit failure

BMI > 35

HbA1c > 8%

Group 0: normal care
Group 1: titrate liraglutide up to 3mg or max tolerated
Group 2: endobarrier followed by liraglutide

Group 1: + liraglutide + combine
2 year end hormones

ABC: HRA audit failures

BMI > 35

HbA1c > 8%

Became ≥7.5%

Group 0: Normal case

Group 1: Titrate lira up to 3mg as max bleol

Group 2: End dose accelerated followed by half strength

Group 3: " + Lira 3mg + Combine 3"
Became 4 contributing centres

ABCD now audit failures

Group 0 "normal case"

Group 1: titrate lime up to 3mg as max bleed

Group 2: endoscopist followed by keep score

Group 3: "lima 3mg"

Group 4: " + lima 3mg + combine 3"
Became 4 contributing centres

Became Dr Sen Gupta!
Became the endobarrier plus liraglutide 1.2mg group

Group 0 = usual case
Group 1 = titrate liragl up to 3mg as max between
Group 2 = endobarr + liragl 3mg + combine 3mg
Became the endobarrier plus liraglutide 1.2mg group

Became the endobarrier instead of liraglutide group

Group 0: Normal case

Group 1: Titrate liraglutide up to 3mg as max dose after

Group 2: EndobARRIER plus liraglutide followed by half dose of

Group 3: + Lira 3mg + Continue 3mg
Became the endobarrier plus liraglutide 1.2mg group

Became the endobarrier instead of liraglutide group

Became the liraglutide 1.8mg group
Fundi

AICD pay for endobronchial laser provided here

Customer requests we collaborate

N? - ask statistic

✓  🔴

✓  🔴

✓  🔴

✓  🔴
Concept & timelines for the trial

- EASD 2011
- 2012-3 grant, ethics, R&D approval
- July 2013 – first patient treated
- April 2016 – 1-year complete for all patients
- March 2017 – 2-year results
Aim

To investigate the effects of adding proximal intestinal exclusion to GLP-1RA therapy not achieving targets, on weight and HbA1c compared to either treatment alone.
INCLUSION CRITERIA:

- Type 2 diabetes
- Liraglutide treated for ≥6 months
- HbA1c ≥58mmol/mol (7.5%)
- Obesity, BMI ≥35kg/m²
- Stable weight, HbA1c (3 months)

EXCLUSION CRITERIA:

- Safety considerations:
  - Bleeding risk: aspirin, warfarin
  - Infection
  - Pregnancy
- Conditions interfering with endobARRIER placement/ findings
Study design:
Open label, multicentre, parallel group, randomised controlled trial

Trial Registrations:
ISRCTN00151053
NCTNCT02055014
Study design:
Open label, multicentre, parallel group, randomised controlled trial

- 3-monthly visits: interview, anthropometry, blood tests (fbc, u&e, lft, amylase, lipids, HbA1c)
- Primary outcome: HbA1c at 2 years
- Subgroup MRI liver and pancreas – baseline and 4 months
Results – Piya Sen Gupta

- Flowsheet of study subjects
- Baseline characteristics
- Efficacy:
  - weight
  - HbA1c and diabetes medications
  - Cardiovascular risk
  - Liver fat
Flowsheet of study subjects (n70)

Assessed for eligibility (n=195)
Assessed for eligibility (n=195)

Excluded (n=110)
Did not meet inclusion criteria (n= 54)
Had exclusion criteria (n=38)
Declined to participate (n= 11)
Other (n=7)
Flowsheet of study subjects (n=70)

Assessed for eligibility (n=195)

Excluded after randomisation (n=15)
- Wanted specific allocation only (n=13)
- Emigrated (n=1)
- Unrelated SAE (n=1)

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- Other (n=7)

n70

TREATMENT GROUP

EndobARRIER + liraglutide: 24
EndobARRIER: 24
Liraglutide 1.8mg: 22

Intention to treat analysis
### Baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EndobARRIER +liraglutide N=24</th>
<th>EndobARRIER N=24</th>
<th>Liraglutide N=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.0±11.7</td>
<td>50.7±8.4</td>
<td>54.0±10.1</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>41.7</td>
<td>29.2</td>
<td>36.4</td>
</tr>
<tr>
<td>Ethnicity (% Caucasian)</td>
<td>66.7</td>
<td>70.8</td>
<td>72.7</td>
</tr>
<tr>
<td>*Diabetes duration (yrs)</td>
<td>11.2 (6.7-17.1)</td>
<td>10.3 (7.8-12.7)</td>
<td>13.3 (9.0-18.4)</td>
</tr>
<tr>
<td>Taking insulin (%)</td>
<td>58.3</td>
<td>25.0</td>
<td>45.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>40.3±4.8</td>
<td>41.7±4.9</td>
<td>40.6±4.4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>112.8±20.4</td>
<td>115.6±19.4</td>
<td>113.9±14.9</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>81.5±14.9</td>
<td>78.1±19.0</td>
<td>82.5±18.8</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>9.6±1.4</td>
<td>9.3±1.7</td>
<td>9.7±1.7</td>
</tr>
</tbody>
</table>

*interquartile range

No significant differences between groups
Impact of treatment on weight over 1 year

Weight (Kg) mean ± 1SE

Time since treatment (months)

Weight loss at 1yr vs base

**P<0.001, ***P<0.0001
Impact of treatment on HbA1c over 1 year

HbA1c (mmol/mol) mean ± 1SE

HbA1c reduction at 1yr vs base

-2.1%  -1.2%  -1.3%
P=0.06  P=0.07

Time since treatment (months)
% frequency of diabetes medications at baseline by treatment group

E+L: Eritetolol, L: Liretalon

- Metformin
- Insulin
- Sulphonylurea
- Pioglitazone
- DPPIV inhibitor
- SGLT2 inhibitor
Number of new/ stopped diabetes medications started in each intervention group

- New diabetes drugs started: 3, 14, -1
- Diabetes drugs stopped: -6, 7, -2

P = 0.01
Change in total daily dose of insulin by treatment group

E+L: \(-76\) (-96 to -15) \(p=0.02\)

E: \(-14\) (-20 to 34) \(p=0.07\)

L: \(-28\) (-49 to 14) \(p=0.03\)
Impact of treatment on 10-year cardiovascular risk

<table>
<thead>
<tr>
<th>10-Year CV risk score parameters</th>
<th>Q-risk2</th>
<th>UKPDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Sex, Ethnicity, Smoking status</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Postcode</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Diabetes status</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Duration of diabetes, HbA1c</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Hypertension status, Rheumatoid arthritis, CKD IV-V</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Cholesterol:HDL</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>BMI</td>
<td>✔</td>
<td></td>
</tr>
</tbody>
</table>

Q-risk2 at baseline
- 38.7% intermediate (10-20%) risk
- 40.0% high (>20%) risk
Impact of treatment on 10-year cardiovascular risk

Q-risk2

UKPDS

*  

**
Liver fat pre- and post-MR images

Pre-endobarrier

4-months later
Liver fat pre- and post-MR images

Pre-endobarrier

Fat fraction 22.4%

4-months later

Fat fraction 0.5%
Liver fat – n8

Mean hepatic fat fraction fell from 15.9±9.4% to 2.9±4.5% post-endobARRIER (87.5±25.2% reduction), 
P=0.0026
Mean pancreatic fat fraction fell from 6.9% to 1.3% post-endobARRIER, $P=0.02$
Safety and tolerability – Barbara McGowan

- Serious adverse events
- Quality of life
- Satisfaction scores
### Safety Data

**Table of Serious Adverse Events (related)**

<table>
<thead>
<tr>
<th>Event</th>
<th>Early removal ✓ or X</th>
<th>EndobARRIER +liraglutide</th>
<th>EndobARRIER</th>
<th>Liraglutide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal symptoms</td>
<td>✓</td>
<td>3</td>
<td>2</td>
<td>---</td>
</tr>
<tr>
<td>Symptomatic cholelithiasis</td>
<td>✓</td>
<td>---</td>
<td>2</td>
<td>---</td>
</tr>
<tr>
<td>GI Bleed</td>
<td>✓</td>
<td>---</td>
<td>1</td>
<td>---</td>
</tr>
<tr>
<td>Obstruction</td>
<td>✓</td>
<td>1</td>
<td>1</td>
<td>---</td>
</tr>
<tr>
<td>Complicated removal</td>
<td>n/a</td>
<td>---</td>
<td>1</td>
<td>---</td>
</tr>
<tr>
<td>Liver abscess</td>
<td>X</td>
<td>---</td>
<td>2</td>
<td>---</td>
</tr>
</tbody>
</table>

5/48 (10.4%) cases had serious complications and all had a full recovery following endobARRIER removal.
Liver abscess - case 1

• 51yr Caucasian female
• Base BMI 53.9kg/m², HbA1c 73mmol/mol (8.8%)
• 01/07/2014 – EndobARRIER implant
• 6 weeks later – admitted to a local hospital while on holiday with nausea, vomiting, fevers and abdominal pain
• → Glasgow CT abdomen:

Attempted US-guided drainage was unsuccessful
• IV Tazocin 12 days, PO ciprofloxacin 16 weeks as she refused removal
• At 1-year EndobARRIER removed – weight loss 18.9kg, HbA1c +0.9%

After 10 weeks antibiotics
Liver abscess – case 2

- 48yr Afrocaribbean male
- Base BMI 44.3kg/m², HbA1c 67mmol/mol (8.3%)
- 30/09/2013 – Endobarrier implant
- At 1-year – DNA’d planned removal, seen at 14 months
- 10 days later – Admitted with septic shock, hyperosmolar hyperglycaemic state glucose 47.4mmol/l, Ur42, Cr348, bili 28, ALT100, AlP140, CRP 239
- 10/12/2014 CT abdomen – 13x10x12cm right lobe hepatic abscess
- Abscess drained twice – 500mls pus removed and IV then PO antibiotics
- Abscess improved
- Feb 2015 – Endobarrier removal
Liver abscesses

- FDA pivotal trial in USA – ENDO trial
- Design: RCT double blind, sham control, 500 patients, 25 centres
- July 2015, ENDO trial was terminated early (325/500 enrolled) due to 7 /217 (3.2%) cases of hepatic abscess (exceeded safety threshold 2%)
- Liver abscesses occurred 40-424 days after implant

- 3000 cases worldwide since 2009 – liver abscess rate ~ 0.73%

- Recommendations under consideration:
  - Antibiotic cover for implant and explant procedures
  - Shortened implant period (9 months)
EQ-5D quality of life – health state at 1-year

“Indicate how good or bad your health state is today in your opinion (the best state you can imagine is marked 100, the worst state you can imagine is marked 0.)”

E+L: \[ 77.6 \pm 13.5 \]
E: \[ 76.4 \pm 17.4 \] \[ p=0.79 \]
L: \[ 74.9 \pm 18.1 \] \[ p=0.79 \] \[ p=0.58 \]
### Patient satisfaction – NHS friends and family test

“How likely would you be to recommend the treatment you have had in this research study to family and friends based on your experience?”

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very likely</td>
<td>89.5%</td>
</tr>
<tr>
<td>Likely</td>
<td>85.7%</td>
</tr>
<tr>
<td>Neither</td>
<td>88.9%</td>
</tr>
<tr>
<td>Likely/unlikely</td>
<td></td>
</tr>
<tr>
<td>Unlikely</td>
<td></td>
</tr>
<tr>
<td>Very unlikely</td>
<td></td>
</tr>
<tr>
<td>Don’t know</td>
<td></td>
</tr>
</tbody>
</table>
Summary

- In E+L group HbA1c fell by 22.8 mmol/mol (2.1%) from 81.5 (9.6%) to 58.7 mmol/mol (7.5%) and weight fell by 12.4 kg from 112.8kg to 100.4 kg
- Both endobARRIER groups produced reduction in weight with a reduction in liver and pancreatic fat
- E+L group demonstrated a trend towards superiority with HbA1c reduction at 1-year, achieved with:
  - reduction in other diabetes medications
  - reduction in 10-year cardiovascular risk
- Safety profile is reasonable – ongoing clinical vigilance during the implant period is advised
- Patient satisfaction levels are high
These data suggest that adding proximal intestinal exclusion in patients with suboptimally performing GLP1-RA therapy rather than switching to it or increasing GLP-1RA dose, has a useful role in the management of refractory diabetes and obesity.
Acknowledgements

All study participants

Endoscopy team: Mark Anderson, Louise Bensaid, Ross Carter, Ed Fogden, David Galloway, Bu Hayee, Lesley Sadler
Research Nurses/ CRF facility: Alison Begg, Elka Giemza, Manju Joy, Fiona Kinney, Fran Lloyd, Hilary Peddie, Andrew Pernet, Bula Wilson, Louisa Green, Noah Yogo
Fellows: Ramdeep Bajwa, Chris Kueh, Siang Lee, Sebastian Lugg, Laura McCreight, Lois Murray
Administration: Melissa Cull, Rosa DaCosta, Vikram Johal, Ben Stothard, Melanie Wyres
R&D: Jocelyn Bell, Sinead Collinge
Statistician: Andrew Blann
Data monitoring committee: Cliff Bailey, John McClure, Parth Narendran
Association of British Clinical Diabetologists
NIHR/ Wellcome Trust King’s Clinical Research Facility