DIABAUD 3

GLYCAEMIC CONTROL IN CHILDREN AND ADOLESCENTS UNDER 15 YEARS OF AGE WITH TYPE 1 DIABETES IN SCOTLAND

Final Report

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on behalf of:
The Scottish Study Group for the Care of Diabetes in the Young

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SUMMARY

DIABAUD 3: GLYCAEMIC CONTROL IN CHILDREN AND ADOLESCENTS UNDER 15 YEARS OF AGE WITH TYPE 1 DIABETES IN SCOTLAND

Background: The Scottish Study Group for the Care of Diabetes in the Young (SSGCDY) established the DIABAUD Project to deliver high quality information on the outcome of the clinical care of children with Type 1 diabetes (T1D) in Scotland. The primary management of T1D is aimed at maintaining good glycaemic control to minimise the risk of complications.

Aim: The aim of DIABAUD 3 was to provide prospective data on the effectiveness of the clinical care strategies employed in the management of T1D in young people in Scotland and to investigate whether there had been a change in glycaemic control between DIABAUD 2 and 3. The information would allow each clinical centre to interpret their efforts against the recommendations of SIGN guidelines.

Methods: Study 1: Data was analysed from a cross-sectional survey in Scottish children (DIABAUD 3) of current treatment and factors which might influence glycaemic control. Study 2: Data was analysed from a record linkage in the subgroup of children who participated in DIABAUD 2 and DIABAUD 3 to assess treatment and results over time.

Results: DIABAUD 3 confirmed that glycaemic control remains unsatisfactory in children and adolescents with a high percentage of subjects falling outside the targets described in accepted guidelines, placing the majority at a high risk of future micro-vascular complications. The overall mean HbA_{1c} was 9.2% (SD 1.54). Only 9.7% of subjects achieved the NICE recommended target of an HbA_{1c} equal to or < 7.5%.

Subjects 10 years and over had a mean HbA_{1c} of 9.5% (SD 1.6) compared with all other ages 8.9%. HbA_{1c} increased with age and is significantly worse during adolescence. There was no association between HbA_{1c} and sex. The mean HbA_{1c} was 9.2% for both males and females.

While the majority of subjects were on two injections per day (51%), there had been a significant increase in patients treated with three injections per day (split evening dose) in DIABAUD 3 compared with DIABAUD 2 (D3, 43% versus D2, 2%). In DIABAUD 2, 94% of subjects were on two injections per day. Less than 10% of patients in DIABAUD 3 were on multiple insulin therapy (MDI- i.e. 4 or more injections per day). There was no significant association found between HbA_{1c} and number of injections per day. Only four (2.5%) subjects were recorded as using an insulin pump.

No association was found between HbA_{1c} and family history of diabetes in mothers or fathers. No significant difference was found in HbA_{1c} levels between subjects living with one or both parents.

The average HbA_{1c} for DIABAUD 2 v. DIABAUD 3 was similar: 8.9 v. 9.2% respectively. Mean HbA_{1c} was significantly higher in patients audited in both studies: D2, 8.6% (SD 1.23), D3 9.6% (SD 1.6). This result was expected because of the known deterioration in HbA_{1c} with age. In 70.2% of subjects HbA_{1c} increased. The numbers of subjects on more than two injections per day increased from 1.3% to 46.8% but most of these were on three injections per day rather than true multiple daily injections. There was no association found between HbA_{1c} levels in DIABAUD 2 and DIABAUD 3. Thus there is no evidence that the best controlled children in DIABAUD 2 were the best controlled in DIABAUD 3 (or that the worst controlled stayed the worst controlled).

Summary: The SSGCDY, through the success of the DIABAUD project, have developed an infrastructure ideally suited to produce high quality data on the evaluation of the delivery of clinical care of Scottish children with T1D. DIABAUD 3 has demonstrated that for the majority of children and adolescents the main clinical outcome of glycaemic control is sub-optimal for the majority and disturbingly poor for a significant number. The situation failed to improve between 1997 and 2004.

A significant change from DIABAUD 2 to DIABAUD 3 in insulin therapy was the use of three insulin injections per day, by splitting the evening insulin dose. This clinical strategy, however, failed to have any impact on glycaemic control. The expected deterioration with age continued.

During the period of DIABAUD 3 the use of an intensive approach to insulin therapy by multiple dosing of insulin (MDI – 4 or more injections per day as a "basal bolus") or continuous subcutaneous insulin infusion (CSII – insulin pump therapy) was limited, despite the evidence in the literature that this clinical strategy, when employed by a multidisciplinary health team, together with a clinical support package is the most effective method of improving glycaemic control and thereby reducing the risk of long-term microvascular complications.

Conclusion: The challenge of improving glycaemic control remains for young people with T1D in Scotland and requires from their health professionals a significant change in strategy with an increased use of "intensive insulin regimens" combined with appropriate support package.

DIABAUD 3

GLYCAEMIC CONTROL IN CHILDREN AND ADOLESCENTS UNDER 15 YEARS OF AGE WITH TYPE 1 DIABETES IN SCOTLAND

1. Introduction

1.1. The Scottish Study Group for the Care of Diabetes in the Young (SSGCDY) is an organisation capable of delivering high quality information on the clinical care of children with Type 1 diabetes (T1D) in Scotland [1].

1.2. In 1998 the SSGCYD completed a national audit of the outcome of clinical care of young people with T1D - DIABAUD[2] – which was submitted to the Clinical Resource and Audit Group the following year. The audit was received with significant praise and the findings were published in Diabetes Care[2]. The findings of DIABAUD 2 were summarised as follows:

1.2.1. "The overall glycaemic control of diabetes in young people in Scotland was equivalent to an HbA1c of 9.1% in the DCCT. This placed the majority of children at a high risk of the long-term complications of diabetes in later adult life. A significant variation existed in the mean HbA1c seen in different centres throughout Scotland. Several factors were significantly associated with poor glycaemic control. However adjustment for these associations with glycaemic control did not explain the significant centre differences in attained average glycaemic control seen across the country. The SSGCYD suggested that factors not analysed in Diabaud2 (e.g. deployment of resources, organisation of the clinical structure, strategies of care, clinic philosophy) are the determinants that appear to influence glycaemic control in individuals. The group speculated that the style of utilisation of optimum resources is the key factor in achieving good glycaemic control."

1.3. The accepted international biochemical standard for the measurement of glycaemic control is glycosylated haemoglobin (HbA_{1c}) and longitudinal assessment is the best predictor of future morbidity[3]. Clinical Governance demands that providers of care should evaluate constantly their performance – if possible against recognised standards. Any attempt to do this with diabetes necessitates some method of comparison of glycaemic control in patient groups (clinics).

1.4. The SSGCDY register of T1D in the under 15 years age group is one of the best registers of its kind, complying with international guidelines[4]. Since its inception, the register has provided reliable incidence and prevalence data – confirming that Scotland has a high incidence with a 2% rise per annum of T1D. Its capture-recapture methodology enhances the basic system of notification, by clinicians, of new patients and ensures >98% ascertainment. The register provided the bedrock for DIABAUD 2 by ensuring that all eligible patients were targeted. Prior to DIABAUD 2 only two national studies (Denmark[5] and France[6]) had been performed using a central HbA_{1c}, standardised against DCCT [7]. Both studies, however, had an ascertainment rate of patients of below 70%. DIABAUD 2 achieved an ascertainment >94%.

1.5. SIGN Publication 55[8] is the first and major step towards the collection of clinically important data for the purposes of Clinical Governance of T1D in Scotland, recently supplemented by Guidelines for T1D in adults, children and adolescents by the National Institute for Clinical Excellence (NICE), Department of Health [9]. T1D care is a specialty where the clinical teams are agreed on the basic dataset that is supported, for the most part, by a sound evidence base. A Shared Care Dataset (for clinical, as opposed to epidemiological, use) has been approved. With the infrastructure already in place, a proven track record and a willingness and desire to lead the way in Scotland, the SSGCDY contracted with the NHSiS to deliver to the Commissioners of health care the minimum dataset on children with T1D in an aggregated and anonymised form. For children,

who generally have short duration diabetes, this will usually represent more of an audit of process than outcome.

1.6. DIABAUD 3 was, therefore, established as a follow on from DIABAUD 2 as a continuing national audit on the care and outcome of Type 1 diabetes (T1D) in Scotland.

1.7. It differed in content from DIABAUD 2 with additional information on natural history of T1D and the frequency of data collection from the patients (annually as against at every visit). The main outcomes assessed were glycaemic control, clinical episodes, use of service, insulin therapy and concomitant disease. The data set was designed using the recommendations and guidelines in practice from SIGN 55[8].

1.8. The audit and data set was agreed by the full membership of the Scottish Study Group for the Care of Diabetes in the Young (SSGCDY: Current Chairman Dr Donald Pearson; Secretary Dr Ken Robertson).

1.9. The methodology was based on DIABAUD 2: The national register based in Aberdeen (Coordinator Mrs Aileen Robertson; Curator Professor Norman Waugh) supplied up-to-date notification of patients. Using a unique SSGCDY number, records were transferred to the DIABAUD Office in Dundee and recorded anonymously. Individual centres were then notified on patients eligible for DIABAUD 3 and asked to perform the annual review and collection of information.

1.10. Central to the audit was the independent measure of glycaemic control (HbA_{1c}) measured in a central laboratory (Edinburgh, Dr Peter Rae).

1.11. DIABAUD 3 started in January 2002 and finished in March 2004.

1.12. The membership of the SSGCYD represents all NHS Health boards across Scotland and all were invited to participate in the National Audit

2. Aims and objectives

The aim of this audit project was to investigate glycaemic control in Scottish children and adolescents under 15 years of age and to assess whether it had improved since DIABAUD 2. DIABAUD 3 provided prospective data on the effectiveness of the clinical care strategies employed in the management of T1D in young people in Scotland. The information allowed each clinical centre to interpret their efforts against each other and against the recommendations of SIGN guidelines for the care of children and adolescents.

2.1. Prospectively obtain annually the minimum data set from each patient <15years age with T1D in Scotland.
2.2. To measure in a central laboratory on each patient an HbA_{1c} level, standardised against DCCT.
2.3. To assess the effectiveness of clinical management across Scotland against standards outlined by the SIGN data set and agreed by the SSGCDY
2.4. To report and delineate areas with inequality of process and outcome and consider measures to enhance the efficacy of care strategies.
2.5. To deliver the basic demographic, clinical and statistical information required to achieve Clinical Governance of Type 1 diabetes in the young.

3. Methodology

3.1. In this audit project two sets of data were analysed, DIABAUD 3 (D3) data and linked data from DIABAUD 2 (D2) and DIABAUD 3.

3.2. The data set was established and agreed by the SSGDCD in March 2002. Each centre was then visited by the DIABAUD 3 Co-ordinator (Ms Teresa Torrance) and the details of the audit explained and confirmed.

3.3. DIABAUD 3 Data:

3.3.1. This data set contained information on Scottish children and adolescents under 15 years of age with T1D. Data collection started in August 2002. All subjects who were under 15 years of age at the date of their clinic appointment were to be included in the study. Data were collected prospectively. Information was collected on the DIABAUD 3 Registration Form (***Appendix 1***), detailing:

date of birth; date of diagnosis; postcode; sex; ethnic origin; home structure; family history of diabetes; clinical characteristics; insulin regimen; height and weight.

3.3.2. Samples for HbA_{1c} were taken at the time of data collection and analysed locally and also sent to the Central laboratory in Edinburgh. The laboratory's variant analyser was traceable to the DCCT under the National Glycohaemoglobin Standardisation Program [3].

3.4. DIABAUD 3 Data Entry and Handling:

3.4.1. Data was entered on a paper copy and either transferred by post or electronically to the DIABAUD office at Dundee. This data was then transferred to the DIABAUD / SSGCYD Register office in Aberdeen, where it was anonymised and coded. All data was subject to the Data Protection Act and all patients signed an informed consent form at the base unit.

3.4.2. The data were validated against the SSGCYD Register to check on completeness of coverage and individual items of data, e.g. date of birth, date of diagnosis and sex. The SSGCYD Register conforms to quality control guidelines.

3.4.3. Subsequently HbA_{1c} results were received directly from a central laboratory in Edinburgh to Dundee and then linked to the data in Aberdeen

3.5. DIABAUD 3 Centre Selection:

3.5.1. All Scottish regions had been invited to take part. Subjects under 15 years of age were included. Centres with a recruitment rate of at least 80% were included.

3.6. DIABAUD 2 and DIABAUD 3 Linked Data:

3.6.1. This data set contained information on a cohort of subjects who participated in both DIABAUD 2 and DIABAUD 3 Audits. Not all of the subjects who participated in D2 took part in D3. Reasons for this include departure of those who had transferred to adult clinics and those who had been diagnosed since D2. It was beyond the scope of this study to follow-up all D2 subjects.

3.7. Statistical Analysis:

3.7.1. Analysis of the data was performed with SPSS Version 11.0 software.

3.7.2. Summary statistics are expressed as means (standard deviation).

3.7.3. Factors likely to be associated with glycaemic control were investigated by two-tailed independent t tests. Pearson correlation and two-tailed paired t tests were performed in the linked data analysis.

3.7.4. A p value of <0.05 was considered significant and 95% confidence intervals are stated. The main outcome measure was glycated haemoglobin (HbA_{1c}).

4. Results

4.1. DIABAUD 3

4.1.1. Participating Regions: Of the 15 Scottish Health Boards, 14 took part in DIABAUD3. Five were subsequently excluded because they failed to achieve a recruitment rate of 80% or over.

4.1.2. Subjects:

4.1.2.1. Patients who were 15 years of age or over were then excluded. This left a total of 1152 subjects in the present analysis. The total number of children diagnosed with T1D in the nine regions included was 1228. The characteristics of the 1152 subjects are given in **Table 1**.

Table 1			n	%
Total Subjects			1152	100.0
Sex				
Female			559	48.5
Male			593	51.5
Age	Female	Male	Total	
less than 5	33 (5.9%)	44 (7.4%)	77	6.7
5 to 9	174 (31.1%)	185 (31.2%)	359	31.2
10 to 14	352 (63%)	364 (61.4%)	716	62.2
Insulin Regimen				
1 per day			5	0.4
2 per day			587	51.0
3 per day			498	43.2
4 or more per day			27	2.3
Pump			4	0.3
Not Known			31	2.7
Family History	Female	Male	Total	
Mother	27 (4.8%)	16 (2.7%)	43	3.7
Father	42 (7.5%)	43 (7.3%)	85	7.4
Family Status				
Both Parents at Home			819	71.1
One Parent Family			191	16.6
Other			94	8.2
Not Known			48	4.2

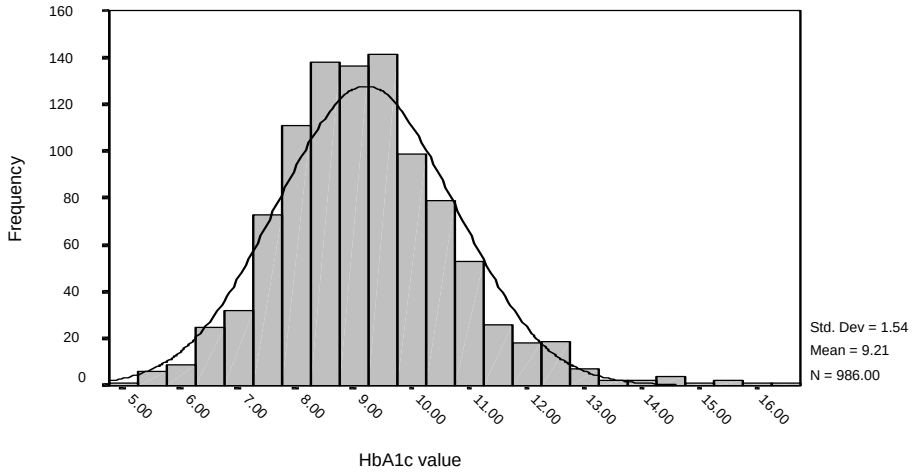
4.1.2.2. There were 559 (48.5%) females and 593 (51.5%) males. The average age of the subjects was 10.5 (SD 3.1), their ages ranging from 1.1 to 14.99. The majority of subjects (62.2%) were in the 10 to14 age group. Of all subjects, 51% were on two injections per day. Only 4 subjects were on insulin pumps. There were 43 (3.7%) subjects who had a mother with diabetes and 85 (7.4%) who had a father with diabetes. There were 191 subjects (16.6%) from one-parent families.

4.1.3. Glycaemic control (HbA_{1c}):

4.1.3.1. HbA_{1c} results were recorded for 986 subjects.

4.1.3.2. HbA_{1c} was normally distributed therefore means (SD) are quoted and parametric tests used. A histogram showing the distribution of HbA_{1c} results is shown in **Figure 1.** There were no outliers.

Figure 1 Distribution of HbA_{1c} Results



4.1.3.3. The overall mean HbA_{1c} was 9.2% (SD1.54). Among the 986 subjects, the lowest recorded HbA_{1c} was 5% and the highest 16.4%.

4.1.3.4. The HbA_{1c} results were grouped into bands. **Table 2** shows the bands of control for comparison with D2 giving the percentage of subjects in each group. A bar chart showing the numbers in each group is shown in **Figure 2**.

4.1.3.5. Mean HbA_{1c} was less than 7% in 5.5% of subjects, 7-8.9% in 41% of subjects, 9-10.9% in 42.2% of subjects and 11% and over in 11.4% of subjects. A comparison of HbA_{1c} results between D2 and D3 and given in **Figure 3**.

Table 2: Percentage of subjects in HbA_{1c} bands for comparison with D2

HbA_{1c} Band	Frequency	Percent
Under 7%	54	5.5
7 to 8.9%	404	41.0
9 to 10.9%	416	42.2
11% and over	112	11.4
Total	986	100.0

Figure 2: Number of subjects in HbA_{1c} bands for comparison with D2

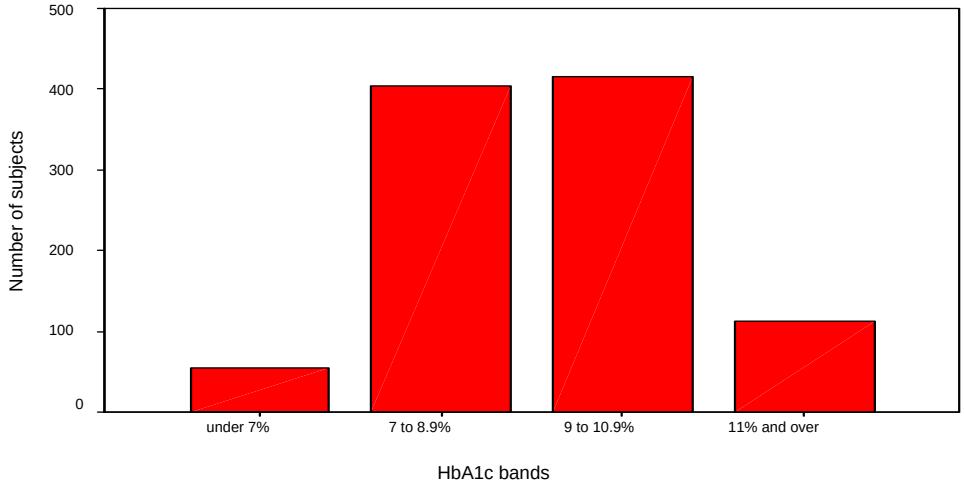
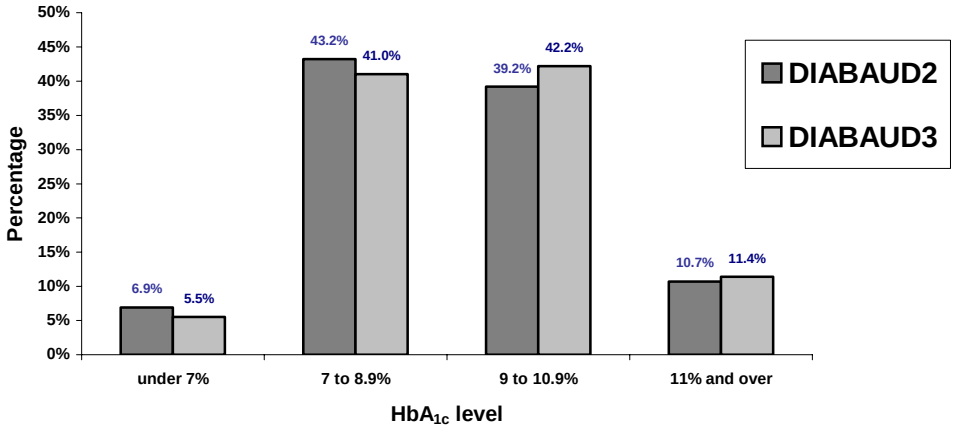


Figure 3: Comparison of HbA_{1c} Results between D2 and D3

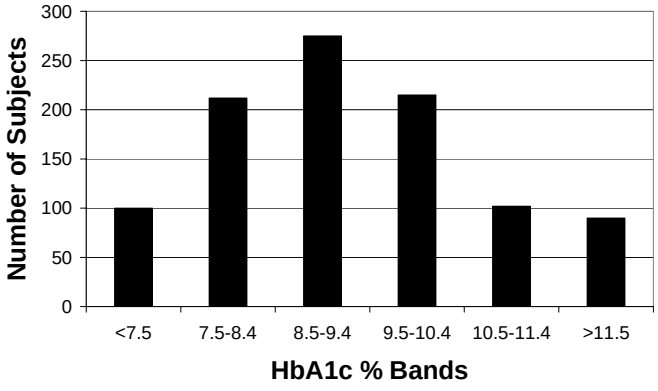


4.1.3.6. Bands of control were also established for comparison with target guidelines. Details are shown in **Table 3 and Figure 4**. Only 9.7% of subjects achieved the target of less than 7.5%.

Table 3: Percentage of subjects in HbA_{1c} bands for comparison with target guidelines

HbA_{1c} Band	Frequency	Percent
Under 7.5%	96	9.7
7.5 to 8.4%	216	21.9
8.5 to 9.4%	279	28.3
9.5 to 10.4%	219	22.2
10.5 to 11.4%	101	10.2
11.5% and over	75	7.6
Total	986	100.0

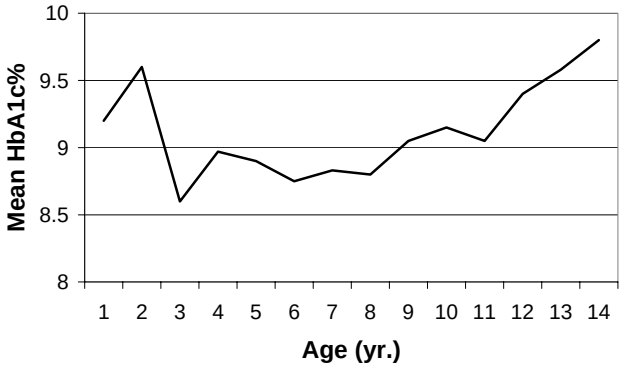
Figure 4: Number of subjects in HbA_{1c} Bands for Comparison with Target Guidelines



4.1.4. HbA_{1c} and Age

4.1.4.1. The mean age of the 986 subjects was 10.6 (SD 3.1), their ages ranging from 1.1 to 14.9. **Figure 5** shows HbA_{1c} levels by age. The lowest HbA_{1c} levels were recorded at age three and the highest at age 14. There is a steep rise in HbA_{1c} levels from age 11 onwards.

Figure 5 HbA_{1c} level by age



4.1.4.2. HbA_{1c} by age group: **Table 4** shows mean HbA_{1c} by age group. Subjects 10 years and over had a mean HbA_{1c} of 9.4% (SD 1.6) compared with all other ages 8.9%. To consider the difference in the means of the groups, after checking the assumptions of normality and constant variance, an independent two-sample t test was performed. As only 70 subjects were in the 0 to 4.9 age group, the remaining two groups were compared. The difference between the two means was 0.53%, 95% CI {0.31, 0.74}. Mean HbA_{1c} was significantly worse in the older child (p=0.00).

Table 4 Mean HbA_{1c} by age group

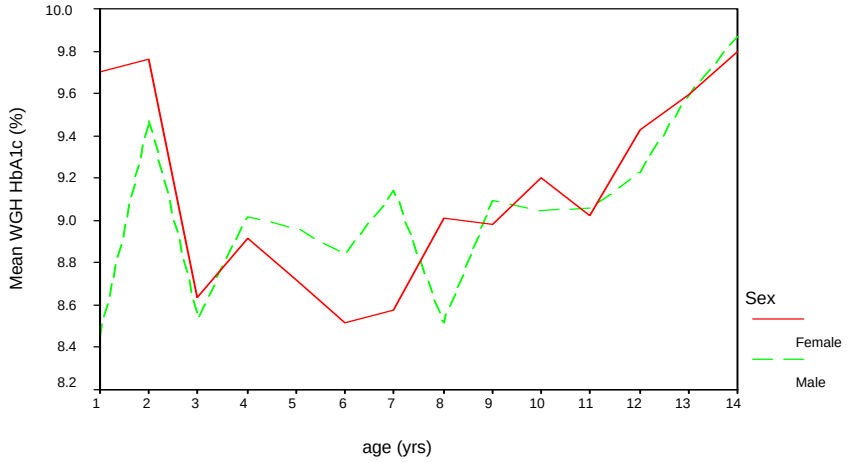
Age Group	n	Mean HbA_{1c} (%)	Std. Deviation (%)
0 to 4.9	70	8.9	1.31
5 to 9.9	302	8.9	1.40
10 to 14.9	614	9.4	1.60
Total	986	9.2	1.54

4.1.5. HbA_{1c} by sex

4.1.5.1. Of the 986 subjects, 478 were females and 508 males.

4.1.5.2. There was no difference in mean HbA_{1c} between sexes. The mean HbA_{1c} for females was 9.2% (SD 1.56) and for males, 9.2% (SD 1.51). **Figure 6** shows HbA_{1c} level by age giving a comparison between males and females.

Figure 6: HbA_{1c} level by age – comparison between males and females



4.1.6. HbA_{1c} and Insulin Regimen

4.1.6.1. The majority of subjects were on two or three injections per day.

4.1.6.2. Only five (0.51%) subjects were on one injection per day, 24 (2.4%) on four or more per day and only four (2.5%) on insulin pump. These groups were excluded from this analysis because they were too small to draw valid conclusions.

4.1.6.3. There was no significant difference in mean HbA_{1c} between those on two injections per day (9.1%) (SD 1.54) and three per day (9.3%) (SD 1.49) ($p = 0.15$). The difference between the two means was 0.15%, 95% CI {-0.34, 0.05}. **Table 5** details the number of subjects on different regimens and their associated mean HbA_{1c}.

Table 5: Insulin Regimens and mean HbA_{1c}

Insulin Regimen	n	Percent	Mean HbA_{1c} (%)	Std. Deviation (%)
1 per day	5	0.51	8.5	0.83
2 per day	488	49.49	9.1	1.54
3 per day	440	44.60	9.3	1.49
4 or more per day	24	2.40	9.3	1.54
Pump	4	2.50	8.3	0.92
Not Known	25	0.40	9.7	2.20
Total	986	100.0	9.2	1.54

4.1.7. HbA_{1c} and family history

4.1.7.1. Of the 986 subjects, 37 had a mother with a history of diabetes and 68 had a father with a history of diabetes. No association was found between HbA_{1c} and family history of diabetes in mothers or fathers. Subjects who had a mother with a history of diabetes had a mean HbA_{1c} of 9.2% (SD 1.48), a father with a history of diabetes 9.2% (SD1.8) and no family history, 9.2% (SD 1.5).

4.1.8. HbA_{1c} and family status

4.1.8.1. Of the 986 subjects, 731 (74%) lived with both parents, while 164 (16.7%) were from one-parent families. Subjects living with both parents had a mean HbA_{1c} of 9.1% (SD 1.49). Subjects from one-parent families had a mean HbA_{1c} of 9.3% (SD 1.65). No significant difference in mean HbA_{1c} was found between these two groups ($p = 0.095$). The difference between the two means was 0.22%, 95% CI {-0.48, 0.34}.

4.2. DIABAUD 2 and DIABAUD 3 LINKED DATA

4.2.1. Subjects: This data set contained information on a cohort of 549 subjects who participated in both D2 and D3. HbA_{1c} results were missing for 83 subjects in the linked cohort. These subjects were excluded which left a total of 466 in the cohort who participated in D2 and D3.

4.2.2. The characteristics of the 466 subjects are given in **Table 6**.

Table 6: Characteristics of 466 subjects participating in D2 and D3

	n	%	n	%
Total	466	100.0		
Sex				
Female	226	48.5		
Male	240	51.5		
Age yr	D2		D3	
Mean Age	7.3 (SD 2.3)		11.9 (SD 2.3)	
Min / Max Age	0.9 / 12.4		5.1/ 16.8	
Insulin Regimen	D2 n	%	D3 n	%
1 per day	14	3.0	1	0.2
2 per day	445	95.7	230	51.2
3 per day	3	0.6	196	43.7
4 or more per day	3	0.6	22	4.9
Pump	Unknown		0	
Not Known	1		17	
Mean HbA_{1c}	8.6%(SD 1.23%)		9.6%(SD .6%)	

4.2.3. There were 226 (48.5%) females and 240 (51.5%) males. The average age of the subjects was 7.3 (SD 2.3) years at D2 and 11.9 (SD 2.3) at D3.

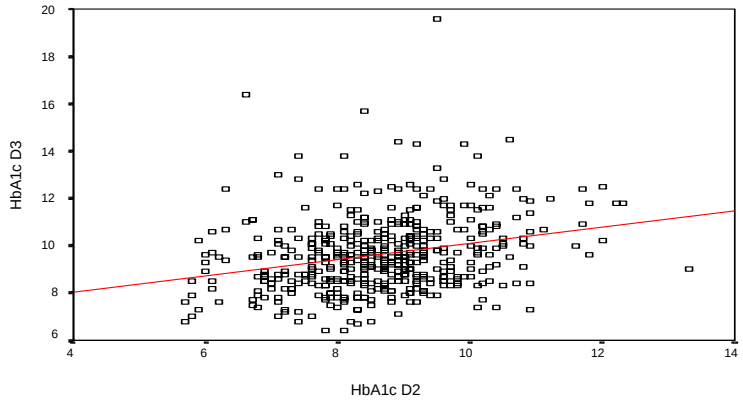
4.2.3.1. The majority of subjects (95.7%) were on two injections per day in D2 with only 0.6% on three injections per day. Percentage of subjects on two injections per day in D3 was 51.2%, while 43.7% were on three injections per day in D3.

4.2.4. The number of subjects on four or more injections rose from 3 (0.6%) in D2 to 22 (4.9%) in D3. There were no subjects on insulin pumps. The mean HbA_{1c} was 8.6% (SD 1.23) in D2 and 9.6% (SD 1.6) in D3. This rise is as expected with age (see **Figure 5**). Despite the marked increase in the proportion of subjects on three injections per day, there was no improvement in HbA_{1c}.

4.2.5. The differences in HbA_{1c} levels between D2 and D3 were normally distributed. To consider average difference between the observations for each individual and the variability of these differences, a paired t test was performed. The mean difference was 0.98%, 95% CI={0.82, 1.13} (p=0.00). There was a significant difference in mean HbA_{1c} levels between D2 and D3.

4.2.6. A scatter plot is shown in **Figure 7** showing the degree of association between D2 and D3 HbA_{1c} levels. Linear regression was performed. Pearson correlation was calculated as r = 0.26 (p=0.00). For absolute values of r, 0.2 – 0.39 is regarded as weak (41). This shows a weak association between D2 and D3 HbA_{1c} levels. Adjusted R^2 gave a value of 0.067, therefore the relationship between D2 and D3 explains only a small percentage, 7% of the variation in D3 HbA_{1c}.

Figure 7: Scatter plot showing relationship between D2 HbA_{1c} and D3 HbA_{1c}



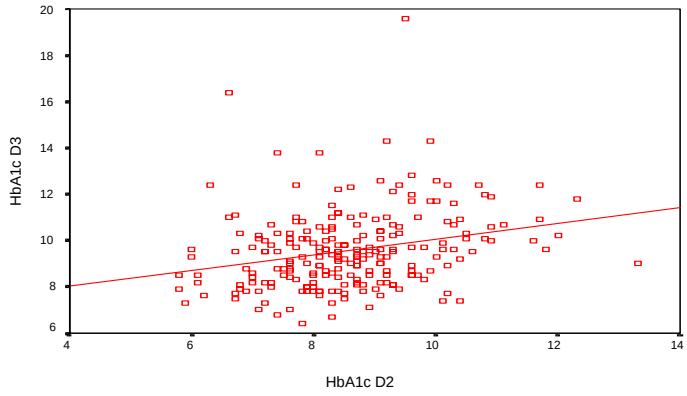
4.2.7. These results show little evidence of "tracking" whereby those with the lowest HbA_{1c} levels in D2 might have been expected to have the lowest levels in D3.

4.2.8. Insulin Regimen:

4.2.8.1. The groups of subjects on one or four or more injections a day were excluded from this analysis because they were too small to draw valid conclusions. The number of subjects on two injections a day in D2 was 445. Of these subjects, 224 were on two injections a day in D3 and 187 were on three injections per day.

4.2.8.2. A scatter plot is shown in **Figure 8** showing the degree of association between D2 and D3 HbA_{1c} levels in these subjects (r = 0.257; p=0.00). Adjusted R^2 gave a value of 0.062, therefore the relationship between D2 and D3 explains only 6% of the variation in D3 HbA_{1c} in this group.

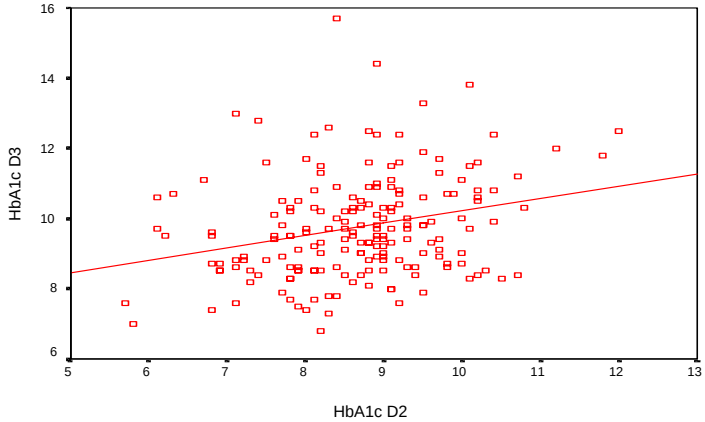
Figure 8 Scatter plot showing relationship between D2 HbA_{1c} and D3 HbA_{1c} in subjects who were on 2 injections per day in D2 and D3



4.2.9. To consider average difference between the observations for each individual and the variability of these differences, a paired t test was performed. The mean difference was 1%, 95% CI={0.76, 1.24} (p=0.00). There was a significant difference in mean HbA_{1c} levels between D2 and D3 in this group of subjects. The mean HbA_{1c} value in D2 was 8.6% (SD 1.3) and in D3 9.6% (SD 1.7).

4.2.10. Subjects on 2 injections per day in D2 and 3 injections per day in D3: A scatter plot is shown in **Figure 9** showing the degree of association between D2 and D3 HbA_{1c} levels in these subjects (r = 0.267; p=0.00). This shows a weak association between D2 and D3 HbA_{1c} levels. Adjusted R^2 gave a value of 0.067, therefore the relationship between D2 and D3 explains only 7% of the variation in D3 HbA_{1c} in this group

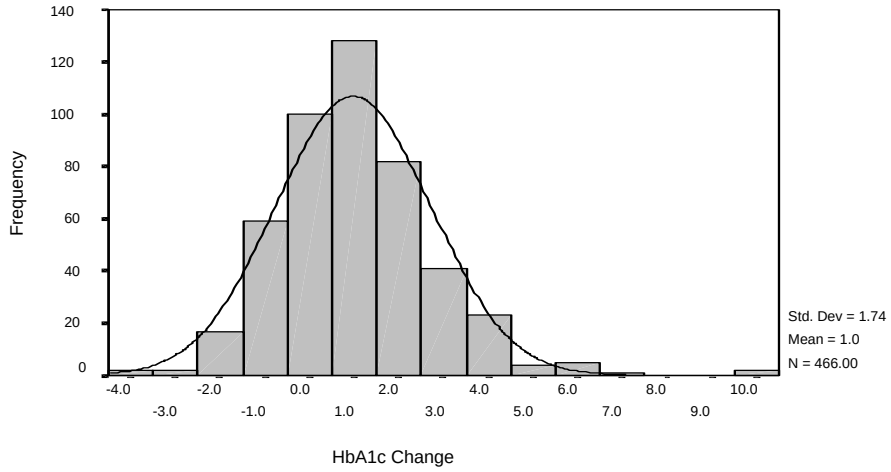
Figure 9: Scatter plot showing relationship between D2 HbA_{1c} and D3 HbA_{1c} in subjects who were on 2 injections per day in D2 and 3 injections per day in D3



4.2.11. To consider average difference between the observations for each individual and the variability of these differences, a paired t test was performed. The mean difference was 1.076%, 95% CI={0.85, 1.30} (p=0.00). There was a significant difference in mean HbA_{1c} levels between D2 and D3 in this group of subjects. The mean HbA_{1c} value in D2 was 8.7% (SD 1.1) and in D3 9.7% (SD 1.46).

4.2.12. Change in HbA_{1c} levels: **Figure 10** shows that the differences in HbA_{1c} levels between D2 and D3 are normally distributed. Overall, the mean change was 1% (SD 1.74). In 27.9% of subjects, HbA_{1c} reduced. There was no change in HbA_{1c} in 1.9% of subjects. In 70.2%, HbA_{1c} increased.

Figure 10 Distribution of HbA_{1c} change between D2 and D3



4.2.13. In the group of subjects who were on two injections per day in both D2 and D3, HbA_{1c} in 29.5% of subjects reduced, in 1.3% of subjects there was no change and in 69.2% HbA_{1c} increased. In the group of subjects who were on two injections per day in D2 and three injections per day in D3, HbA_{1c} in 21.9% of subjects reduced, in 2.7% of subjects there was no change and in 75.4% HbA_{1c} increased.

4.3. COMPARISON OF GLYCAEMIC CONTROL BETWEEN DIABAUD 2 AND DIABAUD 3

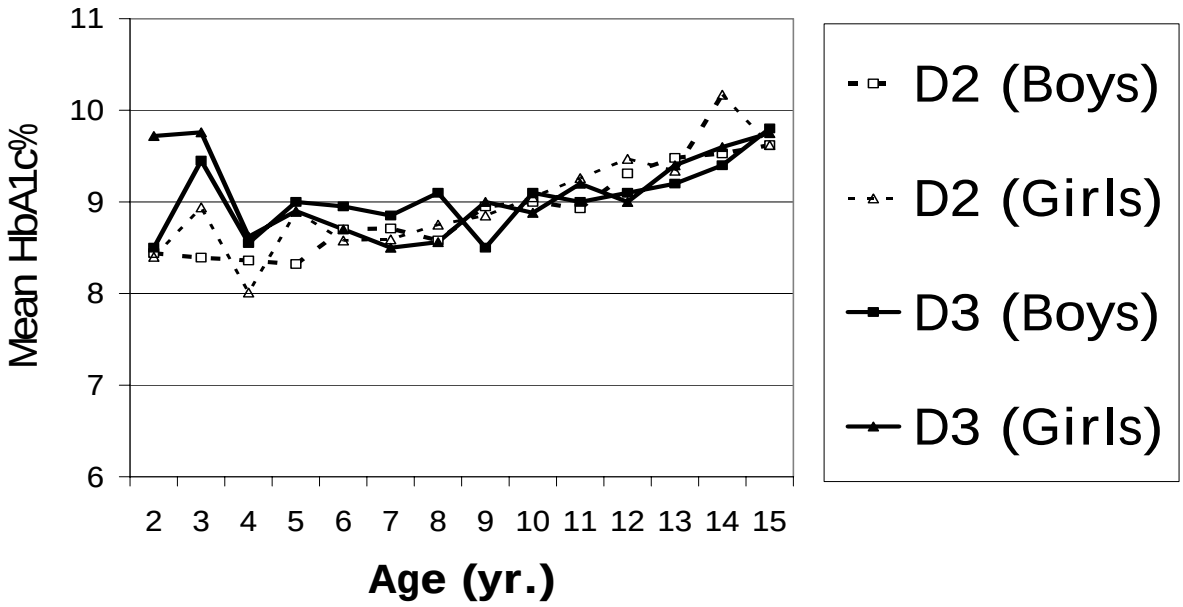
4.3.1. e pattern of distribution of glycaemic control across Scotland comparing DIABAUD 2 (D2 -1997 to 1998) and DIABAUD 3 (D3 – 2002 to 2004) is shown in **Figure 11**.

4.3.2. In both studies glycaemic control was significantly worse in the older child in both studies:

- (DIABAUD 2 mean HbA_{1c} (%) age range 10 to 15 yr 9.5% v. all other ages 8.6%:
- DIABAUD 3 mean HbA_{1c} (%) age range 10 to 15 yr 9.4% v. all other ages 8.9%) $p<0.001$.

4.3.3. No significant differences between boys and girls.

Figure 11: Rise in Hba1c with age (<15yr.) with Type 1 Diabetes in Diabaud 2 (D2) and Diabaud 3 (D3) studies



Glycaemic control was significantly worse in the older child in both studies: (D2 mean HbA1c (%) age range 10 to 15 yr 9.5% v. all other ages 8.6%: D3 mean HbA1c (%) age range 10 to 15 yr 9.4% v. all other ages 8.9%) p<0.001. No significant differences between boys and girls

4.3.4. The comparison of the continuous variables by regression analysis in both D2 and D3 are given in **Table 7**. In both D2 and D3 cohorts HbA1c rose with age. After adjustment for other variables in the combined datasets, insulin regimen was not a significant predictor of HbA1c (F=0.19, df=3, 1774; p=0.90). Clearly much of the 0.22% worsening in HbA1c can be explained by differences between other variables.

Table 7: Comparison of D2 v D3 continuous variables

	D2			D3						
	n	Mean	SD	n	Mean	SD	p	Mean diff	95% CI	
Age of Subjects	1147	10.02	3.25	1152	10.54	3.11	0.000	0.52	0.26	0.78
Duration of Diabetes	1147	3.65	3.09	1151	4.1	3.03	0.000	0.45	0.20	0.70
Height SDS	1145	0.19	1.05	1136	0.26	1.28	0.125	0.08	-0.02	0.17
Weight SDS	1146	0.54	0.94	1138	0.75	1.06	0.000	0.21	0.13	0.30
BMI SDS	1145	0.61	0.92	1133	0.86	1.12	0.000	0.24	0.16	0.33
Dose on entry to clinic	1146	32.9	20.3	1133	42.7	27.33	0.000	9.8	7.8	11.8
Dose per kg	1146	0.83	0.30	1126	0.97	0.38	0.00	0.14	0.11	0.17
HbA_{1c}%	1147	8.99	1.51	986	9.21	1.54	0.001	0.22	0.09	0.35

Adjusted for	D2 / D3 n / n	Difference in mean HbA_{1c} D3-D2 (95%CI)	p
-	1147, 986	0.22 (0.09, 0.35)	0.001
Age, Duration	1147, 985	0.14 (0.02, 0.27)	0.03
Age, Duration, Region,	1147, 985	0.14 (0.02, 0.27)	0.03
Age, Duration, Region, Pubertal status	974, 847	0.08 (-0.05, 0.22)	0.23
Age, Duration, Region, Pubertal status, BMI SDS	972, 839	0.11 (-0.03, 0.24)	0.13
Age, Duration, Region, Pubertal status, BMI SDS, Dose/kg	972, 832	0.04 (-0.10,0.17)	0.62
Age, Duration, Region, Pubertal status, BMI SDS, Dose/kg, Insulin regimen	972, 820	0.03 (-0.14, 0.19)	0.77

5. Summary of Results

5.1. DIABAUD 3 confirmed that glycaemic control remains unsatisfactory in children and adolescents with a high percentage of subjects falling outside the targets described in accepted guidelines placing the majority at a high future risk of diabetic complications.

5.2. The overall mean HbA_{1c} was 9.2% (SD 1.54)

5.3. Only 9.7% of subjects achieved the NICE recommended target of an HbA_{1c} equal to or than 7.5%.

5.4. HbA_{1c} and Age: Subjects 10 years and over had a mean HbA_{1c} of 9.5% (SD 1.6) compared with all other ages 8.9%. The finding that HbA_{1c} increases with age and is significantly worse during adolescence is well supported by the vast majority of previous studies[6, 7, 10].

5.5. HbA_{1c} and sex: The results of this study found no association between HbA_{1c} and sex, which is consistent with previous studies[6, 7, 10]. The mean HbA_{1c} was 9.2% for both males and females. **Figure 6** shows that age-related HbA_{1c} levels are similar for males and females. However, caution should be exercised when interpreting this figure, as there were low numbers of subjects at each age, ranging from 2 to 85 subjects.

5.6. HbA_{1c} and Insulin regimen: While the majority of subjects were on two injections per day (51%), there had been a significant increase in patients treated with three injections per day (split evening dose) in DIABAUD 3 compared with DIABAUD 2 (D3, 43% versus D2, 2%). In DIABAUD 2, 94% of subjects were on two injections per day. Less than 10% of patients in DIABAUD 3 were on multiple insulin therapy (MDI- i.e. 4 or more injections per day). There was no significant association found between HbA_{1c} and number of injections per day consistent with other reports[10].

5.7. Only four (2.5%) subjects were recorded as using an insulin pump.

5.8. HbA_{1c} and family history: No association was found between HbA_{1c} and family history of diabetes in mothers or fathers. This is at odds with DIABAUD 2 which reported that a family history of T1D was associated with significantly poorer glycaemic control, but only when there was a sibling with diabetes. However, these results may not be comparable since in DIABAUD 3 subjects with a family history of other types of diabetes were included.

5.9. HbA_{1c} and family status: No significant difference was found in HbA_{1c} levels between subjects living with one or both parents. This finding is not consistent with other studies. DIABAUD 2 reported that the absence of one or both parents was associated with poor control. The present analysis, however, only compared two-parent families with one-parent families.

5.10. Linkage of individual patients participating in DIABAUD 2 and 3.

5.10.1. Mean HbA_{1c} was significantly higher in patients audited in both studies: D2, 8.6% (SD 1.23), D3, 9.6% (SD 1.6). This result was expected because of the known deterioration in HbA_{1c} with age. In 70.2% of subjects HbA_{1c} increased. The numbers of subjects on more than two injections per day increased from 1.3% to 46.8% but most of these were on three injections per day rather than true multiple daily injections.

5.10.2. No improvement in HbA_{1c} was observed in the group who were on two injections per day in D2 and three injections per day in D3 (9.7%) compared to those who stayed on two injections per day (9.6%).

5.10.3. There was little association found between HbA_{1c} levels in DIABAUD 2 and DIABAUD 3. Thus there is no evidence that the best controlled children in DIABAUD 2 were the best controlled in DIABAUD 3 (or that the worst controlled stayed the worst controlled).

6. Strengths and limitations of study

6.1. DIABAUD 3 (like DIABAUD 2) was a population-based survey increasing the chance that the findings obtained are representative of children and adolescents with T1D in the population as a whole.

6.2. The data were checked and validated by the SSG Register to ensure accuracy.

6.3. All blood samples were sent to a central laboratory which removed variations in results due to different analytical techniques of measuring HbA_{1c}.

6.4. Both projects are descriptive studies, which are able to describe the phenomenon of interest and observed associations, but which cannot provide robust evidence about cause and effect relationships. For example, the finding in DIABAUD2 that subjects on three injections per day had better control does not prove that three injections per day give better control. Confounding factors may have distorted the results.

6.5. DIABAUD 3 aimed at comprehensive recruitment of all children and adolescents less than 15 years age in Scotland. In practice, however, it would generally not be possible to achieve 100% recruitment for a number of reasons: patients move home; some miss appointments or do not attend regularly; there may be problems in obtaining blood samples; when several centres are involved in a study, there is more complex administration and more staff involved; some staff may not know details of the study; there were changes in consultant staffing in several areas; patients not included in the study may be unrepresentative in some way.

6.6. In this study, centres with at least 80% recruitment were included in order to minimise bias, based on the criteria set by The Journal of Evidence-Based Medicine [11]. This still leaves 20% of the population who have not participated and who may differ in some important way from participants and thus results may be biased.

6.7. In the present study a response rate of 93% (1152 out of 1228) was achieved for the nine regions included. It seems likely that the results were representative of those nine regions and that the regions included were representative of Scotland as a whole.

6.8. Several centres had technical and resource difficulties in completing a sufficient return for inclusion in the analysis. Informal discussions with these centres suggest that a major problem for these groups was in the availability of dedicated staff for blood sampling and completion of the documentation. The study also coincided with a major change in several centres of senior personnel, responsible for the service in their locality.

7. Conclusion

7.1. The Scottish Study Group for the Care of Diabetes in the Young (SSGCDY), through the success of the DIABAUD project, have developed an infrastructure ideally suited to high quality data on the evaluation of the delivery of clinical care of Scottish children with Type 1 diabetes mellitus.

7.2. The DIABAUD Project has demonstrated that for the majority of children and adolescents the main clinical outcome of glycaemic control is sub-optimal for the majority and disturbingly poor for a significant number. The situation failed to improve between 1997 and 2004.

7.3. A significant change from DIABAUD 2 to DIABAUD 3 in insulin therapy is the use of three insulin injections per day, by splitting the evening insulin dose. This clinical strategy, however, failed to have any impact on glycaemic control. The expected deterioration with age continued.

7.4. The use of an intensive approach to insulin therapy by multiple dosing of insulin (MDI – 4 or more injections per day as a "basal bolus") or continuous subcutaneous insulin infusion (CSII – insulin pump therapy) currently is very limited in Scotland, despite the evidence in the literature that this clinical strategy, when employed by a multidisciplinary health team together with a clinical support package, is the most effective method of improving glycaemic control and thereby reducing the risk of long-term microvascular complications [8, 9].

7.5. The challenge of improving glycaemic control remains for young people with T1D in Scotland and requires from their health professionals a significant change in strategy with an increased use of "intensive insulin regimens" combined with appropriate support package.

8. Action(s) Required/Recommendations For The Future

8.1. The SSGCYD should continue to contract with NHS Quality Improvement Scotland to produce a regular report (every 3-4 years) on the management and outcome of young people with T1D, based on a central laboratory evaluation of glycaemic control together with first class epidemiological and demographic information.

8.2. Findings from future evaluations will continue to support the clinical governance of diabetes in the young, with the aim of eradicating any inequalities of outcome of care seen across the country, together with optimising the clinical outcome of these young people, who continue to have an unacceptable risk of early morbidity and mortality.

8.3. NHS Boards should review the local implementation of "intensive insulin therapy" in appropriate patients with T1D, and encourage a major effort to improve the main clinical outcome of glycaemic control by the use of multiple daily insulin therapy or insulin pump therapy.

8.4. The DIABAUD project supported and organised by the members of the SSGCYD should be considered as a foundation of a managed clinical network for Type 1 diabetes in the young in Scotland.

9. Dissemination

THE DIABAUD 3 report will be circulated to the following organisations:

- The Membership of the SSGCYD
- The Scottish Diabetes Committee
- Chairman of Diabetes Advisory Committees
- Diabetes UK, Scotland
- Juvenile Diabetes Research Foundation, Scotland

Several Scientific Papers are under construction from the report.

Presentations of the results will be made in local, national and international arenas.
E.g. SSGCDY bi-annual meetings; Diabetes UK Annual Scientific Meetings; Royal College of Paediatrics and Child Health Spring Meeting; International Society of Paediatric and Adolescent Diabetes.

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