

Research Article

A Retrospective Study in 5,989 Patients with Type 1 Diabetes in 10 Outpatient Diabetes Clinics in Sweden of the Frequency of Measuring HbA1c in Clinical Practice

Viktorija Matuleviciene^{1,2}, Stig Attvall^{2,3}, Magnus Ekelund⁴, Mark Clements⁵, Sofia Dahlqvist¹, Martin Fahlén⁶, Aldina Pivodic⁷, Börje Haraldsson⁸ and Marcus Lind^{1,2*}

¹Department of Medicine, NU-Hospital Organization, Sweden

²Department of Molecular and Clinical Medicine, University of Gothenburg, Sweden

³Department of Medicine, Sahlgrenska University Hospital, Sweden

⁴Department of Medicine, Helsingborg Hospital, Helsingborg, Sweden

⁵Children's Mercy Hospital, Kansas City, USA

⁶Department of Medicine, Kungälvs Hospital, Kungälv, Sweden

⁷Statistiska Konsult gruppen, Gothenburg, Sweden

⁸Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

*Corresponding author: Marcus Lind, Department of Medicine NU-Hospital Organization and Department of Molecular and Clinical medicine, University of Gothenburg, Gothenburg, 451 80 Uddevalla, Sweden, Tel: +46 (0) 10 435 00 00; Fax: +46 (0) 10 435 71 66; E-mail: lind.marcus@telia.com

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Abstract

Aim: Guidelines for the treatment of type 1 diabetes generally recommend quarterly or more frequent Haemoglobin A1c (HbA1c) assessment in patients with inadequate glycaemic control. The purpose of the current study was to evaluate to what extent these guidelines are followed in clinical practice in Sweden.

Method: We studied 5989 patients with type 1 diabetes from 10 outpatient diabetes clinics in Sweden from 1 January 2005 to 31 December 2009. Data on HbA1c measurement frequency were obtained from the Diab-Base electronic medical records database, where HbA1c measurements are recorded together with other patient characteristics, including treatment and other general risk factors for diabetic complications. The frequency of HbA1c measurements was obtained for all patients by calendar year, care unit, and during time periods where glucose was classified as well controlled (HbA1c<=7.0%) or inadequate (HbA1c 7.0% or higher).

Results: The mean annual number of HbA1c assessments when glucose control was inadequate was 1.83 compared with 1.58 during well controlled time-periods. In 35.4% of cases the next HbA1c check following an HbA1c >7% was performed within 4 months. The probability of a subsequent assessment in the 4 months following an HbA1c value>7.0% increase in patients treated with continuous subcutaneous insulin infusion (CSII), OR=1.57 (1.46-1.69). Differences were also noted by care unit, age, gender, glycaemic control, calendar year, and weight and diabetes duration.

Conclusion: In patients with type 1 diabetes, HbA1c is measured less frequently in clinical practice in Sweden than guidelines recommend, although patients with CSII and treated in certain care units receive more frequent assessments.

Keywords: Type 1 diabetes mellitus; HbA1c; Diabetic complications; Insulin pump; Availability; Diabetes care

Background

Diabetes mellitus remains a growing public health problem. There are approximately 385 million people worldwide with diabetes (types 1 and 2), and the prevalence is predicted to rise to 500 million by 2030 [1]. The prevalence of type 1 diabetes mellitus is highest in Scandinavian countries and has increased in several countries during the last decades [2-4]. The costs associated with diabetes account for more than 10% of the entire European health budget, with diabetes complications accounting for a major part of these costs [5,6].

Good glycaemic control is crucial in preventing complications in patients with type 1 diabetes [7,8]. Recommended therapy for obtaining good glycaemic control is intensive therapy including multiple daily doses of insulin, frequent blood glucose measurements, and regular Glycosylated Haemoglobin (HbA1c) monitoring [7,9-12]. Currently, less than 20% of adult type 1 diabetic patients in Sweden achieve good glycaemic control (<7.0%), and around 25% have very poor glycaemic control (<8.6% [13]), as poor as when patients in studies have received only basal insulin once or twice a day without any prandial insulin [7]. In Sweden, patients with type 1 diabetes have free access to novel insulin analogues, self-measurement of blood glucose (glucose-monitoring strips and meters), HbA1c tests, while insulin pumps are reimbursed when glycaemic control is inadequate.

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Since many patients with type 1 diabetes in Sweden have poor glycaemic control, despite the widespread availability of novel treatment strategies, it is possible that barriers exist achieving adherence with blood glucose measurements, achieving proper insulin dosing, or providing basic diabetes care.

To support the intensive treatment strategy, diabetes guidelines generally recommend visits to a diabetes educator or physician with HbA1c monitoring performed at least every third month in patients with inadequate glycaemic control [9-12]. To our knowledge there are few studies examining adherence to these guidelines in clinical practice. Therefore, we examined the frequency of visits to 10 outpatient diabetes clinics in Sweden that included HbA1c checks over a 5-year period and evaluated potential explanatory factors for more frequent glycaemic monitoring.

Methods

Data source

Data were obtained from an electronic medical records system (Diab-Base, Journalia AB, Sweden), which is used at 10 hospital-based diabetes clinics that treat adult outpatients (18 years or older) in Sweden [14]). Most clinics in Sweden have used Diab-Base since around the year 2000. The system has been described in detail and has been used in several studies of diabetes treatments among patients with both types 1 and 2 diabetes [14-18]. Briefly, the system includes information about risk factors, treatment, and complications that are recorded during clinical visits. All risk factor measurements, such as HbA1c, blood pressure, blood lipids, body mass index (BMI), type of diabetes, and insulin dose, are tracked electronically. In addition, type of insulin delivery, either continuous subcutaneous insulin infusion (CSII) or Multiple Daily Injections (MDI) can be tracked electronically, as along with information on diabetic complications.

Current cohort and data analysis

The current cohort included patients with type 1 diabetes studied from 1 January 2005 to 31 December 2009. The frequency of HbA1c measurements was assessed for all patients, as well as by calender year, diabetes outpatient clinic (also further on denoted care unit), and period of time when patients achieved good (HbA1c \leq 7.0%) and inadequate glycemic control (HbA1c>7.0%). Potential predictors for receiving a subsequent HbA1c check within 4 and 7 months after an HbA1c value >7.0% were examined, including age, sex, type of insulin delivery (MDII or CSII), diabetes duration, HbA1c level, weight, BMI, insulin dose (U/kg), and care unit.

Statistics

The mean number of HbA1c checks for the entire cohort was calculated as the mean value resulting from the annual means of all HbA1c checks for each individual patient. The mean number of HbA1c checks during periods with an HbA1c>7.0% was calculated with the corresponding methodology during the periods of time when an HbA1c>7.0% was identified until a subsequent check identified a novel value \leq 7.0%. The corresponding methodology was similarly used to estimate the mean number of HbA1c checks during patient periods with HbA1c \leq 7.0%.

To predict the likelihood of having an HbA1c check in 4 and 7 months following an HbA1c>7.0% at any time during the study,

Generalized Estimating Equations (GEE) models with a compound symmetry covariance matrix were used to allow for adjustment of within-individual correlations [19]. Univariate GEE models were used to identify the statistically significant predictors that affected the outcome.

Stepwise logistic regression was used for selection of independent predictors that were statistically significant. Once variables were selected, the GEE models were performed including the selected variables to obtain the adjusted odds-ratios (OR), 95% Confidence Intervals (CI) and associated p-values. Imputation of missing weight, BMI, and insulin doses was performed by using last observation carried forward. All tests were two-tailed and conducted at the 0.05 significance level.

Results

In total, there were 5,989 patients with type 1 diabetes evaluated. Patient characteristics for the whole cohort at first visit during the years 2005 to 2009 as well as in relation to the number of annual HbA1c measurements are presented in Table 1a. Distribution of mean number of annual HbA1c measurements by care unit is given in Table 1b.

	Total	<1	1-<2	2-<3	3-<4	>=4
	(n=5989)	(n=569)	(n=2894)	(n=2050)	(n=371)	(n=105)
Age (years)	42.9 (16.1)	42.6 (16.7)	43.2 (16.0)	44.0 (16.0)	37.4 (14.9)	37.4 (15.3) 34.9 (16.1:
	41.7 (16.0; 89.5) n=5989	39.7 (17.3; 87.1) n=569	41.7 (16.2; 85.3) n=2894	44.1 (16.2; 89.5) n=2050	35.7 (16.0; 79.4) n=371	78.4) n=105
Sex						
Male	3327 (55.6%)	350 (61.5%)	1663 (57.5%)	1082 (52.8%)	179 (48.2%)	53 (50.5%)
Female	2662 (44.4%)	219 (38.5%)	1231 (42.5%)	968 (47.2%)	192 (51.8%)	52 (49.5%)
CSII						
No	4724 (78.9%)	506 (88.9%)	2423 (83.7%)	1506 (73.5%)	223 (60.1%)	66 (62.9%)
Yes	1265 (21.1%)	63 (11.1%)	471 (16.3%)	544 (26.5%)	148 (39.9%)	39 (37.1%)
Diabetes duration (years)	20.9 (14.8)	21.9 (14.7)	21.1 (14.6)	21.5 (15.1)	15.9 (14.2)	15.8 (15.0) 14.3 (-0.0:
	19.1 (-0.9; 78.4) n=5636	20.4 (-0.0; 68.7) n=502	19.1 (-0.9; 78.4) n=2719	20.2 (-0.9; 69.1) n=1960	13.6 (-0.2; 59.1) n=358	55.2) n=97
BMI (kg/m ²)*	25.3 (12.1) 25.0 (14.0; 806.0)	25.0 (4.0) 24.0 (16.0; 43.0)	25.3 (16.7) 25.0 (14.0; 806.0)	25.2 (3.9) 25.0 (15.0; 42.0) n=1615	25.1 (4.1) 24.0 (15.0; 42.0)	26.3 (5.4) 26.0 (17.0; 46.0) n=55

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	n=4643	n=428	n=2292		n=253	
Weight (kg)*	75.7 (14.1) 74.6 (32.0; 150.0) n=4979	76.3 (15.0) 75.0 (41.5; 148.8) n=458	75.7 (14.1) 74.5 (32.0; 150.0) n=2444	75.6 (13.8) 74.7 (43.6; 140.1) n=1731	74.3 (14.2) 74.0 (44.4; 132.0) n=280	77.1 (18.0) 75.2 (47.3; 123.0) n=66
Insulin dose (unit/kg)*	0.63 (0.26) 0.60 (0.00; 5.80) n=4762	0.66 (0.28) 0.60 (0.00; 2.40) n=433	0.62 (0.25) 0.60 (0.00; 5.80) n=2343	0.63 (0.25) 0.60 (0.00; 3.90) n=1674	0.64 (0.31) 0.60 (0.00; 3.40) n=257	0.74 (0.31) 0.70 (0.30; 1.70) n=55

For categorical variables n (%) is presented.

For continuous variables Mean (SD) / Median / (Min; Max) / n= is presented.

* Missing values are imputed by using last observation carry forward (LOCF) in case patient existed in DiabBase before 2005.

Table 1a: Patient characteristics at first visit during years 2005 and 2009 in DiabBase in total and in relation to the number of mean number of annual HbA1c measurements performed during same period.

	<1 (n=569)	1-<2 (n=2894)	2-<3 (n=2050)	3-<4 (n=371)	>=4 (n=105)
Unit 1	6.1%	35.6%	53.8%	4.2%	0.4%
Unit 2	16.3%	58.4%	16.9%	5.6%	2.8%
Unit 3	12.2%	54.2%	29.1%	3.7%	0.8%
Unit 4	3.8%	36.0%	48.0%	9.0%	3.2%
Unit 5	7.5%	58.7%	31.5%	2.4%	0.0%
Unit 6	10.9%	56.0%	26.2%	5.0%	1.9%
Unit 7	5.6%	30.0%	52.3%	10.9%	1.2%
Unit 8	12.2%	56.5%	26.4%	3.8%	1.1%
Unit 9	7.6%	53.2%	32.5%	6.1%	0.6%
Unit 10	3.3%	20.9%	39.6%	22.5%	13.7%

Table 1b: Distribution of mean number of annual HbA1cmeasurements performed during years 2005-2009 by care unit

The mean age of patients with 3 or more HbA1c checks per year was 37.4 years, compared to 42.9 years for the entire cohort. Females comprised 44.4% of the entire cohort, compared to 51.8% and 49.5% among patients with 3 to 4 annual HbA1c checks and 4 or more annual HbA1c checks, respectively, p=0.0022 for test between <3 vs. \geq 3 HbA1c checks. Diabetes duration was 20.9 years among the entire cohort, compared to 15.9 and 15.8 years, respectively, in patients with 3 to 4 and 4 or more HbA1c checks per year, p<0.0001 for test vs.<3 HbA1c checks. Among the entire cohort, 21.1% had CSII, compared to 39.9% and 37.1%, respectively, in patients with 3 to 4 and 4 or more

annual HbA1c checks, p<0.0001 for test vs.<3 HbA1c checks. In unit 10 there were 36.2% of patients having 3 or more HbA1c checks per year, p<0.0001 for test vs.<3 HbA1c checks, whereas fewer than 10% of patients had 3 or more annual HbA1c checks in most other care units (Table 1b).

The mean annual number of HbA1c measurements increased moderately, from 1.72 in 2005 to 1.90 in 2009, p=0.0021 for trend over years, with a mean of 1.78 over the study period (Table 2). There was an increase p<0.0001 in the mean HbA1c level, from 7.92% in 2005 to 8.05% in 2009 (Table 2). The proportion of patients reaching a target HbA1c of \leq 7.0% varied, from a low of 18.6% in 2009 to a high of 22.9% in 2007 (Table 2).

	Mean number of yearly visit	Mean HbA1c (%, NGSP)	First yearly HbA1c<=7 (%, NGSP)				
Year 2005	1.72 (1.11) 2.00 (0.00; 8.00) n=4852	7.92 (1.24) 7.83 (4.58; 16.29) n=4255	912 (21.4%)				
Year 2006	1.74 (1.11) 2.00 (0.00; 9.00) n=4937	7.94 (1.25) 7.87 (4.53; 14.57) n=4392	927 (21.1%)				
Year 2007	1.79 (1.11) 2.00 (0.00; 14.00) n=5075	7.91 (1.27) 7.78 (4.43; 14.66) n=4565	1047 (22.9%)				
Year 2008	1.89 (1.12) 2.00 (0.00; 11.00) n=5149	8.00 (1.25) 7.87 (4.62; 15.81) n=4738	965 (20.4%)				
Year 2009	1.90 (1.15) 2.00 (0.00; 10.00) n=5092	8.05 (1.27) 7.92 (4.15; 14.57) n=4769	888 (18.6%)				
Mean during 2005-2009	1.78 (0.80) 1.80 (0.00; 9.00) n=5989	8.00 (1.21) 7.90 (4.43; 14.64) n=5854					
For categorical variables n (%) is presented.							

For continuous variables Mean (SD)/Median/(Min: Max)/n=is presented.

Table 2: Distribution of number of yearly visits, HbA1c levels and HbA1c <=7 (%, NGSP) by calendar year</th>

The mean number of HbA1c measurements during time periods where HbA1c was >7.0% and \leq 7.0% was 1.83 and 1.58, respectively. In 35.4% of cases the next HbA1c check following an HbA1c >7% was performed within 4 months. Table 3 contains the univariable and multivariable predictors for a novel HbA1c check within 4 and 7 months, respectively, after an HbA1c >7.0%. In multivariable models, younger age, female sex, shorter diabetes duration, treatment with CSII, later calendar year, lower weight, higher HbA1c, and care unit were independently associated with an HbA1c check within 4 months. With the exception of younger age, the same variables were independent predictors of an HbA1c check within 7 months. The odds ratios for an HbA1c check within 4 and 7 months was 1.57 (1.46-1.69)

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and 1.50 (1.40-1.62,) respectively, for patients using CSII versus MDI, the OR was 1.37 (1.34-1.41) and 1.21 (1.17-1.24) for each 1 percentage

unit increase in HbA1c, and 2.92 (2.50-3.42) and 2.88 (2.40-3.47) for the care unit with the highest OR versus all other care units.

	Probability of having a novel HbA1c check within 4 months after an HbA1c>7%				Probability of having a novel HbA1c check within 7 months after an HbA1c>7%			
	Univariable	nivariable Multivariable Multi		Multivariable				
	OR		OR		OR		OR	
Variable	(95% CI)	p-value	(95% CI)	p-value	(95% CI)	p-value	(95% CI)	p-value
Sex (1=Male; 2=Female)	1.20 (1.12-1.28)	<.0001	1.12 (1.05-1.21)	0.0017	1.19 (1.12-1.27)	<.0001	1.12 (1.05-1.20)	0.0007
Current age (by 10 years)	0.87 (0.85-0.89)	<.0001	0.94 (0.92-0.96)	<.0001	0.95 (0.93-0.97)	<.0001		
Diabetes duration (by 10 years)	0.89 (0.87-0.91)	<.0001	0.93 (0.91-0.96)	<.0001	0.97 (0.95-0.99)	0.0060	0.97 (0.95-0.99)	0.0098
CSII (0=No; 1=Yes)	1.65 (1.54-1.78)	<.0001	1.57 (1.46-1.69)	<.0001	1.54 (1.43-1.66)	<.0001	1.50 (1.40-1.62)	<.0001
Current weight (by 10 kg)	0.97 (0.94-1.00)	0.030	0.97 (0.94-1.00)	0.023	0.98 (0.97-1.00)	0.048	0.98 (0.96-1.00)	0.027
Current BMI (kg/m ²)	0.99 (0.98-1.00)	0.039			1.00 (0.99-1.00)	0.56		
Current insulin dose (unit/kg)	0.99 (0.88-1.11)	0.82			0.99 (0.89-1.11)	0.89		
Current calendar year	1.13 (1.11-1.15)	<.0001	1.14 (1.12-1.17)	<.0001	1.17 (1.15-1.19)	<.0001	1.18 (1.16-1.20)	<.0001
Current HbA1c (%, NGSP)	1.38 (1.34-1.41)	<.0001	1.37 (1.34-1.41)	<.0001	1.22 (1.19-1.25)	<.0001	1.21 (1.17-1.24)	<.0001
Unit 1 (0=No; 1=Yes)	0 .85 (0.72-1.00)	0.056			1.60 (1.40-1.84)	<.0001	1.94 (1.68-2.24)	<.0001
Unit 2 (0=No; 1=Yes)	1.14 (1.00-1.31)	0.052			0.64 (0.56-0.72)	<.0001	0.80 (0.70-0.91)	0.0007
Unit 3 (0=No; 1=Yes)	0.80 (0.74-0.87)	<.0001	0.86 (0.78-0.96)	0.0061	0.77 (0.72-0.82)	<.0001		
Unit 4 (0=No; 1=Yes)	1.63 (1.48-1.80)	<.0001	1.56 (1.38-1.77)	<.0001	1.64 (1.48-1.82)	<.0001	1.92 (1.72-2.15)	<.0001
Unit 5 (0=No; 1=Yes)	0.56 (0.47-0.65)	<.0001	0.55 (0.46-0.65)	<.0001	0.94 (0.84-1.06)	0.33		
Unit 6 (0=No; 1=Yes)	0.83 (0.76-0.92)	0.0003	0.82 (0.73-0.93)	0.0012	0.68 (0.62-0.74)	<.0001	0.85 (0.78-0.93)	0.0005
Unit 7 (0=No; 1=Yes)	1.17 (1.08-1.26)	0.0002	1.13 (1.02-1.26)	0.024	1.74 (1.59-1.89)	<.0001	1.91 (1.75-2.09)	<.0001
Unit 8 (0=No; 1=Yes)	0.79 (0.69-0.90)	0.0004	0.75 (0.65-0.87)	0.0002	0.75 (0.67-0.85)	<.0001		
Unit 9 (0=No; 1=Yes)	0.91 (0.78-1.06)	0.25			0.94 (0.82-1.07)	0.34		

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Unit 10 (0=No; 1=Yes)	2.83 (2.45-3.26)	<.0001	2.92 (2.50-3.42)	<.0001	2.41 (2.00-2.89)	<.0001	2.88 (2.40-3.47)	<.0001		
Generalized Estimating Equation (GEE) models have been used as they allow for adjustment of within-individual correlation.										
Odds-ratio (OR) is describing the effect of the predictor on the outcome variable per 1 unit except for the variables current age, diabetes duration and current weight for which OR is expressing the effect by 10 units.										
The OR for a unit is compared is expressing the effect compared to all other units.										

Table 3: Probability of having a novel HbA1c check within 4 months and 7 months respectively after an HbA1c>7 (%, NGSP), univariable and multivariable GEE model.

The relationship between HbA1c level and probability of having an HbA1c check within 4 months indicated a monotonically increasing probability by higher HbA1c up to 11% (Figure 1a). The probability of having an HbA1c check was higher among patients with diabetes duration less than 10 years, but no clear pattern was seen beyond 10 years (Figure 1b).



Figure 1: A) The probability of having HbA1c checked in 4 months and in 7 months after an HbA1c above 7.0% in relation to the current HbA1c-level. B) The probability of having HbA1c checked in 4 months and in 7 months after an HbA1c above 7.0% in relation to diabetes duration (by 10 year-intervals).

Discussion

This retrospective study of 5989 patients with type 1 diabetes from 10 outpatient diabetes clinics in Sweden during years 2005-2009, shows that annual HbA1c checks were performed less frequently than advocated in clinical guidelines. During the follow-up period, there were 1.75 annual HbA1c checks, on average, during patient periods with HbA1c \geq 7.0%, while clinical guidelines suggest a check at least every 3rd month after the initial elevated value. In only 35.4% of cases the next HbA1c check following an HbA1c >7% was performed within 4 months. The frequency of annual HbA1c checks was significantly higher for patients treated with CSII compared to MDI, younger individuals compared to older, those with shorter diabetes duration, females, patients with higher HbA1c, and for certain care units. The probability of having an HbA1c check within 4 months after an HbA1c check with a value \geq 7.0% was approximately 50% greater in individuals treated with CSII compared to MDI. Moreover, the probability of a follow-up HbA1c check at 4 months in patients with inadequate glycaemic control differed between certain care units, with a nearly three-fold increased likelihood among the care unit performing the most annual checks, when compared to the mean number of checks in other care units.

To our knowledge, there is only a single study examining the frequency of HbA1c measurements in patients with type 1 diabetes [20]. In Germany and the UK, electronic medical records were examined from 1,910 and 1,500 patients with type 1 diabetes, respectively, treated in the primary care setting. Patients received, on average, 1.1 annual HbA1c checks in Germany and 2.0 annual checks in the U.K., and investigators concluded that HbA1c checks were underused in both countries. However, we found no previous work examining potential predictors for receiving more frequent annual HbA1c checks in patients with type 1 diabetes, such as those reported here (e.g., CSII and care unit). Recent studies of the frequency of HbA1c measurements in patients with type 2 diabetes or without specifying the type of diabetes, have reported that HbA1c checks are underused in the UK and Australia, without generally examining various predictors for more frequent HbA1c checks [21,22].

One possible explanation for type 1 diabetes patients receiving relatively few HbA1c checks at diabetes care units in Sweden could be a general lack of resources. However, insulin are free, as are glucose monitoring strips, HbA1c tests and insulin pumps if MDI is not used to target good glycaemic control, which is distinguishable from many other countries. Another more likely explanation may therefore be that the number of visits and checks of HbA1c have not been a proper focus of attention in evaluating the quality of diabetes care. In Sweden, the frequency of visits for diabetes care and HbA1c checks are not recorded in the national diabetes registry or in various economic

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programs that support care units [13]. Since the mean HbA1c-level during recent years has increased on a national level in patients with type 1 diabetes in Sweden [13], despite increased use of advanced therapies such as CSII, it is possible that there may be problems in the basic care structure for intensive glycaemic therapy. In addition to fewer visits including HbA1c checks, as shown in this study, compliance with regular blood glucose measurements and insulin dosing may also explain these findings.

The number of blood glucose (BG) measurements performed in patients with type 1 diabetes has shown a strong association to the HbA1c-level [23,24]. Good compliance with BG checks has been associated with larger drops in HbA1c than novel therapies such as CSII or insulin analogues [14,23-27]. This may also be reasonable from a clinical perspective since dosage of insulin will not be optimised by bolus correction if BG is not measured before meals. There are yet no studies in Sweden of the general frequency of BG measurements in patients with type 1 diabetes, but our clinical experience is that it is difficult for many patients to comply with BG measurements 4 times per day as advocated in guidelines. One hypothesis is therefore that a reason why HbA1c is not improving in Sweden in spite of patients receiving more modern treatments can be general barriers to adhere to intensive treatment strategies. More frequent clinical visits to diabetes outpatient clinics than the relatively low rate shown here may be essential in supporting patients to comply with BG measurements and insulin dosage, besides other general treatment strategies included in modern diabetes care.

The likelihood of having an HbA1c check within 4 months was approximately 50% greater for patients treated with CSII compared to MDI. It is noteworthy that although if the lower bound of the 95% CI would be true, there was an OR of 1.46 supporting a greater likelihood in the probability of having HbA1c checked for patients treated with CSII compared to MDI. Moreover, when evaluating the likelihood of receiving an HbA1c check within 7 months, the OR was 1.50 in favour of CSII also supporting this difference in availability of care depending on treatment. One possible explanation is that patients on CSII need more visits for support regarding technical issues and complications with the therapy. However, it does not seem reasonable that patients with MDI should receive considerably less diabetes care: also noticing that MDI is a much less expensive therapy. The variation found in HbA1c checks in relation to care unit may implicate a need for recommendations on the number of visits including HbA1c checks in quality registers and be a focus in the care at outpatient diabetic clinics. Although relatively few HbA1c checks were performed, it was encouraging that more checks existed the higher the HbA1c, since it could be hypothesized that patients with very high HbA1c would have had fewer checks due to worse adherence to patient visits. The fact that patients with shorter diabetes duration had more checks of HbA1c seems appropriate since we could show that this was mainly contributed by more visits during the first years after diagnosis, when more attention and education to the patient is generally needed.

The present study is limited in that psychosocial variables were not available for study. It is possible that various psychosocial variables may be related to the probability of having an HbA1c check.

Family situation, working situation, educational level, area of living (rural/urban) could possibly all be related to the willingness and possibility to attend clinical visits. Today, some psychosocial variables exist in the Diab-Base system. For future research, care units could be promoted to register these variables to a greater extent, and the number of variables could possibly be extended. Another limitation is

that we did not have information whether patients were scheduled for a check of HbA1c but did not attend or whether patients did not receive a visit. However, from clinical experience of diabetes care in Sweden the absolute majority of patients attend their scheduled visits. Our results are therefore probably explained mainly by care givers not giving patients the opportunity to visits in accordance with guidelines. To improve availability of HbA1c checks, increased resources from care givers may be essential but the responsibility for the individual physician and diabetes educator may also be of concern. Another variable that may have been of interest to evaluate is hypoglycaemia, but this is difficult to record properly in clinical practice for several reasons and the data were judged to be insufficient in the current electronical medical record system. Our finding that more checks were performed in women must be interpreted with caution since it was not possible to exclude periods of pregnancy in all instances, which may result in unknown confounder, although the total time of pregnancy is likely very small compared to all patient years without pregnancy. We did not evaluate explicit visits but the checks of HbA1c per se, but it is noteworthy that in Sweden HbA1c evaluations are in the absolute majority of cases performed in connection to a visit to a physician or diabetes educator.

In our analyses we used the time frame of having an HbA1c check within 4 months and not 3 months as advocated in guidelines. The reason is that it may be difficult to schedule visits at exactly 3 months in clinical practice due to practical reasons such as family situation or work situation for the patient. The time frame of one extra month was set relatively conservatively to not overestimate patients not having an HbA1c check in accordance with guidelines. In correspondence when evaluating patient characteristics associated to not having an HbA1c check even in 6 months, we used an extended time frame by 1 month.

In conclusion, patients with type 1 diabetes at 10 outpatient diabetes clinics in Sweden had fewer HbA1c checks than advocated in clinical guidelines. More frequent HbA1c checks may improve glycaemic control in the Swedish population. Patients with MDI need to attain extra attention. The frequency of HbA1c checks varies strongly by care unit and needs to be evaluated at the individual diabetes outpatient clinic. Our literature review shows that there previously has been little focus on evaluating the availability of the basic diabetes care in patients with type 1 diabetes. The basic support in diabetes care is probably most crucial in reducing diabetic complications and to give full support to novel therapies to obtain maximal benefit and from a safety perspective.

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Author Disclosure Statement

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References

- Whiting DR, Guariguata L, Weil C, Shaw J (2011) IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res ClinPract 94: 311-321.
- Imkampe AK, Gulliford MC (2011) Trends in Type 1 diabetes incidence in the UK in 0- to 14-year-olds and in 15- to 34-year-olds, 1991-2008. Diabet Med 28: 811-814.
- 3. Galler A, Stange T, Müller G, Näke A, Vogel C, et al. (2010) Incidence of childhood diabetes in children aged less than 15 years and its clinical and metabolic characteristics at the time of diagnosis: data from the Childhood Diabetes Registry of Saxony, Germany. Horm Res Paediatr 74: 285-291.
- 4. Ragnar Hanås (2008) Typ 1 Diabetes hos barn, ungdomarochungavuxna Hur du blir expert på din egen diabetes (Type 1 Diabetes in children, youth and young adults - How you become an expert on your diabetes).
- Menzin J, Korn JR, Cohen J, Lobo F, Zhang B, et al. (2010) Relationship between glycemic control and diabetes-related hospital costs in patients with type 1 or type 2 diabetes mellitus. J Manag Care Pharm 16: 264-275.
- McKinlay J, Marceau L (2000) US public health and the 21st century: diabetes mellitus. Lancet 356: 757-761.
- 7. Diabetes Control and Complications Trial Research Group (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 329: 977-986.
- Nathan DM, Cleary PA, Backlund JY, Genuth SM, Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group (2005) Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med 353: 2643-2653.
- American Diabetes Association (2014) Standards of medical care in diabetes--2014. Diabetes Care 37 Suppl 1: S14-80.
- 10. Type 1 diabetes: Diagnosis and management of type 1 diabetes in children, young people and adults. Available at: http://egap.evidence.nhs.uk/type-1-diabetes-cg15/guidance#blood-glucose-control-and-insulin-therapy, accessed 8 Jan 2014.
- Canadian Diabetes Association Clinical Practice Guidelines Expert Committee (2013) Canadian Diabetes Association 2013. Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes 37: S1-S212.
- National Board of Health and Welfare (2010) Nationella Riktlinjer för diabetesvården. (National Guidelines for Diabetes Care) http:// www.socialstyrelsen.se/nationellariktlinjerfordiabetesvarden, accessed 10 May 2014.
- Swedish National Diabetes Register, Annual Report 2012. Available at: https://www.ndr.nu/pdf/Annual_Report_NDR_2012.pdf, accessed 8 Jan 2014.

- 14. Carlsson BM, Attvall S, Clements M, Gumpeny SR, Pivodic A, et al. (2013) Insulin pump-long-term effects on glycemic control: an observational study at 10 diabetes clinics in Sweden. Diabetes TechnolTher 15: 302-307.
- 15. Anderson J, Attvall S, Sternemalm L, Pivodic A, Fahlén M, et al. (2011) Effect on glycemic control by short- and long-term use of continuous glucose monitoring in clinical practice. J Diabetes SciTechnol 5: 1472-1479.
- Carlsson BM, Andersson PN, Alnervik J, Carstensen J, Lind M (2012) Availability of insulin pump therapy in clinical practice. Diabet Med 29: 1055-1059.
- Lind M, Fahlén M, Happich M, Odén A, Eliasson B (2009) The effect of insulin lispro on glycemic control in a large patient cohort. Diabetes TechnolTher 11: 51-56.
- Lind M, Odén A, Fahlén M, Eliasson B (2009) The true value of HbA1c as a predictor of diabetic complications: simulations of HbA1c variables. PLoS One 4: e4412.
- 19. (2006) Applied Mixed Models in Medicine (2nd edn). Helen Brown and Robin Prescott, Wiley.
- 20. Kostev K, Grunow S, Rockel T (2012) HbA1c testing frequency in primary care diabetes patients in Germany and in the UK. ISPOR 15th annual European congress research abstracts. Value in Health 15: A519.
- National Institute of Clinical Studies (2008) Evidence-Practice Gaps Report Volume
 1: A review of developments: 2004–2007. Measuring glycated haemoglobin in
 diabetes management. Canberra: National Health and Medical Research Council:
 18-19.
- 22. Driskell OJ, Holland D, Hanna FW, Jones PW, Pemberton RJ, Tran M, Fryer AA (2012) Inappropriate requesting of glycated hemoglobin (HbA1c) is widespread: assessment of prevalence, impact of national guidance, and practice-to-practice variability. Clin Chem 58 (5): 906-915.
- 23. Hansen MV, Pedersen-Bjergaard U, Heller SR, Wallace TM, Rasmussen AK, et al. (2009) Frequency and motives of blood glucose self-monitoring in type 1 diabetes. Diabetes Res ClinPract 85: 183-188.
- 24. Miller KM, Beck RW, Bergenstal RM, Goland RS, Haller MJ, T1D Exchange Clinic Network (2013) Evidence of a strong association between frequency of selfmonitoring of blood glucose and hemoglobin A1c levels in T1D exchange clinic registry participants. Diabetes Care 36: 2009-2014.
- Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J (2010) Continuous subcutaneous insulin infusion (CSII) versus multiple insulin injections for type 1 diabetes mellitus. Cochrane Database Syst Rev: CD005103.
- 26. Singh SR, Ahmad F, Lal A, Yu C, Bai Z, et al. (2009) Efficacy and safety of insulin analogues for the management of diabetes mellitus: a meta-analysis. CMAJ 180: 385-397.
- Plank J, Siebenhofer A, Berghold A, Jeitler K, Horvath K, et al. (2005) Systematic review and meta-analysis of short-acting insulin analogues in patients with diabetes mellitus. Arch Intern Med 165: 1337-1344.