SubCutaneous Insulin: Pumps or Injections

Randomised controlled trial of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type I diabetes mellitus.

EudraCT number: 2010-023792-25

ISRCTN: 29255275

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Date	31/07/2017		
Protocol Version and Date	Version 7.0 (01/08/2016)		

Report Amendments Change Control

Updated report version no.	Report section changed	Description of change	Date changed	Initials
2.0	6.2 Study population • 6.2.1 Data sets analysed	Updated Figure 6.2-1 to account for the additional permanent change of insulin delivery* i.e. 1 more from CSII to MDI between 9m-12m.	31/07/2017	AMc
2.0	6.2 Study population • 6.2.2 Protocol deviations	Updated Table 6.2-5 to account for the additional permanent change of insulin delivery* i.e. 1 more major protocol deviation.	31/07/2017	AMc
2.0	6.6.1.2 HbA1c measured 12 months after randomisation – Per-protocol	Updated Table 6.6-5, Table 6.6-6, Table 6.6-7 and Table 6.6-8 and to account for the additional permanent change of insulin delivery* i.e. 1 less patient CSII patient included in the primary outcome per-protocol analysis.	31/07/2017	AMc
2.0	6.7 Additional analyses • 6.7.1 Permanent change to insulin delivery method	Updated Figure 6.7-1 to account for the additional permanent change of insulin delivery* i.e. 1 more from CSII to MDI in the primary outcome ITT meta-analysis for Alder Hey.	31/07/2017	AMc
		Updated Table 6.7-1, Table 6.7-2 and Table 6.7-3 to account for the additional permanent change of insulin delivery* i.e. further details added.	31/07/2017	AMc
	6.7 Additional analyses • Safety data – EUDRA-CT – Post-hoc	To upload the adverse event data to EUDRA-CT database the descriptions are required to be (1) summarised as non-serious AEs and serious AEs and (2) be MedDRA coded using System Organ Class (SOC) and Preferred Term (PT). All adverse events were MedDRA coded and agreed by the Chief Investigator after unblinding hence why labelled post-hoc.	31/07/2017	AMc

* The SCIPI trial database was unlocked to add one additional 'Form 13 Permanent Change To Insulin Delivery Method' for an patient Alder Hey patient.

1. Table of Contents

2. List of Tables and Figures

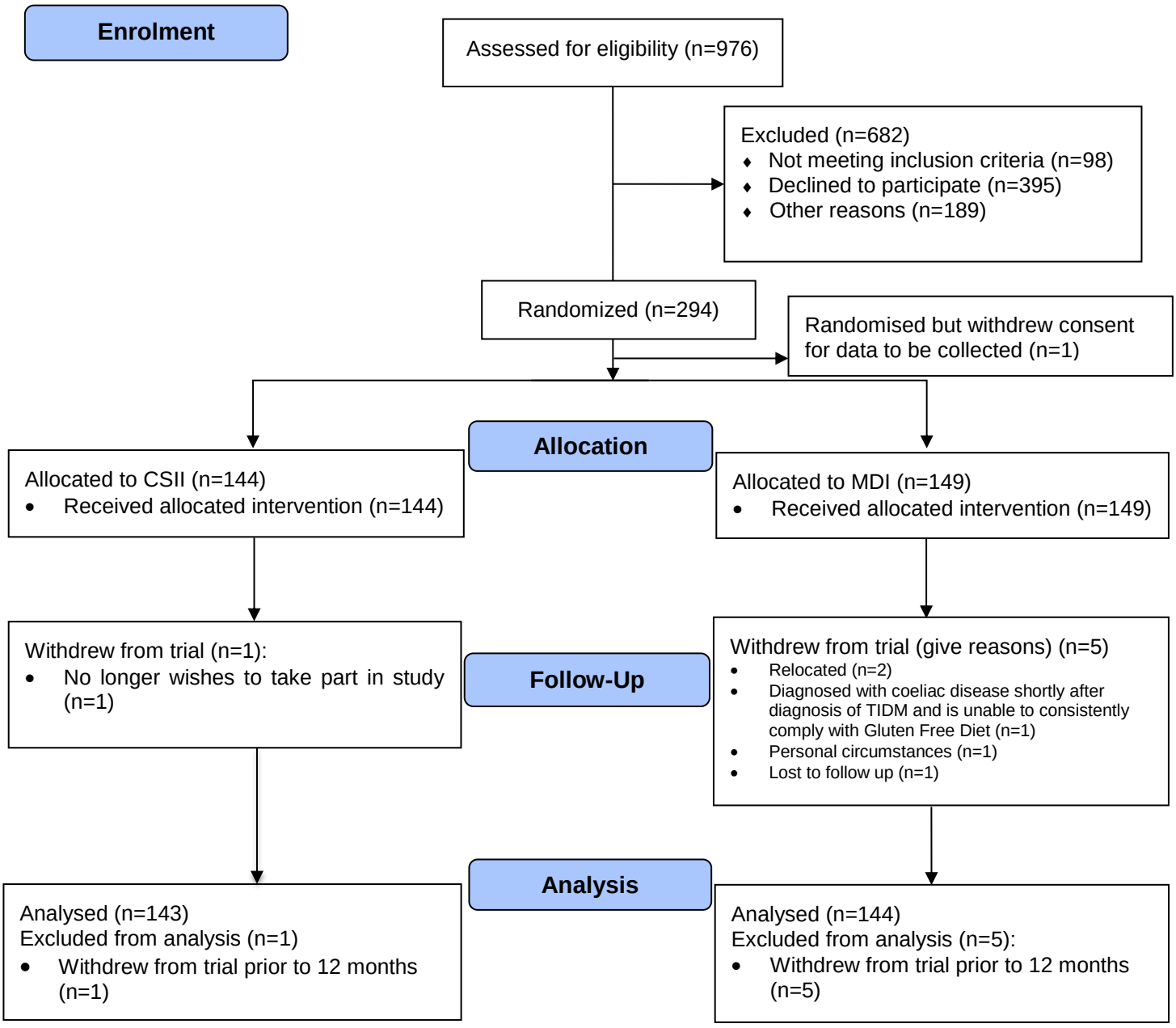
List of Tables

List of Figures

3. CONSORT diagram

3.1 CONSORT 2010 Flow Diagram

Figure 3.1-1: CONSORT 2010 Flow Diagram



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4. Randomisation checking

A statistical quality assurance check was performed to check for missing randomisation numbers and whether any had been randomised out of sequence. There are no missing randomisation numbers and no numbers randomised out of sequence.

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5. Recruitment

5.1 Recruitment summary

Summary

- Total number randomised = 294
- Date of first randomisation: 31/05/2011
- Date of last trial randomisation: 23/03/2015
- Total centres participated = 15 (3 site closure(s): See Table 5.1-1 for further details)

Table 5.1-1: Site closure reasons

Site	Initiation date	Date closed	Reason for closing early
Cardiff	19/12/2011	09/09/2014	Lack of staff resources
Doncaster	26/04/2012	02/09/2014	Financial and invoicing issues
Mid-Staffordshire	16/07/2013	29/12/2014	Unforeseen Trust changes (Mid Staff and North Staff hospitals merging and ward closure)

Note: Table provided by Trial Management.

5.2 Screening rates by site

Table 5.2-1: Screening and consent by site (All protocol versions combined, but consent rate broken down by protocol versions)
≤v3: Protocol versions 1-3 (covering recruitment period from 16/05/2011-16/08/2012).
≥v4: Protocol versions 4-5 (covering recruitment period from 17/08/2012-31/03/2015).
[A]-[F] cells used for denominators in percentage calculations for other cells.
[dx] denominator is [x]; [dx+y] denominator is [x]+[y].

Site (Initiation date)	Total screens [A]	Total not eligible (%) [B] [dA]	Total eligible (%) [C] [dA]	Eligible but consent not sought							Eligible and consent sought but refused				Total consented (%) [F] [dE+F]	Rando-mised
				Lack of trained staff (%) [dD]		Reason not recorded (%) [dD]		Consultant decision (%) [dD]		Total (%) [D] [dC]	MDI pref (%) [dE]	Pump pref (%) [dE]	Other (%) [dE]	Total (%) [E]		
				(≤v3)	(≥v4)	(≤v3)	(≥v4)	(≤v3)	(≥v4)							
Total	**976**	**98 (10)**	**878 (90)**	**18 (38.3)**	**34 (23.9)**	**0 (0)**	**22 (15.5)**	**29 (61.7)**	**86 (60.6)**	**189 (21.5)**	**259 (65.6)**	**36 (9.1)**	**100 (25.3)**	**395 (57.3)**	**294 (42.7)**	**294**
Alder Hey (16/05/2011)	163	19 (11.7)	144 (88.3)	16 (94.1)	19 (55.9)	0 (0)	0 (0)	1 (5.9)	15 (44.1)	51 (35.4)	33 (80.5)	3 (7.3)	5 (12.2)	41 (44.1)	52 (55.9)	52
Newcastle (18/07/2011)	90	7 (7.8)	83 (92.2)	0 (0)	2 (18.2)	0 (0)	1 (9.1)	2 (100)	8 (72.7)	13 (15.7)	41 (69.5)	4 (6.8)	14 (23.7)	59 (84.3)	11 (15.7)	11
Birmingham (27/10/2011)	97	9 (9.3)	88 (90.7)	1 (5.9)	3 (15)	0 (0)	4 (20)	16 (94.1)	13 (65)	37 (42)	12 (40)	12 (40)	6 (20)	30 (58.8)	21 (41.2)	21
Cardiff (19/12/2011)	68	7 (10.3)	61 (89.7)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	2 (3.3)	34 (85)	1 (2.5)	5 (12.5)	40 (67.8)	19 (32.2)	19
Oxford (23/12/2011)	135	16 (11.9)	119 (88.1)	0 (0)	6 (40)	0 (0)	4 (26.7)	6 (100)	5 (33.3)	21 (17.6)	35 (56.5)	2 (3.2)	25 (40.3)	62 (63.3)	36 (36.7)	36
Doncaster (26/04/2012)	39	3 (7.7)	36 (92.3)	1 (50)	0 (0)	0 (0)	1 (33.3)	1 (50)	2 (66.7)	5 (13.9)	9 (75)	2 (16.7)	1 (8.3)	12 (38.7)	19 (61.3)	19
Southampton (12/06/2012)	77	11 (14.3)	66 (85.7)	0 (0)	0 (0)	0 (0)	0 (0)	3 (100)	12 (100)	15 (22.7)	14 (66.7)	0 (0)	7 (33.3)	21 (41.2)	30 (58.8)	30
Nottingham (20/07/2012)	86	7 (8.1)	79 (91.9)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	4 (80)	5 (6.3)	11 (84.6)	0 (0)	2 (15.4)	13 (17.6)	61 (82.4)	61
Blackburn (24/05/2013)	48	4 (8.3)	44 (91.7)	0 (0)	0 (0)	0 (0)	6 (60)	0 (0)	4 (40)	10 (22.7)	18 (78.3)	3 (13)	2 (8.7)	23 (67.6)	11 (32.4)	11
Mid Staffordshire (16/07/2013)	22	2 (9.1)	20 (90.9)	0 (0)	2 (33.3)	0 (0)	1 (16.7)	0 (0)	3 (50)	6 (30)	6 (50)	2 (16.7)	4 (33.3)	12 (85.7)	2 (14.3)	2
East Surrey (23/08/2013)	45	3 (6.7)	42 (93.3)	0 (0)	0 (0)	0 (0)	3 (50)	0 (0)	3 (50)	6 (14.3)	21 (75)	3 (10.7)	4 (14.3)	28 (77.8)	8 (22.2)	8
Ipswich	26	2	24	0	0	0	0	0	6	6	6	1	5	12	6	6

(23/10/2013)		(7.7)	(92.3)	(0)	(0)	(0)	(0)	(0)	(100)	(25)	(50)	(8.3)	(41.7)	(66.7)	(33.3)	
Sheffield (04/12/2013)	32	5 (15.6)	27 (84.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (25)	2 (10)	13 (65)	20 (74.1)	7 (25.9)	7
Norfolk and Norwich (17/01/2014)	39	3 (7.7)	36 (92.3)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)	7 (87.5)	8 (22.2)	11 (57.9)	1 (5.3)	7 (36.8)	19 (67.9)	9 (32.1)	9
Preston (10/07/2014)	9	0 (0)	9 (100)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	3 (75)	4 (44.4)	3 (100)	0 (0)	0 (0)	3 (60)	2 (40)	2

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Table 5.2-2: Screening and consent by protocol version

≤v3: Protocol versions 1-3 (covering recruitment period from 16/05/2011-16/08/2012).
≥v4: Protocol versions 4-5 (covering recruitment period from 17/08/2012-31/03/2015).
[A]-[F] cells used for denominators in percentage calculations for other cells.
[dx] denominator is [x]; [dx+y] denominator is [x]+[y].

Protocol version	Patient count N (%)	Total screens [A]	Total not eligible (%) [B] [dA]	Total eligible (%) [C] [dA]	Eligible but consent not sought							Eligible and consent sought but refused				Total consented (%) [F] [dE+F]	Rando-mised
					Lack of trained staff (%) [dD]		Reason not recorded (%) [dD]		Consultant decision (%) [dD]		Total (%) [D] [dC]	MDI pref (%) [dE]	Pump pref (%) [dE]	Other (%) [dE]	Total (%) [E]		
					(≤v3)	(≥v4)	(≤v3)	(≥v4)	(≤v3)	(≥v4)							
Total	**Overall**	**976**	**98 (10)**	**878 (90)**	**18 (38.3)**	**34 (23.9)**	**0 (0)**	**22 (15.5)**	**29 (61.7)**	**86 (60.6)**	**189 (21.5)**	**259 (65.6)**	**36 (9.1)**	**100 (25.3)**	**395 (57.3)**	**294 (42.7)**	**294**
1-3	**Overall**	**273**	**42 (15.4)**	**231 (84.6)**	**18 (38.3)**	**-**	**0 (0)**		**29 (61.7)**	**-**	**47 (20.3)**	**87 (77)**	**6 (5.3)**	**20 (17.7)**	**113 (61.4)**	**71 (38.6)**	**71**
4-5	**Overall**	**703**	**56 (8)**	**647 (92)**	**-**	**34 (23.9)**	**-**	**22 (15.5)**	**-**	**86 (60.6)**	**142 (21.9)**	**172 (61)**	**30 (10.6)**	**80 (28.4)**	**282 (55.8)**	**223 (44.2)**	**223**

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Table 5.2-3: Summary key changes from protocol v3 to v4 to boost recruitment

	Change type	Protocol v3	Protocol v4
1	Inclusion / exclusion criteria	Parent/legal representative of the patient not able to fill out study material	Parent/legal representative of the patient are not able to comply with the treatment regimen and study visits
2	Inclusion / exclusion criteria	Patient (aged 8 years and above) is not able to fill out study material	Parent/legal representative of the patient are not able to comply with the treatment regimen and study visits
3	Inclusion / exclusion criteria	First degree family member (sibling or parent) with TIDM	Sibling with existing TIDM
4	Inclusion / exclusion criteria	N/A	New reason: Has a known thyroid condition and are in a non euthyroid state
5	Inclusion / exclusion criteria	N/A	New reason: Has Coeliac disease and are unable to maintain a gluten free diet
6	Guidance / consent	Recruitment window period 10 days following diagnosis	Additional guidance and change to recruitment window period to 14 days and further guidance on patients being approached and consented as soon after diagnosis as possible

Note: Table constructed from information listed in SCIPI trial protocol v4.0.

Table 5.2-4: Screening log version 3 and version 4 reason codes

V3 code	Screening log version 3 reason codes	V4 code	Screening log version 4 reason codes
A	Age not appropriate (less than 7 months, greater than 15 years)	**A**	Age not appropriate (less than 7 months, greater than 15 years)
B	Treated previously for diabetes	**B**	Treated previously for diabetes
Cv3	Parent/legal representative of the patient not able to fill out study material (Version 3.0 protocol only)	**Cv4**	Parent/legal representative of the patient are not able to comply with the treatment regimen and study visits (Version 4.0 protocol only)
Dv3	Patient (aged 8 years and above) is not able to fill out study material (Version 3.0 protocol only)	**Dv4**	Parent/legal representative of the patient are not able to comply with the treatment regimen and study visits (Version 4.0 protocol only)
E	Haemoglobinopathy	**E**	Haemoglobinopathy
F	Co-existing pathology conditions likely to affect glycaemic control	**F**	Co-existing pathology conditions likely to affect glycaemic control
G	Psychological/psychiatric disorders	**G**	Psychological/psychiatric disorders
H	Receipt of medication likely to affect glycaemic control	**H**	Receipt of medication likely to affect glycaemic control
Iv3	Allergy to a component of insulin aspart or insulin glargine	**Iv4**	Sibling with existing TIDM (Version 4.0 protocol only)
Jv3	First degree family member (sibling or parent) with TIDM (Version 3.0 protocol only)	**Jv4**	Allergy to a component of insulin aspart or insulin glargine (Version 4.0 protocol only)
		Kv4	Has a known thyroid condition and are in a non euthyroid state (Version 4.0 protocol only)

V3 code	Screening log version 3 reason codes	V4 code	Screening log version 4 reason codes
		Lv4	Has Coeliac disease and are unable to maintain a gluten free diet (Version 4.0 protocol only)

Note: Table constructed from comparing screening log case report forms v4.0 and v3.0.

Table 5.2-5: Reasons for ineligibility at screening – Protocol up to version 3.0 [N ineligible = 42]

Note: Ineligible patients may fail on 1 or more reasons for ineligibility.

Site	Total screens	Total not eligible	A	B	C_v3	D_v3	E	F	G	H	I_v3	J_v3
Total	**273**	**42**	**19 (45.2%)**	**1 (2.4%)**	**7 (16.7%)**	**1 (2.4%)**	**0 (0%)**	**7 (16.7%)**	**13 (31%)**	**7 (16.7%)**	**0 (0%)**	**20 (47.6%)**
00086 -Doncaster Royal Infirmary	11	1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
00114 -Southampton University Hospitals NHS Trust	16	3	5 (166.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)	0 (0%)	0 (0%)	1 (33.3%)
00133 -Birmingham Childrens Hospital	39	7	0 (0%)	1 (14.3%)	5 (71.4%)	0 (0%)	0 (0%)	0 (0%)	1 (14.3%)	0 (0%)	0 (0%)	0 (0%)
00213 -Nottingham University Hospital NHS Trust	21	5	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	1 (20%)	0 (0%)	0 (0%)	3 (60%)
00243 -Alder Hey Childrens NHS Foundation Trust	62	10	0 (0%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)	3 (30%)	2 (20%)	5 (50%)	0 (0%)	6 (60%)
04913 -Cardiff and Value University Local Health Board	30	5	2 (40%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	1 (20%)	0 (0%)	1 (20%)	0 (0%)	2 (40%)
05042 -Oxford Radcliffe Hospitals NHS Trust	48	7	2 (28.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (14.3%)	1 (14.3%)	0 (0%)	5 (71.4%)
12617 -The Newscastle Upon Tyne Hospitals NHS	46	4	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)	2 (50%)	0 (0%)	0 (0%)	2 (50%)

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Table 5.2-6: Reasons for ineligibility at screening – Protocol version 4.0 only [N ineligible = 56]

Note: Ineligible patients may fail on 1 or more reasons for ineligibility.

Site	Total screens	Total not eligible	A	B	C_v4	D_v4	E	F	G	H	I_v4	J_v4	K_v4	L_v4
Total	**703**	**56**	**19 (33.9%)**	**1 (1.8%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**7 (12.5%)**	**13 (23.2%)**	**7 (12.5%)**	**24 (42.9%)**	**0 (0%)**	**2 (3.6%)**	**2 (3.6%)**
00036 -Norfolk and Norwich University Hospitals NHS Foundation Trust	39	3	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (66.7%)	0 (0%)	0 (0%)	0 (0%)
00086 -Doncaster Royal Infirmary	28	2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)
00104 -Stafford Hospital, Mid Staffordshire NHS Trust	22	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
00114 -Southampton University Hospitals NHS Trust	61	8	5 (62.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (12.5%)	2 (25%)	0 (0%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)
00133 -Birmingham Childrens Hospital	58	2	0 (0%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
00148 -The Ipswich Hospital	26	2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	1 (50%)	0 (0%)
00160 -Royal Preston Hospital	9	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
00213 -Nottingham University Hospital NHS Trust	65	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
00243 -Alder Hey Childrens NHS Foundation Trust	101	9	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (33.3%)	2 (22.2%)	5 (55.6%)	3 (33.3%)	0 (0%)	0 (0%)	0 (0%)
00248 -Sheffield Childrens NHS Trust	32	5	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	2 (40%)	0 (0%)	0 (0%)	0 (0%)
00326 -East Surrey Hospital, Surrey and Sussex Healthcare NHS trust	45	3	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (66.7%)	0 (0%)	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)
01527 -Royal Blackburn Hospital, East Lancashire NHS Trust	48	4	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (50%)	0 (0%)	1 (25%)	0 (0%)

Site	Total screens	Total not eligible	A	B	C_v4	D_v4	E	F	G	H	I_v4	J_v4	K_v4	L_v4
04913 -Cardiff and Value University Local Health Board	38	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
05042 -Oxford Radcliffe Hospitals NHS Trust	87	9	2 (22.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (11.1%)	1 (11.1%)	6 (66.7%)	0 (0%)	0 (0%)	1 (11.1%)
12617 -The Newcastle Upon Tyne Hospitals NHS	44	3	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)	0 (0%)	2 (66.7%)	0 (0%)	0 (0%)	0 (0%)

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Table 5.2-7: Time of recruitment events from date of diagnosis

		Consent obtained	Patient declined		
			MDI preference	CSII preference	Other reason
Days from diagnosis to Screening	N	291	257	36	97
	Mean	1.34	1.48	1.33	1.72
	SD	1.58	1.7	1.43	1.86
	Median	1	1	1	1
	Min	0	0	0	0
	Max	9	12	7	10
	Missing	3	2	0	3
First informed about SCIPI	N	289	254	35	91
	Mean	1.49	1.69	1.8	1.69
	SD	1.4	1.6	2.22	1.62
	Median	1	1	1	1
	Min	0	0	0	0
	Max	9	12	11	10
	Missing	5	5	1	9
PIS provided	N	289	246	33	84
	Mean	2.26	2.49	2.79	2.64
	SD	1.85	1.91	2.98	2.17
	Median	2	2	2	2
	Min	0	0	0	0
	Max	9	12	16	11
	Missing	5	13	3	16
Approached for consent	N	289	220	25	75
	Mean	5.45	6.07	6.88	6.52
	SD	3.14	2.9	4.04	2.77
	Median	5	6	7	7
	Min	1	0	1	1
	Max	14	13	20	14
	Missing	5	39	11	25
Randomised	N	292	0	0	0
	Mean	5.78			
	SD	3.22			
	Median	5			
	Min	1			
	Max	15			
	Missing	2			

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Table 5.2-8: Demographic characteristics of screened patients

		Consent obtained	Patient declined		
			MDI preference	CSII preference	Other reason
Days from diagnosis to					
Age (years)	N	293	259	36	100
	Mean	8.98	10	8.1	8.85
	SD	4.13	3.76	4.27	4.09
	Median	9.69	10.48	8.075	9.08
	Min	0.7	0.41	1.28	0.98
	Max	16	16	15.15	15.7
	Missing	1	0	0	0
Age N(%)	N	293	259	36	100
	Birth to 6 months	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)
	7 months to 4 years	67 (22.9%)	32 (12.4%)	9 (25%)	23 (23%)
	5 to 11 years	146 (49.8%)	135 (52.1%)	18 (50%)	52 (52%)
	12 to 15 years	79 (27%)	90 (34.7%)	9 (25%)	25 (25%)
	16+ years	1 (0.3%)	1 (0.4%)	0 (0%)	0 (0%)
	Missing	1	0	0	0
Gender N(%)	N	293	259	36	100
	Female	140 (47.8%)	121 (46.7%)	17 (47.2%)	46 (46%)
	Male	153 (52.2%)	138 (53.3%)	19 (52.8%)	54 (54%)
	Missing	1	0	0	0
Ethnicity N(%)	N	292	259	36	100
	Asian or Asian British	6 (2.1%)	4 (1.5%)	1 (2.8%)	4 (4%)
	Black or British Black	3 (1%)	2 (0.8%)	2 (5.6%)	1 (1%)
	British White	242 (82.9%)	228 (88%)	25 (69.4%)	81 (81%)
	Chinese	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Indian	4 (1.4%)	1 (0.4%)	0 (0%)	2 (2%)
	Mixed	10 (3.4%)	6 (2.3%)	2 (5.6%)	1 (1%)
	Not stated	3 (1%)	12 (4.6%)	1 (2.8%)	4 (4%)
	Other	5 (1.7%)	1 (0.4%)	0 (0%)	1 (1%)
	Other White	14 (4.8%)	3 (1.2%)	1 (2.8%)	5 (5%)
	Pakistani	5 (1.7%)	2 (0.8%)	4 (11.1%)	1 (1%)
	Missing	2	0	0	0
Deprivation score* N(%)	N	280	241	33	94
	Mean	23.26	24.01	28.51	21.65

	SD	18.53	18.19	16.57	16.17
	Median	17.045	17.96	27.65	17.06
	Min	1.62	1.18	3.9	2.95
	Max	77.23	74.35	63.86	71.91
	Missing	14	18	3	6

* Deprivation score is measured 0 to 100; 100 being worst possible deprivation.

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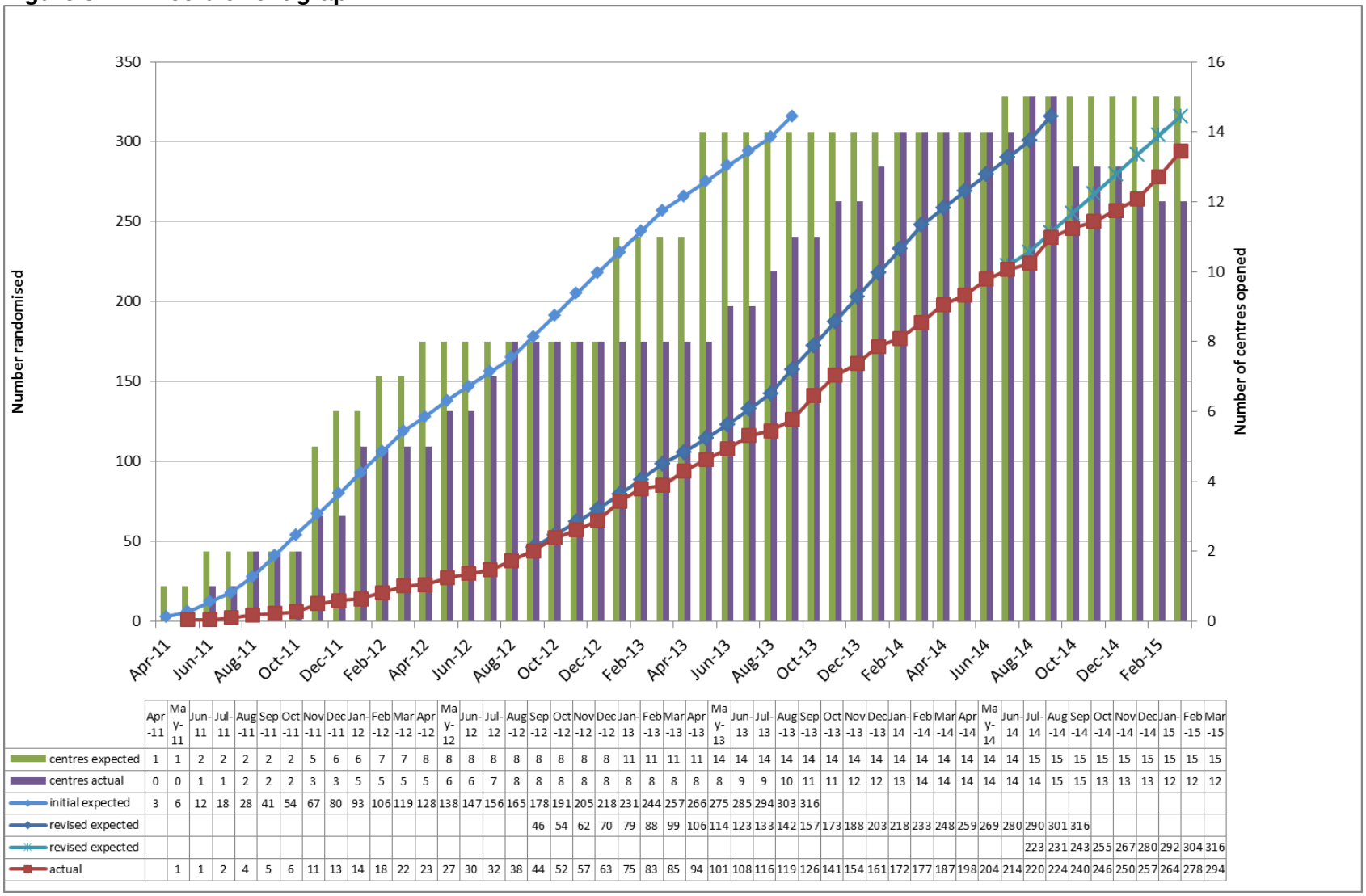
Figure 5.2-1: Recruitment graph



	Apr-11	May-11	Jun-11	Jul-11	Aug-11	Sep-11	Oct-11	Nov-11	Dec-11	Jan-12	Feb-12	Mar-12	Apr-12	May-12	Jun-12	Jul-12	Aug-12	Sep-12	Oct-12	Nov-12	Dec-12	Jan-13	Feb-13	Mar-13	Apr-13	May-13	Jun-13	Jul-13	Aug-13	Sep-13	Oct-13	Nov-13	Dec-13	Jan-14	Feb-14	Mar-14	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15
centres expected	1	1	2	2	2	2	2	5	6	6	7	7	8	8	8	8	8	8	8	8	8	11	11	11	11	14	14	14	14	14	14	14	14	14	14	14	14	14	15	15	15	15	15	15	15	15
centres actual	0	0	1	1	2	2	2	3	3	5	5	5	5	6	6	7	8	8	8	8	8	8	8	8	8	8	9	9	10	11	11	12	12	13	14	14	14	14	14	14	15	15	13	13	13	12	12	12
initial expected	3	6	12	18	28	41	54	67	80	93	106	119	128	138	147	156	165	178	191	205	218	231	244	257	266	275	285	294	303	316																		
revised expected																		46	54	62	70	79	88	99	106	114	123	133	142	157	173	188	203	218	233	248	259	269	280	290	301	316						
revised expected																																							223	231	243	255	267	280	292	304	316
actual		1	1	2	4	5	6	11	13	14	18	22	23	27	30	32	38	44	52	57	63	75	83	85	94	101	108	116	119	126	141	154	161	172	177	187	198	204	214	220	224	240	246	250	257	264	278	294

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6. Results

6.1 Baseline characteristics

Note: One randomised patient withdrew and requested all their data to be deleted so therefore all summaries are based on 293 patients throughout.

6.1.1 Demographic details

Table 6.1-1: Demographic details

	CSII	MDI	Total
Age at randomisation (years)			
Missing	0	0	0
N	144	149	293
Mean (SD)	9 (4.1)	9.1 (4.1)	9.1 (4.1)
Median (IQR)	9.9 (5.7, 12.2)	9.4 (5.8, 12.5)	9.8 (5.7, 12.3)
(Min, Max)	(0.8, 16)	(0.7, 15.4)	(0.7, 16)
Age cat (strata cat): n (%)			
Missing	0	0	0
N	144	149	293
7mths – <5 yrs	33 (22.9%)	32 (21.5%)	65 (22.2%)
5 – <12 yrs	71 (49.3%)	76 (51%)	147 (50.2%)
12-15 yrs	40 (27.8%)	41 (27.5%)	81 (27.6%)
Age cat (EudraCT): n (%)			
Missing	0	0	0
N	144	149	293
Infants and toddlers	8 (5.6%)	6 (4%)	14 (4.8%)
Children	96 (66.7%)	102 (68.5%)	198 (67.6%)
Adolescents	40 (27.8%)	41 (27.5%)	81 (27.6%)
Gender: n (%)			
Missing	0	0	0
N	144	149	293
Female	71 (49.3%)	69 (46.3%)	140 (47.8%)
Male	73 (50.7%)	80 (53.7%)	153 (52.2%)
Ethnicity: n (%)			
Missing	1	3	4
N	143	146	289
Asian or Asian British	3 (2.1%)	3 (2.1%)	6 (2.1%)
Black or British Black	0 (0%)	3 (2.1%)	3 (1%)
British White	124 (86.7%)	118 (80.8%)	242 (83.7%)
Indian	2 (1.4%)	2 (1.4%)	4 (1.4%)
Mixed	4 (2.8%)	6 (4.1%)	10 (3.5%)
Other White	6 (4.2%)	8 (5.5%)	14 (4.8%)
Other	3 (2.1%)	2 (1.4%)	5 (1.7%)
Pakistani	1 (0.7%)	4 (2.7%)	5 (1.7%)
Deprivation score* (continuous)			

	CSII	MDI	Total
Missing	7	6	13
N	137	143	280
Mean (SD)	25 (19.4)	21.6 (17.6)	23.3 (18.5)
Median (IQR)	19.4 (8.9, 37.9)	14.7 (7.8, 31.8)	17 (8.4, 35.8)
(Min, Max)	(1.8, 77.1)	(1.6, 77.2)	(1.6, 77.2)
Deprivation score* (quintile categories): n (%)			
Missing	7	6	13
N	137	143	280
1 (<=8.49)	32 (23.4%)	40 (28%)	72 (25.7%)
2 (8.5 – 13.79)	23 (16.8%)	30 (21%)	53 (18.9%)
3 (13.8 – 21.35)	18 (13.1%)	22 (15.4%)	40 (14.3%)
4 (21.36 – 34.17)	25 (18.2%)	18 (12.6%)	43 (15.4%)
5 (>=34.18)	39 (28.5%)	33 (23.1%)	72 (25.7%)

* Deprivation score is measured 0 to 100; 100 being worst possible deprivation.

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6.1.2 Baseline disease characteristics

Table 6.1-2: Baseline disease characteristics

	CSII	MDI	Total
BMI SDS			
Missing	20	17	37
N	124	132	256
Mean (SD)	0.2 (1.3)	0.1 (1.4)	0.1 (1.3)
Median (IQR)	0.2 (-0.7, 0.9)	0.1 (-0.8, 1)	0.2 (-0.8, 1)
(Min, Max)	(-2.9, 4.2)	(-4.6, 3.5)	(-4.6, 4.2)
Height SDS			
Missing	20	17	37
N	124	132	256
Mean (SD)	0.3 (1.1)	0.3 (1.1)	0.3 (1.1)
Median (IQR)	0.1 (-0.4, 1.1)	0.4 (-0.3, 1.1)	0.3 (-0.4, 1.1)
(Min, Max)	(-2.3, 3.3)	(-4.8, 2.4)	(-4.8, 3.3)
Local HbA1c (mmol/mol)			
Missing	22	27	49
N	122	122	244
Mean (SD)	105.9 (24.2)	103.6 (26.3)	104.7 (25.2)
Median (IQR)	105 (87, 122)	103 (83, 126)	104.7 (85.5, 125)
(Min, Max)	(58, 184)	(55, 172.1)	(55, 184)
Central HbA1c (mmol/mol)			
Missing*	80	78	158

	CSII	MDI	Total
N	64	71	135
Mean (SD)	101.2 (24.9)	96.4 (24)	98.7 (24.4)
Median (IQR)	102.5 (81.5, 127)	93 (79, 119)	100 (80, 126)
(Min, Max)	(38, 130)	(50, 130)	(38, 130)
HbA1c[#] (mmol/mol)			
Missing	12	18	30
N	132	131	263
Mean (SD)	104.6 (24.4)	102.6 (26.7)	103.6 (25.5)
Median (IQR)	105 (87.5, 127)	103 (81, 127)	105 (84, 127)
(Min, Max)	(38, 184)	(50, 172.1)	(38, 184)
Blood glucose (mmol/L)			
Missing	3	3	6
N	141	146	287
Mean (SD)	26.8 (9.2)	26.9 (10)	26.9 (9.6)
Median (IQR)	26.2 (20.2, 32.5)	25.6 (19.5, 32.6)	25.7 (19.7, 32.5)
(Min, Max)	(5.1, 56)	(5.7, 69.5)	(5.1, 69.5)
Blood pH			
Missing	17	16	33
N	127	133	260
Mean (SD)	7.3 (0.2)	7.3 (0.1)	7.3 (0.2)
Median (IQR)	7.4 (7.3, 7.4)	7.4 (7.2, 7.4)	7.4 (7.3, 7.4)
(Min, Max)	(6, 7.6)	(6.8, 7.5)	(6, 7.6)
Thyroid test result: n (%)			
Not done[$]	25	19	44
Missing	7	6	13
N	112	124	236
Abnormal	6 (5.4%)	3 (2.4%)	9 (3.8%)
Normal	105 (93.8%)	118 (95.2%)	223 (94.5%)
Results unobtainable	1 (0.9%)	3 (2.4%)	4 (1.7%)
Coeliac screen test result: n (%)			
Not done[$]	28	30	58
Missing	14	10	24
N	102	109	211
Abnormal	3 (2.9%)	9 (8.3%)	12 (5.7%)
Normal	97 (95.1%)	97 (89%)	194 (91.9%)
Results unobtainable	2 (2%)	3 (2.8%)	5 (2.4%)
Islet Cell Antibodies test result: n (%)			
Not done[$]	39	34	73
Missing	17	17	34
N	88	98	186
Negative	35 (39.8%)	31 (31.6%)	66 (35.5%)
Positive	39 (44.3%)	53 (54.1%)	92 (49.5%)
Results unobtainable	1 (1.1%)	4 (4.1%)	5 (2.7%)

	CSII	MDI	Total
Weak Positive	13 (14.8%)	10 (10.2%)	23 (12.4%)
GAD 65 Antibodies test result: n (%)			
Not done$	65	65	130
Missing	13	14	27
N	66	70	136
Equivocal	4 (6.1%)	4 (5.7%)	8 (5.9%)
Negative	11 (16.7%)	16 (22.9%)	27 (19.9%)
Positive	50 (75.8%)	50 (71.4%)	100 (73.5%)
Results unobtainable	1 (1.5%)	0 (0%)	1 (0.7%)
Health Utilities Index			
Not done (HUI not completed properly)	7	3	10
Missing (HUI not completed at all)	22	19	41
N	115	127	242
Mean (SD)	0.9 (0.19)	0.9 (0.1)	0.9 (0.1)
Median (IQR)	1.0 (0.8, 1.0)	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)
(Min, Max)	(0.5, 1.0)	(0.4, 1.0)	(0.4, 1.0)
Conmeds prescribed up to baseline: n (%)			
Missing	2	0	2
N	142	149	291
No	102 (71.8%)	114 (76.5%)	216 (74.2%)
Yes	40 (28.2%)	35 (23.5%)	75 (25.8%)

* High levels of missing data for 'Central HbA1c' because the central laboratory for sending all blood samples to for measuring HbA1c was only set up part-way through the trial.
# When available central lab HbA1c measurement taken in preference of local lab HbA1c measurement.
$ Test not a requirement of the study protocol.

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6.2 Study population

6.2.1 Data sets analysed

Table 6.2-1: Data sets analysed

Population	CSII	MDI	Total
Screened	N/A	N/A	976
Randomised	144 (49.1%)	149 (50.9%)	293
Intention-to-treat	144 (49.1%)	149 (50.9%)	293
Per-protocol	88 (55.0%)	72 (45.0%)	160
Safety	144 (49.1%)	149 (50.9%)	293

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Table 6.2-2: Discontinuation rates at each follow-up time-point

Time-point	CSII (n=144)	MDI (n=149)	Total (n=293)
Any time-point	1 (0.7%)	5 (3.4%)	6 (2.0%)
=0 months	0 (0%)	0 (0%)	0 (0%)
0<WD<3 months	0 (0%)	0 (0%)	0 (0%)
=3 month visit	0 (0%)	0 (0%)	0 (0%)
3<WD<6 months	0 (0%)	0 (0%)	0 (0%)
=6 months	0 (0%)	1 (0.7%)	1 (0.3%)
6<WD<9 months	0 (0%)	1 (0.7%)	1 (0.3%)
=9 month visit	0 (0%)	0 (0%)	0 (0%)
9<WD<12 months	1 (0.7%)	3 (2.0%)	4 (1.4%)

See

Table **6.2-3** for summary of reasons for discontinuation.

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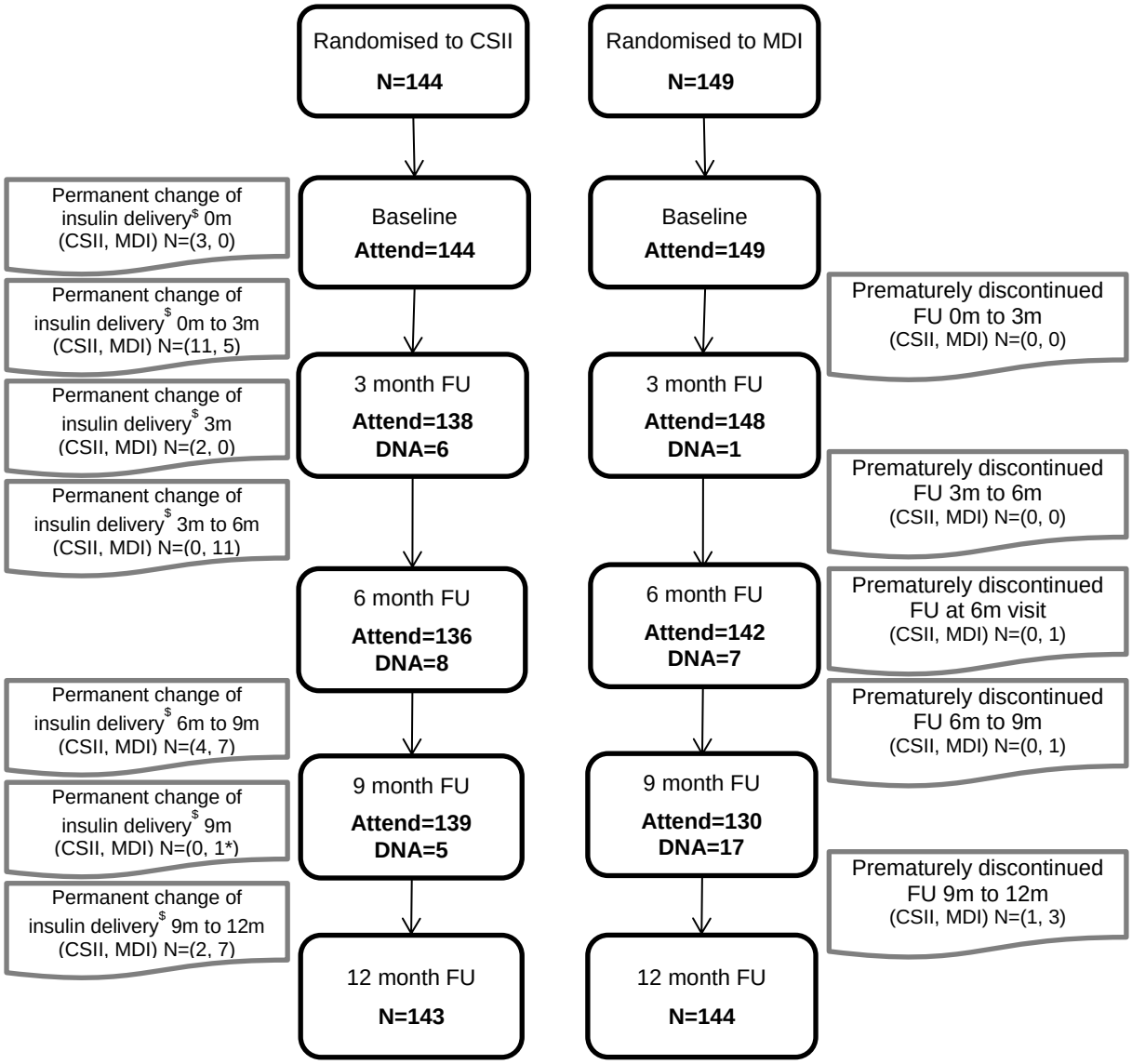
Figure 6.2-1: Completeness of follow-up



$ Permanent change of insulin delivery from randomised treatment listed but continuing FU.
* Patient changed from MDI to ‘Injections TDS regime’.

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The time points of permanent change to insulin delivery method are summarised by age strata in Table 6.7-1.

Line listings of permanent change to insulin delivery method showing the ages at change and last HbA1c (mmol/mol) measurement are provided in Table 6.7-2

Table 6.2-3: Reasons for discontinuing randomised treatment allocation

Rand No	Rand date	WD date	Treatment	Who	Reason (Verbatim)
00036104	26/9/2014	3/6/2015	MDI	Decision of Clinician	Other Specify: 'moved out of area'
00086211	27/6/2014	27/6/2015	CSII	Decision of Parent/legal representative; Decision of Participant (withdrawal of consent)	Other Specify: 'no longer wishes to take part in study'
00114305	10/1/2014	10/10/2014	MDI	Decision of Clinician	Other Specify: 'Patient diagnosed with coeliac disease shortly after diagnosis of TIDM and is unable to consistently comply with Gluten Free Diet'
00243203	1/2/2012	10/1/2013	MDI	Decision of Clinician	Other Specify: 'participant attended visit with foster parent. No consent. therefore unable to collect data.'
00326302	2/2/2015	29/6/2015	MDI	Decision of Parent/legal representative; Decision of Participant (withdrawal of consent)	Other Specify: 'family returned to America to live'
04913207	4/7/2014	28/7/2015	MDI	Unobtainable	Other Specify: 'dna'd 2x appointments, lst to follow up'

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Table 6.2-4: Summary of the explanatory notes of non-allocation of randomised treatment

Site	Rand no	Randomised treatment	Permanent change to	Rand date	Permanent change date	Decision	Reason
00213 Nottingham	00213102	CSII	MDI	9/1/2013	9/1/2013	Parent	Parent preference
05042 Oxford	05042207	CSII	MDI	28/9/2012	28/9/2012	Parent; Patient	Other: Participant was not sure he wanted a pump to deliver insulin
05042 Oxford	05042214	CSII	MDI	2/12/2013	2/12/2013	Clinician; Parent	Poor glycaemic control - b. Frequent hyperglycaemia; Parent preference

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6.2.2 Protocol deviations

Protocol deviations are summarised in Table 6.2-5.

Table 6.2-5: Protocol deviations

Protocol deviations	CSII (n = 144)	MDI (n = 149)	Overall (n = 293)
Any protocol deviation	**97 (67.4%)**	**117 (78.5%)**	**214 (73%)**
Deviations relating to inclusion and exclusion criteria	**0 (0%)**	**0 (0%)**	**0 (0%)**
Deviations relating to treatment and follow-up visits:			
At least one major:	57 (39.6%)	77 (51.7%)	134 (45.7%)
Start of study treatment from diagnosis being > 10 days (protocol v3)	1 (0.7%)	1 (0.7%)	2 (0.7%)
Start of study treatment from diagnosis being > 14 days (protocol v4)	1 (0.7%)	3 (2%)	4 (1.4%)
Scheduled 12 month follow-up visit falling outside the +/-15 day window	36 (25%)	49 (32.9%)	85 (29%)
Permanent change of insulin delivery	22 (15.3%)	31 (20.8%)	53 (18.1%)
Useage of non-protocol specified insulin**	10 (6.9%)	13 (8.7%)	23 (7.8%)
At least one minor:	**70 (48.6%)**	**87 (58.4%)**	**157 (53.6%)**
At least three minor:	**0 (0%)**	**0 (0%)**	**0 (0%)**
Scheduled 3 month follow-up visit falling outside the +/-15 day window	34 (23.6%)	44 (29.5%)	78 (26.6%)
Scheduled 6 month follow-up visit falling outside the +/-15 day window	43 (29.9%)	48 (32.2%)	91 (31.1%)
Scheduled 9 month follow-up visit falling outside the +/-15 day window	44 (30.6%)	39 (26.2%)	83 (28.3%)
At least one major and/or at least three minor:	**57 (39.6%)**	**77 (51.7%)**	**134 (45.7%)**

* One permanent switch of insulin delivery method was from MDI to 'Injections TDS regime'
** Does not include Levemir/Detemir.

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Table 6.2-6: Visit assessment timings – Categorical

	Visit	Summary	CSII	MDI	Total
Number of days from diagnosis	**0m (protocol v3)**	DNA	0	0	0
		Missing	1	0	1
		N	35	35	70
		V3 OK	34 (97.1%)	34 (97.1%)	68 (97.1%)
		V3 Out of range	1 (2.9%)	1 (2.9%)	2 (2.9%)
	0m (protocol v4)	DNA	0	0	0
		Missing	1	1	2
		N	107	113	220
		V4 OK	106 (99.1%)	110 (97.3%)	216 (98.2%)
		V4 Out of range	1 (0.9%)	3 (2.7%)	4 (1.8%)
Number of days outside visit window	**3m**	DNA	6	1	7
		Missing	0	0	0
		N	138	148	286
		OK	104 (75.4%)	104 (70.3%)	208 (72.7%)
		Earlier than -15 days	10 (7.2%)	16 (10.8%)	26 (9.1%)
		Later than +15 days	24 (17.4%)	28 (18.9%)	52 (18.2%)
	6m	DNA	8	7	15
		Missing	0	0	0
		N	136	142	278
		OK	93 (68.4%)	94 (66.2%)	187 (67.3%)
		Earlier than -15 days	14 (10.3%)	15 (10.6%)	29 (10.4%)
		Later than +15 days	29 (21.3%)	33 (23.2%)	62 (22.3%)
	9m	DNA	5	17	22
		Missing	0	0	0
		N	139	130	269
		OK	95 (68.3%)	91 (70%)	186 (69.1%)
		Earlier than -15 days	11 (7.9%)	16 (12.3%)	27 (10%)
		Later than +15 days	33 (23.7%)	23 (17.7%)	56 (20.8%)
	12m	DNA	0	0	0
		Missing	0	0	0
		N	143	144	287
		OK	107 (74.8%)	95 (66%)	202 (70.4%)
		Earlier than -15 days	9 (6.3%)	14 (9.7%)	23 (8%)
		Later than +15 days	27 (18.9%)	35 (24.3%)	62 (21.6%)

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Table 6.2-7: Visit assessment timings – Continuous

	Visit	Summary	CSII	MDI	Total
Number of days from diagnosis	**0m (protocol v3)**	DNA	0	0	0
		Missing	1	0	1
		N	35	35	70
		Mean (SD)	8.1 (1.9)	6.7 (3.3)	7.4 (2.8)
		Median (IQR)	8 (7, 10)	7 (4, 10)	8 (5, 10)
		(Min, Max)	(4, 14)	(1, 11)	(1, 14)
	0m (protocol v4)	DNA	0	0	0
		Missing	1	1	2
		N	107	113	220
		Mean (SD)	10.6 (3.1)	7.4 (4.4)	9 (4.1)
		Median (IQR)	12 (8, 13)	7 (4, 12)	10 (6, 12)
		(Min, Max)	(2, 16)	(1, 17)	(1, 17)
Number of days outside visit window	**3m**	DNA	6	1	7
		Missing	0	0	0
		N	138	148	286
		Mean (SD)	1.1 (10.2)	2.6 (12.9)	1.9 (11.7)
		Median (IQR)	1 (-6, 9)	1.5 (-7, 9)	1 (-7, 9)
		(Min, Max)	(-28, 34)	(-21, 53)	(-28, 53)
	6m	DNA	8	7	15
		Missing	0	0	0
		N	136	142	278
		Mean (SD)	1.3 (13.2)	3.5 (13.5)	2.4 (13.4)
		Median (IQR)	2 (-10, 10)	2.5 (-7, 11)	2 (-8, 10)
		(Min, Max)	(-32, 44)	(-26, 49)	(-32, 49)
	9m	DNA	5	17	22
		Missing	0	0	0
		N	139	130	269
		Mean (SD)	4.5 (14.3)	2.2 (12.1)	3.4 (13.3)
		Median (IQR)	4 (-6, 13)	1.5 (-6, 9)	2 (-6, 12)
		(Min, Max)	(-25, 42)	(-34, 48)	(-34, 48)
	12m	DNA	0	0	0
		Missing	0	0	0
		N	143	144	287
		Mean (SD)	3.3 (11.7)	3.7 (14.6)	3.5 (13.2)
		Median (IQR)	2 (-5, 10)	2.5 (-7, 9.5)	2 (-5, 10)
		(Min, Max)	(-18, 54)	(-27, 98)	(-27, 98)

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6.3 Compliance with treatment

See Table 6.2-5: Protocol **deviations** for details.

6.4 Unblinding

This trial is open-label.

6.5 Safety data

The safety analysis data set contains all participants that were randomised and received at least one dose of trial medication. Participants AEs/SAEs are included in the method of insulin delivery they were actually receiving at the time of AE/SAE onset to take into account any participants that temporarily changed (Form 17: Insulin delivery) or permanently changed (Form 13: Permanent change to insulin delivery) their mode of insulin delivery at any point throughout the trial.

6.5.1 Adverse events

The incidence of related AEs by treatment group were:

- 54 AEs in 36 patients that were on CSII at the time of the AE. IDR* was 25.0 patients with at least one event per 100-person-years.
- 17 AEs in 16 patients that were on MDI at the time of the AE. IDR* was 10.5 patients with at least one event per 100-person-years.

* The incidence density rate (IDR) is the number of patients with at least one new case per population at risk in a given time period. The denominator here is the sum of the person-time in years for each treatment group (accounting for treatment switches) of the at risk population.

Table 6.5-1: Overview of related AEs by site and overall (All AEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**54**	**36 (25)**	**17**	**16 (10.5)**	**71**	**50* (16.9)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	3	3 (46.7)	1	1 (45.1)	4	4 (46.3)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	3	1 (10.6)	0	0 (0)	3	1 (5.3)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	10	8 (48.2)	6	5 (37.8)	16	12[#] (40.3)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	3	2 (66.9)	2	2 (67)	5	4 (67)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	2	2 (6.2)	2	2 (6.6)	4	4 (6.4)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	12	6 (25)	1	1 (3.4)	13	6[#] (11.2)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	2	2 (52.9)	2	2 (28.2)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	1	1 (23.2)	0	0 (0)	1	1 (13.5)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	1	1 (20)	0	0 (0)	1	1 (9.1)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	6	4 (43.2)	1	1 (9.6)	7	5 (25.4)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	5	4 (30.3)	1	1 (4.5)	6	5 (14.1)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	8	4 (69)	1	1 (19.7)	9	5 (46)

***** Two patients experienced AEs on both treatment arms.
****** One patient experienced AEs on both treatment arms.

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Table 6.5-2: Overview of related AEs by site and overall (Device AEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**29**	**21 (14.6)**	**3**	**3 (2)**	**32**	**24 (8.1)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	2	2 (31.1)	0	0 (0)	2	2 (23.1)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	3	1 (10.6)	0	0 (0)	3	1 (5.3)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	5	4 (24.1)	1	1 (7.6)	6	5 (16.8)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	2	2 (66.9)	0	0 (0)	2	2 (33.5)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	2	2 (6.2)	0	0 (0)	2	2 (3.2)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	7	4 (16.6)	0	0 (0)	7	4 (7.5)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	1	1 (26.5)	1	1 (14.1)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	0	0 (0)	0	0 (0)	0	0 (0)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	2	1 (10.8)	0	0 (0)	2	1 (5.1)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	3	2 (15.1)	0	0 (0)	3	2 (5.6)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	3	3 (51.8)	1	1 (19.7)	4	4 (36.8)

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Table 6.5-3: Overview of related AEs by site and overall (Carer error AEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**6**	**3 (2.1)**	**4**	**4 (2.6)**	**10**	**7 (2.4)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	0	0 (0)	0	0 (0)	0	0 (0)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	0	0 (0)	0	0 (0)	0	0 (0)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	0	0 (0)	2	2 (15.1)	2	2 (6.7)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	1	1 (33.4)	1	1 (33.5)	2	2 (33.5)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	0	0 (0)	0	0 (0)	0	0 (0)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	0	0 (0)	1	1 (3.4)	1	1 (1.9)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	0	0 (0)	0	0 (0)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	0	0 (0)	0	0 (0)	0	0 (0)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	0	0 (0)	0	0 (0)	0	0 (0)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	1	1 (7.6)	0	0 (0)	1	1 (2.8)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	4	1 (17.3)	0	0 (0)	4	1 (9.2)

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Table 6.5-4: Overview of related AEs by site and overall (Meter error AEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**3**	**3 (2.1)**	**1**	**1 (0.7)**	**4**	**4 (1.4)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	0	0 (0)	0	0 (0)	0	0 (0)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	0	0 (0)	0	0 (0)	0	0 (0)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	3	3 (18.1)	1	1 (7.6)	4	4 (13.4)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	0	0 (0)	0	0 (0)	0	0 (0)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	0	0 (0)	0	0 (0)	0	0 (0)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	0	0 (0)	0	0 (0)	0	0 (0)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	0	0 (0)	0	0 (0)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	0	0 (0)	0	0 (0)	0	0 (0)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	0	0 (0)	0	0 (0)	0	0 (0)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	0	0 (0)	0	0 (0)	0	0 (0)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)

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Table 6.5-5: Overview of related AEs by site and overall (Incidental illness AEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**6**	**6 (4.2)**	**3**	**3 (2)**	**9**	**9 (3)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	0	0 (0)	0	0 (0)	0	0 (0)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	0	0 (0)	0	0 (0)	0	0 (0)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	2	2 (12.1)	0	0 (0)	2	2 (6.7)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	0	0 (0)	1	1 (33.5)	1	1 (16.7)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	0	0 (0)	1	1 (3.3)	1	1 (1.6)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	1	1 (4.2)	0	0 (0)	1	1 (1.9)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	0	0 (0)	0	0 (0)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	1	1 (23.2)	0	0 (0)	1	1 (13.5)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	1	1 (10.8)	0	0 (0)	1	1 (5.1)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	1	1 (7.6)	1	1 (4.5)	2	2 (5.6)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)

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Table 6.5-6: Overview of related AEs by site and overall (Other AEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**10**	**9 (6.2)**	**6**	**6 (3.9)**	**16**	**15 (5.1)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	1	1 (15.6)	1	1 (45.1)	2	2 (23.1)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	0	0 (0)	0	0 (0)	0	0 (0)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	0	0 (0)	2	2 (15.1)	2	2 (6.7)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	0	0 (0)	0	0 (0)	0	0 (0)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	0	0 (0)	1	1 (3.3)	1	1 (1.6)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	4	3 (12.5)	0	0 (0)	4	3 (5.6)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	1	1 (26.5)	1	1 (14.1)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	0	0 (0)	0	0 (0)	0	0 (0)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	1	1 (20)	0	0 (0)	1	1 (9.1)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	3	3 (32.4)	1	1 (9.6)	4	4 (20.3)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	0	0 (0)	0	0 (0)	0	0 (0)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	1	1 (17.3)	0	0 (0)	1	1 (9.2)

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Table 6.5-7: Summary of related AE by adverse event description code

		Total person years (total patients)			CSII		MDI		Total	
Category	**Description**	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
All	**Diabetic Ketoacidosis**	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**2**	**2 (1.4)**	**0**	**0 (0)**	**2**	**2 (0.7)**
	Insulin administration error	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**2**	**2 (1.4)**	**5**	**5 (3.3)**	**7**	**6 (2)**
	Pump Failure	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**4**	**3 (2.1)**	**0**	**0 (0)**	**4**	**3 (1)**
	Severe Hypoglycaemia	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**6**	**6 (4.2)**	**2**	**2 (1.3)**	**8**	**8 (2.7)**
	Site Infections	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**8**	**7 (4.9)**	**0**	**0 (0)**	**8**	**7 (2.4)**
	other - specify	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**32**	**22 (15.3)**	**10**	**10 (6.6)**	**42**	**32 (10.8)**
Device	Diabetic Ketoacidosis	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	Pump Failure	144.1 (144)	151.9 (149)	296.1 (293)	4	3 (2.1)	0	0 (0)	4	3 (1)
	Severe Hypoglycaemia	144.1 (144)	151.9 (149)	296.1 (293)	2	2 (1.4)	0	0 (0)	2	2 (0.7)
	Site Infections	144.1 (144)	151.9 (149)	296.1 (293)	8	7 (4.9)	0	0 (0)	8	7 (2.4)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	14	11 (7.6)	3	3 (2)	17	14 (4.7)
Carer error	Insulin administration error	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	4	4 (2.6)	5	5 (1.7)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	5	2 (1.4)	0	0 (0)	5	2 (0.7)
Meter error	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	3	3 (2.1)	1	1 (0.7)	4	4 (1.4)
Incidental illness	Insulin administration error	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	5	5 (3.5)	3	3 (2)	8	8 (2.7)
Other	Diabetic Ketoacidosis	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	Insulin administration error	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	1	1 (0.7)	1	1 (0.3)
	Severe Hypoglycaemia	144.1 (144)	151.9 (149)	296.1 (293)	4	4 (2.8)	2	2 (1.3)	6	6 (2)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	5	4 (2.8)	3	3 (2)	8	7 (2.4)

***** One patient experienced Insulin administration error on both treatment arms (separate categories).

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Table 6.5-8: Listing of related AEs – CSII (taken at time of AE onset)

Notes:
[a] *Consumable* includes: 'Catheter', 'Cannula', 'Cartridge', 'Set', 'Transfer set', etc.
[b] *Insulin drug* includes: 'Insulin aspart', 'Insulin glargine'
[c] *Insulin delivery device* includes: 'MDI pens', 'Insulin pump'
[d] Intervention listed if *relationship* is 'possible', 'probably', 'almost certainly'.
-7 Field not active for earlier versions of Related Adverse Event CRF.
-8 Data unobtainable (i.e. queried and confirmed missing).

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
1	00036 Norfolk and Norwich University Hospitals NHS	00036103	No	Device	Switched trt	Site Infections	Mild	Almost Certainly	N/A	Consumable - omnipod cannula / Almost Certainly / Expected	Concomitant medications	Resolved
2	00036 Norfolk and Norwich University Hospitals NHS	00036106	No	Device	Rand trt	Site Infections	Mild	Probably	Unrelated	Consumable - cannula / Almost Certainly / Expected	Concomitant medications	Resolved
3	00086 Doncaster Royal Infirmary	00086103	No	Device	Rand trt	Other - specify: Allergy	Mild	Probably	Unlikely	Consumable - Cannulae / Almost Certainly / Unexpected	None	Not resolved / ongoing
4	00086 Doncaster Royal Infirmary	00086103	No	Device	Rand trt	Other - specify: Skin Reaction	Mild	Probably	Unlikely	Consumable - cannula / Almost Certainly / Unexpected	Concomitant medications	Not resolved / ongoing
5	00086 Doncaster Royal Infirmary	00086103	No	Device	Rand trt	Other - specify: hypoglycemia	Mild	Possibly	Almost Certainly	Insulin delivery device - Pump / Possibly / Expected	Other - specify / A&E Visit	Resolved
6	00114 Southampton University Hospitals NHS Trust	00114206	No	Device	Switched trt	Site Infections	Moderate	Almost Certainly	Probably	Consumable - pod cannula / Possibly / Expected	Concomitant medications	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
7	00114 Southampton University Hospitals NHS Trust	00114207	No	Device	Rand trt	Other - specify: pain at cannula insertion site	Mild	Probably	Unrelated	Consumable - pump cannula / Probably / Expected	Other - specify / changed from pump to using MDI	Resolved
8	00114 Southampton University Hospitals NHS Trust	00114207	No	Device	Rand trt	Other - specify: pain at cannula site	Mild	Probably	Unrelated	Consumable - pump cannula / Probably / Expected	Other - specify / changed from using pump to using MDI from 5 / 11 / 14 to 14 / 11 / 14	Resolved
9	00114 Southampton University Hospitals NHS Trust	00114210	No	Device	Rand trt	Other - specify: pump failure - higher blood sugars than usual but no ketones.	Mild	Almost Certainly	Unrelated	Insulin delivery device - Pump / Almost Certainly / Expected	Other - specify / changed to mdi temporarily	Resolved
10	00114 Southampton University Hospitals NHS Trust	00114213	No	Device	Switched trt	Pump Failure	Moderate	Almost Certainly	Unlikely	Insulin delivery device - Pump / Possibly / Expected; Glucometer / Almost Certainly / Expected	Other - specify / come off p[ump and gave injections of aspart and garline insulin instead	Resolved
11	00148 Ipswich Hospital	00148101	No	Device	Rand trt	Other - specify: brusing to cannula site after falling on it	Moderate	Almost Certainly	Unrelated	Consumable - cannula / Almost Certainly / Unexpected	Other - specify / cannula site changed	Resolved
12	00148 Ipswich Hospital	00148203	No	Device	Rand trt	Other - specify: tubing broke at leur lock end. blood glucose levels rose.	Mild	Almost Certainly	Unrelated	Consumable - set / Almost Certainly / Expected	Other - specify / tubing changed and correction doses given	Resolved
13	00213 Nottingham University Hospital NHS Trust	00213105	No	Device	Rand trt	Other - specify: Hyperglycemia	Mild	Probably	Almost Certainly	Insulin delivery device - Pump / Almost Certainly / Expected; Consumable - infusion set / Possibly / Expected	Other - specify / pump set change	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
14	00213 Nottingham University Hospital NHS Trust	00213108	Yes	Device	Rand trt	Diabetic Ketoacidosis	Moderate	Possibly	Almost Certainly	Insulin delivery device - Pump / Possibly / Unexpected	General admission	Resolved
15	00243 Alder Hey Childrens NHS Foundation Trust	00243103	No	Device	Rand trt	Other - specify: lost cannula tip required x ray of area.	Mild	- 7	- 9	Consumable - Catheter / Almost Certainly / Unexpected	Other - specify / X - Ray	Resolved
16	00243 Alder Hey Childrens NHS Foundation Trust	00243201	No	Device	Rand trt	Site Infections	Moderate	- 7	- 8	Consumable - Catheter / Possibly / Expected	Concomitant medications	Resolved
17	00243 Alder Hey Childrens NHS Foundation Trust	00243201	No	Device	Rand trt	Pump Failure	Moderate	- 7	- 8	Insulin delivery device - Pump / Almost Certainly / Expected	Other - specify / Missing reason	Resolved
18	00243 Alder Hey Childrens NHS Foundation Trust	00243201	No	Device	Rand trt	Pump Failure	Mild	- 7	- 8	Consumable - Catheter / Almost Certainly / Unexpected	Other - specify / Ultrasound and surgical review 18 / 05 / 2012. NAD surgeon advised discharge home	Resolved
19	00243 Alder Hey Childrens NHS Foundation Trust	00243201	Yes	Device	Rand trt	Site Infections	Moderate	- 7	- 8	Consumable - canula (cleo) / Almost Certainly / Expected	General admission	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
20	00243 Alder Hey Childrens NHS Foundation Trust	00243205	No	Device	Rand trt	Site Infections	Mild	- 7	Almost Certainly	Insulin drug - Insulin aspart / Possibly / Expected; Insulin delivery device - Pump / Possibly / Expected; Consumable - Cannula / Almost Certainly / Expected	Concomitant medications	Resolved
21	00243 Alder Hey Childrens NHS Foundation Trust	00243401	No	Device	Rand trt	Other - specify: cannulae falling out - mum ran out of cannula - no supply available.	Mild	- 7	- 7	Consumable - Catheter / Almost Certainly / Expected	Other - specify / New canunula inserted and supply given	Resolved
22	04913 Cardiff and Vale University Local Health Board	04913106	No	Device	Rand trt	Pump Failure	Moderate	Possibly	Possibly	Insulin delivery device - Pump / Possibly / Unexpected; Consumable - cartridges / Possibly / Unexpected	Other - specify / advised to ring roche	Resolved
23	04913 Cardiff and Vale University Local Health Board	04913106	No	Device	Rand trt	Other - specify: hyperglycemia x2 episodes	Mild	Possibly	Possibly	Insulin delivery device - Pump / Possibly / Unexpected	Other - specify / new pump	Resolved
24	05042 Oxford Radcliffe Hospitals NHS Trust	05042102	No	Device	Rand trt	Site Infections	Mild	- 7	Almost Certainly	Consumable - Rapid D link cannula / Possibly / Expected	Concomitant medications	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
25	05042 Oxford Radcliffe Hospitals NHS Trust	05042102	No	Device	Rand trt	Severe Hypoglycaemia	Moderate	- 7	Almost Certainly	Insulin drug - Insulin aspart / Possibly / Expected; Insulin delivery device - Pump / Possibly / Expected; Consumable - Not specified / Possibly / Unexpected; Consumable - Not specified / Possibly / Expected	Concomitant medications	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
26	05042 Oxford Radcliffe Hospitals NHS Trust	05042204	No	Device	Rand trt	Severe Hypoglycaemia	Moderate	Possibly	Possibly	Insulin drug - Insulin aspart / Possibly / Expected; Insulin delivery device - Pump / Possibly / Expected; Glucometer / Possibly / Expected; Consumable - rapid cannulas / Possibly / Expected; Consumable - cartridges / Possibly / Expected; Consumable - transfer sets / Possibly / Expected	Concomitant medications	Resolved with sequelae
27	12617 The Newcastle Upon Tyne Hospitals NHS	12617203	No	Device	Rand trt	Other - specify: high blood sugar - negative ketones	Mild	Almost Certainly	Unrelated	Consumable - Infusion set / Almost Certainly / Expected	Other - specify / Changed infusion set x2	Resolved
28	12617 The Newcastle Upon Tyne Hospitals NHS	12617304	No	Device	Rand trt	Other - specify: High blood sugars	Mild	Almost Certainly	Unrelated	Consumable - Infusion set / Almost Certainly / Expected	Other - specify / Chnaged infusion set twice	Resolved
29	12617 The Newcastle Upon Tyne Hospitals NHS	12617305	No	Device	Rand trt	Site Infections	Moderate	Almost Certainly	Possibly	Consumable - Infusion Set / Almost Certainly / Expected	Concomitant medications	Ongoing at final follow - up

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
30	00114 Southampton University Hospitals NHS Trust	00114209	No	Meter error	Switched trt	Other - specify: Episode of high blood glucose levels (no ketones) due to handset failure.	Mild	Almost Certainly	Unrelated	Glucometer / Almost Certainly / Expected	Other - specify / new handset sent by roche	Resolved
31	00114 Southampton University Hospitals NHS Trust	00114210	No	Meter error	Rand trt	Other - specify: handset failiure	Severe	Almost Certainly	Unrelated	Glucometer / Almost Certainly / Expected	Other - specify / phonecall to diabetes nurse and roche careline	Resolved
32	00114 Southampton University Hospitals NHS Trust	00114303	No	Meter error	Rand trt	Other - specify: handset not checking blood sugars - blood sugars higher than normal (no ketones)	Mild	Almost Certainly	Unlikely	Glucometer / Possibly / Expected	Other - specify / Roche careline contacted - new handset to be sent to patient	Resolved
33	00148 Ipswich Hospital	00148101	No	Carer error	Rand trt	Other - specify: device problem caused by human error - to much insulin used by grandparent. hypoglycemia as result of	Moderate	Almost Certainly	Unrelated	Insulin drug - Insulin aspart / Almost Certainly / Expected; Insulin delivery device - Pump / Almost Certainly / Unexpected; Glucometer / Almost Certainly / Expected	Other - specify / paed reg contacted for advice, gluco tabs and milk given. pump suspended overnight. glucose checked.	Resolved
34	05042 Oxford Radcliffe Hospitals NHS Trust	05042213	Yes	Carer error	Rand trt	Insulin administration error: admitted following insulin overdose, parent miscalculated bolus dose, dextrose given to correct	Moderate	Almost Certainly	- 9	Insulin drug - Insulin aspart / Almost Certainly / Expected	General admission	Resolved
35	12617 The Newcastle Upon Tyne Hospitals NHS	12617304	No	Carer error	Rand trt	Other - specify: High blood glucose after changing infusion set	Mild	Almost Certainly	Unrelated	Consumable - Infusion set / Almost Certainly / Expected	Other - specify / Telephone advice from specialist nurse	Resolved
36	12617 The Newcastle Upon Tyne Hospitals NHS	12617304	No	Carer error	Rand trt	Other - specify: High blood glucose after changing infusion set	Mild	Almost Certainly	Unrelated	Consumable - Infusion set / Almost Certainly / Expected	Other - specify / Changed to another infusion set	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
37	12617 The Newcastle Upon Tyne Hospitals NHS	12617304	No	Carer error	Rand trt	Other - specify: High blood sugar after changing infusion set	Mild	Almost Certainly	Unrelated	Consumable - Infusion set / Almost Certainly / Expected	Other - specify / Changed Infusion set twice	Resolved
38	12617 The Newcastle Upon Tyne Hospitals NHS	12617304	No	Carer error	Rand trt	Other - specify: High blood sugar after changing infusion set	Mild	Almost Certainly	Unrelated	Consumable - Infusion set / Almost Certainly / Expected	Other - specify / Replaced infusion set	Resolved
39	00114 Southampton University Hospitals NHS Trust	00114102	No	Incidental illness	Rand trt	Other - specify: fungal scrotal + penile infection	Mild	Unrelated	Possibly		Concomitant medications	Resolved
40	00114 Southampton University Hospitals NHS Trust	00114103	Yes	Incidental illness	Switched trt	Other - specify: gastroenteritis	Moderate	Unrelated	Possibly		General admission	Resolved
41	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Yes	Incidental illness	Rand trt	Insulin administration error: ear infection - high blood glucose and ketones	Moderate	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Expected	General admission	Resolved
42	00326 East Surrey Hospital	00326101	No	Incidental illness	Rand trt	Other - specify: abdominal pain	Moderate	Unlikely	Possibly		Other - specify / investigations	Not resolved / ongoing
43	04913 Cardiff and Vale University Local Health Board	04913103	Yes	Incidental illness	Rand trt	Other - specify: Pyrexia; Hyperglycaemia	Mild	Unlikely	Almost Certainly		General admission	Resolved
44	05042 Oxford Radcliffe Hospitals NHS Trust	05042219	Yes	Incidental illness	Rand trt	Other - specify: not eating	Moderate	Unrelated	Possibly		General admission	Resolved
45	00036 Norfolk and Norwich University Hospitals NHS	00036105	No	Other	Rand trt	Severe Hypoglycaemia	Mild	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Expected	Other - specify / able to take oral hypo tx	Resolved
46	00243 Alder Hey Childrens NHS Foundation Trust	00243105	No	Other	Rand trt	Severe Hypoglycaemia	Moderate	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Expected	Other - specify / Brought to A + E observed 90 mins then discharged	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
47	00243 Alder Hey Childrens NHS Foundation Trust	00243201	Yes	Other	Rand trt	Severe Hypoglycaemia	Severe	- 7	- 8	Insulin drug - Insulin aspart / Almost Certainly / Expected	General admission	Resolved
48	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Yes	Other	Rand trt	specify: hyperglycaemia ketones	Mild	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Expected	General admission	Resolved
49	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Yes	Other	Rand trt	specify: hyperglycaemia ketones	Mild	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Expected	General admission	Resolved
50	01527 Royal Blackburn Hospital	01527301	No	Other	Rand trt	specify: Hyperglycaemia	Mild	N/A	Almost Certainly		Other - specify / Additional insulin given	Resolved
51	04913 Cardiff and Vale University Local Health Board	04913101	No	Other	Rand trt	specify: Hyperglycaemia	Moderate	Unlikely	Almost Certainly		Other - specify / Review in Hospital Assessement area	Resolved
52	04913 Cardiff and Vale University Local Health Board	04913103	Yes	Other	Rand trt	Diabetic Ketoacidosis	Mild	Unlikely	Almost Certainly		General admission	Not resolved / ongoing
53	04913 Cardiff and Vale University Local Health Board	04913203	Yes	Other	Rand trt	specify: Moderate hypoglycaemia	Moderate	- 7	Almost Certainly		General admission	Resolved
54	12617 The Newcastle Upon Tyne Hospitals NHS	12617204	No	Other	Rand trt	Severe Hypoglycaemia	Severe	Unrelated	Almost Certainly		Other - specify / seen at A &E then home	Resolved

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Table 6.5-9: Listing of related AEs – MDI (taken at time of AE onset)

Notes:
[a] *Consumable* includes: 'Catheter', 'Cannula', 'Cartridge', 'Set', 'Transfer set', etc.
[b] *Insulin drug* includes: 'Insulin aspart', 'Insulin glargine'
[c] *Insulin delivery device* includes: 'MDI pens', 'Insulin pump'
[d] Intervention listed if *relationship* is 'possible', 'probably', 'almost certainly'.
-7 Field not active for earlier versions of Related Adverse Event CRF.
-8 Data unobtainable (i.e. queried and confirmed missing).

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
1	00114 Southampton University Hospitals NHS Trust	00114105	No	Device	Rand trt	Other - specify: hyperglycemia	Mild	Possibly	Almost Certainly	Insulin drug - Insulin aspart / Possibly / Unexpected	Other - specify / whent to gp gave advice to give additional insulin aspart.	Resolved
2	00248 Sheffield Childrens NHS Foundation Trust	00248303	No	Device	Rand trt	Other - specify: stinging at inj site	Moderate	Possibly	Unrelated	Insulin drug - Insulin glargine / Probably / Expected	Other - specify / potentially change to levemir	Not resolved / ongoing
3	12617 The Newcastle Upon Tyne Hospitals NHS	12617303	No	Device	Rand trt	Other - specify: Stininging at injection site after glargine given	Mild	Almost Certainly	Unrelated	Insulin drug - Insulin glargine / Almost Certainly / Expected	None	Not resolved / ongoing
4	00114 Southampton University Hospitals NHS Trust	00114213	No	Meter error	Rand trt	Other - specify: expert glucoresulting in high variability in glucose levels.	Mild	Almost Certainly	Unrelated	Glucometer / Almost Certainly / Expected	Other - specify / change of glucomter, glucometer returned to roche as requested by roche.	Resolved
5	00114 Southampton University Hospitals NHS Trust	00114213	No	Carer error	Rand trt	Insulin administration error: reastarted pump when had active glagine	Moderate	Almost Certainly	Unlikely	Insulin drug - Insulin aspart / Possibly / Unexpected; Insulin drug - Insulin glargine / Probably / Unexpected	Other - specify / patient restarted pump without using temp basal rate having had glargine 10hrs earlier.	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
6	00114 Southampton University Hospitals NHS Trust	00114304	Yes	Carer error	Rand trt	Insulin administration error: missed insulin glargine over several days due to non conpliance with diabetes treatment and behaviou	Moderate	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Unexpected; Insulin drug - Insulin glargine / Almost Certainly / Unexpected	General admission	Resolved
7	00148 Ipswich Hospital	00148301	No	Carer error	Rand trt	Insulin administration error: 6 units glargine should of given 4 units error by participant, high blood glucose as result	Mild	Almost Certainly	Unrelated	Insulin drug - Insulin glargine / Probably / Expected; Insulin delivery Insulin pen injector / Almost Certainly / Expected	Other - specify / paed reg on call advised to give extra food test over night and reduce am glargine if glucose low	Resolved
8	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Yes	Carer error	Switched trt	Insulin administration error: high blood glucose lvels with ketones due to insufficient insulin.	Mild	Almost Certainly	Probably	Insulin drug - Insulin aspart / Probably / Expected; Insulin drug - Insulin glargine / Probably / Expected	General admission	Resolved
9	00148 Ipswich Hospital	00148102	No	Incidental illness	Rand trt	Other - specify: hypoglycaemia - not eating	Mild	Unlikely	Probably		Other - specify / observed on ward in view of age	Resolved
10	00213 Nottingham University Hospital NHS Trust	00213304	Yes	Incidental illness	Switched trt	Other - specify: Major Social concerns	Moderate	N/A	Almost Certainly		General admission	Resolved
11	05042 Oxford Radcliffe Hospitals NHS Trust	05042214	Yes	Incidental illness	Switched trt	Other - specify: Vomiting Bug	Moderate	Unrelated	Possibly		Concomitant medications	Resolved

	Site	Rand no	Serious-ness	Category	Treatment taken during AE onset	Description	Severity	Relationship to interventions	Relationship to disease under study	PI assessment Trial intervention [a,b,c] / Relationship [d] / Expectedness [a]	Action taken	Outcome
12	00036 Norfolk and Norwich University Hospitals NHS	00036104	No	Other	Rand trt	Severe Hypoglycaemia	Moderate	Almost Certainly	Unrelated	Insulin drug - Insulin aspart / Almost Certainly / Expected	Other - specify / hypo treatment glucogel	Resolved
13	00114 Southampton University Hospitals NHS Trust	00114101	Yes	Other	Rand trt	specify: Hyperglycaemia	Severe	- 7	- 7	Insulin drug - Insulin aspart / Possibly / Unexpected; Insulin drug - Insulin glargine / Possibly / Unexpected; Insulin delivery Insulin pen injector / Possibly / Unexpected	Other - specify / Hospital review	Resolved
14	00114 Southampton University Hospitals NHS Trust	00114301	Yes	Other	Rand trt	Insulin administration error: Hyperglycaemia	Moderate	- 7	Almost Certainly		General admission	Resolved
15	00213 Nottingham University Hospital NHS Trust	00213102	Yes	Other	Switched trt	specify: Hypoglycaemia - resolved	Mild	Possibly	Almost Certainly	Insulin drug - Insulin aspart / Possibly / Expected	General admission	Resolved
16	00248 Sheffield Childrens NHS Foundation Trust	00248101	No	Other	Rand trt	Severe Hypoglycaemia	Moderate	Almost Certainly	Almost Certainly	Insulin drug - Insulin aspart / Almost Certainly / Expected	None	Resolved
17	04913 Cardiff and Vale University Local Health Board	04913204	Yes	Other	Rand trt	specify: High BGS and ketones	Mild	Unlikely	Almost Certainly		General admission	Resolved

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6.5.2 Serious adverse events

The incidence of related SAEs by treatment group were:

- 14 SAEs in 9 patients that were on CSII at the time of the SAE. IDR* was 6.2 patients with at least one event per 100-person-years.
- 8 SAEs in 8 patients that were on MDI at the time of the SAE. IDR* was 5.3 patients with at least one event per 100-person-years.

* The incidence density rate (IDR) is the number of patients with at least one new case per population at risk in a given time period. The denominator here is the sum of the person-time in years for each treatment group (accounting for treatment switches) of the at risk population.

Table 6.5-10: Overview of related SAEs by site and overall (All SAEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**14**	**9 (6.2)**	**8**	**8 (5.3)**	**22**	**16 (5.4)**
00036 Norfolk and Norwich University Hospitals NHS	6.4 (4)	2.2 (5)	8.6 (9)	0	0 (0)	0	0 (0)	0	0 (0)
00086 Doncaster Royal Infirmary	9.5 (9)	9.3 (9)	18.8 (18)	0	0 (0)	0	0 (0)	0	0 (0)
00104 Stafford Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00114 Southampton University Hospitals NHS Trust	16.6 (14)	13.2 (16)	29.8 (30)	1	1 (6)	3	3 (22.7)	4	4 (13.4)
00133 Birmingham Childrens Hospital	11.5 (12)	9.8 (9)	21.3 (21)	0	0 (0)	0	0 (0)	0	0 (0)
00148 Ipswich Hospital	3 (3)	3 (3)	6 (6)	0	0 (0)	0	0 (0)	0	0 (0)
00160 Royal Preston Hospital	0 (0)	2.1 (2)	2.1 (2)	0	0 (0)	0	0 (0)	0	0 (0)
00213 Nottingham University Hospital NHS Trust	32.2 (31)	30.3 (30)	62.5 (61)	1	1 (3.1)	2	2 (6.6)	3	3 (4.8)
00243 Alder Hey Childrens NHS Foundation Trust	24 (26)	29.3 (26)	53.3 (52)	5	2 (8.3)	1	1 (3.4)	6	2 (3.7)
00248 Sheffield Childrens NHS Foundation Trust	3.3 (4)	3.8 (3)	7.1 (7)	0	0 (0)	0	0 (0)	0	0 (0)
00326 East Surrey Hospital	4.3 (3)	3.1 (5)	7.4 (8)	0	0 (0)	0	0 (0)	0	0 (0)
01527 Royal Blackburn Hospital	5 (5)	5.9 (6)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)
04913 Cardiff and Vale University Local Health Board	9.3 (9)	10.4 (10)	19.7 (19)	5	3 (32.4)	1	1 (9.6)	6	4 (20.3)
05042 Oxford Radcliffe Hospitals NHS Trust	13.2 (18)	22.3 (18)	35.5 (36)	2	2 (15.1)	1	1 (4.5)	3	3 (8.5)
12617 The Newcastle Upon Tyne Hospitals NHS	5.8 (6)	5.1 (5)	10.9 (11)	0	0 (0)	0	0 (0)	0	0 (0)

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Table 6.5-11: Overview of related SAEs by site and overall (Device SAEs)

	Total person years (total patients)			CSII		MDI		Total	
	CSII	MDI	Total	Events	Patients (IDR)	Events	Patients (IDR)	Events	Patients (IDR)
Overall	144.1 (144)	151.9 (149)	296.1 (293)	2	2 (1.4)	-	-	2	2 (0.7)

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Table 6.5-12: Overview of related SAEs by site and overall (Carer error SAEs)

	Total person years (total patients)			CSII		MDI		Total	
	CSII	MDI	Total	Events	Patients (IDR)	Events	Patients (IDR)	Events	Patients (IDR)
Overall	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	2	2 (1.3)	3	3 (1)

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Table 6.5-13: Overview of related SAEs by site and overall (Meter error SAEs)

	Total person years (total patients)			CSII		MDI		Total	
	CSII	MDI	Total	Events	Patients (IDR)	Events	Patients (IDR)	Events	Patients (IDR)
Overall	144.1 (144)	151.9 (149)	296.1 (293)	-	-	-	-	-	-

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Table 6.5-14: Overview of related SAEs by site and overall (Incidental illness SAEs)

	Total person years (total patients)			CSII		MDI		Total	
	CSII	MDI	Total	Events	Patients (IDR)	Events	Patients (IDR)	Events	Patients (IDR)
Overall	144.1 (144)	151.9 (149)	296.1 (293)	6	5 (3.5)	2	2 (1.3)	8	7 (2.4)

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Table 6.5-15: Overview of related SAEs by site and overall (Other SAEs)

	Total person years (total patients)			CSII		MDI		Total	
Site name	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
Overall	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**5**	**4 (2.8)**	**4**	**4 (2.6)**	**9**	**8 (2.7)**

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Table 6.5-16: Summary of related serious adverse events by adverse event description code

		Total person years (total patients)			CSII		MDI		Total	
Category	**Description**	**CSII**	**MDI**	**Total**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**	**Events**	**Patients (IDR)**
All	**Diabetic Ketoacidosis**	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**2**	**2 (1.4)**	**0**	**0 (0)**	**2**	**2 (0.7)**
	Insulin administration error	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**2**	**2 (1.4)**	**3**	**3 (2)**	**5**	**4 (1.4)**
	Pump Failure	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**0**	**0 (0)**	**0**	**0 (0)**	**0**	**0 (0)**
	Severe Hypoglycaemia	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**1**	**1 (0.7)**	**0**	**0 (0)**	**1**	**1 (0.3)**
	Site Infections	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**1**	**1 (0.7)**	**0**	**0 (0)**	**1**	**1 (0.3)**
	other - specify	**144.1 (144)**	**151.9 (149)**	**296.1 (293)**	**8**	**6 (4.2)**	**5**	**5 (3.3)**	**13**	**11 (3.7)**
Device	Diabetic Ketoacidosis	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	Pump Failure	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	0	0 (0)	0	0 (0)
	Severe Hypoglycaemia	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	0	0 (0)	0	0 (0)
	Site Infections	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	0	0 (0)	0	0 (0)
Carer error	Insulin administration error	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	2	2 (1.3)	3	3 (1)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	0	0 (0)	0	0 (0)

Meter error	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	0	0 (0)	0	0 (0)
Incidental illness	Insulin administration error	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	5	4 (2.8)	2	2 (1.3)	7	6 (2)
Other	Diabetic Ketoacidosis	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	Insulin administration error	144.1 (144)	151.9 (149)	296.1 (293)	0	0 (0)	1	1 (0.7)	1	1 (0.3)
	Severe Hypoglycaemia	144.1 (144)	151.9 (149)	296.1 (293)	1	1 (0.7)	0	0 (0)	1	1 (0.3)
	other - specify	144.1 (144)	151.9 (149)	296.1 (293)	3	2 (1.4)	3	3 (2)	6	5 (1.7)

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Table 6.5-17: Relationship and expectedness of insulin drug

Events (Randomisation no / CTRC SAE no) are classified into the following 5 categories:

SAEs in CSII group (N events=14)				
Related* SAE (n=6)				Unrelated SAE (n=8)
Unexpected (n=0)		Expected (n=6)		
SUSAR Involving insulin drug (n=0)	Not involving insulin drug (n=0)	Involving insulin drug (n=4)	Not involving insulin drug (n=2)	
		(Other) 00243201/02 (Other) 04913103/04 (Carer error) 05042213/13 (Other) 00243313/20	(Device) 00243201/01 (Incidental illness) 04913103/10	(Incidental illness) 04913101/06 (Incidental illness) 04913103/11 (Other) 04913103/12 (Incidental illness) 05042219/15 (Incidental illness) 00243313/17 (Incidental illness) 00114103/18 (Other) 00243313/19 (Device) 00213108/22
SAEs in MDI group (N events=8)				
Related* SAE (n=4)				Unrelated SAE (n=4)
Unexpected (n=1)		Expected (n=3)		
SUSAR Involving insulin drug (n=1)	Not involving insulin drug (n=0)	Involving insulin drug (n=3)	Not involving insulin drug (n=0)	
(Other) 00114101/05		(Other) 00213102/08 (Carer error) 00114304/16 (Carer error) 00243313/21		(Other) 00114301/03 (Incidental illness) 00213304/07 (Other) 04913204/09 (Incidental illness) 05042214/14

* Related = possibly, probably or almost certainly.

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Table 6.5-18: SAE listing of related serious adverse events – CSII (taken at time of SAE onset)

Notes:
[a] *Consumable* includes: 'Catheter', 'Cannula', 'Cartridge', 'Set', 'Transfer set', etc.
[b] *Insulin drug* includes: 'Insulin aspart', 'Insulin glargine'
[c] *Insulin delivery device* includes: 'MDI pens', 'Insulin pump'
[d] Intervention listed if *relationship* is 'possible', 'probably', 'almost certainly'.

SAE no	Site	Rand_no	AE category and description	Description	CI assessment of seriousness	**Trial intervention** [a,b,c] **/ Relationship** [d] **/ Expectedness**		Action taken	Outcome
						CI	PI		
1	00243 Alder Hey Childrens NHS Foundation Trust	00243201	Device -Site Infections	Swelling and redness at site of infection. Follow up: Needed surgical drainage of collection at Cannula site (in theatre). Treated with IV and then oral antibiotics. Final Report: Discharged home after 48 hrs IV antibiotics to complete 7 days oral antibiotics. Reviewed after 3 days by practice nurse for dressing change and 7 days later by practice nurse - no problems. No further action needed and all resolved.	Required Hospitalisation	Consumable / Almost certainly / Expected		Hospital admission; Treatment with medication; Other- Drainage of collection at cannula site (in theatre)	Resolved
2	00243 Alder Hey Childrens NHS Foundation Trust	00243201	Other -Severe Hypoglycaemia	Seizures realted to possible hypoglycaemia.	Required Hospitalisation	Insulin drug - Insulin aspart / Almost certainly / Expected; Insulin delivery device - Insulin Pump / Almost certainly / Expected; Consumable / Almost certainly / Expected; Consumable / Almost certainly / Expected		Dose reduced; Temporary interruption; Hospital admission; Attendance at A and E	Resolved
4	04913 Cardiff and Vale University	04913203	Other -other - specify: Moderate hypoglycaemia	Call to diabetes nurses on-call phone. Patient hypo with 1.8 reading, mum tested blood sugar 5.0mmol Mum stated patient	Required Hospitalisation	Insulin drug - Insulin aspart / Almost certainly / Expected		Dose reduced; Hospital admission;	Resolved

SAE no	Site	Rand_no	AE category and description	Description	CI assessment of seriousness	Trial intervention [a,b,c] / Relationship [d] / Expectedness		Action taken	Outcome
						CI	PI		
	Local Health Board			dizzy, confused and sleepy, Mum called back 5 minutes later and tetsted B.S. and now 14mmol/l, and patient perked up. mum called back back 30 mins later B.S. 7mmol/l, mum concerned about symptoms advised mum to come to childrens's emergency department. Sent to emergency department likley honeymoon period onsnet.				Attendance at A and E	
6	04913 Cardiff and Vale University Local Health Board	04913101	Incidental illness -other - specify: Gastroentiritis	Call to diabetes on-call phone. Patient vommiting and had diarrhea throughout the night. Patient developed blood ketones and fluctuating blood sugars. Advised patient and mother to present to children assessment unit. No acidosis, clinically dehydrated, IV fluids for 24 hours insulin pump working and infusing throughout, patient discharged 24 hourslater 18/02/2013 at 14:30hrs	Required Hospitalisation			Dose reduced; Insulin Dose increased; Hospital admission; Other-Attendance at Childrens Emergency Assessment unit	Resolved
10	04913 Cardiff and Vale University Local Health Board	04913103	Incidental illness -other - specify: Chicken pox	High blood sugar readings, 29.5mmol/l and blood ketones 3.3mmol/l. Patient sleepy, eating very little but drinking. Advised mum on on-call phone to present to children's assessment. Likely not in DKA, increased CSII baal rates. During Hospital admission chicken pox appeared. Discharged home 14/06/2013	Required Hospitalisation	Insulin delivery device - Insulin Pump / Possibly / Expected; Consumable / Possibly / Expected; Consumable / Possibly / Expected; Consumable / Possibly / Expected		Insulin Dose increased; Hospital admission; Other-Attendance at Children's Assessment Unit	Resolved
11	04913 Cardiff and Vale	04913103	Incidental illness -other - specify: Pyrexia; Hyperglycaemia	Parent observed high temperature 40.2 degrees cand called out of hours GP who	Required Hospitalisation			Insulin Dose increased;	Resolved

SAE no	Site	Rand_no	AE category and description	Description	CI assessment of seriousness	Trial intervention [a,b,c] / Relationship [d] / Expectedness		Action taken	Outcome
						CI	PI		
	University Local Health Board			advised presentation to Hosiptal. Patient admitted to General Paediatric Ward overnight observations.Eratic blood glucose levels throughout admission, no ketosis. Patient discharged home 18 hours later. Unknown cause of fever.				Hospital admission	
12	04913 Cardiff and Vale University Local Health Board	04913103	Other -Diabetic Ketoacidosis	Following on from the initial report for thi SAE, the patient was slow to recover post DKA pathway. Blood sugar reading dropped and patient went hypoglycaemic. This was put down to human error in pump set change. Patient discharged home.	Required Hospitalisation			Dose reduced; Temporary interruption; Hospital admission	Resolved
13	05042 Oxford Radcliffe Hospitals NHS Trust	05042213	Carer error -Insulin administration error: admitted following insulin overdose, parent miscalculated bolus dose, dextrose given to correct	Insulin administration error	Required Hospitalisation	Insulin drug - Insulin aspart / Almost certainly / Expected		Dose reduced; Temporary interruption; Hospital admission; Attendance at A and E	Resolved
15	05042 Oxford Radcliffe Hospitals NHS Trust	05042219	Incidental illness -other - specify: not eating	poor appetite hyperglycaemia	Required Hospitalisation			Insulin Dose increased; Hospital admission; Attendance at A and E	Resolved
17	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Incidental illness -Insulin administration error: ear infection- high blood glucose and ketones	participant has ear infection. History of elevated blood glucose levels and blood ketones. Taken off insulin pump onto sliding scale. Resumed to MDI 23/11/20114- back on insulin pump 24/11/2014	Required Hospitalisation			Insulin Dose increased; Temporary interruption; Hospital admission;	Resolved

SAE no	Site	Rand_no	AE category and description	Description	CI assessment of seriousness	Trial intervention [a,b,c] / Relationship [d] / Expectedness		Action taken	Outcome
						CI	PI		
								Attendance at A and E	
18	00114 Southampton University Hospitals NHS Trust	00114103	Incidental illness -other - specify: gastroenteritis	known diabetic on insulin pump admitted with vomiting and raised ketones blood sugars stable around 12. bloods taken, iv fluids commenced 11/10/2014. iv fluids discontinued 12/10/2014 participants ketones down and blood sugars stab;le therefore discharged home 12/10/14.	Required Hospitalisation			Hospital admission	Resolved
19	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Other -other - specify: hyperglycaemia ketones	participant admitted to general ward due to being hyperglycaemic with ketones. Not resolving following 4 sick day doses not in DKA however treated on DKA pathway	Required Hospitalisation			Insulin Dose increased; Temporary interruption; Hospital admission; Attendance at A and E	Resolved with sequelae
20	00243 Alder Hey Childrens NHS Foundation Trust	00243313	Other -other - specify: hyperglycaemia ketones	admitted to general ward. hyperglycaemia and blood ketones not resolving with sick day doses of insulin commenced on D.KA pathway although not in D.K.A	Required Hospitalisation	Insulin drug - Insulin aspart / Almost certainly / Expected		Insulin Dose increased; Temporary interruption; Hospital admission; Attendance at A and E	Resolved
22	00213 Nottingham University Hospital NHS Trust	00213108	Device -Diabetic Ketoacidosis	admitted with diabetic ketoacidosis following a day of high blood glucose levels settled rapidly with iv fluids and insulin kept in hospital for addittional 5 days for education and safeguarding	Required Hospitalisation			Temporary interruption; Hospital admission; Attendance at A and E	Resolved

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Table 6.5-19: SAE listing of related serious adverse events – MDI (taken at time of SAE onset)

Notes:
[a] *Consumable* includes: 'Catheter', 'Cannula', 'Cartridge', 'Set', 'Transfer set', etc.
[b] *Insulin drug* includes: 'Insulin aspart', 'Insulin glargine'
[c] *Insulin delivery device* includes: 'MDI pens', 'Insulin pump'
[d] Intervention listed if *relationship* is 'possible', 'probably', 'almost certainly'.

SAE no	Site	Rand no	AE category and description	Description	CI assessment of seriousness	**Trial intervention** [a,b,c] **/ Relationship** [d] **/ Expectedness**		Action taken	Outcome
						CI	PI		
3	00114 Southampton University Hospitals NHS Trust	00114301	Other -Insulin administration error: Hyperglycaemia	Participant had blood sugar 28mmol no ketone testing strips - called ward for advice. Advised to go to nearest hospital to have ketones checked (by local hospital - advice given). In A&E nightime Lantus injection given by parent, keteones reported to be negative subsequently novorapid and actrapid doeses given by A&E department. Participant then admitted to paediatric ward due to insulin overdose, risk of hypoglycaemia. Overnight stay (pt and family not in local area during this event).	Required Hospitalisation; Medically significant / important			Hospital admission; Attendance at A and E	Resolved
5	00114 Southampton University Hospitals NHS Trust	00114101	Other -other - specify: Hyperglycaemia	Seen at home visit 14/01/2013 Insulin pen, injection technique all checked and OK. High blood sugars and ketones resolved with increased insulin doses glargine and novorapid. Please see attached sheet (file note) for detail.	Required Hospitalisation		Insulin drug - Insulin aspart / Probably / Unexpected; Insulin drug - Insulin glargine / Probably / Unexpected	Insulin Dose increased	Resolved
7	00213 Nottingham University Hospital NHS Trust	00213304	Incidental illness -other - specify: Major Social concerns	High blood glucose levels and attended OPD for Pump start but had not tested any blood glucose levels for 4 days. Mum had not collected a new prescription for testing strips despite arranging for her to collect strips at both hospital. Hospitalised to arrange safeguarding meeting.	Medically significant / important			Temporary interruption; Hospital admission; Other-Referral to social care	Resolved
8	00213 Nottingham	00213102	Other -other - specify: Hypoglycaemia -	Had low blood glucose level (BGL) recorded at hime (1.4) fully	Required Hospitalisation	Insulin drug - Insulin aspart /		Dose reduced;	Resolved

SAE no	Site	Rand no	AE category and description	Description	CI assessment of seriousness	Trial intervention [a,b,c] / Relationship [d] / Expectedness		Action taken	Outcome
						CI	PI		
	University Hospital NHS Trust		resolved	concious and treated with study treatment. Parents concerned and attended ED. BGL normal then and during admission. Case not discussed with diabetes team, else would not have been admitted.		Almost certainly / Expected		Hospital admission; Attendance at A and E	
9	04913 Cardiff and Vale University Local Health Board	04913204	Other -other - specify: High BGS and ketones	Patient admitted to General Paediatric Ward due to Gastroentritis. He developed ketones and vommited he required overnight IV fluids.He tolerated diet and fluids the following morning and was subsequently discharged home. MDI treatment continued as normal through the event. Event resolved.	Required Hospitalisation			Hospital admission	Resolved
14	05042 Oxford Radcliffe Hospitals NHS Trust	05042214	Incidental illness -other - specify: Vomiting Bug	Vomiting bug	Required Hospitalisation			Temporary interruption; Hospital admission; Treatment with medication	Resolved
16	00114 Southampton University Hospitals NHS Trust	00114304	Carer error -Insulin administration error: missed insulin glargine over several days due to non conpliance with diabetes treatment and behaviou	participant was admitted with a history of blood sugar of 21.1.ketones 5.5 at 6pm at home normal blood ph. he had a 2 day history of feeling unwell. participant admitted missing glargine dose on 01/11/2014 and x2 novorapid doses on 02/11/2014. novorapid dose given with evening meal on 02/11/2014 together with evening meal on 02/11/2014 together with a correction dose, prior to hospital admission participant rechecked following clerking in hospital.blood sugar 16 + ketones 0.8	Required Hospitalisation	Insulin drug - Insulin aspart / Almost certainly / Expected; Insulin drug - Insulin glargine / Almost certainly / Expected		Hospital admission	Resolved
21	00243 Alder Hey	00243313	Carer error -Insulin administration error:	admitted to general medical ward with high blood glucose levels and	Required Hospitalisation	Insulin drug - Insulin aspart /		Insulin Dose increased;	Resolved

SAE no	Site	Rand no	AE category and description	Description	CI assessment of seriousness	Trial intervention [a,b,c] / Relationship [d] / Expectedness		Action taken	Outcome
						CI	PI		
	Childrens NHS Foundation Trust		high blood glucose lvels with ketones due to insufficient insulin.	blood ketones not in DKA.		Probably / Expected; Insulin drug - Insulin glargine / Probably / Expected		Hospital admission	

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6.6 Efficacy data

The membership of the analysis set for each outcome was determined and documented and reasons for participant exclusion given prior to the randomisation lists being requested.

The principle of intention-to-treat, as far as practically possible, was the main strategy of the analysis adopted for the primary outcome and all the secondary outcomes. These analyses were conducted on all randomised participants, in the group to which they were allocated, and for whom the outcome(s) of interest have been observed/measured. No imputations were made.

6.6.1 Primary efficacy assessment - $HbA1_c$ measured 12 months after randomisation

6.6.1.1 $HbA1_c$ measured 12 months after randomisation – ITT

Table 6.6-1: HbA1c measured 12 months after randomisation – Completeness of data (ITT)

Analysis status	Reason	CSII	MDI	Total
Included	Included	143 (99.3%)	142 (95.3%)	285 (97.3%)
Excluded	No local reason=(home visit); No central reason=(Quantity not sufficient)	0 (0%)	1 (0.7%)	1 (0.3%)
	No local reason=(home visit, see below); No central reason=(no sample received at labs)	0 (0%)	1 (0.7%)	1 (0.3%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)

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Table 6.6-2: HbA1c measured 12 months after randomisation – Lab value used for analysis (ITT)

Age strata	Lab value used for PO analysis (ITT)	CSII	MDI
<5 years	Central	22 (66.7%)	26 (83.9%)
	Local	11 (33.3%)	5 (16.1%)
5-11 years	Central	58 (82.9%)	58 (80.6%)
	Local	12 (17.1%)	14 (19.4%)
12+ years	Central	32 (80%)	33 (84.6%)
	Local	8 (20%)	6 (15.4%)
Total	**Central**	**112 (77.8%)**	**117 (78.5%)**
	Local	**31 (21.5%)**	**25 (16.8%)**

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Table 6.6-3: HbA1c measured 12 months after randomisation – Results (ITT)

Age-group	HbA1c (mmol/mol) at 12 months	CSII	MDI	Total	Least Squares Mean CSII (95% CI)	Least Squares Mean MDI (95% CI)	Least Squares Mean Difference between treatment groups (CSII-MDI) across all age-groups (95% CI)	P-value
7mths - < 5yrs	Missing	0	0	0	60.9 (58.5,63.3)	58.5 (56.1,60.9)	2.4 (-0.4, 5.3)	0.09
	N	33	31	64				
	Mean (SD)	63.9 (12.1)	58.4 (9.9)	61.2 (11.3)				
	Median (IQR)	63.6 (56, 71)	58 (51, 65)	62.5 (54, 69)				
	(Min, Max)	(40, 88)	(36, 83)	(36, 88)				
5yrs - <12yrs	Missing	0	0	0				
	N	70	72	142				
	Mean (SD)	58 (11.4)	59.3 (11.4)	58.7 (11.4)				
	Median (IQR)	57 (50, 65)	58 (49, 65)	57 (50, 65)				
	(Min, Max)	(33, 92)	(43, 89)	(33, 92)				
12yrs - <16yrs	Missing	0	0	0				
	N	40	39	79				
	Mean (SD)	61.3 (13.3)	54.7 (14.7)	58.1 (14.3)				
	Median (IQR)	63.5 (50.5, 69.5)	51 (45, 66)	58 (45, 68)				
	(Min, Max)	(35, 84)	(31, 94)	(31, 94)				
Overall	**Missing**	**0**	**0**	**0**				
	N	**143**	**142**	**285**				
	Mean (SD)	**60.3 (12.3)**	**57.9 (12.2)**	**59.1 (12.3)**				
	Median (IQR)	**60 (52, 68)**	**57 (48, 65)**	**58 (50, 67)**				
	(Min, Max)	**(33, 92)**	**(31, 94)**	**(31, 94)**				

Note: Lower mmol/mol indicates better glycaemic control.

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Figure 6.6-1: Primary outcome results Meta-Analysis and Forest plot across sites (ITT)

Study or Subgroup	CSII Mean	CSII SD	CSII Total	MDI Mean	MDI SD	MDI Total	Weight	Mean Difference IV, Fixed, 95% CI
00036 Norfolk and Norwich University Hospitals NHS	60.7555	11.9268604	4	49.25	8.0156098	4	3.7%	11.51 [-2.58, 25.59]
00086 Doncaster Royal Infirmary	55.25	10.9642275	8	59.6666667	11.6404467	9	6.3%	-4.42 [-15.17, 6.33]
00104 Stafford Hospital	0	0	0	57	4.2426407	2		Not estimable
00114 Southampton University Hospitals NHS Trust	64.2142857	15.5324899	14	61.1333333	13.0376743	15	6.6%	3.08 [-7.39, 13.56]
00133 Birmingham Childrens Hospital	61.5	13.541183	12	59.5555556	11.7910041	9	6.2%	1.94 [-8.92, 12.81]
00148 Ipswich Hospital	56.6666667	8.3864971	3	48.3333333	4.7258156	3	6.1%	8.33 [-2.56, 19.23]
00160 Royal Preston Hospital	0	0	0	67.5	7.7781746	2		Not estimable
00213 Nottingham University Hospital NHS Trust	57.7741935	11.1376529	31	55.8666667	13.6879845	30	18.5%	1.91 [-4.37, 8.18]
00243 Alder Hey Childrens NHS Foundation Trust	58.6923077	11.3517196	26	55.1666667	12.7370281	24	16.2%	3.53 [-3.18, 10.23]
00248 Sheffield Childrens NHS Foundation Trust	64	13.2916014	4	52.6666667	10.7857931	3	2.3%	11.33 [-6.52, 29.18]
00326 East Surrey Hospital	61.2	4.5077711	3	69.25	10.8435849	4	5.2%	-8.05 [-19.84, 3.74]
01527 Royal Blackburn Hospital	61.07983	12.6936387	5	61.6666667	11.2368442	6	3.6%	-0.59 [-14.89, 13.72]
04913 Cardiff and Vale University Local Health Boa	59.3333333	9.8361578	9	61.5555556	9.0015431	9	9.6%	-2.22 [-10.93, 6.49]
05042 Oxford Radcliffe Hospitals NHS Trust	62.3333333	15.8336945	18	54.7647059	10.9231944	17	9.0%	7.57 [-1.40, 16.54]
12617 The Newcastle Upon Tyne Hospitals NHS	68.3333333	8.2623645	6	68.8	9.2032603	5	6.7%	-0.47 [-10.90, 9.96]
Total (95% CI)			**143**			**142**	**100.0%**	**2.16 [-0.54, 4.86]**

Heterogeneity: Chi² = 11.21, df = 12 (P = 0.51); I² = 0%
Test for overall effect: Z = 1.57 (P = 0.12)

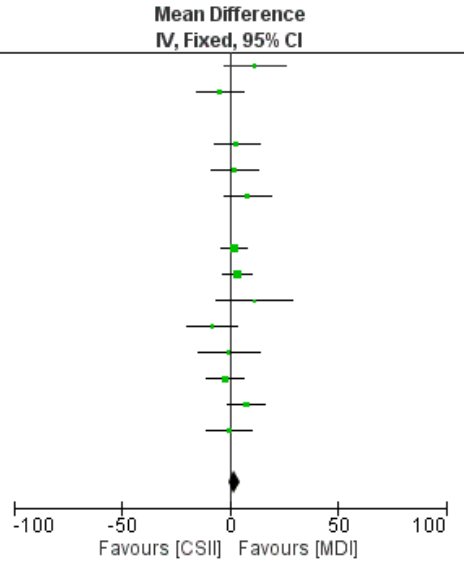

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Table 6.6-4: Baseline characteristics of children that were randomised and have a primary outcome measurement (ITT)

	CSII	MDI	Total
Age at randomisation (years)			
Missing	0	0	0
N	143	142	285
Mean (SD)	9.1 (4.1)	9 (4.2)	9 (4.1)
Median (IQR)	9.9 (5.6, 12.3)	9.3 (5.7, 12.5)	9.7 (5.7, 12.3)
(Min, Max)	(0.8, 16)	(0.7, 15.4)	(0.7, 16)
Age cat (strata cat)			
Missing	0	0	0
N	143	142	285
7mths – <5 yrs	33 (23.1%)	31 (21.8%)	64 (22.5%)
5 – <12 yrs	70 (49%)	72 (50.7%)	142 (49.8%)
12-15 yrs	40 (28%)	39 (27.5%)	79 (27.7%)
Age cat (EudraCT)			
Missing	0	0	0
N	143	142	285
Infants and toddlers	8 (5.6%)	6 (4.2%)	14 (4.9%)
Children	95 (66.4%)	97 (68.3%)	192 (67.4%)
Adolescents	40 (28%)	39 (27.5%)	79 (27.7%)
Gender			
Missing	0	0	0
N	143	142	285
Female	71 (49.7%)	64 (45.1%)	135 (47.4%)
Male	72 (50.3%)	78 (54.9%)	150 (52.6%)
Ethnicity			
Missing	1	3	4
N	142	139	281
Asian or Asian British	3 (2.1%)	3 (2.2%)	6 (2.1%)
Black or British Black	0 (0%)	3 (2.2%)	3 (1.1%)
British White	124 (87.3%)	112 (80.6%)	236 (84%)
Indian	2 (1.4%)	2 (1.4%)	4 (1.4%)
Mixed	4 (2.8%)	6 (4.3%)	10 (3.6%)
Not stated	0 (0%)	0 (0%)	3 (1.1%)
Other	2 (1.4%)	2 (1.4%)	4 (1.4%)
Other White	6 (4.2%)	7 (5%)	13 (4.6%)
Pakistani	1 (0.7%)	4 (2.9%)	5 (1.8%)
Deprivation score (continuous)			
Missing	7	6	13
N	136	136	272
Mean (SD)	25 (19.4)	20.9 (17)	22.9 (18.3)
Median (IQR)	19.3 (8.9, 38.5)	13.9 (7.7, 29.5)	16.7 (8.3, 35)
(Min, Max)	(1.8, 77.1)	(1.6, 73.9)	(1.6, 77.1)
Deprivation score (quintile			

	CSII	MDI	Total
categories)			
Missing	7	6	13
N	136	136	272
1 (<=8.49)	32 (23.5%)	39 (28.7%)	71 (26.1%)
2 (8.5 – 13.79)	23 (16.9%)	29 (21.3%)	52 (19.1%)
3 (13.8 – 21.35)	18 (13.2%)	22 (16.2%)	40 (14.7%)
4 (21.36 – 34.17)	24 (17.6%)	16 (11.8%)	40 (14.7%)
5 (>=34.18)	39 (28.7%)	30 (22.1%)	69 (25.4%)

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Figure 6.6-2: HbA1c mmol/mol – Mean profile plots (<5 years old) (ITT) – Post-hoc analysis

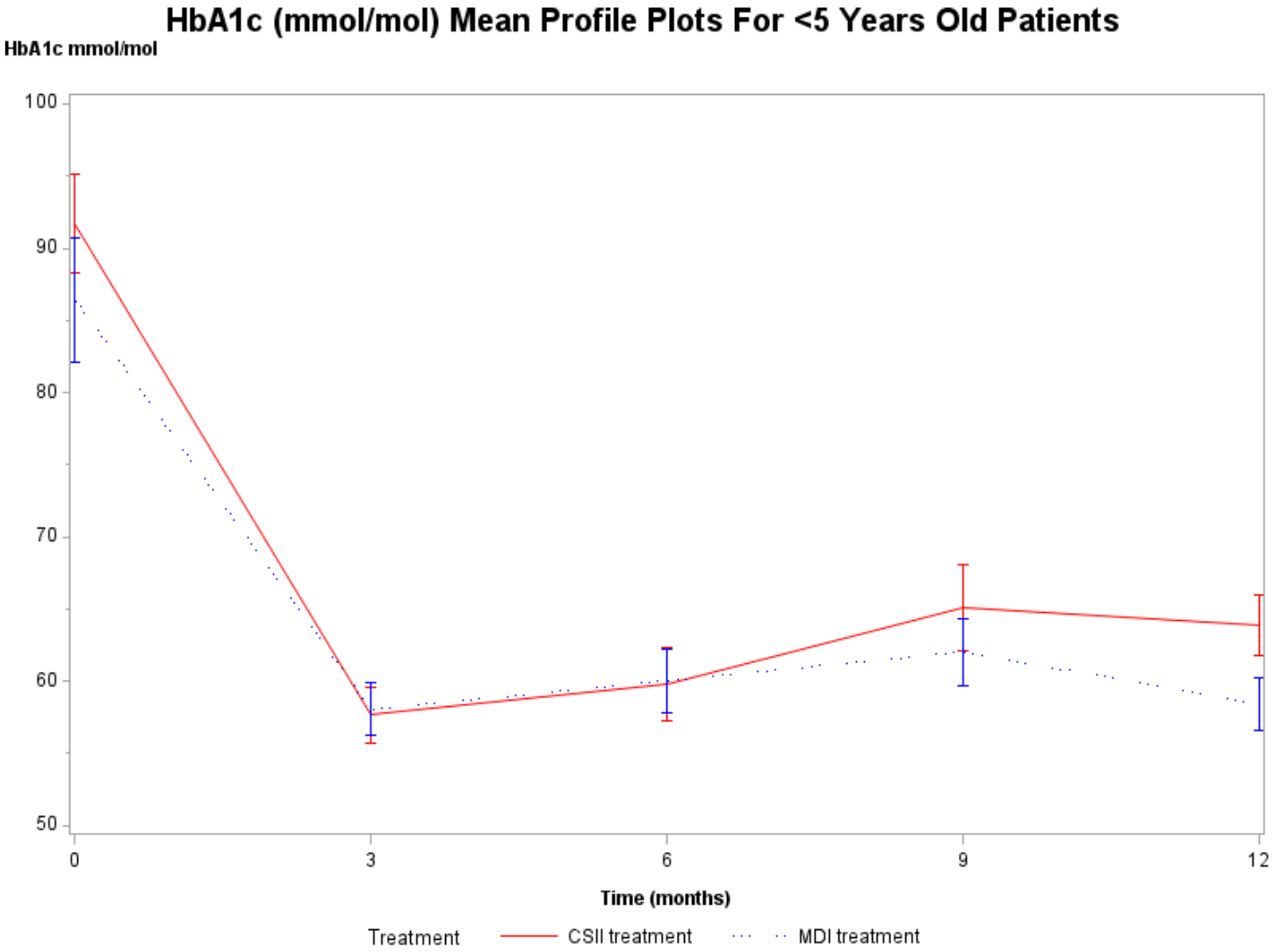

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Figure 6.6-3: HbA1c mmol/mol – Mean profile plots (5-11 years old) (ITT) – Post-hoc analysis

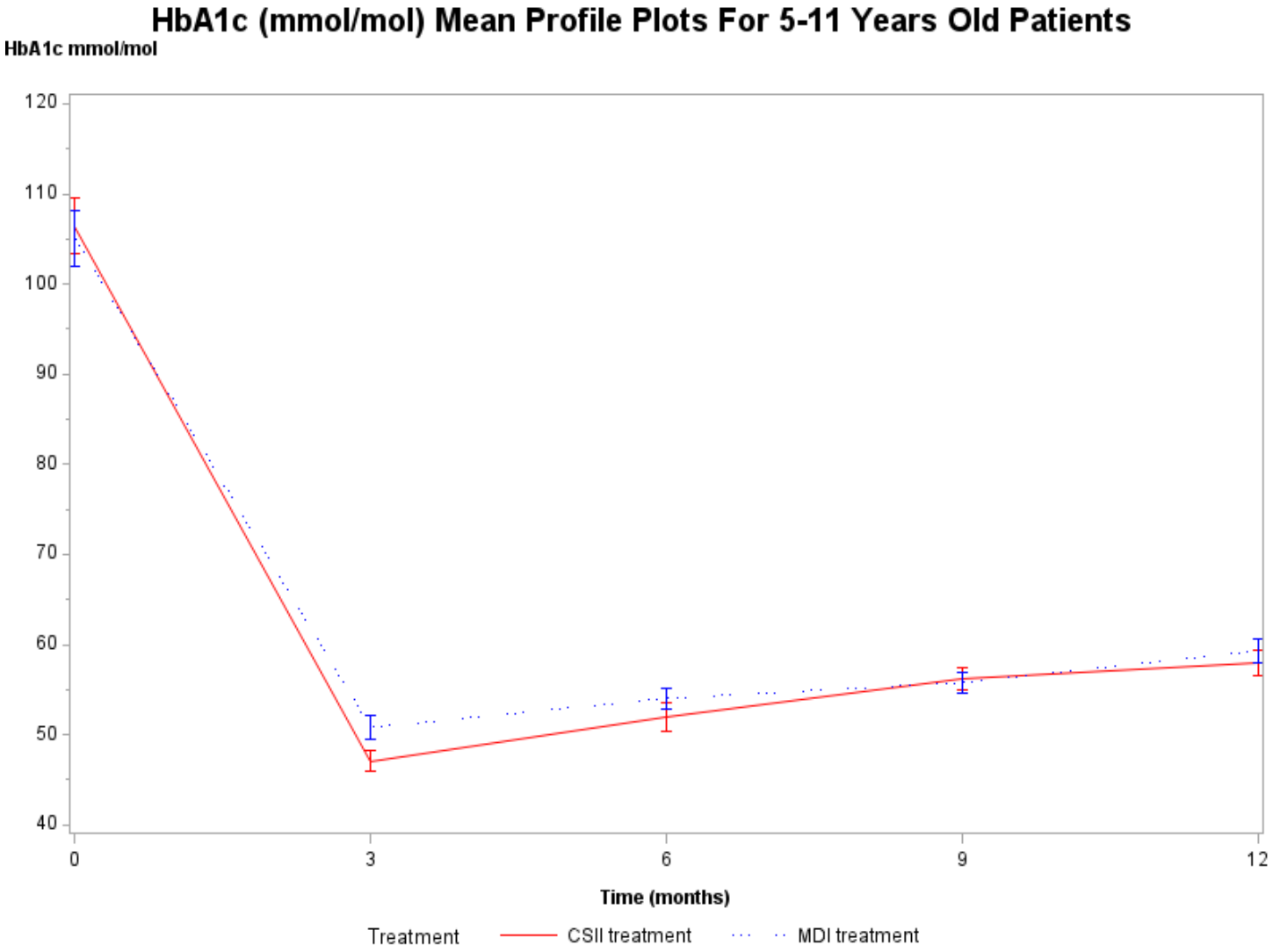

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Figure 6.6-4: HbA1c mmol/mol – Mean profile plots (12+ years old) (ITT) – Post-hoc analysis

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6.6.1.2 HbA1c measured 12 months after randomisation – Per-protocol

The per protocol analysis set is defined as those participants without a major protocol deviation or less than three minor deviations as specified within the monitoring plan. See Table 6.2-5 for summary of protocol deviations.

Table 6.6-5: HbA1c measured 12 months after randomisation – Completeness of data (Per-protocol)

Analysis status	Reason	CSII	MDI	Total
Included	Included	87 (60.4%)	66 (44.3%)	153 (52.2%)
Excluded	At least one major PD	56 (38.9%)	76 (51%)	132 (45.1%)
	At least one major PD and were also excluded from ITT analysis: (WD from study prior to 12 months)	1 (0.7%)	1 (0.7%)	2 (0.7%)
	Excluded from ITT analysis: (No local reason=(home visit); No central reason=(Quantity not sufficient))	0 (0%)	1 (0.7%)	1 (0.3%)
	Excluded from ITT analysis: (No local reason=(home visit, see below); No central reason=(no sample received at labs))	0 (0%)	1 (0.7%)	1 (0.3%)
	Excluded from ITT analysis: (WD from study prior to 12 months)	0 (0%)	4 (2.7%)	4 (1.4%)

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Table 6.6-6: HbA1c measured 12 months after randomisation – Lab value used for analysis (Per-protocol)

Age strata	Lab value used for PO analysis (per-protocol)	CSII	MDI
<5 years	Central	15 (65.2%)	11 (100%)
	Local	8 (34.8%)	-
5-11 years	Central	34 (82.9%)	27 (84.4%)
	Local	7 (17.1%)	5 (15.6%)
12+ years	Central	18 (78.3%)	20 (87%)
	Local	5 (21.7%)	3 (13%)
Total	**Central**	**67 (77.0%)**	**58 (87.9%)**
	Local	**20 (23.0%)**	**8 (12.1%)**

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Table 6.6-7: HbA1c measured 12 months after randomisation – Results (Per-protocol)

Age-group	HbA1c at 12 months	CSII	MDI	Total	Least Squares Mean CSII (95% CI)	Least Squares Mean MDI (95% CI)	Least Squares Mean Difference between treatment groups (CSII-MDI) across all age-groups (95% CI)	P-value
7mths - < 5yrs	Missing	0	0	0	60.2 (56.4,63.9)	59.3 (55.3,63.3)	0.9 (-3.2, 5)	0.67
	N	23	11	34				
	Mean (SD)	62.6 (13.1)	56.2 (11)	60.5 (12.6)				
	Median (IQR)	63 (54, 71)	56 (48, 68)	60.5 (52, 70)				
	(Min, Max)	(40, 88)	(36, 70)	(36, 88)				
5yrs - <12yrs	Missing	0	0	0				
	N	41	32	73				
	Mean (SD)	57.9 (11.8)	59.7 (10.8)	58.7 (11.3)				
	Median (IQR)	57 (50, 63)	61 (50.5, 65)	58 (50, 65)				
	(Min, Max)	(33, 90)	(43, 83)	(33, 90)				
12yrs - <16yrs	Missing	0	0	0				
	N	23	23	46				
	Mean (SD)	57.6 (14.2)	57.8 (16.8)	57.7 (15.4)				
	Median (IQR)	58 (43, 67)	57 (45, 73)	57.5 (44, 67)				
	(Min, Max)	(35, 83)	(32, 94)	(32, 94)				
Overall	**Missing**	**0**	**0**	**0**				
	N	**87**	**66**	**153**				
	Mean (SD)	**59 (12.8)**	**58.4 (13.1)**	**58.8 (12.9)**				
	Median (IQR)	**58 (50, 67)**	**57.5 (47, 67)**	**58 (48, 67)**				
	(Min, Max)	**(33, 90)**	**(32, 94)**	**(32, 94)**				

Note: Lower mmol/mol indicates better glycaemic control.

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Table 6.6-8: Baseline characteristics of children that were randomised and have a primary outcome measurement (Per-protocol)

	CSII	MDI	Total
Age at randomisation (years)			
Missing	0	0	0
N	87	66	153
Mean (SD)	8.6 (4.2)	9.7 (4.2)	9.1 (4.2)
Median (IQR)	9.1 (4.7, 12.2)	10.1 (7.1, 13.7)	9.3 (5.7, 12.5)
(Min, Max)	(0.8, 16)	(0.9, 15.3)	(0.8, 16)
Age cat (strata cat)			
Missing	0	0	0
N	87	66	153
7mths – <5 yrs	23 (26.4%)	11 (16.7%)	34 (22.2%)
5 – <12 yrs	41 (47.1%)	32 (48.5%)	73 (47.7%)
12-15 yrs	23 (26.4%)	23 (34.8%)	46 (30.1%)
Age cat (EudraCT)			
Missing	0	0	0
N	87	66	153
Infants and toddlers	6 (6.9%)	3 (4.5%)	9 (5.9%)
Children	58 (66.7%)	40 (60.6%)	98 (64.1%)
Adolescents	23 (26.4%)	23 (34.8%)	46 (30.1%)
Gender			
Missing	0	0	0
N	87	66	153
Female	44 (50.6%)	29 (43.9%)	73 (47.7%)
Male	43 (49.4%)	37 (56.1%)	80 (52.3%)
Ethnicity			
Missing	1	1	2
N	86	65	151
Asian or Asian British	0 (0%)	2 (3.1%)	2 (1.3%)
Black or British Black	0 (0%)	3 (4.6%)	3 (2%)
British White	78 (90.7%)	51 (78.5%)	129 (85.4%)
Indian	2 (2.3%)	1 (1.5%)	3 (2%)
Mixed	3 (3.5%)	5 (7.7%)	8 (5.3%)
Not stated	0 (0%)	0 (0%)	1 (0.7%)
Other	0 (0%)	2 (3.1%)	2 (1.3%)
Other White	2 (2.3%)	1 (1.5%)	3 (2%)
Pakistani	1 (1.2%)	0 (0%)	1 (0.7%)
Deprivation score (continuous)			
Missing	5	4	9
N	82	62	144
Mean (SD)	21.7 (18.9)	21 (16.8)	21.4 (18)
Median (IQR)	13.7 (8.4, 31.8)	15.1 (8.4, 30.9)	14.4 (8.4, 31.4)
(Min, Max)	(2.1, 67.9)	(1.6, 73.9)	(1.6, 73.9)

	CSII	MDI	Total
Deprivation score (quintile categories)			
Missing	5	4	9
N	82	62	144
1 (<=8.49)	22 (26.8%)	16 (25.8%)	38 (26.4%)
2 (8.5 – 13.79)	19 (23.2%)	14 (22.6%)	33 (22.9%)
3 (13.8 – 21.35)	12 (14.6%)	11 (17.7%)	23 (16%)
4 (21.36 – 34.17)	10 (12.2%)	7 (11.3%)	17 (11.8%)
5 (>=34.18)	19 (23.2%)	14 (22.6%)	33 (22.9%)

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Table 6.6-9: HbA1c measured 12 months after randomisation – Measurement of local lab HbA1c at 12 months

Age strata	Local lab HbA1c reason (Verbatim)	CSII	MDI
<5 years	HbA1c measured	33 (100%)	31 (96.9%)
5-11 years	HbA1c measured	69 (97.2%)	70 (92.1%)
	additional visit Hba1c analyser not available	-	1 (1.3%)
	home visit	-	1 (1.3%)
	no clinic runnning was unable to undertake HbA1c locally as DCA advantage was not available	1 (1.4%)	-
12+ years	HbA1c measured	39 (97.5%)	36 (87.8%)
	No reason provided	-	1 (2.4%)
	insufficient sample	-	1 (2.4%)
	non clinic visit	1 (2.5%)	-
	not a routine clinic visit HbA1c analyser unavailable	-	1 (2.4%)
Total	HbA1c measured	141 (97.9%)	137 (91.9%)
	No reason provided	-	1 (0.7%)
	additional visit Hba1c analyser not available	-	1 (0.7%)
	home visit	-	1 (0.7%)
	insufficient sample	-	1 (0.7%)
	no clinic runnning was unable to undertake HbA1c locally as DCA advantage was not available	1 (0.7%)	-
	non clinic visit	1 (0.7%)	-
	not a routine clinic visit HbA1c analyser unavailable	-	1 (0.7%)

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Table 6.6-10: HbA1c measured 12 months after randomisation – Measurement of central lab HbA1c at 12 months

Age strata	Central lab HbA1c reason (Verbatim)	CSII	MDI
<5 years	HbA1c measured	23 (69.7%)	26 (81.3%)
	Quantity not sufficient	5 (15.2%)	4 (12.5%)
	no record of log at site	1 (3%)	-
	no sample recieved at labs	-	1 (3.1%)
	participant did not wish to do this	1 (3%)	-
	prior to Version 4 of protocol being received at site	2 (6.1%)	-
	sample not taken unable to obtain blood 2 attempts made on 2 separate days	1 (3%)	-
5-11 years	HbA1c measured	59 (83.1%)	59 (77.6%)
	None returned from lab	1 (1.4%)	-
	Quantity not sufficient	5 (7%)	8 (10.5%)
	Test not performed	-	1 (1.3%)
	bloods not taken	1 (1.4%)	-
	no sample record	-	1 (1.3%)
	no staff available- home visit	1 (1.4%)	-
	prior to Version 4 of protocol being received at site	3 (4.2%)	3 (3.9%)
12+ years	HbA1c measured	32 (80%)	33 (80.5%)
	DNA'd appointment only minimal data available	-	1 (2.4%)
	DNA'd multiple appointments	-	1 (2.4%)
	Quantity not sufficient	4 (10%)	3 (7.3%)
	prior to Version 4 of protocol being received at site	4 (10%)	1 (2.4%)
Total	HbA1c measured	114 (79.2%)	118 (79.2%)
	None returned from lab	1 (0.7%)	-
	Quantity not sufficient	14 (9.7%)	15 (10.1%)
	Test not performed	-	1 (0.7%)
	bloods not taken	1 (0.7%)	2 (1.4%)
	no record of log at site	1 (0.7%)	-
	no sample recieved at labs	-	1 (0.7%)
	no sample record	-	1 (0.7%)
	no staff available- home visit	1 (0.7%)	-
	participant did not wish to do this	1 (0.7%)	-
	prior to Version 4 of protocol being received at site	9 (6.3%)	4 (2.7%)
	sample not taken unable to obtain blood 2 attempts made on 2 separate days	1 (0.7%)	-

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6.6.2 Secondary outcome 1: Percentage of participants in each group with 12-month $HbA1_c$ < 48 mmol/mol

Table 6.6-11: Percentage of participants in each group with 12-month HbA1c < 48 mmol/mol – Completeness of data (ITT)

Analysis status	Reason	CSII	MDI	Total
Included	Included	143 (99.3%)	142 (95.3%)	285 (97.3%)
Excluded	No local reason=(home visit); No central reason=(Quantity not sufficient)	0 (0%)	1 (0.7%)	1 (0.3%)
	No local reason=(home visit, see below); No central reason=(no sample received at labs)	0 (0%)	1 (0.7%)	1 (0.3%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)

Note: This table is exactly the same for the HbA1c < 58.5 analysis.

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Table 6.6-12: Percentage of participants in each group with 12-month HbA1c < 48 mmol/mol – Results (ITT)

	CSII	MDI	Overall	Difference in percentages (CSII-MDI) (95% CI)	Risk ratio (95% CI)	Chi-square *p*-value
HbA1c < 48 mmol/mol at 12 mths FU: n (%)	**143**	**142**	**285**	-5.0% (-14.0%, 3.9%)	0.75 (0.46,1.25)	0.28
No	121 (84.6%)	113 (79.6%)	234 (82.1%)			
Yes	22 (15.4%)	29 (20.4%)	51 (17.9%)			

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Table 6.6-13: Percentage of participants in each group with 12-month HbA1c < 58.5 mmol/mol – Results (ITT)

	CSII	MDI	Overall	Difference in percentages (CSII-MDI) (95% CI)	Risk ratio (95% CI)	Chi-square *p*-value
HbA1c < 58.5 mmol/mol at 12 mths FU: n (%)	**143**	**142**	**285**	-8.8% (-2.9%, 20.4%)	0.84 (0.67,1.06)	0.16
No	77 (53.8%)	64 (45.1%)	141 (49.5%)			
Yes	66 (46.2%)	78 (54.9%)	144 (50.5%)			

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6.6.3 Secondary efficacy outcome 2: Incidence of severe hypoglycaemia

Table 6.6-14: Incidence of severe hypoglycaemia – Results (ITT)

	CSII	MDI	Overall	Relative risk (95% CI)	*p*-value
At least one event of Severe Hypoglycaemia (Yes/No)				3.1 (0.6, 15.1)	0.17
N	144	149	293		
No	138 (95.8%)	147 (98.7%)	285 (97.3%)		
Yes	6* (4.2%)	2* (1.3%)	8 (2.7%)		

WARNING: 50% of the cells have expected counts less than 5. Chi-Square may not be a valid test.
* All incidences of severe hypoglycaemia were in separate patients.

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6.6.4 Secondary efficacy outcome 3: Incidence of diabetic ketoacidosis

Table 6.6-15: Incidence of diabetic ketoacidosis – Results (ITT)

	CSII	MDI	Overall	Relative risk (95% CI)**	*p*-value**
At least one event of Diabetic Ketoacidosis (Yes/No)				5.2 (0.3, 106.8)	0.24
N	144	149	293		
No	142 (98.6%)	149 (100%)	291 (99.3%)		
Yes	2* (1.4%)	0 (0%)	2* (0.7%)		

WARNING: 50% of the cells have expected counts less than 5. Chi-Square may not be a valid test.
* Both incidences of diabetic ketoacidosis were in two separate patients.
** Logit estimator used a correction of 0.5 in every cell of that contained a zero.

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6.6.5 Secondary efficacy outcome 4: Change in BMI SDS

Table 6.6-16: Change in BMI SDS – Completeness of data (ITT)

Time-point	BMI	CSII	MDI	Total
BMI (0m)	N	144	149	293
	Measured	124 (86.1%)	132 (88.6%)	256 (87.4%)
	Missing data	20 (13.9%)	17 (11.4%)	37 (12.6%)
BMI (12m)	N	144	149	293
	Measured	142 (98.6%)	138 (92.6%)	280 (95.6%)
	Missing data	1 (0.7%)	6 (4%)	7 (2.4%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)
BMI (at both 0m and 12m)	N	144	149	293
	Measured	122 (84.7%)	122 (81.9%)	244 (83.3%)
	Missing data	21 (14.6%)	22 (14.8%)	43 (14.7%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)

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Table 6.6-17: Change in BMI SDS – Results (ITT)

Time-point	BMI	CSII	MDI	Total	Mean Difference (95% CI)	P-value
BMI (0m)	N	124	132	256	0.1 (0, 0.3)*	0.13*
	Mean (SD)	0.2 (1.3)	0.1 (1.3)	0.1 (1.3)		
	Median (IQR)	0.2 (-0.7, 0.9)	0.1 (-0.8, 1)	0.2 (-0.8, 1)		
	(Min, Max)	(-2.9, 4.2)	(-4, 3.5)	(-4, 4.2)		
BMI (12m)	N	142	138	280		
	Mean (SD)	0.8 (1.1)	0.7 (1)	0.7 (1.1)		
	Median (IQR)	0.8 (0.1, 1.5)	0.6 (0, 1.4)	0.6 (0, 1.4)		
	(Min, Max)	(-1.8, 4.1)	(-2.7, 3)	(-2.7, 4.1)		
BMI (12m - 0m)	N	122	122	244		
	Mean (SD)	0.6 (0.8)	0.5 (0.8)	0.5 (0.8)		
	Median (IQR)	0.5 (0.1, 1)	0.4 (-0.1, 0.9)	0.5 (0, 0.9)		
	(Min, Max)	(-1.4, 3.4)	(-1.1, 5.3)	(-1.4, 5.3)		

* Primary analysis used (12m BMI SDS – baseline BMI SDS) as the outcome variable with baseline BMI SDS, age strata, treatment and centre (random effect) as covariates. A secondary analysis uses 12m BMI SDS as the outcome with the same covariates. Both analyses give the same treatment difference, 95% confidence interval and p-value.

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6.6.6 Secondary efficacy outcome 5: Height

Table 6.6-18: Height – Completeness of data (ITT)

Time-point	Height	CSII	MDI	Total
Height (0m)	N	144	149	293
	Measured	124 (86.1%)	132 (88.6%)	256 (87.4%)
	Missing data	20 (13.9%)	17 (11.4%)	37 (12.6%)
Height (12m)	N	144	149	293
	Measured	142 (98.6%)	138 (92.6%)	280 (95.6%)
	Missing data	1 (0.7%)	6 (4%)	7 (2.4%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)
Height (at both 0m and 12m)	N	144	149	293
	Measured	122 (84.7%)	122 (81.9%)	244 (83.3%)
	Missing data	21 (14.6%)	22 (14.8%)	43 (14.7%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)

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Table 6.6-19: Height – Results (ITT)

Time-point	Height	CSII	MDI	Total	Mean Difference (95% CI)	P-value
Height (0m)	N	124	132	256	-0.1 (-0.2, 0)*	0.10*
	Mean (SD)	0.3 (1.1)	0.3 (1)	0.3 (1)		
	Median (IQR)	0.1 (-0.4, 1.1)	0.4 (-0.3, 1.1)	0.3 (-0.3, 1.1)		
	(Min, Max)	(-2.3, 3.3)	(-2.9, 2.4)	(-2.9, 3.3)		
Height (12m)	N	142	138	280		
	Mean (SD)	0.2 (1.1)	0.3 (1)	0.3 (1)		
	Median (IQR)	0.1 (-0.6, 1)	0.3 (-0.3, 1)	0.2 (-0.5, 1)		
	(Min, Max)	(-2.1, 3.5)	(-2.7, 2.3)	(-2.7, 3.5)		
Height (12m - 0m)	N	122	122	244		
	Mean (SD)	-0.1 (0.5)	0 (0.4)	0 (0.4)		
	Median (IQR)	0 (-0.2, 0.2)	0 (-0.2, 0.2)	0 (-0.2, 0.2)		
	(Min, Max)	(-2.8, 0.7)	(-1.7, 1.6)	(-2.8, 1.6)		

* Primary analysis used (12m HEIGHT SDS – baseline HEIGHT SDS) as the outcome variable with baseline HEIGHT SDS, age strata, treatment and centre (random effect) as covariates. A secondary analysis uses 12m HEIGHT SDS as the outcome with the same covariates. Both analyses give the same treatment difference, 95% confidence interval and p-value.

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6.6.7 Secondary efficacy outcome 6: Insulin requirements

Table 6.6-20: Insulin requirements – Completeness of data (ITT)

Analysis status	Reason	CSII	MDI	Total
Included	Included	87 (60.4%)	64 (43%)	151 (51.5%)
Excluded	No dose data	56 (38.9%)	76 (51%)	132 (45.1%)
	No dose data and weight not recorded	0 (0%)	2 (1.3%)	2 (0.7%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)
	Weight not recorded	0 (0%)	2 (1.3%)	2 (0.7%)

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Table 6.6-21: Insulin requirements – Results (ITT)

strata	Insulin requirements (Units/kg/day)	CSII	MDI	Total	Least Squares Mean Difference between treatment groups (CSII-MDI) across all age-groups	p-value
7mths - < 5yrs	Missing	0	0	0	0.1 (0, 0.2)	0.01
	N	24	13	37		
	Mean (SD)	0.7 (0.2)	0.7 (0.1)	0.7 (0.2)		
	Median (IQR)	0.8 (0.6, 0.8)	0.6 (0.6, 0.7)	0.7 (0.6, 0.8)		
	(Min, Max)	(0.3, 1.2)	(0.4, 0.9)	(0.3, 1.2)		
5yrs - <12yrs	Missing	0	0	0		
	N	45	38	83		
	Mean (SD)	0.6 (0.2)	0.6 (0.3)	0.6 (0.3)		
	Median (IQR)	0.6 (0.5, 0.8)	0.6 (0.4, 0.7)	0.6 (0.4, 0.8)		
	(Min, Max)	(0.2, 1.2)	(0, 1.2)	(0, 1.2)		
12yrs - <16yrs	Missing	0	0	0		
	N	18	13	31		
	Mean (SD)	0.8 (0.2)	0.5 (0.4)	0.7 (0.3)		
	Median (IQR)	0.8 (0.6, 0.9)	0.7 (0, 0.8)	0.7 (0.5, 0.9)		
	(Min, Max)	(0.4, 1.2)	(0, 0.9)	(0, 1.2)		
Overall	**Missing**	**0**	**0**	**0**		
	N	**87**	**64**	**151**		
	Mean (SD)	**0.7 (0.2)**	**0.6 (0.3)**	**0.6 (0.3)**		
	Median (IQR)	**0.7 (0.5, 0.8)**	**0.6 (0.4, 0.8)**	**0.6 (0.5, 0.8)**		
	(Min, Max)	**(0.2, 1.2)**	**(0, 1.2)**	**(0, 1.2)**		

Note: The Estimated G matrix was not positive definite which indicates that the variance component in the RANDOM statement (site) are estimated to be zero so were removed from the model.

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6.6.8 Secondary efficacy outcome 7: Paediatric Quality of Life (PedsQL)

Table 6.6-22: Paediatric Quality of Life (PedsQL) – Completeness of data (ITT)

Note: 1 CSII patient that DNA 6-month visit provided a completed child PedsQL questionnaire; The parents/carers of 1 CSII patient and 1 MDI patient that DNA their 6-month visit provided a completed parent/carer PedsQL questionnaire

	6 months			12 months		
	CSII	**MDI**	**Total**	**CSII**	**MDI**	**Total**
Child (Diabetes)						
N	144	149	293	144	149	293
Included	100 (69.4%)	108 (72.5%)	208 (71%)	108 (75%)	107 (71.8%)	215 (73.4%)
DNA 6 months	7 (4.9%)	7 (4.7%)	14 (4.8%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	6 (4.2%)	6 (4%)	12 (4.1%)	7 (4.9%)	8 (5.4%)	15 (5.1%)
Only5/11 questions answered	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	1 (0.3%)
Questionnaire section not completed	1 (0.7%)	1 (0.7%)	2 (0.7%)	1 (0.7%)	3 (2%)	4 (1.4%)
Too young for questionnaire	30 (20.8%)	27 (18.1%)	57 (19.5%)	26 (18.1%)	26 (17.4%)	52 (17.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Child (Treatment I)						
N	144	149	293	144	149	293
Included	100 (69.4%)	107 (71.8%)	207 (70.6%)	109 (75.7%)	107 (71.8%)	216 (73.7%)
DNA 6 months	7 (4.9%)	7 (4.7%)	14 (4.8%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	6 (4.2%)	6 (4%)	12 (4.1%)	7 (4.9%)	8 (5.4%)	15 (5.1%)
Questionnaire section not completed	1 (0.7%)	2 (1.3%)	3 (1%)	1 (0.7%)	3 (2%)	4 (1.4%)
Too young for questionnaire	30 (20.8%)	27 (18.1%)	57 (19.5%)	26 (18.1%)	26 (17.4%)	52 (17.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Child (Treatment II)						
N	144	149	293	144	149	293
Included	100 (69.4%)	107 (71.8%)	207 (70.6%)	108 (75%)	107 (71.8%)	215 (73.4%)
DNA 6 months	7 (4.9%)	7 (4.7%)	14 (4.8%)	0 (0%)	0 (0%)	0 (0%)

	6 months			12 months		
	CSII	**MDI**	**Total**	**CSII**	**MDI**	**Total**
No questionnaire completed	6 (4.2%)	6 (4%)	12 (4.1%)	7 (4.9%)	8 (5.4%)	15 (5.1%)
Only3/7 questions answered	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	1 (0.3%)
Questionnaire section not completed	1 (0.7%)	2 (1.3%)	3 (1%)	1 (0.7%)	3 (2%)	4 (1.4%)
Too young for questionnaire	30 (20.8%)	27 (18.1%)	57 (19.5%)	26 (18.1%)	26 (17.4%)	52 (17.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Child (Worry)						
N	144	149	293	144	149	293
Included	99 (68.8%)	106 (71.1%)	205 (70%)	109 (75.7%)	105 (70.5%)	214 (73%)
DNA 6 months	7 (4.9%)	7 (4.7%)	14 (4.8%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	6 (4.2%)	6 (4%)	12 (4.1%)	7 (4.9%)	8 (5.4%)	15 (5.1%)
Only1/3 questions answered	1 (0.7%)	1 (0.7%)	2 (0.7%)	0 (0%)	0 (0%)	0 (0%)
Questionnaire section not completed	1 (0.7%)	2 (1.3%)	3 (1%)	1 (0.7%)	5 (3.4%)	6 (2%)
Too young for questionnaire	30 (20.8%)	27 (18.1%)	57 (19.5%)	26 (18.1%)	26 (17.4%)	52 (17.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Child (Communication)						
N	144	149	293	144	149	293
Included	98 (68.1%)	106 (71.1%)	204 (69.6%)	106 (73.6%)	105 (70.5%)	211 (72%)
DNA 6 months	7 (4.9%)	7 (4.7%)	14 (4.8%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	6 (4.2%)	6 (4%)	12 (4.1%)	7 (4.9%)	8 (5.4%)	15 (5.1%)
Only1/3 questions answered	1 (0.7%)	0 (0%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Questionnaire section not completed	2 (1.4%)	3 (2%)	5 (1.7%)	4 (2.8%)	5 (3.4%)	9 (3.1%)
Too young for questionnaire	30 (20.8%)	27 (18.1%)	57 (19.5%)	26 (18.1%)	26 (17.4%)	52 (17.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Child (Overall)						
N	144	149	293	144	149	293

	6 months			12 months		
	CSII	**MDI**	**Total**	**CSII**	**MDI**	**Total**
Included	98 (68.1%)	104 (69.8%)	202 (68.9%)	104 (72.2%)	104 (69.8%)	208 (71%)
1/5 incomplete sections	1 (0.7%)	3 (2%)	4 (1.4%)	5 (3.5%)	2 (1.3%)	7 (2.4%)
2/5 incomplete sections	1 (0.7%)	0 (0%)	1 (0.3%)	0 (0%)	1 (0.7%)	1 (0.3%)
3/5 incomplete sections	0 (0%)	1 (0.7%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
DNA 6 months	7 (4.9%)	7 (4.7%)	14 (4.8%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	6 (4.2%)	6 (4%)	12 (4.1%)	7 (4.9%)	8 (5.4%)	15 (5.1%)
Questionnaire section not completed	1 (0.7%)	1 (0.7%)	2 (0.7%)	1 (0.7%)	3 (2%)	4 (1.4%)
Too young for questionnaire	30 (20.8%)	27 (18.1%)	57 (19.5%)	26 (18.1%)	26 (17.4%)	52 (17.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Parent (Diabetes)						
N	144	149	293	144	149	293
Included	127 (88.2%)	128 (85.9%)	255 (87%)	132 (91.7%)	125 (83.9%)	257 (87.7%)
DNA 6 months	7 (4.9%)	6 (4%)	13 (4.4%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	10 (6.9%)	14 (9.4%)	24 (8.2%)	11 (7.6%)	17 (11.4%)	28 (9.6%)
Questionnaire section not completed	0 (0%)	1 (0.7%)	1 (0.3%)	0 (0%)	2 (1.3%)	2 (0.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Parent (Treatment I)						
N	144	149	293	144	149	293
Included	127 (88.2%)	127 (85.2%)	254 (86.7%)	131 (91%)	125 (83.9%)	256 (87.4%)
DNA 6 months	7 (4.9%)	6 (4%)	13 (4.4%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	10 (6.9%)	14 (9.4%)	24 (8.2%)	11 (7.6%)	17 (11.4%)	28 (9.6%)
Only1/4 questions answered	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	1 (0.3%)
Questionnaire section not completed	0 (0%)	2 (1.3%)	2 (0.7%)	0 (0%)	2 (1.3%)	2 (0.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Parent (Treatment II)						

	6 months			12 months		
	CSII	**MDI**	**Total**	**CSII**	**MDI**	**Total**
N	144	149	293	144	149	293
Included	126 (87.5%)	128 (85.9%)	254 (86.7%)	131 (91%)	125 (83.9%)	256 (87.4%)
DNA 6 months	7 (4.9%)	6 (4%)	13 (4.4%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	10 (6.9%)	14 (9.4%)	24 (8.2%)	11 (7.6%)	17 (11.4%)	28 (9.6%)
Only3/7 questions answered	1 (0.7%)	0 (0%)	1 (0.3%)	1 (0.7%)	0 (0%)	1 (0.3%)
Questionnaire section not completed	0 (0%)	1 (0.7%)	1 (0.3%)	0 (0%)	2 (1.3%)	2 (0.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Parent (Worry)						
N	144	149	293	144	149	293
Included	127 (88.2%)	128 (85.9%)	255 (87%)	131 (91%)	125 (83.9%)	256 (87.4%)
DNA 6 months	7 (4.9%)	6 (4%)	13 (4.4%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	10 (6.9%)	14 (9.4%)	24 (8.2%)	11 (7.6%)	17 (11.4%)	28 (9.6%)
Only1/3 questions answered	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	1 (0.3%)
Questionnaire section not completed	0 (0%)	1 (0.7%)	1 (0.3%)	0 (0%)	2 (1.3%)	2 (0.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Parent (Communication)						
N	144	149	293	144	149	293
Included	124 (86.1%)	127 (85.2%)	251 (85.7%)	130 (90.3%)	123 (82.6%)	253 (86.3%)
DNA 6 months	7 (4.9%)	6 (4%)	13 (4.4%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	10 (6.9%)	14 (9.4%)	24 (8.2%)	11 (7.6%)	17 (11.4%)	28 (9.6%)
Questionnaire section not completed	3 (2.1%)	2 (1.3%)	5 (1.7%)	2 (1.4%)	4 (2.7%)	6 (2%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)
Parent (Overall)						
N	144	149	293	144	149	293
Included	124 (86.1%)	125 (83.9%)	249 (85%)	128 (88.9%)	123 (82.6%)	251 (85.7%)

	6 months			12 months		
	CSII	**MDI**	**Total**	**CSII**	**MDI**	**Total**
1/5 incomplete sections	2 (1.4%)	3 (2%)	5 (1.7%)	3 (2.1%)	2 (1.3%)	5 (1.7%)
2/5 incomplete sections	1 (0.7%)	0 (0%)	1 (0.3%)	1 (0.7%)	0 (0%)	1 (0.3%)
4/5 incomplete sections	0 (0%)	1 (0.7%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
DNA 6 months	7 (4.9%)	6 (4%)	13 (4.4%)	0 (0%)	0 (0%)	0 (0%)
No questionnaire completed	10 (6.9%)	14 (9.4%)	24 (8.2%)	11 (7.6%)	17 (11.4%)	28 (9.6%)
Questionnaire section not completed	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.3%)	2 (0.7%)
WD from study prior to 12 months	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	5 (3.4%)	6 (2%)

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Table 6.6-23: Paediatric Quality of Life (PedsQL) – Results summary at 6m and 12m (ITT)

		6 months			12 months		
Questionnaire age-group	**Summary**	**CSII**	**MDI**	**Total**	**CSII**	**MDI**	**Total**
Children 5-7 years old (6 & 12 month follow-up)	Child (Diabetes)						
	N	12	22	34	14	19	33
	Mean (SD)	56.8 (13.4)	61 (10.4)	59.5 (11.5)	66.7 (16.9)	59.6 (16)	62.6 (16.5)
	Median (IQR)	54.5 (50, 63.6)	59.1 (50, 72.7)	56.8 (50, 68.2)	68.2 (63.6, 79.3)	63.6 (50, 72.7)	63.6 (54.5, 72.7)
	(Min, Max)	(31.8, 81.8)	(40.9, 77.3)	(31.8, 81.8)	(27.3, 90.9)	(22.7, 77.3)	(22.7, 90.9)
Children 8-12 years old (6 & 12 month follow-up)	Child (Diabetes)						
	N	59	55	114	57	55	112
	Mean (SD)	63 (16.9)	62.3 (15)	62.7 (15.9)	68.7 (15.8)	63.9 (16.1)	66.4 (16.1)
	Median (IQR)	65.9 (49.6, 77.3)	63.6 (50, 74.4)	63.6 (50, 75)	70.5 (54.5, 79.5)	61.4 (50, 77.3)	65.9 (52.3, 79.5)
	(Min, Max)	(25, 100)	(29.5, 100)	(25, 100)	(36.4, 100)	(37.2, 93.2)	(36.4, 100)
Children 13-16 years old (6 & 12 month follow-	Child (Diabetes)						
	N	29	31	60	37	33	70
	Mean (SD)	68.2 (16.4)	64.3 (15.3)	66.2 (15.8)	62.9 (16.8)	61.6 (17.3)	62.3 (16.9)

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
up)	Median (IQR)	65.9 (56.8, 75)	61.4 (56.8, 72.7)	63.6 (56.8, 73.9)	61.4 (54.5, 71.9)	59.1 (52.3, 72.7)	61.1 (52.3, 72.7)
	(Min, Max)	(40.9, 100)	(40.9, 100)	(40.9, 100)	(27.3, 100)	(29.5, 90.9)	(27.3, 100)
Children 5-7 years old (6 & 12 month follow-up)	Child (Treatment I)						
	N	12	22	34	14	19	33
	Mean (SD)	77.3 (18.3)	79.8 (16.1)	79 (16.7)	81.3 (16.8)	75.7 (22.2)	78 (20)
	Median (IQR)	76.6 (62.5, 93.8)	82.8 (75, 87.5)	78.1 (75, 87.5)	75 (75, 100)	75 (62.5, 87.5)	75 (62.5, 100)
	(Min, Max)	(50, 100)	(37.5, 100)	(37.5, 100)	(50, 100)	(12.5, 100)	(12.5, 100)
Children 8-12 years old (6 & 12 month follow-up)	Child (Treatment I)						
	N	59	54	113	57	55	112
	Mean (SD)	79.3 (17.9)	74.7 (19.6)	77.1 (18.8)	83.7 (15.5)	77.2 (20.5)	80.5 (18.3)
	Median (IQR)	87.5 (68.8, 93.8)	75 (68.8, 87.5)	81.3 (68.8, 93.8)	87.5 (75, 93.8)	81.3 (62.5, 93.8)	81.3 (75, 93.8)
	(Min, Max)	(31.3, 100)	(12.5, 100)	(12.5, 100)	(25, 100)	(18.8, 100)	(18.8, 100)
Children 13-16 years old (6 & 12 month follow-up)	Child (Treatment I)						
	N	29	31	60	38	33	71
	Mean (SD)	79.7 (21.2)	79.5 (14.2)	79.6 (17.8)	76.6 (21.2)	74.8 (15.3)	75.8 (18.6)
	Median (IQR)	87.5 (75, 93.8)	81.3 (75, 87.5)	81.3 (75, 93.8)	81.3 (68.8, 93.8)	75 (62.5, 87.5)	75 (68.8, 87.5)
	(Min, Max)	(6.3, 100)	(43.8, 100)	(6.3, 100)	(25, 100)	(31.3, 100)	(25, 100)
Children 5-7 years old (6 & 12 month follow-up)	Child (Treatment II)						
	N	12	22	34	13	19	32
	Mean (SD)	80.1 (19.3)	83.2 (12.9)	82.1 (15.3)	82.3 (18.1)	79.9 (15.3)	80.9 (16.3)
	Median (IQR)	85.7 (67.9, 95.4)	83.7 (73.5, 92.9)	85.7 (71.4, 92.9)	85.7 (73.5, 100)	78.6 (71.4, 92.9)	80.1 (72.4, 95.4)
	(Min, Max)	(42.9, 100)	(57.1, 100)	(42.9, 100)	(35.7, 100)	(55.1, 100)	(35.7, 100)
Children 8-12 years old (6 & 12 month follow-up)	Child (Treatment II)						
	N	59	54	113	57	55	112
	Mean (SD)	87.9 (11.9)	83.7 (14.5)	85.9 (13.3)	89.6 (11.6)	84.8 (17.6)	87.2 (15)
	Median (IQR)	92.9 (82.1, 96.4)	85.7 (77.6, 96.4)	89.3 (78.6, 96.4)	92.9 (82.1, 100)	92.9 (75, 100)	92.9 (82.1, 100)
	(Min, Max)	(45.9, 100)	(39.3, 100)	(39.3, 100)	(53.1, 100)	(16.3, 100)	(16.3, 100)

Questionnaire age-group	Summary	6 months			12 months		
		CSII	**MDI**	**Total**	**CSII**	**MDI**	**Total**
Children 13-16 years old (6 & 12 month follow-up)	Child (Treatment II)						
	N	29	31	60	38	33	71
	Mean (SD)	90.1 (13.8)	87.2 (10.7)	88.6 (12.3)	84 (16.7)	85.3 (12.4)	84.6 (14.8)
	Median (IQR)	96.4 (87.2, 100)	85.7 (82.1, 96.4)	92.9 (82.1, 98)	91.3 (75, 96.4)	85.7 (78.6, 96.4)	89.3 (75, 96.4)
	(Min, Max)	(50, 100)	(60.7, 100)	(50, 100)	(42.9, 100)	(50, 100)	(42.9, 100)
Children 5-7 years old (6 & 12 month follow-up)	Child (Worry)						
	N	11	21	32	14	19	33
	Mean (SD)	74.2 (26.2)	77.8 (24.9)	76.6 (25)	77.4 (31.1)	68.4 (28.8)	72.2 (29.7)
	Median (IQR)	66.7 (66.7, 100)	83.3 (66.7, 100)	83.3 (66.7, 100)	100 (50, 100)	66.7 (50, 100)	83.3 (50, 100)
	(Min, Max)	(16.7, 100)	(16.7, 100)	(16.7, 100)	(16.7, 100)	(0, 100)	(0, 100)
Children 8-12 years old (6 & 12 month follow-up)	Child (Worry)						
	N	59	54	113	57	53	110
	Mean (SD)	81.2 (16.8)	75.8 (20.7)	78.6 (18.9)	82.5 (17.7)	78 (23.4)	80.3 (20.6)
	Median (IQR)	83.3 (75, 91.7)	79.2 (58.3, 91.7)	83.3 (66.7, 91.7)	83.3 (75, 100)	83.3 (66.7, 100)	83.3 (66.7, 100)
	(Min, Max)	(33.3, 100)	(25, 100)	(25, 100)	(16.7, 100)	(8.3, 100)	(8.3, 100)
Children 13-16 years old (6 & 12 month follow-up)	Child (Worry)						
	N	29	31	60	38	33	71
	Mean (SD)	80.5 (22.1)	77.2 (17.9)	78.8 (19.9)	73 (23.2)	74.5 (23.3)	73.7 (23.1)
	Median (IQR)	83.3 (66.7, 100)	83.3 (66.7, 91.7)	83.3 (66.7, 91.7)	75 (50, 100)	75 (58.3, 100)	75 (50, 100)
	(Min, Max)	(25, 100)	(33.3, 100)	(25, 100)	(33.3, 100)	(25, 100)	(25, 100)
Children 5-7 years old (6 & 12 month follow-up)	Child (Communication)						
	N	11	22	33	14	18	32
	Mean (SD)	56.1 (38.2)	77.3 (23.9)	70.2 (30.5)	57.1 (33.1)	80.6 (25.7)	70.3 (31)
	Median (IQR)	50 (16.7, 100)	83.3 (66.7, 100)	66.7 (50, 100)	58.3 (33.3, 83.3)	83.3 (66.7, 100)	75 (50, 100)
	(Min, Max)	(0, 100)	(33.3, 100)	(0, 100)	(0, 100)	(0, 100)	(0, 100)
Children 8-12 years old (6 &	Child (Communication)						
	N	58	55	113	54	54	108

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
12 month follow-up)	Mean (SD)	82.2 (18.3)	72 (25.3)	77.2 (22.5)	79.7 (23.7)	75.6 (26.6)	77.6 (25.2)
	Median (IQR)	83.3 (75, 100)	75 (58.3, 91.7)	83.3 (66.7, 100)	91.7 (66.7, 100)	83.3 (58.3, 100)	83.3 (58.3, 100)
	(Min, Max)	(16.7, 100)	(0, 100)	(0, 100)	(8.3, 100)	(0, 100)	(0, 100)
Children 13-16 years old (6 & 12 month follow-up)	Child (Communication)						
	N	29	29	58	38	33	71
	Mean (SD)	86.2 (15.5)	81.6 (19.7)	83.9 (17.7)	81.6 (18.1)	76.8 (26.4)	79.3 (22.3)
	Median (IQR)	91.7 (75, 100)	83.3 (75, 100)	87.5 (75, 100)	83.3 (66.7, 100)	83.3 (66.7, 100)	83.3 (66.7, 100)
	(Min, Max)	(50, 100)	(16.7, 100)	(16.7, 100)	(33.3, 100)	(0, 100)	(0, 100)
Children 5-7 years old (6 & 12 month follow-up)	Child (Overall)						
	N	11	21	32	13	18	31
	Mean (SD)	67.3 (15.4)	73 (9)	71 (11.7)	72.6 (15.5)	70 (15.2)	71.1 (15.1)
	Median (IQR)	75 (51.5, 80.4)	70.9 (67.9, 80.4)	71.4 (67, 80.4)	78.6 (60.7, 85.7)	76.4 (60.7, 81.6)	76.8 (60.7, 82.1)
	(Min, Max)	(41.1, 83.4)	(55.4, 87.5)	(41.1, 87.5)	(39.3, 89.3)	(30.4, 85.7)	(30.4, 89.3)
Children 8-12 years old (6 & 12 month follow-up)	Child (Overall)						
	N	58	54	112	54	53	107
	Mean (SD)	75.9 (12.6)	71.8 (13.2)	73.9 (13)	79 (12)	74.4 (14.3)	76.7 (13.3)
	Median (IQR)	79.1 (66.6, 84.8)	71.5 (64.3, 80.4)	75.9 (66.3, 83.6)	81.7 (70.7, 88.4)	76.8 (64.3, 85.7)	77.7 (70.5, 87.8)
	(Min, Max)	(45.5, 94.1)	(40.2, 99.1)	(40.2, 99.1)	(44.6, 100)	(39.8, 96.4)	(39.8, 100)
Children 13-16 years old (6 & 12 month follow-up)	Child (Overall)						
	N	29	29	58	37	33	70
	Mean (SD)	78.6 (13)	75.9 (11.6)	77.2 (12.3)	73.7 (13.8)	72.4 (14.4)	73.1 (14)
	Median (IQR)	79.5 (71.4, 87.6)	75.9 (67, 82.1)	76.9 (69.6, 85.7)	75 (63.4, 84.8)	73.2 (60.7, 79.3)	74.7 (60.7, 84.8)
	(Min, Max)	(43.8, 99.1)	(50, 98.2)	(43.8, 99.1)	(47.3, 95.5)	(35.7, 94.6)	(35.7, 95.5)
Parents / carers 2-4 years old (6 & 12 month follow-up)	Parent (Diabetes)						
	N	25	18	43	22	18	40
	Mean (SD)	62 (16)	58.1 (11.1)	60.4 (14.1)	62.7 (17.1)	56.2 (16.2)	59.8 (16.8)
	Median (IQR)	62 (54.5, 65.9)	58.1 (47.7, 65.9)	61.4 (47.7, 65.9)	59.1 (47.7, 75)	56.8 (43.2, 68.2)	56.8 (46.6, 72.7)

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
	(Min, Max)	(27.3, 97.7)	(38.6, 75)	(27.3, 97.7)	(33.1, 97.7)	(27.3, 81.8)	(27.3, 97.7)
Parents / carers 5-7 years old (6 & 12 month follow-up)	Parent (Diabetes)						
	N	14	23	37	17	18	35
	Mean (SD)	66.2 (12)	61.4 (13.9)	63.2 (13.2)	68.3 (15.4)	60.8 (15.7)	64.5 (15.8)
	Median (IQR)	65.9 (59.1, 77.3)	59.1 (50, 72.7)	61.4 (54.5, 72.7)	65.9 (56.8, 77.3)	61.4 (53.7, 72.7)	65.9 (53.7, 75)
	(Min, Max)	(43.2, 84.1)	(38.6, 90.9)	(38.6, 90.9)	(45.5, 95.5)	(13.6, 81.8)	(13.6, 95.5)
Parents / carers 8-12 years old (6 & 12 month follow-up)	Parent (Diabetes)						
	N	58	58	116	55	55	110
	Mean (SD)	62.9 (14.9)	62.7 (15.3)	62.8 (15)	66.2 (14.6)	60.8 (16.2)	63.5 (15.6)
	Median (IQR)	63.6 (52.3, 75)	61.4 (52.3, 72.7)	61.4 (52.3, 72.7)	65.9 (52.3, 75.2)	61.4 (47.7, 74.4)	63.6 (52.3, 75)
	(Min, Max)	(25, 93.2)	(36.4, 95.5)	(25, 95.5)	(43.2, 100)	(29.5, 97.7)	(29.5, 100)
Parents / carers 13-16 years old (6 & 12 month follow-up)	Parent (Diabetes)						
	N	30	29	59	38	34	72
	Mean (SD)	63.9 (17.4)	60.3 (18.1)	62.1 (17.7)	60.3 (17.7)	61.5 (14)	60.9 (15.9)
	Median (IQR)	58 (52.3, 81.8)	61.4 (50, 72.7)	59.1 (52.1, 75)	59.1 (47.7, 68.2)	61.4 (54.5, 70.5)	61.4 (50, 70.5)
	(Min, Max)	(36.4, 97.7)	(24.8, 100)	(24.8, 100)	(27.3, 100)	(22.7, 90.9)	(22.7, 100)
Parents / carers 2-4 years old (6 & 12 month follow-up)	Parent (Treatment I)						
	N	25	18	43	21	18	39
	Mean (SD)	79.8 (20.5)	69.8 (20.7)	75.6 (20.9)	80.7 (18.9)	73.6 (20.8)	77.4 (19.9)
	Median (IQR)	87.5 (62.5, 100)	68.8 (56.3, 93.8)	75 (56.3, 100)	87.5 (68.8, 93.8)	81.3 (68.8, 87.5)	81.3 (68.8, 87.5)
	(Min, Max)	(37.5, 100)	(31.3, 100)	(31.3, 100)	(31.3, 100)	(18.8, 100)	(18.8, 100)
Parents / carers 5-7 years old (6 & 12 month follow-up)	Parent (Treatment I)						
	N	14	23	37	17	18	35
	Mean (SD)	63.8 (28.4)	69.3 (19.2)	67.2 (22.9)	72.8 (21.5)	69.8 (21.1)	71.3 (21.1)
	Median (IQR)	62.5 (50, 87.5)	68.8 (56.3, 81.3)	68.8 (56.3, 81.3)	81.3 (56.3, 87.5)	71.9 (56.3, 87.5)	75 (56.3, 87.5)
	(Min, Max)	(0, 100)	(31.3, 100)	(0, 100)	(37.5, 100)	(25, 100)	(25, 100)
Parents / carers	Parent (Treatment I)						

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
8-12 years old (6 & 12 month follow-up)	N	58	57	115	55	55	110
	Mean (SD)	71.3 (20.3)	67.9 (20.8)	69.6 (20.5)	69.1 (18.7)	66.9 (19.6)	68 (19.1)
	Median (IQR)	75 (56.3, 87.5)	68.8 (56.3, 87.5)	68.8 (56.3, 87.5)	68.8 (56.3, 81.3)	62.5 (56.3, 81.3)	68.8 (56.3, 81.3)
	(Min, Max)	(25, 100)	(12.5, 100)	(12.5, 100)	(25, 100)	(25, 100)	(25, 100)
Parents / carers 13-16 years old (6 & 12 month follow-up)	Parent (Treatment I)						
	N	30	29	59	38	34	72
	Mean (SD)	65.2 (22.3)	61.3 (18.1)	63.3 (20.3)	67.3 (22.1)	62.3 (21.9)	64.9 (22)
	Median (IQR)	68.8 (43.8, 81.3)	62.5 (50, 75)	62.5 (50, 81.3)	68.8 (50, 81.3)	62.5 (43.8, 81.3)	68.8 (50, 81.3)
	(Min, Max)	(25, 100)	(31.3, 100)	(25, 100)	(25, 100)	(12.5, 100)	(12.5, 100)
Parents / carers 2-4 years old (6 & 12 month follow-up)	Parent (Treatment II)						
	N	25	18	43	22	18	40
	Mean (SD)	85.4 (13.6)	74.2 (16.6)	80.8 (15.7)	88.6 (10.9)	82.7 (14.8)	85.9 (13)
	Median (IQR)	91.8 (82.1, 96.4)	73.2 (61.2, 85.7)	82.1 (69.4, 96.4)	92.3 (85.7, 92.9)	87.8 (75, 93.9)	90.8 (80.4, 93.4)
	(Min, Max)	(49, 100)	(40.8, 100)	(40.8, 100)	(59.7, 100)	(45.9, 100)	(45.9, 100)
Parents / carers 5-7 years old (6 & 12 month follow-up)	Parent (Treatment II)						
	N	14	23	37	16	18	34
	Mean (SD)	84.2 (14.4)	82.8 (9.8)	83.3 (11.6)	84.8 (14.3)	77.6 (15.3)	81 (15.1)
	Median (IQR)	91.3 (75, 96.4)	82.1 (75, 92.9)	85.7 (75, 93.9)	85.7 (70.2, 100)	76.8 (64.3, 92.9)	82.1 (65.3, 96.4)
	(Min, Max)	(57.1, 98)	(64.3, 100)	(57.1, 100)	(64.3, 100)	(50, 98)	(50, 100)
Parents / carers 8-12 years old (6 & 12 month follow-up)	Parent (Treatment II)						
	N	58	58	116	55	55	110
	Mean (SD)	86.4 (12.7)	80.9 (15.3)	83.7 (14.3)	86.8 (13.5)	81.1 (16.6)	83.9 (15.3)
	Median (IQR)	87.2 (77.6, 98)	82.1 (71.4, 92.9)	85.7 (73.5, 96.4)	89.3 (81.6, 100)	85.7 (67.9, 92.9)	89.3 (75, 96.4)
	(Min, Max)	(50, 100)	(39.3, 100)	(39.3, 100)	(44.9, 100)	(16.3, 100)	(16.3, 100)
Parents / carers 13-16 years old (6 & 12 month	Parent (Treatment II)						
	N	29	29	58	38	34	72
	Mean (SD)	84.6 (15.1)	79.4 (15)	82 (15.1)	80.7 (16.4)	77.7 (19.6)	79.3 (17.9)

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
follow-up)	Median (IQR)	85.7 (77.6, 98)	82.1 (64.3, 92.9)	85.7 (73.5, 93.9)	81.9 (64.3, 96.4)	78.6 (67.9, 92.9)	81.6 (67.9, 96.4)
	(Min, Max)	(42.9, 100)	(55.1, 100)	(42.9, 100)	(39.3, 100)	(32.1, 100)	(32.1, 100)
Parents / carers 2-4 years old (6 & 12 month follow-up)	Parent (Worry)						
	N	25	18	43	21	18	39
	Mean (SD)	63 (29.5)	45.4 (28.6)	55.6 (30.1)	47.9 (28.1)	48.6 (31.9)	48.2 (29.5)
	Median (IQR)	58.3 (33.3, 91.7)	41.7 (25, 58.3)	50 (33.3, 83.3)	41.7 (33.3, 75)	54.2 (25, 66.7)	50 (25, 75)
	(Min, Max)	(8.3, 100)	(0, 100)	(0, 100)	(0, 100)	(0, 100)	(0, 100)
Parents / carers 5-7 years old (6 & 12 month follow-up)	Parent (Worry)						
	N	14	23	37	17	18	35
	Mean (SD)	61.3 (26.7)	75.4 (22)	70 (24.5)	61.3 (29.3)	67.1 (25.2)	64.3 (27)
	Median (IQR)	58.3 (33.3, 83.3)	83.3 (58.3, 91.7)	75 (50, 91.7)	66.7 (33.3, 83.3)	75 (50, 83.3)	75 (41.7, 83.3)
	(Min, Max)	(25, 100)	(25, 100)	(25, 100)	(16.7, 100)	(0, 100)	(0, 100)
Parents / carers 8-12 years old (6 & 12 month follow-up)	Parent (Worry)						
	N	58	58	116	55	55	110
	Mean (SD)	72.1 (20.1)	64.4 (21.3)	68.2 (21)	68.2 (24.3)	67.7 (25.3)	68 (24.7)
	Median (IQR)	75 (58.3, 83.3)	66.7 (50, 83.3)	66.7 (50, 83.3)	75 (50, 91.7)	66.7 (50, 91.7)	70.8 (50, 91.7)
	(Min, Max)	(25, 100)	(25, 100)	(25, 100)	(8.3, 100)	(0, 100)	(0, 100)
Parents / carers 13-16 years old (6 & 12 month follow-up)	Parent (Worry)						
	N	30	29	59	38	34	72
	Mean (SD)	69.2 (24.4)	65.2 (23.5)	67.2 (23.8)	71.9 (21)	66.9 (23.6)	69.6 (22.3)
	Median (IQR)	75 (50, 91.7)	66.7 (50, 83.3)	66.7 (50, 83.3)	75 (50, 83.3)	75 (50, 83.3)	75 (50, 83.3)
	(Min, Max)	(8.3, 100)	(16.7, 100)	(8.3, 100)	(33.3, 100)	(8.3, 100)	(8.3, 100)
Parents / carers 2-4 years old (6 & 12 month follow-up)	Parent (Communication)						
	N	24	19	43	21	17	38
	Mean (SD)	83.7 (25.2)	74.1 (28.7)	79.5 (26.9)	81.3 (25.7)	70.6 (34)	76.5 (29.8)
	Median (IQR)	100 (75, 100)	75 (58.3, 100)	91.7 (66.7, 100)	91.7 (75, 100)	83.3 (50, 100)	91.7 (50, 100)
	(Min, Max)	(0, 100)	(0, 100)	(0, 100)	(25, 100)	(0, 100)	(0, 100)

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
Parents / carers 5-7 years old (6 & 12 month follow-up)	Parent (Communication)						
	N	13	23	36	17	17	34
	Mean (SD)	82.7 (22.4)	84.1 (22.5)	83.6 (22.1)	72.5 (32.1)	80.9 (18.8)	76.7 (26.3)
	Median (IQR)	100 (66.7, 100)	91.7 (75, 100)	95.8 (75, 100)	83.3 (50, 100)	83.3 (66.7, 100)	83.3 (66.7, 100)
	(Min, Max)	(41.7, 100)	(16.7, 100)	(16.7, 100)	(0, 100)	(41.7, 100)	(0, 100)
Parents / carers 8-12 years old (6 & 12 month follow-up)	Parent (Communication)						
	N	58	57	115	54	55	109
	Mean (SD)	78.7 (22.4)	75.7 (26.2)	77.2 (24.3)	80.1 (22.8)	67.2 (26.3)	73.6 (25.4)
	Median (IQR)	83.3 (66.7, 100)	83.3 (58.3, 100)	83.3 (58.3, 100)	87.5 (75, 100)	75 (50, 91.7)	75 (58.3, 100)
	(Min, Max)	(16.7, 100)	(0, 100)	(0, 100)	(0, 100)	(0, 100)	(0, 100)
Parents / carers 13-16 years old (6 & 12 month follow-up)	Parent (Communication)						
	N	29	28	57	38	34	72
	Mean (SD)	77 (28.9)	67.3 (24.1)	72.2 (26.9)	73.2 (26.1)	72.8 (30.7)	73 (28.2)
	Median (IQR)	83.3 (75, 100)	66.7 (50, 91.7)	83.3 (50, 100)	75 (50, 100)	79.2 (58.3, 100)	75 (58.3, 100)
	(Min, Max)	(0, 100)	(25, 100)	(0, 100)	(0, 100)	(0, 100)	(0, 100)
Parents / carers 2-4 years old (6 & 12 month follow-up)	Parent (Overall)						
	N	24	18	42	20	17	37
	Mean (SD)	72.5 (13)	64 (11.5)	68.9 (12.9)	73 (12.7)	67 (15.7)	70.2 (14.3)
	Median (IQR)	72.8 (62.9, 77.2)	61.8 (55.5, 74.1)	68.8 (57, 76.8)	75 (62.1, 82.1)	70.5 (54.7, 79.5)	73.2 (60.7, 80.4)
	(Min, Max)	(54.5, 98.6)	(46.7, 81.6)	(46.7, 98.6)	(52.4, 99.1)	(40.2, 90.2)	(40.2, 99.1)
Parents / carers 5-7 years old (6 & 12 month follow-up)	Parent (Overall)						
	N	13	23	36	16	17	33
	Mean (SD)	72.5 (12.8)	71.8 (8.6)	72 (10.1)	73.1 (15.8)	71 (9.3)	72 (12.7)
	Median (IQR)	70.5 (63.5, 85.7)	69.6 (65.2, 80.4)	69.8 (65.1, 80.8)	75.6 (60.4, 86.6)	72.3 (64.7, 76)	73.2 (63.4, 81.3)
	(Min, Max)	(51.8, 90.2)	(54.7, 84.4)	(51.8, 90.2)	(45.5, 94.6)	(49.1, 86.6)	(45.5, 94.6)
Parents / carers 8-12 years old	Parent (Overall)						
	N	58	56	114	54	55	109

Questionnaire age-group	Summary	6 months			12 months		
		CSII	MDI	Total	CSII	MDI	Total
(6 & 12 month follow-up)	Mean (SD)	72.7 (12.7)	69.9 (13)	71.3 (12.8)	73.9 (11.9)	68.2 (14.9)	71 (13.8)
	Median (IQR)	73.2 (65.2, 84.2)	68.8 (63.4, 78.8)	70.5 (64.3, 81.5)	74.5 (65.9, 81.3)	67.9 (57.1, 77.7)	70.5 (61.6, 80.4)
	(Min, Max)	(31.3, 94.6)	(34.8, 95.8)	(31.3, 95.8)	(39.5, 100)	(34.2, 99.1)	(34.2, 100)
Parents / carers 13-16 years old (6 & 12 month follow-up)	Parent (Overall)						
	N	29	28	57	38	34	72
	Mean (SD)	71.7 (15.4)	66.7 (16.1)	69.3 (15.8)	69 (14.5)	67.5 (15.7)	68.3 (15)
	Median (IQR)	73.2 (59.8, 84.3)	67.6 (55.6, 74.9)	69.6 (58.9, 80.4)	67.3 (58, 80.7)	67.4 (59.8, 79.5)	67.3 (58.9, 80.1)
	(Min, Max)	(42, 99.1)	(35.1, 98.2)	(35.1, 99.1)	(41.1, 96.4)	(19.6, 91.1)	(19.6, 96.4)

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Table 6.6-24: Paediatric Quality of Life (PedsQL) – Modelling results at 12m (ITT)

Type	Least Squares Mean Difference between treatment groups (CSII-MDI) across all questionnaire age-groups	p-value
Child Self-Report	3.1 (-0.6, 6.8)	0.10
Parent/Carer Proxy*	4.1 (0.6, 7.6)	0.02

* The Estimated G matrix was not positive definite which indicates that the variance component in the RANDOM statement (site) are estimated to be zero so were removed from the model.

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Table 6.6-25: Paediatric Quality of Life (PedsQL) – Mean profile plot inclusion status (ITT)

Note: Only Patients that completed the same questionnaire age-group at both 6m and 12m are included in the mean profile plots

	Mean profile plot inclusion status	6-month questionnaire status	12-month questionnaire status	CSII	MDI	Total
Child	Included	Children 13-16 years old	Children 13-16 years old	27 (18.8%)	25 (16.8%)	52 (17.7%)
		Children 5-7 years old	Children 5-7 years old	8 (5.6%)	14 (9.4%)	22 (7.5%)
		Children 8-12 years old	Children 8-12 years old	46 (31.9%)	45 (30.2%)	91 (31.1%)
	Excluded	1/5 incomplete sections	1/5 incomplete sections	1 (0.7%)	1 (0.7%)	2 (0.7%)
		1/5 incomplete sections	Included	0 (0%)	2 (1.3%)	2 (0.7%)
		2/5 incomplete sections	Included	1 (0.7%)	0 (0%)	1 (0.3%)
		3/5 incomplete sections	Included	0 (0%)	1 (0.7%)	1 (0.3%)
		DNA 6 months	1/5 incomplete sections	1 (0.7%)	0 (0%)	1 (0.3%)
		DNA 6 months	Included	6 (4.2%)	3 (2%)	9 (3.1%)
		DNA 6 months	No questionnaire completed	0 (0%)	2 (1.3%)	2 (0.7%)
		DNA 6 months	WD from study prior to 12 months	0 (0%)	2 (1.3%)	2 (0.7%)
		Included	1/5 incomplete sections	2 (1.4%)	1 (0.7%)	3 (1%)
		Included	2/5 incomplete sections	0 (0%)	1 (0.7%)	1 (0.3%)
		Included	No questionnaire completed	4 (2.8%)	5 (3.4%)	9 (3.1%)
		Included	Questionnaire section not completed	0 (0%)	3 (2%)	3 (1%)
		Included	WD from study prior to 12 months	0 (0%)	3 (2%)	3 (1%)
		No questionnaire completed	Included	3 (2.1%)	5 (3.4%)	8 (2.7%)
		No questionnaire completed	No questionnaire completed	1 (0.7%)	1 (0.7%)	2 (0.7%)
		No questionnaire completed	Questionnaire section not completed	1 (0.7%)	0 (0%)	1 (0.3%)
		No questionnaire completed	WD from study prior to 12 months	1 (0.7%)	0 (0%)	1 (0.3%)
		Questionnaire completed but different age questionnaires at 6m and at 12m	Questionnaire completed but different age questionnaires at 6m and at 12m	11 (7.6%)	7 (4.7%)	18 (6.1%)
		Questionnaire section not completed	Included	1 (0.7%)	1 (0.7%)	2 (0.7%)

	Mean profile plot inclusion status	6-month questionnaire status	12-month questionnaire status	CSII	MDI	Total
		Too young for questionnaire	Now old enough and included	1 (0.7%)	1 (0.7%)	2 (0.7%)
		Too young for questionnaire	Now old enough but: 1/5 incomplete sections	1 (0.7%)	0 (0%)	1 (0.3%)
		Too young for questionnaire	Now old enough but: No questionnaire completed	2 (1.4%)	0 (0%)	2 (0.7%)
		Too young for questionnaire	Too young for questionnaire	26 (18.1%)	26 (17.4%)	52 (17.7%)
Parent / Carer	Included	Parents / carers 13-16 years old (6 & 12 month follow-up)	Parents / carers 13-16 years old (6 & 12 month follow-up)	28 (19.4%)	26 (17.4%)	54 (18.4%)
		Parents / carers 2-4 years old (6 & 12 month follow-up)	Parents / carers 2-4 years old (6 & 12 month follow-up)	18 (12.5%)	13 (8.7%)	31 (10.6%)
		Parents / carers 5-7 years old (6 & 12 month follow-up)	Parents / carers 5-7 years old (6 & 12 month follow-up)	10 (6.9%)	15 (10.1%)	25 (8.5%)
		Parents / carers 8-12 years old (6 & 12 month follow-up)	Parents / carers 8-12 years old (6 & 12 month follow-up)	45 (31.3%)	47 (31.5%)	92 (31.4%)
	Excluded	1/5 incomplete sections	2/5 incomplete sections	1 (0.7%)	0 (0%)	1 (0.3%)
		1/5 incomplete sections	Included	1 (0.7%)	1 (0.7%)	2 (0.7%)
		1/5 incomplete sections	No questionnaire completed	0 (0%)	1 (0.7%)	1 (0.3%)
		1/5 incomplete sections	Questionnaire section not completed	0 (0%)	1 (0.7%)	1 (0.3%)
		2/5 incomplete sections	Included	1 (0.7%)	0 (0%)	1 (0.3%)
		4/5 incomplete sections	No questionnaire completed	0 (0%)	1 (0.7%)	1 (0.3%)
		DNA 6 months	Included	6 (4.2%)	3 (2%)	9 (3.1%)
		DNA 6 months	No questionnaire completed	1 (0.7%)	2 (1.3%)	3 (1%)
		DNA 6 months	WD from study prior to 12 months	0 (0%)	1 (0.7%)	1 (0.3%)
		Included	1/5 incomplete sections	2 (1.4%)	1 (0.7%)	3 (1%)
		Included	No questionnaire completed	8 (5.6%)	10 (6.7%)	18 (6.1%)
		Included	Questionnaire section not completed	0 (0%)	1 (0.7%)	1 (0.3%)
		Included	WD from study prior to 12 months	0 (0%)	4 (2.7%)	4 (1.4%)
		No questionnaire completed	1/5 incomplete sections	1 (0.7%)	1 (0.7%)	2 (0.7%)

	Mean profile plot inclusion status	6-month questionnaire status	12-month questionnaire status	CSII	MDI	Total
		No questionnaire completed	Included	6 (4.2%)	10 (6.7%)	16 (5.5%)
		No questionnaire completed	No questionnaire completed	2 (1.4%)	3 (2%)	5 (1.7%)
		No questionnaire completed	WD from study prior to 12 months	1 (0.7%)	0 (0%)	1 (0.3%)
		Questionnaire completed but different age questionnaires at 6m and at 12m	Questionnaire completed but different age questionnaires at 6m and at 12m	13 (9%)	8 (5.4%)	21 (7.2%)

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Figure 6.6-5: Paediatric Quality of Life (PedsQL) – Child mean profile plots (5-7 years old) (ITT)

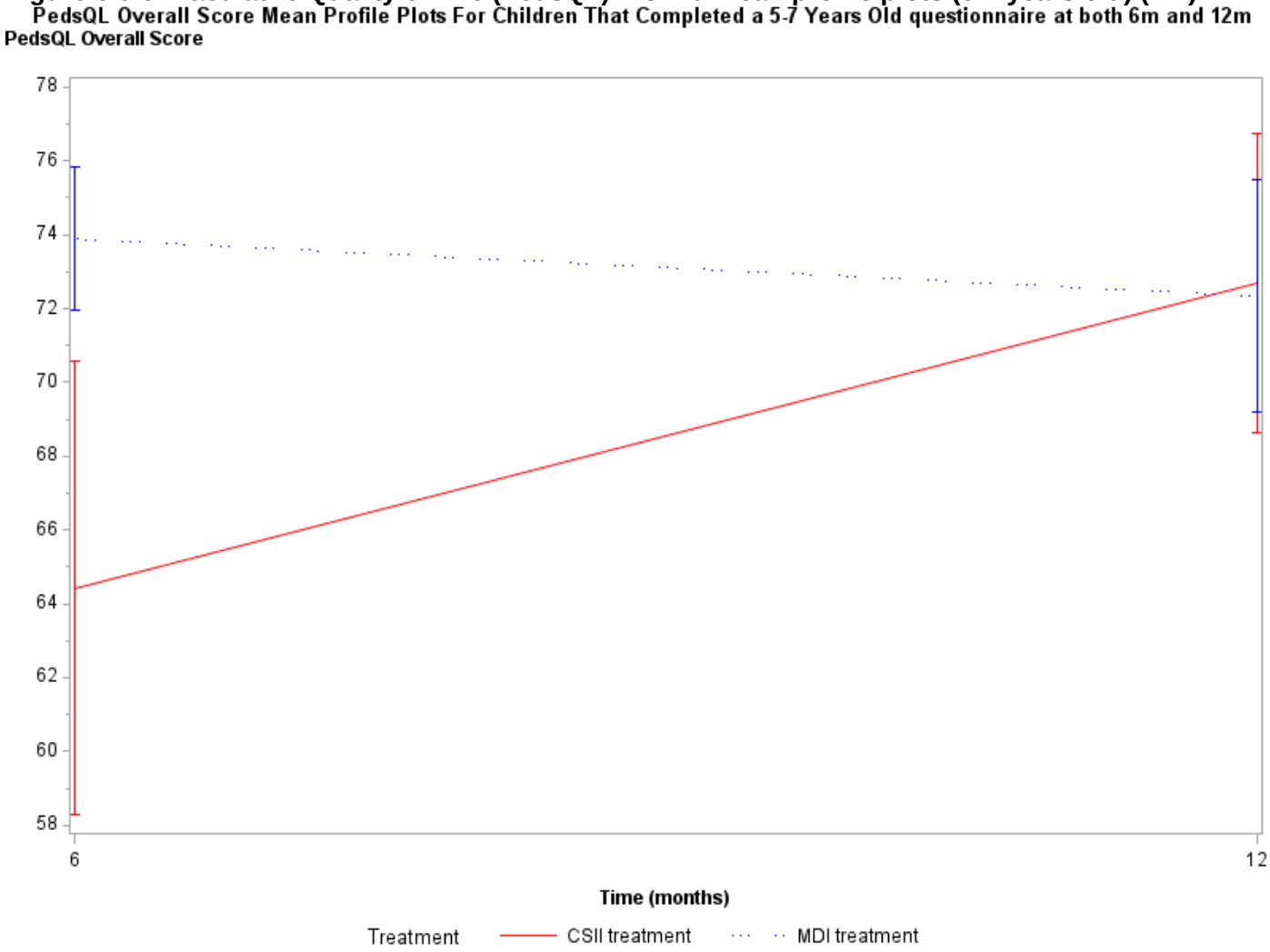

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Figure 6.6-6: Paediatric Quality of Life (PedsQL) – Child mean profile plots (8-12 years old) (ITT)

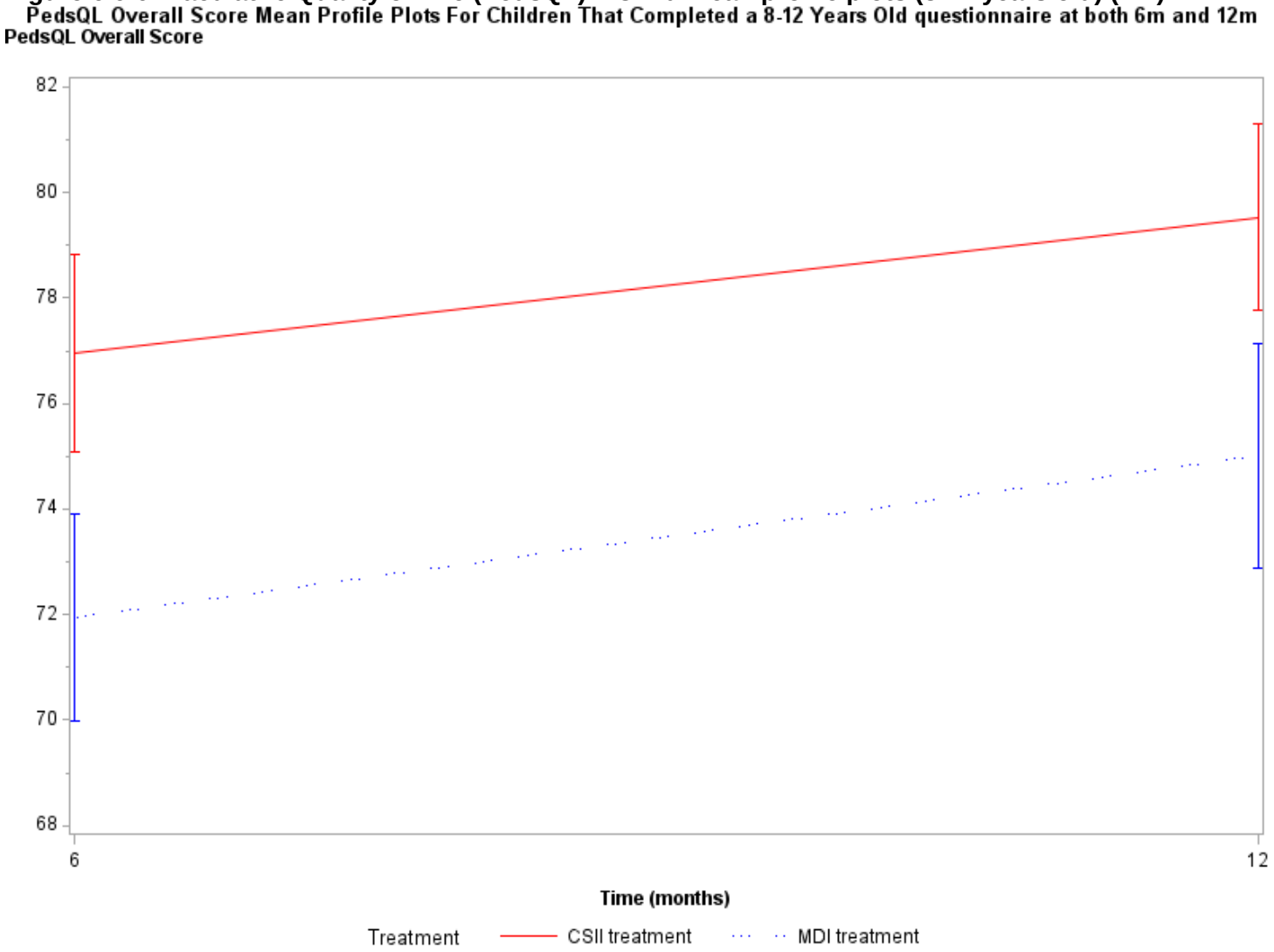

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Figure 6.6-7: Paediatric Quality of Life (PedsQL) – Child mean profile plots (13-16 years old) (ITT)

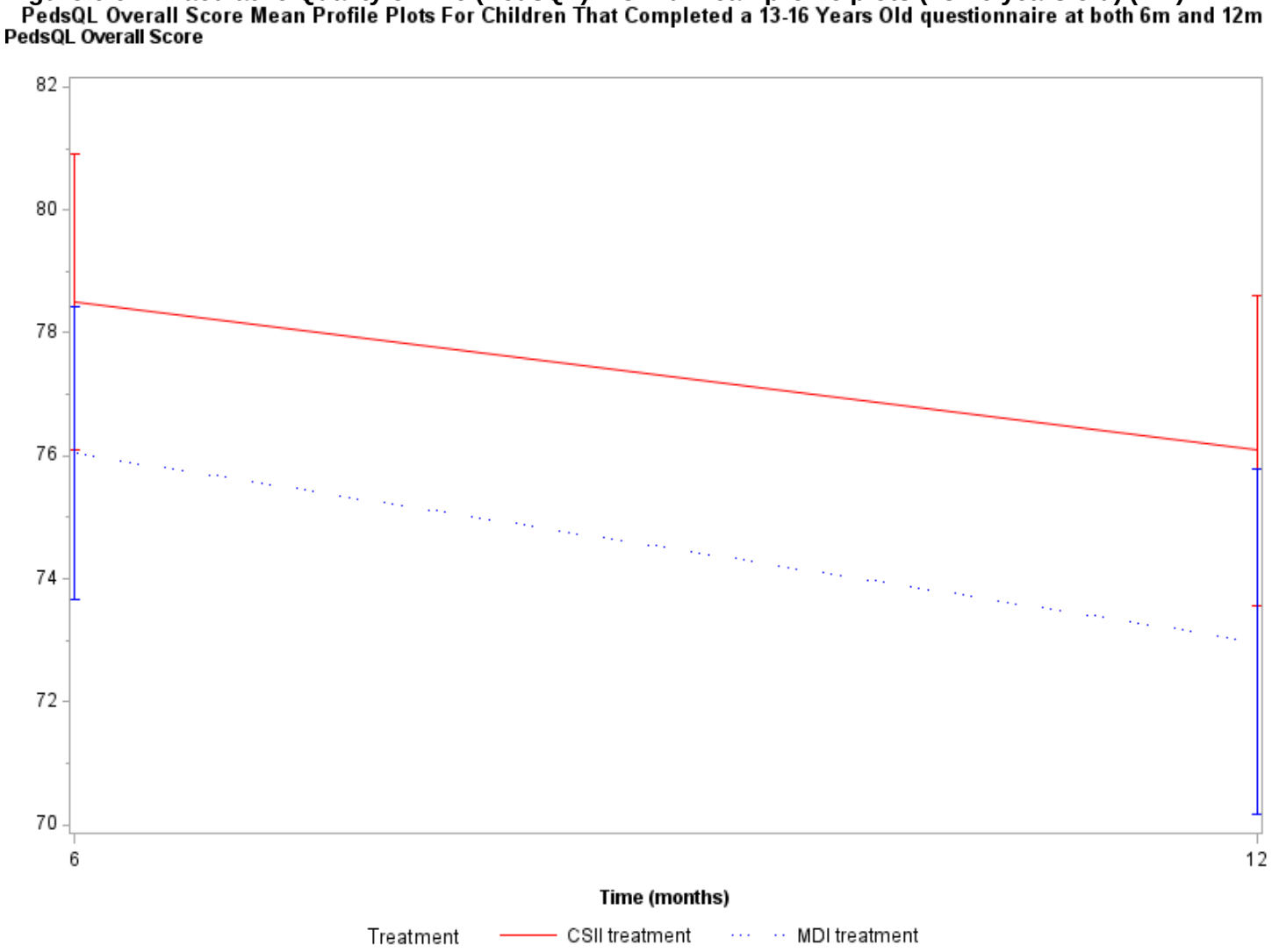

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Figure 6.6-8: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (2-4 years old) (ITT)

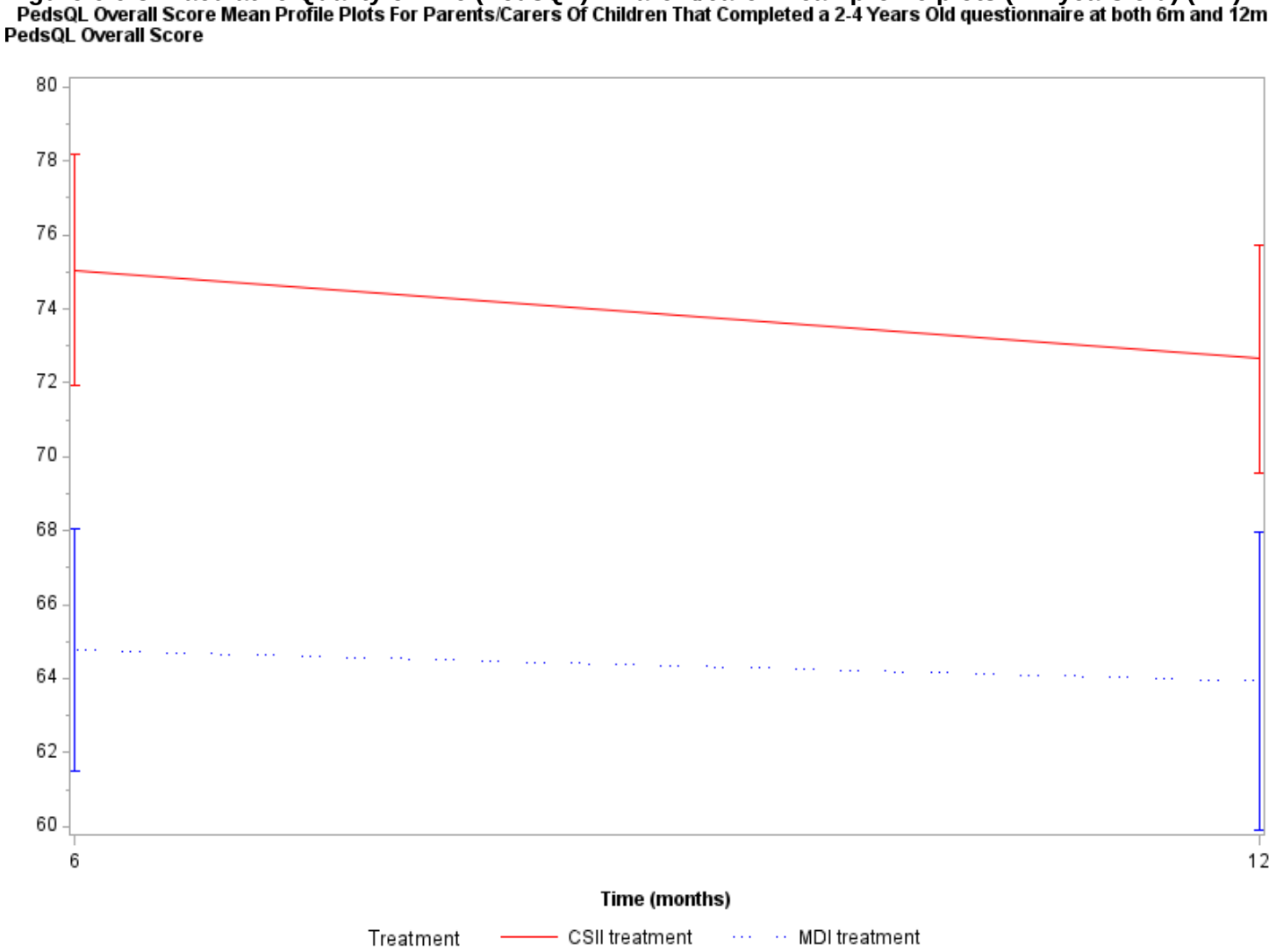

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Figure 6.6-9: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (5-7 years old) (ITT)

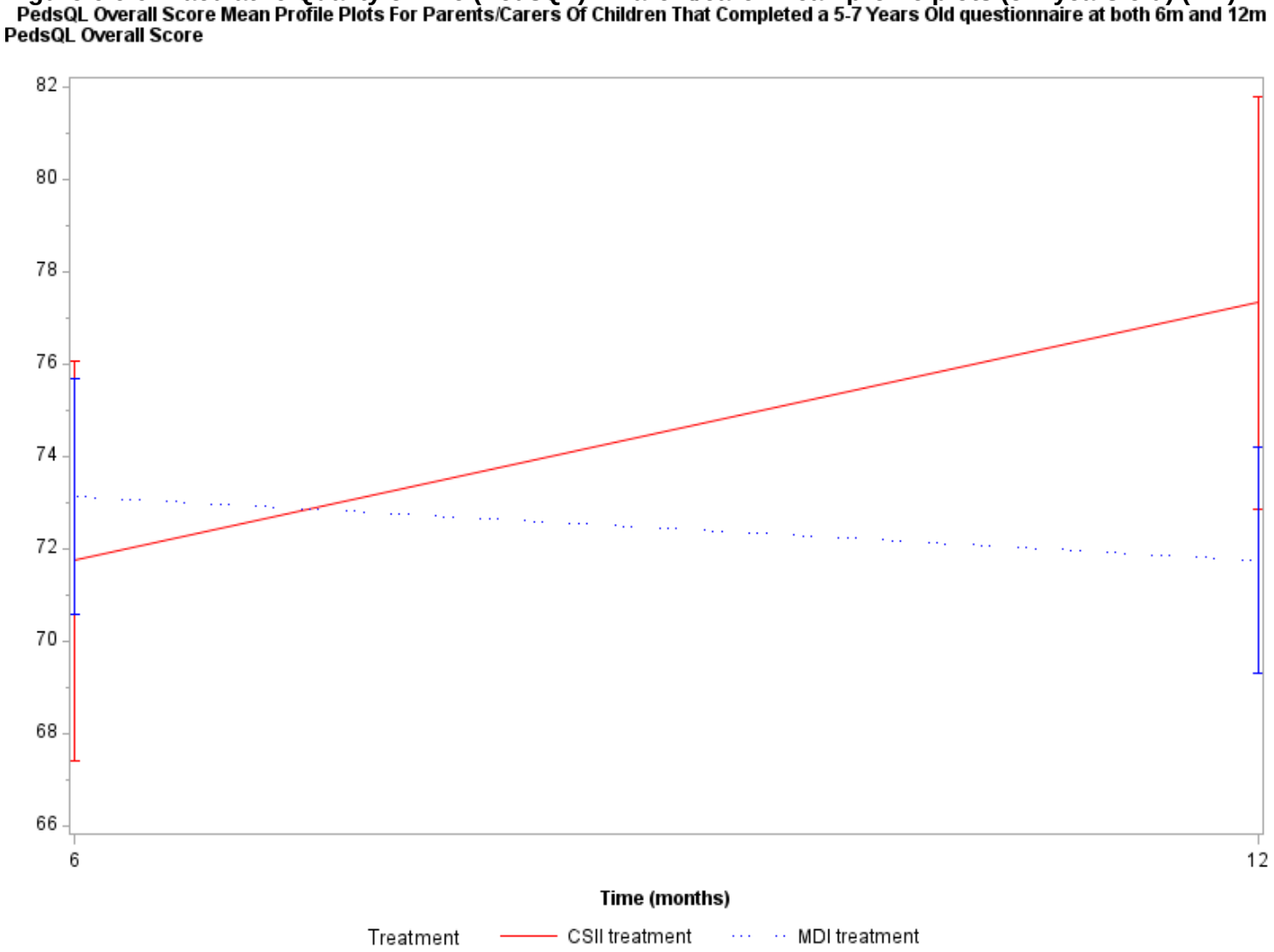

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Figure 6.6-10: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (8-12 years old) (ITT)

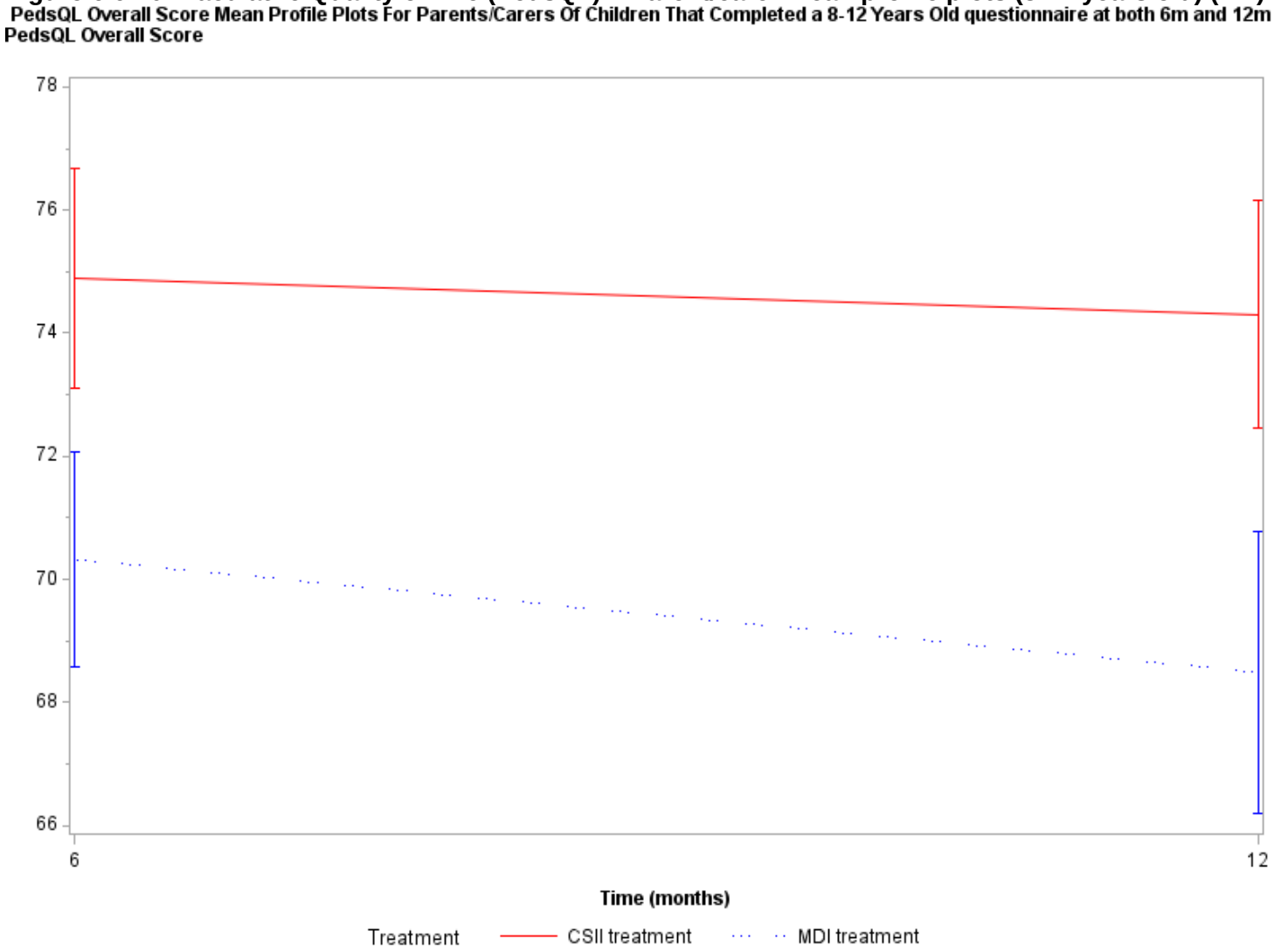

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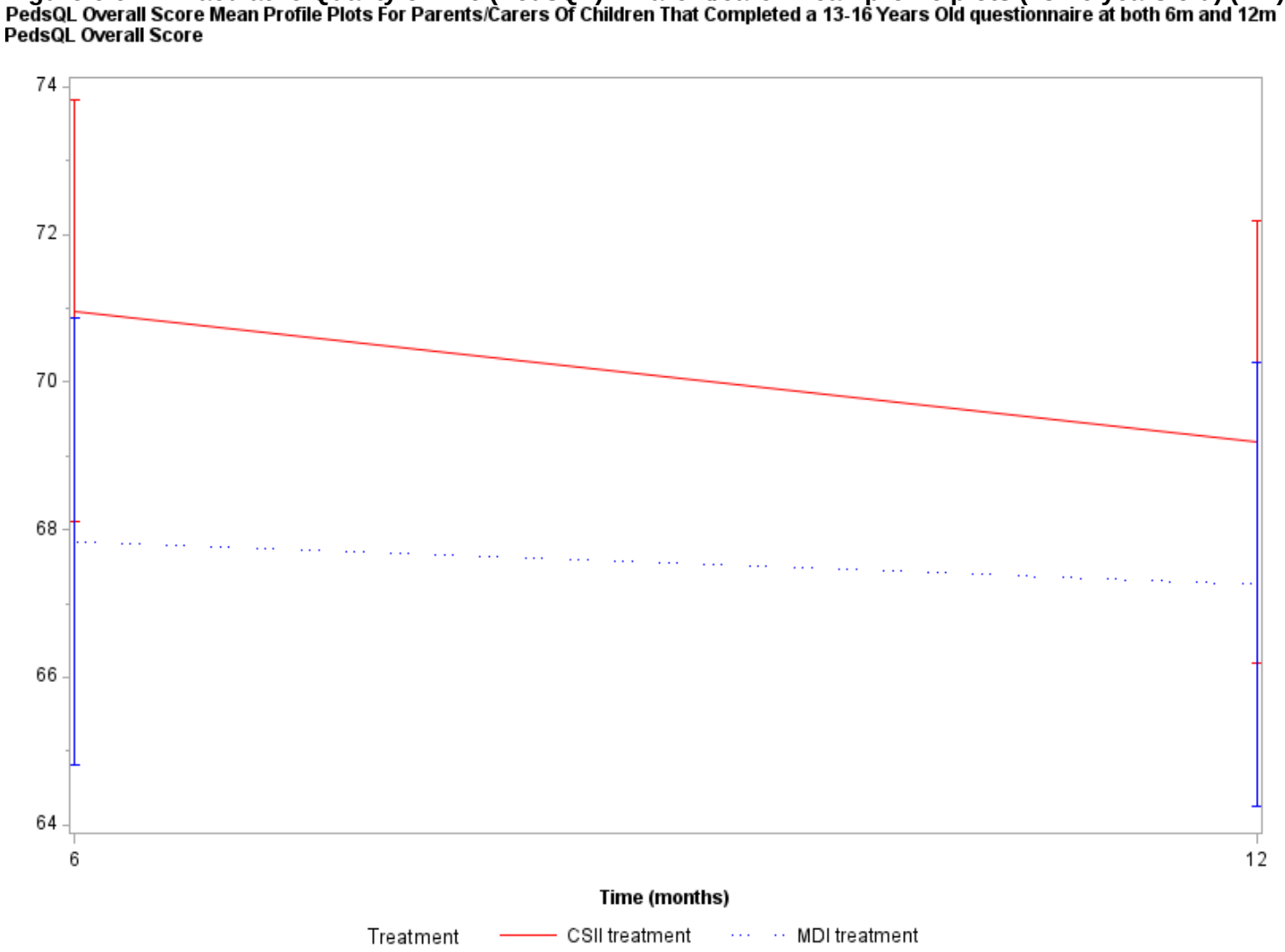
Figure 6.6-11: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (13-16 years old) (ITT)



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6.6.9 Secondary efficacy outcome 8: Cost effectiveness

This analysis is reported separately by Health Economists at Bangor.

6.6.10 Secondary efficacy outcome 9: Partial Remission

Table 6.6-26: Partial Remission – Completeness of data (ITT)

Analysis status	Partial remission at 12 months	CSII	MDI	Total
Included	Included	86 (59.7%)	64 (43%)	150 (51.2%)
Excluded	No HbA1c measurement and no dose data	0 (0%)	2 (1.3%)	2 (0.7%)
	No dose data	57 (39.6%)	75 (50.3%)	132 (45.1%)
	No dose data and weight not recorded	0 (0%)	2 (1.3%)	2 (0.7%)
	WD from study prior to 12 months	1 (0.7%)	5 (3.4%)	6 (2%)
	Weight not recorded	0 (0%)	1 (0.7%)	1 (0.3%)

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Table 6.6-27: Partial Remission – Results summary at 12m (ITT)

	CSII	MDI	Overall	Relative risk (95% CI)	*p*-value
Partial remission at 12 months: n (%)	86	64	150	0.74 (0.45, 1.24)	0.28
No	65 (75.6%)	43 (67.2%)	108 (72.0%)		
Yes	21 (24.4%)	21 (32.8%)	42 (28.0%)		

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Table 6.6-28: Partial Remission – Results summary at 3m, 6m and 9m (ITT)

	CSII	MDI	Overall
Partial remission at 3 months: n (%)	94	91	185
No	32 (34.0%)	34 (37.4%)	66 (35.7%)
Yes	62 (66.0%)	57 (62.6%)	119 (64.3%)
Partial remission at 6 months: n (%)	79	79	158
No	39 (49.4%)	35 (44.3%)	74 (46.8%)
Yes	40 (50.6%)	44 (55.7%)	84 (53.2%)
Partial remission at 9 months: n (%)	92	68	160
No	66 (71.7%)	44 (64.7%)	110 (68.7%)
Yes	26 (28.3%)	24 (35.3%)	50 (31.3%)

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Table 6.6-29: Partial Remission – Summary at each visit (ITT)

	CSII				MDI				Total			
Summary	**03m**	**06m**	**09m**	**12m**	**03m**	**06m**	**09m**	**12m**	**03m**	**06m**	**09m**	**12m**
N	**94**	**79**	**92**	**86**	**91**	**79**	**68**	**64**	**185**	**158**	**160**	**150**
1. Not in partial remission	32 (34%)	30 (38%)	51 (55.4%)	57 (66.3%)	34 (37.4%)	24 (30.4%)	30 (44.1%)	38 (59.4%)	66 (35.7%)	54 (34.2%)	81 (50.6%)	95 (63.3%)
2. Entering partial remission	62 (66%)	4 (5.1%)	0 (0%)	4 (4.7%)	57 (62.6%)	4 (5.1%)	0 (0%)	4 (6.3%)	119 (64.3%)	8 (5.1%)	0 (0%)	8 (5.3%)
3. Remaining in partial remission	0 (0%)	31 (39.2%)	18 (19.6%)	12 (14%)	0 (0%)	34 (43%)	18 (26.5%)	11 (17.2%)	0 (0%)	65 (41.1%)	36 (22.5%)	23 (15.3%)
4. In partial remission (no info from previous visit)	0 (0%)	5 (6.3%)	8 (8.7%)	5 (5.8%)	0 (0%)	6 (7.6%)	6 (8.8%)	6 (9.4%)	0 (0%)	11 (7%)	14 (8.8%)	11 (7.3%)
5. Leaving partial remission	0 (0%)	9 (11.4%)	15 (16.3%)	8 (9.3%)	0 (0%)	11 (13.9%)	14 (20.6%)	5 (7.8%)	0 (0%)	20 (12.7%)	29 (18.1%)	13 (8.7%)

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Table 6.6-30: Partial Remission – Transitions from 6m to 12m (ITT)

	CSII	MDI	Total
Number in PR at 6m	31	31	62
Number still in PR at 12m	18/31 (58.1%)	15/31 (48.4%)	33/62 (53.2%)
Number not in PR at 6m	33	22	55
Number now in PR at 12m	1 (3.0%)	1 (4.6%)	2 (3.6%)

Note: Only patients with a PR Yes/No at both 6m and 12m have been included in the summary.

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Figure 6.6-12: Partial remission – Mean profile plots (<5 years old) (ITT)

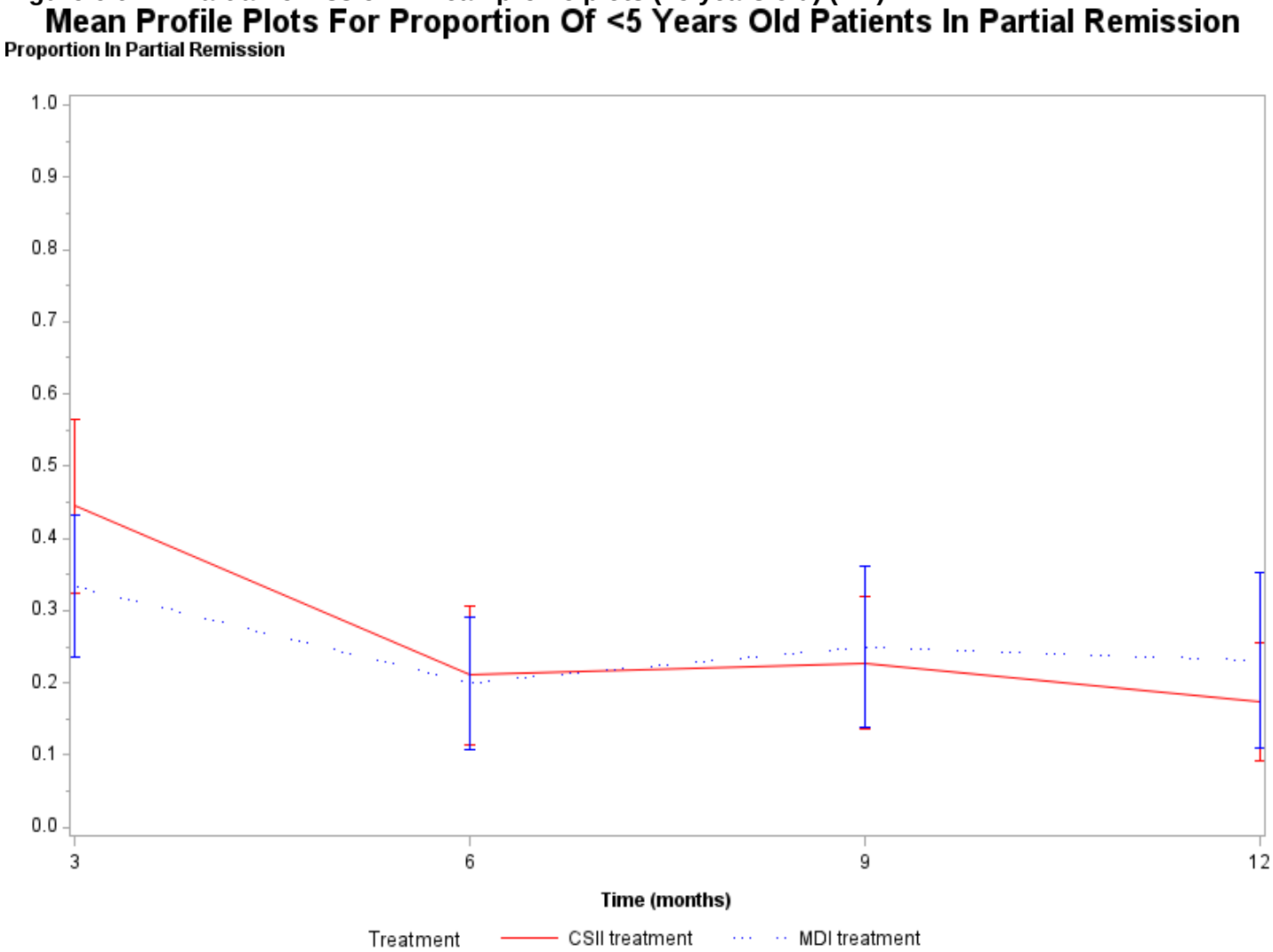

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Figure 6.6-13: Partial remission – Mean profile plots (5-11 years old) (ITT)

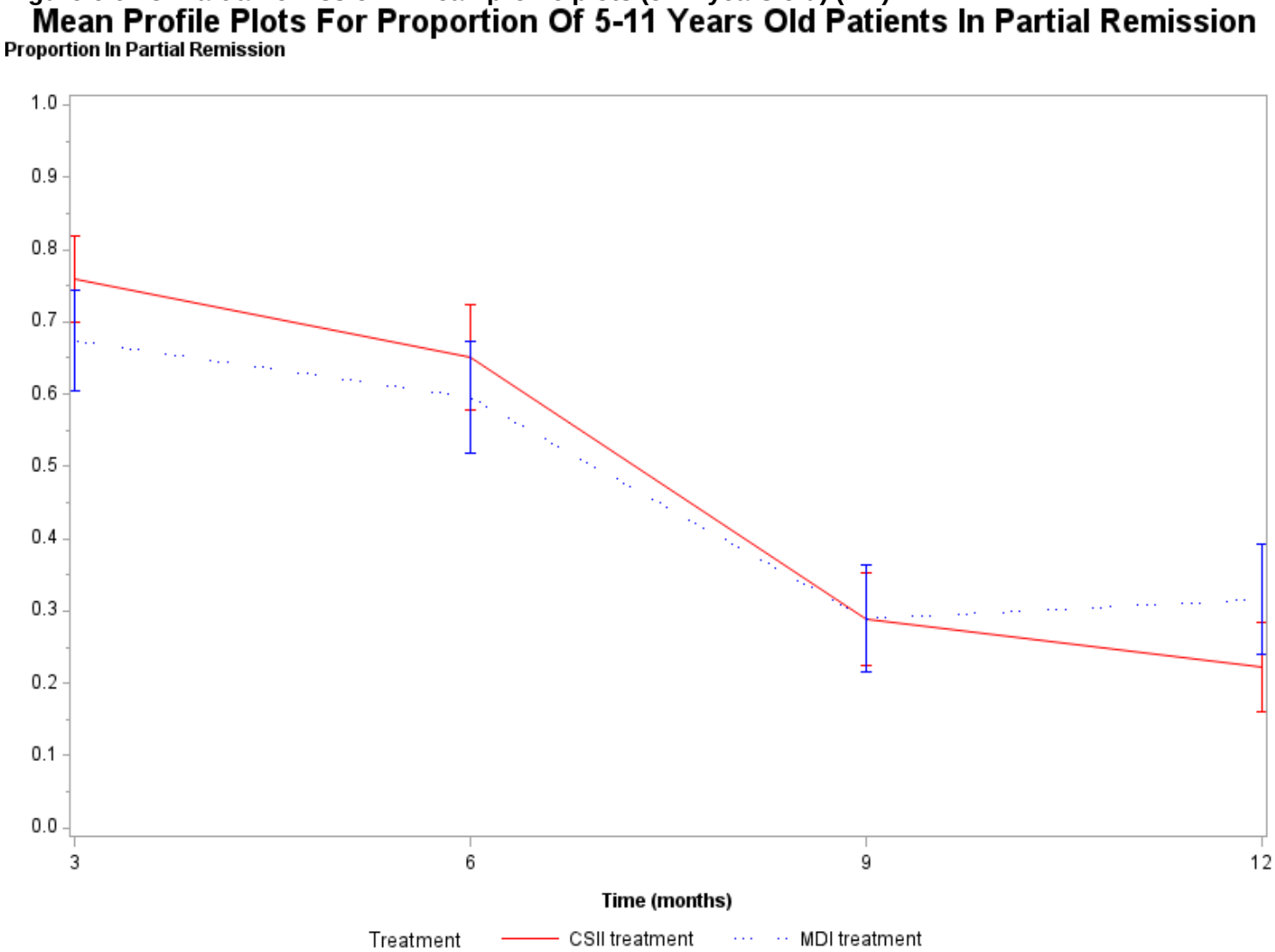

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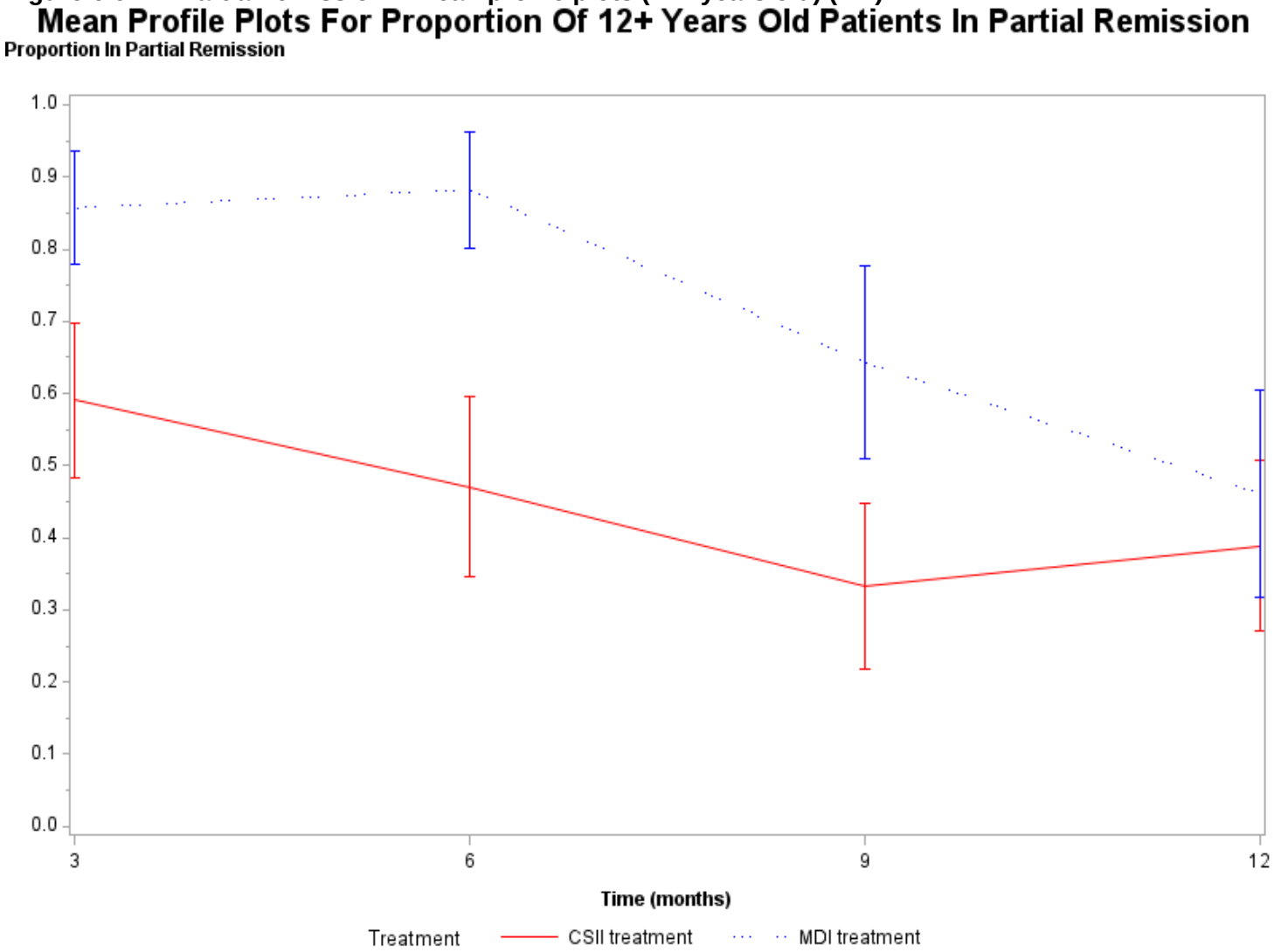
Figure 6.6-14: Partial remission – Mean profile plots (12+ years old) (ITT)



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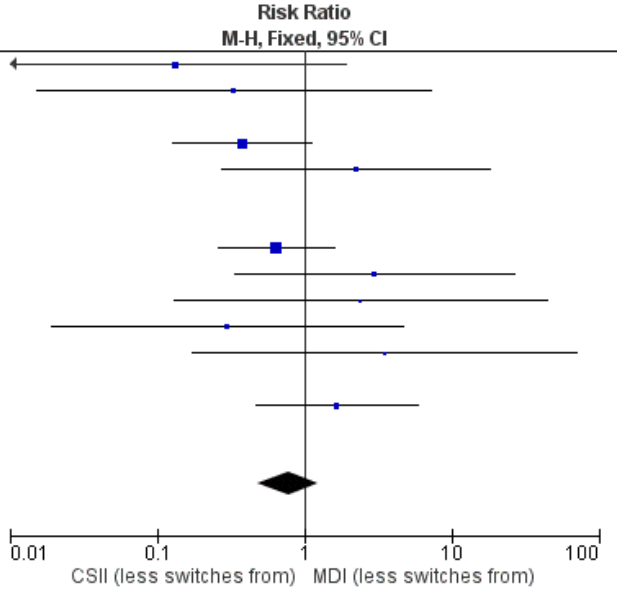
6.7 Additional analyses

6.7.1 Permanent change to insulin delivery method

Figure 6.7-1: Additional Analyses – Permanent change to insulin delivery method split by site – Forest plot (ITT)

Study or Subgroup	CSII (switches to MDI) Events	Total	MDI (Switches to CSII) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
00036 Norfolk and Norwich University Hospitals NHS	0	4	4	5	13.1%	0.13 [0.01, 1.93]
00086 Doncaster Royal Infirmary	0	9	1	9	4.8%	0.33 [0.02, 7.24]
00104 Stafford Hospital	0	0	0	2		Not estimable
00114 Southampton University Hospitals NHS Trust	3	14	9	16	26.8%	0.38 [0.13, 1.14]
00133 Birmingham Childrens Hospital	3	12	1	9	3.7%	2.25 [0.28, 18.22]
00148 Ipswich Hospital	0	3	0	3		Not estimable
00160 Royal Preston Hospital	0	0	0	2		Not estimable
00213 Nottingham University Hospital NHS Trust	6	31	9	30	29.2%	0.65 [0.26, 1.59]
00243 Alder Hey Childrens NHS Foundation Trust	3	26	1	26	3.2%	3.00 [0.33, 26.99]
00248 Sheffield Childrens NHS Foundation Trust	1	4	0	3	1.8%	2.40 [0.13, 44.41]
00326 East Surrey Hospital	0	3	2	5	6.4%	0.30 [0.02, 4.74]
01527 Royal Blackburn Hospital	1	5	0	6	1.5%	3.50 [0.17, 70.94]
04913 Cardiff and Vale University Local Health Boa	0	9	0	10		Not estimable
05042 Oxford Radcliffe Hospitals NHS Trust	5	18	3	18	9.6%	1.67 [0.47, 5.96]
12617 The Newcastle Upon Tyne Hospitals NHS	0	6	0	5		Not estimable
Total (95% CI)		**144**		**149**	**100.0%**	**0.78 [0.48, 1.25]**
Total events	22		30			

Heterogeneity: Chi² = 9.58, df = 9 (P = 0.39); I² = 6%
Test for overall effect: Z = 1.05 (P = 0.30)



Note: There were 53 permanent changes in total (22 randomised to CSII and 31 randomised to MDI). However, one permanent switch of insulin delivery method was from MDI to 'Injections TDS regime' so this has not been included in the meta-analysis as an event.

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Table 6.7-1: Additional Analyses – Permanent change to insulin delivery method – Time point of changes by age strata (ITT) – Post-hoc analysis

	CSII to MDI										MDI to CSII									
	Time point of change										Time point of change									
Strata	**Total Rand**	**0**	**0-3**	**3**	**3-6**	**6**	**6-9**	**9**	**9-12**	**Total Permanent changes**	**Total Rand**	**0**	**0-3**	**3**	**3-6**	**6**	**6-9**	**9**	**9-12**	**Total Permanent changes**
<5 years	**33**	1 (3%)	-	-	-	-	-	-	-	**1 (3%)**	**32**	-	3 (9.4%)	-	4 (12.5%)	-	2 (6.3%)	-	3 (9.4%)	**12 (37.5%)**
5-11 years	**71**	2 (2.8%)	5 (7%)	-	-	-	2 (2.8%)	-	1 (1.4%)	**10 (14.1%)**	**76**	-	1 (1.3%)	-	5 (6.6%)	-	4 (5.3%)	-	4 (5.3%)	**14 (18.4%)**
12+ years	**40**	-	6 (15%)	2 (5%)	-	-	2 (5%)	-	1 (2.5%)	**11 (27.5%)**	**41**	-	1 (2.4%)	-	2 (4.9%)	-	1 (2.4%)	-	-	**4 (9.8%)**
Total	**144**	**3 (2.1%)**	**11 (7.6%)**	**2 (1.4%)**	**-**	**-**	**4 (2.8%)**	**-**	**1 (0.7%)**	**22 (15.3%)**	**149**	**-**	**5 (3.4%)**	**-**	**11 (7.4%)**	**-**	**7 (4.7%)**	**-**	**7 (4.7%)**	**30 (20.1%)**

Note: One patient (5-11 years age strata) changed from MDI to 'Injections TDS regime' at their 9 month visit (not included in the table).

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Table 6.7-2: Additional Analyses – Permanent change to insulin delivery method – Further information line listings (ITT) – Post-hoc analysis

Permanent change from -> to	Age strata	Rand no	DOB	Permanent change date	Timing of change (months)	Age at permanent change (years)	Last HbA1c measurement prior to switch (mmol/mol)	Last HbA1c measurement as the previous or this visit	Last HbA1c measurement visit (months)	Last HbA1c measurement visit date	Days from last HbA1c measurement to permanent change
CSII -> MDI	<5 years	00213102	10/3/2011	9/1/2013	0	1.84	110	This	0m	09/01/2013	0
	5-11 years	00243224	1/8/2008	17/2/2015	0-3	6.55	72	Prev	0m	11/02/2015	6
		05042218	4/4/2004	16/6/2014	0-3	10.2	83	Prev	0m	12/06/2014	4
		00213218	28/7/2004	4/12/2014	6-9	10.35	68	Prev	6m	14/11/2014	20
		05042212	3/5/2003	18/11/2013	0-3	10.55	117	Prev	0m	12/11/2013	6
		00114207	11/6/2003	7/1/2014	0-3	10.58	105	Prev	0m	05/12/2013	33
		05042214	14/3/2003	2/12/2013	0	10.72	114	This	0m	02/12/2013	0
		00133207	26/9/2003	15/7/2014	6-9	10.8	N/A	Prev	6m	DNA appointment	N/A

Permanent change from -> to	Age strata	Rand no	DOB	Permanent change date	Timing of change (months)	Age at permanent change (years)	Last HbA1c measurement prior to switch (mmol/mol)	Last HbA1c measurement as the previous or this visit	Last HbA1c measurement visit (months)	Last HbA1c measurement visit date	Days from last HbA1c measurement to permanent change
		00133209	22/6/2004	17/9/2015	9-12	11.24	58	Prev	9m	09/07/2015	70
		05042207	13/1/2001	28/9/2012	0	11.71	38	This	0m	28/09/2012	0
		00243219	30/5/2002	12/5/2014	0-3	11.95	98	Prev	0m	07/05/2014	5
	12+ years	00133302	10/10/2000	31/7/2013	6-9	12.8	65	Prev	6m	09/05/2013	83
		00114302	12/3/2000	7/5/2013	0-3	13.15	Missing	Prev	0m	03/05/2013	4
		00213313	23/5/2001	4/9/2014	3	13.28	59	This	3m	04/09/2014	0
		00213307	19/1/2000	14/5/2013	0-3	13.32	105	Prev	0m	07/05/2013	7
		01527305	16/10/2001	1/4/2015	0-3	13.46	103	Prev	0m	16/02/2015	44
		05042301	31/10/1999	18/11/2013	0-3	14.05	129	Prev	0m	14/11/2013	4
		00213304	23/3/1999	3/12/2013	6-9	14.7	89	Prev	6m	06/09/2013	88
		00248302	11/8/1999	23/7/2014	0-3	14.95	126	Prev	0m	14/07/2014	9
		00213318	2/6/2000	19/6/2015	3	15.04	50	This	3m	19/06/2015	0
		00114306	12/2/1999	2/4/2014	0-3	15.13	130	Prev	0m	24/03/2014	9
		00243313	22/8/1999	9/1/2015	9-12	15.38	63	Prev	9m	24/11/2014	46
MDI -> CSII	<5 years	00213109	23/9/2013	10/9/2014	0-3	0.96	68	Prev	0m	03/09/2014	7
		00036102	18/3/2012	29/5/2014	0-3	2.2	90	Prev	0m	09/05/2014	20
		00243104	19/7/2011	3/12/2013	9-12	2.38	73	Prev	9m	22/11/2013	11
		00213101	11/5/2010	8/1/2013	3-6	2.66	66	Prev	3m	03/01/2013	5
		00133104	26/12/2010	28/5/2014	9-12	3.42	72	Prev	9m	27/02/2014	90
		00213107	12/10/2010	28/4/2014	0-3	3.54	89	Prev	0m	28/03/2014	31
		00213103	26/8/2009	14/5/2013	3-6	3.72	39	Prev	3m	01/05/2013	13
		00114105	23/6/2011	15/6/2015	9-12	3.98	79	Prev	9m	28/05/2015	18
		00114101	16/4/2009	11/6/2013	3-6	4.15	51.9	Prev	3m	28/03/2013	75
		05042104	12/11/2009	1/5/2014	6-9	4.47	60	Prev	6m	31/03/2014	31
		00114103	24/8/2009	4/6/2014	6-9	4.78	78	Prev	6m	01/05/2014	34

Permanent change from -> to	Age strata	Rand no	DOB	Permanent change date	Timing of change (months)	Age at permanent change (years)	Last HbA1c measurement prior to switch (mmol/mol)	Last HbA1c measurement as the previous or this visit	Last HbA1c measurement visit (months)	Last HbA1c measurement visit date	Days from last HbA1c measurement to permanent change
		00036103	3/12/2009	2/2/2015	3-6	5.17	54	Prev	3m	12/12/2014	52
	5-11 years	00114202	30/8/2007	9/1/2013	0-3	5.36	58.5	Prev	0m	23/11/2012	47
		00086210	18/9/2008	9/2/2015	9-12	6.39	59	Prev	9m	27/10/2014	105
		00213229	23/2/2008	13/10/2015	6-9	7.64	51	Prev	6m	27/07/2015	78
		00114206	19/6/2006	18/2/2014	3-6	7.67	46	Prev	3m	30/01/2014	19
		00114213	14/11/2007	17/11/2015	6-9	8.01	53	Prev	6m	13/08/2015	96
		00326201	12/6/2006	13/1/2015	3-6	8.59	53	Prev	3m	12/12/2014	32
		00114208	22/9/2005	4/6/2014	3-6	8.7	47	Prev	3m	17/04/2014	48
		00213223	23/6/2006	8/6/2015	9-12	8.96	61	Prev	9m	15/04/2015	54
		00326204	1/11/2005	14/9/2015	3-6	9.87	54	Prev	3m	25/06/2015	81
		00213226	5/10/2004	13/10/2015	6-9	11.02	43	Prev	6m	06/08/2015	68
		05042217	6/11/2003	9/4/2015	9-12	11.42	58	Prev	9m	23/02/2015	45
		00213211	17/9/2001	26/9/2013	3-6	12.02	43	Prev	3m	30/08/2013	27
		00114209	8/12/2002	31/3/2015	6-9	12.31	64	Prev	6m	05/02/2015	54
		05042216	25/6/2002	26/11/2014	9-12	12.42	44	Prev	9m	20/10/2014	37
	12+ years	00213306	22/3/2001	29/10/2013	3-6	12.61	38	Prev	3m	31/07/2013	90
		00036303	22/9/2002	2/6/2015	0-3	12.69	133	Prev	0m	18/03/2015	76
		00114301	18/9/1998	25/2/2013	3-6	14.44	38.8	Prev	3m	02/01/2013	54
		00036301	17/11/1999	27/7/2015	6-9	15.69	32	Prev	6m	13/05/2015	75
MDI -> Injections - TDS regime	5-11 years	12617501	5/6/2002	28/6/2012	9	10.06	66	This	9m	28/06/2012	0

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Table 6.7-3: Additional Analyses – Permanent change to insulin delivery method – Reasons line listings (ITT) – Post-hoc analysis

Permanent change from -> to	Age strata	Rand no	Timing of change (months)	Age at permanent change (years)	Person(s) that made decision	Reason(s)	Permanent change due to an adverse event
CSII -> MDI	<5 years	00213102	0	1.84	Parent	Parent preference	No
	5-11 years	00243224	0-3	6.55	Patient	Participant preference	No
		05042218	0-3	10.2	Patient	Participant preference	No
		00213218	6-9	10.35	Clinician; Parent; Patient	Poor concordance with treatment; Participant preference; Parent preference	No
		05042212	0-3	10.55	Parent; Patient	Participant preference; Parent preference	No
		00114207	0-3	10.58	Parent; Patient	Participant preference; Parent preferenceOther: pain at cannula site	No
		05042214	0	10.72	Clinician; Parent	Poor glycaemic control - b. Frequent hyperglycaemia; Parent preference	No
		00133207	6-9	10.8	Patient	Participant preference	No
		00133209	9-12	11.24	Patient	Participant preference	No
		05042207	0	11.71	Parent; Patient	Other: Participant was not sure he wanted a pump to deliver insulin	No
		00243219	0-3	11.95	Parent	Participant preference	No
	12+ years	00133302	6-9	12.8	Parent; Patient	Participant preference; Parent preference	No
		00114302	0-3	13.15	Parent; Patient	Participant preference; Parent preference	No
		00213313	3	13.28	Clinician; Parent; Patient	Participant preference; Parent preference	No
		00213307	0-3	13.32	Parent; Patient	Participant preference; Parent preference	No
		01527305	0-3	13.46	Parent; Patient	Participant preference	No

Permanent change from -> to	Age strata	Rand no	Timing of change (months)	Age at permanent change (years)	Person(s) that made decision	Reason(s)	Permanent change due to an adverse event
		05042301	0-3	14.05	Patient	Participant preference	No
		00213304	6-9	14.7	Clinician; Patient	Poor concordance with treatment	No
		00248302	0-3	14.95	Clinician; Parent; Patient	Participant preference	No
		00213318	3	15.04	Patient	Participant preference	No
		00114306	0-3	15.13	Clinician; Parent; Patient	Participant preference	Yes - AE='Insulin administration error: no adverse effect reported'
		00243313	9-12	15.38	Clinician; Parent; Patient	Poor glycaemic control - b. Frequent hyperglycaemia; Participant preference; Parent preference	Yes - AE='other - specify: hyperglycaemia ketones'
MDI -> CSII	<5 years	00213109	0-3	0.96	Clinician; Parent	Other: age related	No
		00036102	0-3	2.2	Parent	Parent preference	No
		00243104	9-12	2.38	Clinician; Parent	Poor glycaemic control - b. Frequent hyperglycaemia; Parent preference	No
		00213101	3-6	2.66	Clinician; Parent	Poor glycaemic control - a. Debiltating hypoglycaemia; Poor glycaemic control - b. Frequent hyperglycaemia	No
		00133104	9-12	3.42	Clinician	Poor glycaemic control - b. Frequent hyperglycaemia	No
		00213107	0-3	3.54	Clinician; Parent	Poor glycaemic control - a. Debiltating	No

Permanent change from -> to	Age strata	Rand no	Timing of change (months)	Age at permanent change (years)	Person(s) that made decision	Reason(s)	Permanent change due to an adverse event
						hypoglycaemia; Parent preference	
		00213103	3-6	3.72	Clinician; Parent	Other: young age needs smaller insulin quantities	No
		00114105	9-12	3.98	Parent	Other: bruising from injections	No
		00114101	3-6	4.15	Clinician; Parent	Parent preference	No
		05042104	6-9	4.47	Clinician; Parent	Parent preferenceOther: frequent hypoglycaemia	No
		00114103	6-9	4.78	Clinician; Parent	Participant preference; Parent preference	No
		00036103	3-6	5.17	Clinician	Parent preference	No
	5-11 years	00114202	0-3	5.36	Clinician; Parent; Patient	Participant preference; Parent preference	No
		00086210	9-12	6.39	Clinician; Parent; Patient	Poor glycaemic control - b. Frequent hyperglycaemia; Participant preference; Parent preference	No
		00213229	6-9	7.64	Clinician; Parent	Poor concordance with treatment	No
		00114206	3-6	7.67	Clinician; Parent; Patient	Participant preference; Parent preference	No
		00114213	6-9	8.01	Parent; Patient	Participant preference; Parent preference	No
		00326201	3-6	8.59	Patient	Participant preference	No
		00114208	3-6	8.7	Clinician; Parent; Patient	Participant preference; Parent preference	No
		00213223	9-12	8.96	Clinician; Parent; Patient	Participant preference; Parent preference	No
		00326204	3-6	9.87	Clinician;	Participant preference	No

Permanent change from -> to	Age strata	Rand no	Timing of change (months)	Age at permanent change (years)	Person(s) that made decision	Reason(s)	Permanent change due to an adverse event
					Parent; Patient		
		00213226	6-9	11.02	Clinician; Parent; Patient	Poor concordance with treatment; Participant preference; Parent preference	No
		05042217	9-12	11.42	Patient	Participant preference	No
		00213211	3-6	12.02	Clinician; Parent; Patient	Participant preference; Parent preference	No
		00114209	6-9	12.31	Clinician; Parent; Patient	Participant preference; Parent preference	No
		05042216	9-12	12.42	Parent; Patient	Participant preference; Parent preference	No
	12+ years	00213306	3-6	12.61	Clinician; Parent; Patient	Participant preference; Parent preferenceOther: Fear of Hypoglycaemia	No
		00036303	0-3	12.69	Parent; Patient	Participant preference; Parent preference	No
		00114301	3-6	14.44	Clinician; Patient	Parent preference	No
		00036301	6-9	15.69	Patient	Participant preference	No
MDI -> Injections - TDS regime	5-11 years	12617501	9	10.06	Clinician; Parent	Participant preference; Parent preference	No

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6.7.2 Primary efficacy assessment – HbA1c measured 12 months after randomisation (ITT)

Table 6.7-4: Additional Analyses – Primary efficacy assessment – HbA1c measured 12 months after randomisation (ITT)

Analysis	Least-Square Mean Difference between treatment groups (CSII-MDI) across all age-groups (95% CI)	P-value
Primary outcome ITT analysis	*2.4 (-0.5, 5.2)*	*0.10*
Total related AEs as a covariate	2.5 (-0.4, 5.3)	0.09
*Deprivation score (quintile) as a covariate	2.2 (-0.7, 5)	0.14
*Deprivation score (continuous) as a covariate	2.2 (-0.7, 5)	0.14
*Abnormal coeliac screen result as a covariate	1.7 (-1.7, 5.1)	0.33

* Conducted to explore possible imbalance in baseline characteristics between treatment groups.

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6.7.3 Safety data – EUDRA-CT – Post-hoc

To upload the adverse event data to EUDRA-CT database the descriptions are required to be (1) summarised as non-serious AEs and serious AEs and (2) be MedDRA coded using System Organ Class (SOC) and Preferred Term (PT). All adverse events were MedDRA coded and agreed by the Chief Investigator after unblinding hence why labelled post-hoc. Some of the adverse event descriptions needed to be split up to match multiple MedDRA codes. See Table 6.7-5 and Table 6.7-6 for how they were categorised. See Table 6.7-7 for the summary of non-serious AEs and see Table 6.7-8 for the summary of serious AEs.

Table 6.7-5: Additional Analyses – Non-serious AE MedDRA codes used for EUDRA-CT

Category	Randomisation number	AE number	AE description	PT	SOC
Carer error	00114213	3	Insulin administration error: restarted pump when had active glargine	Drug administration error	Injury, poisoning and procedural complications
	00148101	2	Other - specify: device problem caused by human error- to much insulin used by grandparent. hypoglycaemia as result of	Drug administration error	Injury, poisoning and procedural complications
				Hypoglycaemia	Metabolism and nutrition disorders
	00148301	1	Insulin administration error: 6 units glargine should of given 4 units error by participant, high blood glucose as result	Drug administration error	Injury, poisoning and procedural complications
	12617304	1	Other - specify: High blood glucose after changing infusion set	Blood glucose increased	Investigations
	12617304	3	Other - specify: High blood glucose after changing infusion set	Blood glucose increased	Investigations
	12617304	4	Other - specify: High blood sugar after changing infusion set	Blood glucose increased	Investigations
	12617304	5	Other - specify: High blood sugar after changing infusion set	Blood glucose increased	Investigations
Device	00036103	1	Site Infections	Administration site infection	Infections and infestations
	00036106	1	Site Infections	Administration site infection	Infections and infestations
	00086103	1	Other - specify: Allergy	Hypersensitivity	Immune system disorders
	00086103	2	Other - specify: Skin Reaction	Skin reaction	Skin and subcutaneous tissue disorders
	00086103	3	Other - specify: hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	00114105	1	Other - specify: hyperglycaemia	Hyperglycaemia	Metabolism and nutrition disorders

Category	Randomisation number	AE number	AE description	PT	SOC
	00114206	1	Site Infections	Administration site infection	Infections and infestations
	00114207	3	Other - specify: pain at cannula insertion site	Catheter site pain	General disorders and administration site conditions
	00114207	5	Other - specify: pain at cannula site	Catheter site pain	General disorders and administration site conditions
	00114210	2	Other - specify: pump failure- higher blood sugars than usual but no ketones.	Device failure	General disorders and administration site conditions
				Hyperglycaemia	Metabolism and nutrition disorders
	00114213	2	Pump Failure	Device failure	General disorders and administration site conditions
	00148101	1	Other - specify: bruising to cannula site after falling on it	Implant site bruising	General disorders and administration site conditions
	00148203	1	Other - specify: tubing broke at leur lock end. blood glucose levels rose.	Device failure	General disorders and administration site conditions
				Hyperglycaemia	Metabolism and nutrition disorders
	00213105	1	Other - specify: Hyperglycaemia	Hyperglycaemia	Metabolism and nutrition disorders
	00243103	1	Other - specify: lost cannula tip required x ray of area.	Device issue	General disorders and administration site conditions
	00243201	1	Site Infections	Administration site infection	Infections and infestations

Category	Randomisation number	AE number	AE description	PT	SOC
	00243201	2	Pump Failure	Device failure	General disorders and administration site conditions
	00243201	3	Pump Failure	Device failure	General disorders and administration site conditions
	00243205	1	Site Infections	Administration site infection	Infections and infestations
	00243401	1	Other - specify: cannulae falling out - mum ran out of cannula - no supply available.	Device issue	General disorders and administration site conditions
	00248303	1	Other - specify: stinging at inj site	Injection site pain	General disorders and administration site conditions
	04913106	1	Pump Failure	Device failure	General disorders and administration site conditions
	04913106	2	Other - specify: hyperglycaemia x2 episodes	Hyperglycaemia	Metabolism and nutrition disorders
	05042102	1	Site Infections	Administration site infection	Infections and infestations
	05042102	2	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	05042204	1	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	12617203	1	Other - specify: high blood sugar - negative ketones	Blood glucose increased	Investigations
	12617303	1	Other - specify: Stinging at injection site after glargine given	Injection site pain	General disorders and administration site conditions
	12617304	6	Other - specify: High blood sugars	Blood glucose increased	Investigations

Category	Randomisation number	AE number	AE description	PT	SOC
	12617305	1	Site Infections	Administration site infection	Infections and infestations
Incidental illness	00114102	2	Other - specify: fungal scrotal + penile infection	Penile infection	Infections and infestations
				Scrotal infection	Infections and infestations
	00148102	1	Other - specify: hypoglycaemia- not eating	Decreased appetite	Metabolism and nutrition disorders
				Hypoglycaemia	Metabolism and nutrition disorders
	00326101	1	Other - specify: abdominal pain	Abdominal pain	Gastrointestinal disorders
Meter error	00114209	1	Other - specify: Episode of high blood glucose levels (no ketones) due to handset failure.	Blood glucose increased	Investigations
				Hyperglycaemia	Metabolism and nutrition disorders
	00114210	1	Other - specify: handset failure	Device failure	General disorders and administration site conditions
	00114213	1	Other - specify: expert glucometer error- resulting in high variability in glucose levels.	Device failure	General disorders and administration site conditions
	00114303	1	Other - specify: handset not checking blood sugars- blood sugars higher than normal (no ketones)	Device failure	General disorders and administration site conditions
Other	00036104	1	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	00036105	1	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	00243105	1	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders

Category	Randomisation number	AE number	AE description	PT	SOC
	00248101	1	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	01527301	1	Other - specify: Hyperglycaemia	Hyperglycaemia	Metabolism and nutrition disorders
	04913101	3	Other - specify: Hyperglycaemia	Hyperglycaemia	Metabolism and nutrition disorders
	12617204	1	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders

Table 6.7-6: Additional Analyses – Serious AE MedDRA codes used for EUDRA-CT

Category	Randomisation number	AE number	AE description	PT	SOC
Carer error	00114304	1	Insulin administration error: missed insulin glargine over several days due to non-compliance with diabetes treatment and behaviour	Treatment noncompliance	Social circumstances
	00243313	4	Insulin administration error: high blood glucose levels with ketones due to insufficient insulin.	Drug administration error	Injury, poisoning and procedural complications
				Hyperglycaemia	Metabolism and nutrition disorders
	05042213	1	Insulin administration error: admitted following insulin overdose, parent miscalculated bolus dose, dextrose given to correct	Drug administration error	Injury, poisoning and procedural complications
Device	00213108	1	Diabetic Ketoacidosis	Ketoacidosis	Metabolism and nutrition disorders
	00243201	4	Site Infections	Administration site infection	Infections and infestations
Incidental illness	00114103	1	Other - specify: gastroenteritis	Gastroenteritis	Infections and infestations
	00213304	1	Other - specify: Major Social concerns	Social problem	Social circumstances

Category	Randomisation number	AE number	AE description	PT	SOC
	00243313	1	Insulin administration error: ear infection- high blood glucose and ketones	Ear infection	Infections and infestations
				Drug administration error	Injury, poisoning and procedural complications
				Blood glucose increased	Investigations
	04913101	1	Other - specify: Gastroenteritis	Gastroenteritis	Infections and infestations
	04913103	1	Other - specify: Chicken pox	Varicella	Infections and infestations
	04913103	2	Other - specify: Pyrexia; Hyperglycaemia	Pyrexia	General disorders and administration site conditions
				Hyperglycaemia	Metabolism and nutrition disorders
	05042214	2	Other - specify: Vomiting Bug	Vomiting	Gastrointestinal disorders
	05042219	1	Other - specify: not eating	Eating disorder	Psychiatric disorders
Other	00114101	1	Other - specify: Hyperglycaemia	Hyperglycaemia	Metabolism and nutrition disorders
	00114301	1	Insulin administration error: Hyperglycaemia	Drug administration error	Injury, poisoning and procedural complications
				Hyperglycaemia	Metabolism and nutrition disorders
	00213102	1	Other - specify: Hypoglycaemia - resolved	Hypoglycaemia	Metabolism and nutrition disorders
	00243201	5	Severe Hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	00243313	2	Other - specify: hyperglycaemia ketones	Blood ketone body	Investigations
				Hyperglycaemia	Metabolism and nutrition disorders
	00243313	3	Other - specify: hyperglycaemia ketones	Blood ketone body	Investigations
				Hyperglycaemia	Metabolism and nutrition disorders

Category	Randomisation number	AE number	AE description	PT	SOC
	04913103	3	Diabetic Ketoacidosis	Diabetic ketoacidosis	Metabolism and nutrition disorders
	04913203	1	Other - specify: Moderate hypoglycaemia	Hypoglycaemia	Metabolism and nutrition disorders
	04913204	1	Other - specify: High BGS and ketones	Blood glucose increased	Investigations
				Blood ketone body	Investigations

Non-Serious AEs

The incidence of related non-serious AEs by treatment group were:

- 47 AEs in 28 patients that were on CSII at the time of the non-serious AE.
- 10 AEs in 8 patients that were on MDI at the time of the non-serious AE.

Table 6.7-7: Additional Analyses – Non-serious AE summary for EUDRA-CT

		CSII		MDI	
SOC	**PT**	**Patients**	**Events**	**Patients**	**Events**
Gastrointestinal disorders	Abdominal pain	1	1	0	0
General disorders and administration site conditions	Catheter site pain	1	2	0	0
	Device failure	5	8	1	1
	Device issue	2	2	0	0
	Implant site bruising	1	1	0	0
	Injection site pain	0	0	2	2
Immune system disorders	Hypersensitivity	1	1	0	0
Infections and infestations	Administration site infection	7	7	0	0
	Penile infection	1	1	0	0
	Scrotal infection	1	1	0	0
Injury, poisoning and procedural complications	Drug administration error	1	1	2	2
Investigations	Blood glucose increased	3	7	0	0
Metabolism and nutrition disorders	Decreased appetite	0	0	1	1
	Hyperglycaemia	7	7	1	1
	Hypoglycaemia	7	7	3	3
Skin and subcutaneous tissue disorders	Skin reaction	1	1	0	0

Serious AEs

The incidence of serious AEs by treatment group were:

- 19 AEs in 9 patients that were on CSII at the time of the serious AE.
- 11 AEs in 7 patients that were on MDI at the time of the serious AE.

Table 6.7-8: Additional Analyses – Serious AE summary for EUDRA-CT

		CSII			MDI		
SOC	**PT**	**Patients**	**Events (all)**	**Events (related)**	**Patients**	**Events (all)**	**Events (related)**
Gastrointestinal disorders	Vomiting	0	0	0	1	1	1
General disorders and administration site conditions	Pyrexia	1	1	1	0	0	0
Infections and infestations	Administration site infection	1	1	1	0	0	0
	Ear infection	1	1	1	0	0	0
	Gastroenteritis	2	2	1	0	0	0
	Varicella	1	1	0	0	0	0
Injury, poisoning and procedural complications	Drug administration error	1	2	2	2	2	2
Investigations	Blood glucose increased	1	1	1	1	1	1
	Blood ketone body	1	2	2	1	1	1
Metabolism and nutrition disorders	Diabetic ketoacidosis	1	1	1	0	0	0
	Hyperglycaemia	2	3	3	2	3	3
	Hypoglycaemia	2	2	2	1	1	1
	Ketoacidosis	1	1	1	0	0	0
Psychiatric disorders	Eating disorder	1	1	1	0	0	0
Social circumstances	Social problem	0	0	0	1	1	1
	Treatment noncompliance	0	0	0	1	1	1

7. Listings shells

Line listings in ‘Table 5.1-1: Site closure reasons’ are presented in section 5.1.

Line listings in ‘Table 5.2-3: Summary key changes from protocol v3 to v4 to boost recruitment’ are presented in section 5.2.

Line listings in ‘Table 6.2-3 Reasons for discontinuing randomised treatment allocation’ are presented in section 6.2.

Line listings in ‘Table 6.2-4: Summary of the explanatory notes of non-allocation of randomised treatment’ are presented in section 6.2.

Line listings in ‘Table 6.5-8: Listing of related AEs – CSII (taken at time of AE onset)’ are presented in section 6.5.

Line listings in ‘Table 6.5-9: Listing of related AEs – MDI (taken at time of AE onset)’ are presented in section 6.5.

Line listings in ‘Table 6.5-18: SAE listing of related serious adverse events – CSII (taken at time of SAE onset)’ are presented in section 6.5.

Line listings in ‘Table 6.5-19: SAE listing of related serious adverse events – MDI (taken at time of SAE onset)’ are presented in section 6.5.

Line listings in ‘Table 6.7-2: Additional Analyses – Permanent change to insulin delivery method – Further information line listings (ITT)’ are presented in section 6.7.

Line listings in ‘Table 6.7-3: Additional Analyses – Permanent change to insulin delivery method – Reasons line listings (ITT)’ are presented in section 6.7.

8. Plots and graphs

Plot number	Title	Section number of data to be included	Population	x-axis/y-axis
1	CONSORT 2010 Flow Diagram	3.1-1	ITT	N/A
2	Recruitment graph	5.2-1	ITT	X=Date (Mon-Year) / Y1=Number randomised Y2=Number of centres opened
3	Completeness of follow-up	6.2-1	ITT	Numbers and %s (no axes as not a graph)
4	Primary outcome results Meta-Analysis and Forest plot across sites (ITT)	6.6-1	ITT	Mean difference (CSII-MDI) / Centres
5	HbA1c mmol/mol – Mean profile plots (<5 years old) (ITT)	6.6-2	ITT (<5 years old)	Time (months) / HbA1c (mmol/mol)
6	HbA1c mmol/mol – Mean profile plots (5-11 years old) (ITT)	6.6-3	ITT (5-11 years old)	Time (months) / HbA1c (mmol/mol)
7	HbA1c mmol/mol – Mean profile plots (12+ years old) (ITT)	6.6-4	ITT (12+ years old)	Time (months) / HbA1c (mmol/mol)
8	Paediatric Quality of Life (PedsQL) – Child mean profile plots (5-7 years old) (ITT)	6.6-5	ITT (5-7 years old)	Time (months) / PedsQL overall score (0-100)
9	Paediatric Quality of Life (PedsQL) – Child mean profile plots (8-12 years old) (ITT)	6.6-6	ITT (8-12 years old)	Time (months) / PedsQL overall score (0-100)
10	Paediatric Quality of Life (PedsQL) – Child mean profile plots (13-16 years old) (ITT)	6.6-7	ITT (13-16 years old)	Time (months) / PedsQL overall score (0-100)
11	Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (2-4 years old) (ITT)	6.6-8	ITT (2-4 years old)	Time (months) / PedsQL overall score (0-100)
12	Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (5-7 years old) (ITT)	6.6-9	ITT (5-7 years old)	Time (months) / PedsQL overall score (0-100)
13	Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (8-12 years old) (ITT)	6.6-10	ITT (8-12 years old)	Time (months) / PedsQL overall score (0-100)

Plot number	Title	Section number of data to be included	Population	x-axis/y-axis
14	Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (13-16 years old) (ITT)	6.6-11	ITT (13-16 years old)	Time (months) / PedsQL overall score (0-100)
15	Partial remission – Mean profile plots (<5 years old) (ITT)	6.6-12	ITT (<5 years old)	Time (months) / Proportion in partial remission (0-1)
16	Partial remission – Mean profile plots (5-11 years old) (ITT)	6.6-13	ITT (5-11 years old)	Time (months) / Proportion in partial remission (0-1)
17	Partial remission – Mean profile plots (12+ years old) (ITT)	6.6-14	ITT (12+ years old)	Time (months) / Proportion in partial remission (0-1)
18	Additional Analyses – Permanent change to insulin delivery method split by site – Forest plot (ITT)	6.7-1	ITT	Risk ratio (CSII [switches to MDI] / MDI [switches to CSII]) / Centres

Appendix 1: Mapping report contents to SAP

This report has been created following the SCIPI Statistical Analysis Plan V1.0 (dated 13/10/2016).

The following table lists each item (tables, figures and section when applicable) in this report and maps each to the relevant SAP section that describes the methods used to compute it.

Section/subsection of SAP	Item within report	Additional details (if required)
1 to 13	N/A – No analyses listed.	
14.1 Screening, eligibility and recruitment	Figure 3.1-1: CONSORT 2010 Flow Diagram	"Randomised but withdrew consent for data to be collected" box added to diagram prior to the numbers randomised box to show that they were not included in any follow-up or analyses.
	Table 5.1-1: Site closure reasons	Added to provide the reader with further details as to the reasons why some sites closed prior to the end of the recruitment period.
	Table 5.2-1: Screening and consent by site (All protocol versions combined, but consent rate broken down by protocol versions)	
	Table 5.2-2: Screening and consent by protocol version	
	Table 5.2-3: Summary key changes from protocol v3 to v4 to boost recruitment	Added to aid interpretation of the separate recruitment summary tables for protocol versions 3 and 4.
	Table 5.2-4: Screening log version 3 and version 4 reason codes	
	Table 5.2-5: Reasons for ineligibility at screening – Protocol up to version 3.0	
	Table 5.2-6: Reasons for ineligibility at screening – Protocol version 4.0 only	
	Table 5.2-7: Time of recruitment events from date of diagnosis	
	Table 5.2-8: Demographic characteristics of screened patients	
	Figure 5.2-1: Recruitment graph	

Section/subsection of SAP	Item within report	Additional details (if required)
	Table 6.2-2 Discontinuation rates at each follow-up time-point	'0 months', '0<WD<3 months', '3<WD<6 months', '6<WD<9 months' 9<WD<12 months' added as distinct categories in addition to the 3m/6m/9m/12m written in the SAP.
	Figure 6.2-1: Completeness of follow-up	
	Table 6.2-3: Reasons for discontinuing randomised treatment allocation	
	Table 6.2-4: Summary of the explanatory notes of non-allocation of randomised treatment	
15 Protocol deviations	Table 6.2-5: Protocol deviations	
	Table 6.2-6: Visit assessment timings – Categorical	
	Table 6.2-7: Visit assessment timings – Continuous	
16 Unblinding	N/A – No analyses listed	
17.1 Data sets analysed	Table 6.2-1: Data sets analysed	
17.2 Demographic and other baseline characteristics	Table 6.1-1: Demographic details	
	Table 6.1-2: Baseline disease characteristics	
17.3 Compliance with treatment	See section '6.2.2 Protocol deviations' of the report for details.	
17.4.1 Primary Outcome: 12-month HbA1c	Table 6.6-1: HbA1c measured 12 months after randomisation – Completeness of data (ITT)	
	Table 6.6-2: HbA1c measured 12 months after randomisation – Lab value used for analysis (ITT)	Added to provide further information regarding the composition of the primary outcome measurements used in the ITT analysis.
	Table 6.6-3: HbA1c measured 12 months after randomisation – Results (ITT)	Least square means and 95% confidence intervals for CSII and MDI added to aid interpretation of the pre-specified least square mean difference and 95% confidence interval. The overall summary statistics row was also added to aid interpretation.

Section/subsection of SAP	Item within report	Additional details (if required)
	Table 6.6-4: Baseline characteristics of children that were randomised and have a primary outcome measurement (ITT)	Only 8 patients did not contribute to the ITT analysis so there were too few data to summarise in terms of demographics to compare to the baseline population to check that missingness is at random. Therefore, the converse of summarising for those included in the ITT was done instead.
	Figure 6.6-1: Primary outcome results Meta-Analysis and Forest plot across sites (ITT)	
	Figure 6.6-2: HbA1c mmol/mol – Mean profile plots (<5 years old) (ITT)	Post-hoc analysis investigating the HbA1c mean profiles over time.
	Figure 6.6-3: HbA1c mmol/mol – Mean profile plots (5-11 years old) (ITT)	Post-hoc analysis investigating the HbA1c mean profiles over time.
	Figure 6.6-4: HbA1c mmol/mol – Mean profile plots (12+ years old) (ITT)	Post-hoc analysis investigating the HbA1c mean profiles over time.
	Table 6.6-5: HbA1c measured 12 months after randomisation – Completeness of data (Per-protocol)	
	Table 6.6-6: HbA1c measured 12 months after randomisation – Lab value used for analysis (Per-protocol)	Added to provide further information regarding the composition of the primary outcome measurements used in the PP analysis.
	Table 6.6-7: HbA1c measured 12 months after randomisation – Results (Per-protocol)	Least square means and 95% confidence intervals for CSII and MDI added to aid interpretation of the pre-specified least square mean difference and 95% confidence interval. The overall summary statistics row was also added to aid interpretation.
	Table 6.6-8: Baseline characteristics of children that were randomised and have a primary outcome measurement (Per-protocol)	Same reasoning as for the Table 6.6-4 summary table for the ITT analysis set.
	Table 6.6-9: HbA1c measured 12 months after randomisation – Measurement of local lab HbA1c at 12 months	Additional information presented to provide reasons for missing data across age strata. These data were presented within monitoring reports throughout the course of the trial.

Section/subsection of SAP	Item within report	Additional details (if required)
	Table 6.6-10: HbA1c measured 12 months after randomisation – Measurement of central lab HbA1c at 12 months	Additional information presented to provide reasons for missing data across age strata. These data were presented within monitoring reports throughout the course of the trial.
	Table 6.7-4: Additional Analyses – Primary efficacy assessment – HbA1c measured 12 months after randomisation (ITT)	
17.4.2 Secondary Outcome 1: Percentage of participants in each group with $HbA1_c$ < 6.5%	Table 6.6-11: Percentage of participants in each group with 12-month HbA1c < 48 mmol/mol – Completeness of data (ITT)	The following text “Note: This table is exactly the same for the HbA1c < 58.5 analysis” is written below this table in the report to explain why there is no completeness of data table for the ‘HbA1c < 48 mmol/mol’ analysis.
	Table 6.6-12: Percentage of participants in each group with 12-month HbA1c < 48 mmol/mol – Results (ITT)	
	Table 6.6-13: Percentage of participants in each group with 12-month HbA1c < 58.5 mmol/mol – Results (ITT)	Analysis not post-hoc as such as was detailed in earlier version of SCIPI trial protocol. See substantial amendment (01/08/2016): "Updated the HbA1c recommendations in line with the recent NICE guidance: Change to the Secondary Objective. HbA1c reduced from 7.5% to 6.5% and HbA1c also provided in mmol. Change to secondary endpoint - Percentage of participants in each group with HbA1c reduced from <7.5% to <6.5%. Added partial remission and height as endpoints." – Analysis done for completeness.

Section/subsection of SAP	Item within report	Additional details (if required)
17.4.3 Secondary Outcome 2: Incidence of severe hypoglycaemia	Table 6.6-14: Incidence of severe hypoglycaemia – Results (ITT)	SAP says "Severe hypoglycaemia is a type of related adverse event…Cases of hypoglycaemia mild or moderate in severity will not be counted as events for this analysis." – 'Severe hypoglycaemia' is the type of AE and this terminology is used in general clinical practice regardless of adverse event severity so it is, thus, possible to have a moderate or mild 'Severe hypoglycaemia'. Prior to the final analysis being undertaken all cases of 'Severe hypoglycaemia' were queried with site again to double check whether they were happy with the AE type and severity. Individual line listings for all AEs are shown in Table 6.5-8 and Table 6.5-9 so all severities for each 'Severe hypoglycaemia' are shown here.
17.4.4 Secondary Outcome 3: Incidence of diabetic ketoacidosis	Table 6.6-15: Incidence of diabetic ketoacidosis – Results (ITT)	
17.4.5 Secondary Outcome 4: Change in BMI SDS	Table 6.6-16: Change in BMI SDS – Completeness of data (ITT)	
	Table 6.6-17: Change in BMI SDS – Results (ITT)	
17.4.6 Secondary Outcome 5: Height	Table 6.6-18: Height – Completeness of data (ITT)	
	Table 6.6-19: Height – Results (ITT)	
17.4.7 Secondary Outcome 6: Insulin requirements	Table 6.6-20: Insulin requirements – Completeness of data (ITT)	
	Table 6.6-21: Insulin requirements – Results (ITT)	
17.4.8 Secondary Outcome 7: Paediatric Quality of Life: PedsQL	Table 6.6-22: Paediatric Quality of Life (PedsQL) – Completeness of data (ITT)	Summaries presented at 6m in addition to 12m.
	Table 6.6-23: Paediatric Quality of Life (PedsQL) – Results summary at 6m and 12m (ITT)	Summaries presented at 6m in addition to 12m.
	Table 6.6-24: Paediatric Quality of Life (PedsQL) – Modelling results at 6m and 12m (ITT)	
	Table 6.6-25: Paediatric Quality of Life (PedsQL) – Mean profile plot inclusion status (ITT)	Added to help to visualise the results across 6m and 12m.

Section/subsection of SAP	Item within report	Additional details (if required)
	Figure 6.6-5: Paediatric Quality of Life (PedsQL) – Child mean profile plots (5-7 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
	Figure 6.6-6: Paediatric Quality of Life (PedsQL) – Child mean profile plots (8-12 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
	Figure 6.6-7: Paediatric Quality of Life (PedsQL) – Child mean profile plots (13-16 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
	Figure 6.6-8: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (2-4 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
	Figure 6.6-9: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (5-7 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
	Figure 6.6-10: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (8-12 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
	Figure 6.6-11: Paediatric Quality of Life (PedsQL) – Parent/carer mean profile plots (13-16 years old) (ITT)	Added to help to visualise the results across 6m and 12m.
17.4.9 Secondary Outcome 8: Incremental cost per QALY gained	N/A – Analysis undertaken by the Health Economics team at the University of Bangor. They have a separate Health Economics Analysis Plan. See final HTA publication for details.	
17.4.10 Secondary Outcome 9: Partial remission	Table 6.6-26: Partial Remission – Completeness of data (ITT)	
	Table 6.6-27: Partial Remission – Results summary at 12m (ITT)	
	Table 6.6-28: Partial Remission – Results summary at 3m, 6m and 9m (ITT)	
18 Missing data and withdrawals	Table 6.6-4: Baseline characteristics of children that were randomised and have a primary outcome measurement (ITT)	
	Section '14.1 Screening, eligibility and recruitment' of the SAP describes the methods of summarising the withdrawal data in more detail.	
19.1 Additional analyses: Primary outcome	Table 6.7-4: Additional Analyses – Primary efficacy assessment – HbA1c measured 12 months after randomisation (ITT)	

Section/subsection of SAP	Item within report	Additional details (if required)
19.2 Additional analyses: Partial remission	Table 6.6-29: Partial Remission – Summary at each visit (ITT)	
	Table 6.6-30: Partial Remission – Transitions from 6m to 12m (ITT)	
	Figure 6.6-12: Partial remission – Mean profile plots (<5 years old) (ITT)	
	Figure 6.6-13: Partial remission – Mean profile plots (5-11 years old) (ITT)	
	Figure 6.6-14: Partial remission – Mean profile plots (12+ years old) (ITT)	
	N/A – The average length of time participants were in partial remission time to event analysis.	The average length of time participants were in partial remission was a pre-planned analysis to be conducted as a time to event outcome with leaving the partial remission phase as the outcome. As partial remission cannot be measured at baseline (due to the need for insulin data during the 28 days prior not being available) it was to be assumed that all participants at baseline have entered the partial remission phase. Following discussion with the Chief Investigator it was agreed that this analysis did not make any else both clinically and statistically so was not conducted.
19.3 Additional analyses: Permanent changes to insulin delivery	Figure 6.7-1: Additional Analyses – Permanent change to insulin delivery method split by site – Forest plot (ITT)	
	Table 6.7-1: Additional Analyses – Permanent change to insulin delivery method – Time point of changes by age strata (ITT)	Post-hoc analysis to further explore the changes to insulin delivery method.
	Table 6.7-2: Additional Analyses – Permanent change to insulin delivery method – Further information line listings (ITT)	Post-hoc analysis to further explore the changes to insulin delivery method.
	Table 6.7-3: Additional Analyses – Permanent change to insulin delivery method – Reasons line listings (ITT)	Post-hoc analysis to further explore the changes to insulin delivery method.
20.1 Data sets analysed (safety)	Table 6.2-1: Data sets analysed	

Section/subsection of SAP	Item within report	Additional details (if required)
20.2 Presentation of the data (safety)	Table 6.5-1: Overview of related AEs by site and overall (All AEs) serious adverse events – MDI (taken at time of SAE onset)	
	Table 6.5-2: Overview of related AEs by site and overall (Device AEs)	Pre-specified AE categories (harm; device) changed by Chief Investigator to make more clinical sense. This was done during a blinded assessment.
	Table 6.5-3: Overview of related AEs by site and overall (Carer error AEs)	
	Table 6.5-4: Overview of related AEs by site and overall (Meter error AEs)	
	Table 6.5-5: Overview of related AEs by site and overall (Incidental illness AEs)	
	Table 6.5-6: Overview of related AEs by site and overall (Other AEs)	
	Table 6.5-7: Summary of related AE by adverse event description code	
	Table 6.5-8: Listing of related AEs – CSII (taken at time of AE onset)	
	Table 6.5-9: Listing of related AEs – MDI (taken at time of AE onset)	
	Table 6.5-10: Overview of related SAEs by site and overall (All SAEs)	
	Table 6.5-11: Overview of related SAEs by site and overall (Device SAEs)	Pre-specified AE categories (harm; device) changed by Chief Investigator to make more clinical sense. This was done during a blinded assessment.
	Table 6.5-12: Overview of related SAEs by site and overall (Carer error SAEs)	
	Table 6.5-13: Overview of related SAEs by site and overall (Meter error SAEs)	
	Table 6.5-14: Overview of related SAEs by site and overall (Incidental illness SAEs)	
	Table 6.5-15: Overview of related SAEs by site and overall (Other SAEs)	
	Table 6.5-16: Summary of related serious adverse events by adverse event description code	

Section/subsection of SAP	Item within report	Additional details (if required)
	Table 6.5-17: Relationship and expectedness of insulin drug	
	Table 6.5-18: SAE listing of related serious adverse events – CSII (taken at time of SAE onset)	
	Table 6.5-19: SAE listing of related	
	N/A – The number (and percentage) of participants experiencing each AE by severity “Mild”, “Moderate”, or “Severe”)	The number (and percentage) of participants experiencing each AE was a pre-planned analysis to be presented for each treatment arm categorised by severity “Mild”, “Moderate”, or “Severe”). The AEs were presented by number (and percentage) but the severities have just been displayed in the line listings.
	Table 6.7-5: Additional Analyses – Non-serious AE MedDRA codes used for EUDRA-CT	To upload the adverse event data to EUDRA-CT database the descriptions are required to be (1) summarised as non-serious AEs and serious AEs and (2) be MedDRA coded using System Organ Class (SOC) and Preferred Term (PT). All adverse events were MedDRA coded and agreed by the Chief Investigator after unblinding hence why labelled post-hoc.
	Table 6.7-6: Additional Analyses – Serious AE MedDRA codes used for EUDRA-CT	
	Table 6.7-7: Additional Analyses – Non-serious AE summary for EUDRA-CT	
	Table 6.7-8: Additional Analyses – Serious AE summary for EUDRA-CT	
21 References	N/A – No analyses listed	N/A

Consistency With Trial Protocol

Section 9.6 ‘Analysis Plan’ of the SCIPI trial protocol v7.0 (01/08/2016) states:

“The primary outcome HbA1c will be compared between the trial groups using a two group t-test. Difference in means with 95% confidence intervals will be presented. Analysis of covariance will be used to adjust for baseline values (excluding HbA1c measured at baseline) and important prognostic factors.”

These analyses of primary outcome specified were not conducted in preference to least squares regression in accordance with the statistical principles for clinical trials detailed in ICH E9 as the randomisation process was stratified by age category (7mths – <5 yrs, 5 – <12 yrs, 12-15 yrs) and centre.