

Metabolic Control in Type 2 Diabetes Correlates Weakly with Patient Adherence to Oral Hypoglycaemic Treatment

Seng Cheong Loke,¹MBBS, MRCP, FAMS (Endocrinol), Michelle Jong,²MB BCh BAO, MRCP, FAMS (Endocrinol)

Abstract

Introduction: Patient adherence to treatment is viewed as essential to good metabolic control in diabetes. Our primary objective was to determine if self-reported patient adherence correlated strongly with metabolic control. Our secondary objective was to determine the natural grouping of factors which influence adherence. **Materials and Methods:** Data were collected using a questionnaire set with 5-point Likert scales. Primary analysis was done using Spearman's correlation coefficient between self-reported composite adherence scores and HbA1c. Secondary analysis was done using exploratory factor analysis. **Results:** The primary analysis suggests that patient adherence to the treatment regime is weakly correlated to metabolic control. Calculated Spearman's ρ was 0.197, with a two-tailed P value of 0.027. The secondary analysis demonstrates the natural clustering of factors that influence patient adherence to treatment. A 6-factor solution was found to account for most of the variance in the data. We also found that feelings of frustration, anxiety, and depression were associated with a lack of knowledge about diabetes treatment. In addition, belief in traditional medicine correlated strongly with ethnicity. **Conclusion:** A good treatment regime for type 2 diabetes mellitus influences metabolic outcome far more than patient adherence.

Ann Acad Med Singapore 2008;37:15-20

Key words: Factor analysis, Patient non-adherence, Spearman rank correlation coefficient, Traditional medicine

Introduction

Diabetes mellitus is one of the most common chronic diseases affecting Singaporeans. In 2004, 8.2% of the population was afflicted,¹ placing a significant burden on healthcare resources and affecting the well-being of the community.

There is good evidence that tight metabolic control results in reduction of micro- and macro-vascular complications.² Unfortunately, more than half of the patients with diabetes in Singapore have poor control with a mean glycated haemoglobin (HbA1c) of 8.5%.

To achieve good diabetic control, a number of issues must be addressed, the most important of which are the provision of a structured care approach by physicians and improved patient adherence to treatment. Much has been done for the first issue, with accepted clinical practice guidelines and increased resource allocation to primary healthcare providers.³

The issue of patient adherence has been less satisfactorily studied, with relatively little published research in this area.

In addition, there is a need to develop an adequately validated instrument to measure patient adherence to treatment. What research does exist in this area is based mostly in Western countries,⁴ with little that is relevant to the Singaporean context.

Singapore's population is predominantly urban and ethnically diverse. Chinese constitute about three-fourths of the population. Malays form the next largest group, and Indians the third. Traditional beliefs and practices are still widespread, and this affects all areas of life including healthcare. It is thus important to have local data as adherence is heavily influenced by cultural factors.

As such, the primary objective of this study was to determine if self-reported patient adherence correlated strongly with metabolic control, when the treatment regime had been standardised. If this were found to be true, then interventions aimed at improving patient adherence would have a significant beneficial effect.

To develop a statistical instrument to measure patient adherence, it was necessary to study the factors which

¹ Department of Medicine, Faculty of Medicine and Health Science Universiti Putra Malaysia, Malaysia

² Department of Endocrinology, Tan Tock Seng Hospital, Singapore

Address for Correspondence: Dr Loke Seng Cheong, 15 SS 21/3 Damansara Utama, 47400 Petaling Jaya, Selangor, Malaysia.

Email: lokesengcheong@yahoo.com.sg

influence this. Thus, the secondary objective of this study was to determine the natural grouping of factors which influence adherence. This could prove useful in future studies on this subject.

Materials and Methods

Study Premise

The basic premise of the study was that metabolic control in diabetes is determined by both the treatment regime and patient adherence. Standardisation of the treatment regime meant that the sole influence on HbA1c would then be patient adherence (Fig. 1).

From previous studies,^{1,4-8} adherence to treatment is influenced by a number of factors, which can be grouped into 4 broad categories: knowledge, attitude, support, and background. Some of these factors will have a large effect on adherence, while others may only have a minimal effect. The factors are grouped in this way as they correspond to

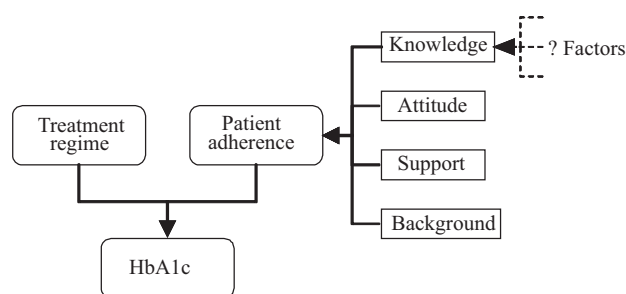


Fig. 1. Relationship between treatment, adherence, and metabolic control.

Table 1. Proposed Factors Which Influence Adherence to Treatment.

Knowledge	Attitude
Education level	Careless attitude**
Belief in traditional medicine###	Frustration with treatment**
Knowledge of treatment*	Unable to accept disease##
Knowledge of complications*	Anxiety/Depression##
From mass media###	Busy schedule
From friends and relatives###	Experience of adverse effects##
From professionals###	Polypharmacy***
Support	Background
Size of household##	Gender#
Family income	Race#
Professional support##	Age#
Supportiveness of family##	

NHS Singapore 1998¹

* Patient education study⁶

DAWN study⁴

** Diabetes non-adherence study⁷

Public awareness study⁵

*** DARTS/MEMO collaboration⁸

Note: factors without explicit references were included after discussion with health care personnel involved in diabetes management. These represent significant local issues which may affect adherence to treatment.

possible interventions which can be employed to reduce non-adherence (Table 1).

Inclusion and Exclusion Criteria

Only patients on oral hypoglycaemic agents who had been followed-up for a minimum of 1 year with at least 3 clinic visits were selected. Patients were excluded from the study if they were anaemic (haemoglobin <10 g/dL), on corticosteroid treatment, taking traditional medicine, on insulin therapy, or had major concomitant illnesses.

Data Collection

The study population consisted of consecutive patients with diabetes mellitus from a single specialist outpatient clinic, under follow-up by the investigators. The treatment regime was standardised according to the Ministry of Health Clinical Practice Guidelines (MOHCPG) for Diabetes Mellitus.⁹ The MOHCPG was used as this is the established local standard for medical practitioners in Singapore involved in the treatment of diabetes. Lifestyle modification is an integral part of the MOHCPG, and this was managed with visits to the dietician, a formal exercise programme for selected overweight and obese patients [body mass index (BMI) >25], smoking cessation advice, and counselling sessions with a nurse educator.

Data were collected in the form of a questionnaire, with individual questions set as 5-point Likert scales (5PLS). These questions were chosen based on previous work done on this subject, which indicated that they may play a role in determining patient adherence (Table 1).

5PLS categories for demographic data were population-adjusted based on statistics from the Singapore census 2000¹⁰ and Diabcare-Singapore 1998¹¹ to give approximately equal numbers in each. The 3 main races, Chinese, Malays and Indians, are represented, along with a fourth catch-all category “Others”, based on Singapore census subdivisions. The last category comprises mainly Eurasians, along with a small number of foreign nationals, in keeping with the cosmopolitan nature of Singapore society.

Metabolic control was graded by HbA1c values on the final clinic visit and categorised into 5PLS. The HbA1c target categories were based on the MOHCPG, with an additional category added at the 10% level.⁹ This cut-off was chosen because of evidence that shows an increase of approximately 50% in deaths and complications related to diabetes compared with a HbA1c of 8%.¹² Absolute HbA1c values were used instead of relative changes, as this reflects a steady state after optimisation of treatment.

Self-reported patient adherence was determined by 2 questions on the frequency of missed and altered medication doses. A final composite result was obtained by adding the scores on these 2 questions.

Patient particulars and personal details were also collected in a similar manner. All questions and instructions were given in the 3 main local languages (English, Mandarin, and Malay). For patients who were illiterate, a member of staff read out the questions verbatim.

A potential difficulty with patient-reported adherence is that it is prone to mis-reporting. To promote greater honesty, all questionnaires were identified only by a study label. Patients were encouraged to fill in the forms themselves, which were then stored in a sealed box.

Analysis One: Does Metabolic Control Correlate Strongly with Patient Adherence?

The first analysis goal was to test the validity of the premise that metabolic control in diabetes was determined by patient adherence, once the treatment regime had been standardised. This was done by calculating Spearman's rank correlation coefficient (ρ) between the composite reported adherence score and HbA1c. Spearman's correlation was chosen as it is more resistant to outliers, unequal variances, non-normality, and non-linearity, which is appropriate for the ordinal dataset being analysed. Power analysis with the program G*power (Faul & Erdfelder, Bonn University 1992) suggested that for a 5% type I error rate (α -level 0.05) and 5% type II error rate (95% power) with ρ of 0.3, a sample size of 111 subjects was needed. For purposes of this analysis, we were interested in $\rho > 0.3$, which would imply at least a moderate correlation.¹³ Smaller correlations would suggest that the underlying premise was invalid.

Analysis Two: To Determine the Natural Grouping of Factors which Influence Adherence

The second analysis goal was to determine if the proposed grouping of factors in Table 1 corresponded to natural factor groups.

As it was expected that the various items on the questionnaire were interrelated, correlation of individual factors with HbA1c could not be tested. Exploratory factor analysis was the preferred method in this situation, where factors were extracted by principal axis factoring, and subjected to Varimax rotation. To determine the number of factors, the Kaiser criterion was used to eliminate components with eigenvalues under 1.0. The Scree plot was then checked according to Cattell's rule to further remove components after the plot levels off. Minimum factor loading was determined by the formula according to Norman and Streiner¹⁴:-

$$FL = \frac{5.152}{\sqrt{N - 2}} \approx 0.46 \text{ where } N = 130$$

Overall sampling adequacy was measured by the Kaiser-Meyer-Olkin (KMO) statistic and Bartlett's Test of Sphericity.

All statistical computations were performed using SPSS for Windows version 12.0 (SPSS Inc, Chicago, Illinois, USA). Only two-tailed tests were used, and all statistical tests were conducted at 5% level of significance.

Results

This study was done with prior ethics approval from the Institutional Ethics Review Board in accordance with current guidelines on Good Clinical Practice, the Declaration of Helsinki, and subsequent relevant versions. As this was done anonymously, informed consent was not required by the ethics review board.

Data from 130 questionnaires were collected and analysed. Patient demographic data is presented in Table 2. All patients were followed up for between 1 and 3 years.

Table 2. Patient Demographic Data (n = 130)

Gender	Male (62, 47.7%)
	Female (68, 52.3%)
Race	Chinese (88, 67.7%)
	Malay (15, 11.5%)
	Indian (25, 19.2%)
	Other (2, 1.5%)
Age (y)	<45 (17, 13.1%)
	45-55 (42, 32.3%)
	56-63 (28, 21.5%)
	64-70 (29, 22.3%)
	>70 (14, 10.8%)
Education	None (25, 19.2%)
	Primary (23, 17.7%)
	Secondary (55, 42.3%)
	ITE/JC (9, 6.9%)
Family income (S\$)	Uni/Poly (18, 13.8%)
	<1500 (53, 40.8%)
	1500-3000 (47, 36.2%)
	3000-4500 (15, 11.5%)
	4500-7000 (9, 6.9%)
Household size (people)	>7000 (6, 4.6%)
	1 (8, 6.2%)
	2 (21, 16.2%)
	3 (33, 25.4%)
	4 (35, 26.9%)
	>4 (33, 25.4%)

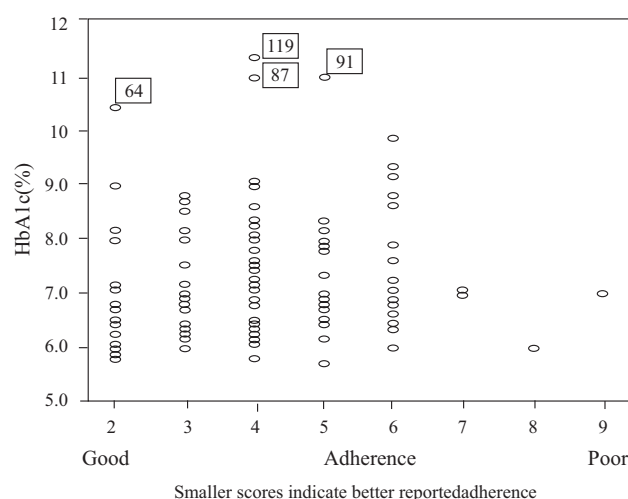


Fig. 2. Scatter plot of HbA1c vs adherence.

Analysis One: Metabolic Control Only Correlates Weakly with Patient Adherence

Our analysis demonstrated that metabolic control correlated only weakly with self-reported adherence to treatment, although there was an upward trend in HbA1c with poorer adherence.

A scatter plot of HbA1c versus reported adherence was generated, and this showed 4 obvious outliers with HbA1c greater than 10% (Fig. 2). As it was possible that these individuals had misreported adherence, or were subject to other confounding factors, they were excluded from this part of the analysis. The calculated ρ was 0.197, with a two-tailed P value of 0.027, which was statistically significant. Even when these outliers were included, calculated ρ was 0.178, with a 2-tailed P value of 0.042.

The scatter plot showed that although there was generally a rise in HbA1c with poorer adherence, this trend was partially obscured by a clustering of HbA1c at lower values. This was confirmed by the frequency plot which showed a normal distribution of HbA1c around a mean of 7%, with a few high outlier values (Fig. 3).

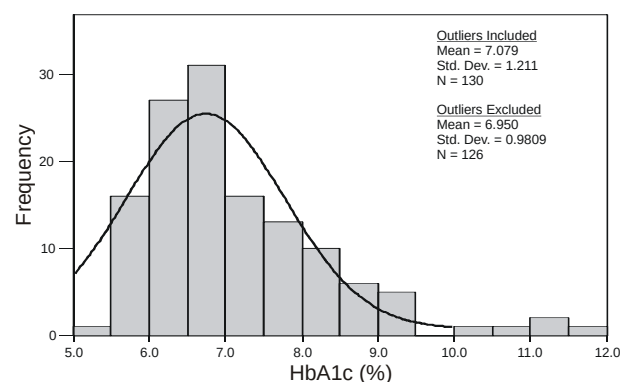


Fig. 3. Frequency plot of HbA1c values.

Analysis Two: Six Natural Factor Groupings were Found

The KMO statistic (0.646) and Bartlett's test (chi square = 681.605, $df = 231$, $P < 0.001$) both suggested that overall sampling was adequate. In general, the KMO statistic should be greater than 0.6 and Bartlett's test should be significant to less than 0.05.

Applying the Kaiser criterion, 7 factors with eigen values greater than 1.0 were found, and the Scree plot further reduced this to a 6-factor solution. These factors were rotated and tabulated with a minimum factor loading of 0.46. They were then cross-referenced against the questionnaire to reveal the underlying structure.

Six natural factors groupings were found, broadly categorised as knowledge of disease, social class, psychological factors, emotional support, patient age and cultural background (Table 3).

Four of these factor groupings comprised related factors which correspond to the proposed factor groups in Table 1. Two of these groups, psychological factors (group 3) and cultural background (group 6), contain dissimilar factors and were hence rechecked with one-way analysis of variance (ANOVA). This gave highly significant differences between groups, and together with the frequency plots confirm the relationship between the individual factors. In all cases, Levene's test of Homogeneity of Variances was not

Table 3. Cross-referenced Factors

Factor	Items from questionnaire	Proposed groupings	Rotation sums of squared loadings	% variance explained
1	Knowledge from mass media, friends, relatives, and professionals.	Knowledge of disease	2.129	9.677
2	Patient background. Gender, education, family income, etc.	Social class	1.736	7.892
3	Knowledge about diabetes treatment. Frustration, depression, and anxiety.	Psychological factors	1.665	7.566
4	Professional support. Supportiveness of family.	Emotional support	1.257	5.714
5	Patient age.		0.965	4.387
6	Belief in traditional medicine. Race.	Cultural background	0.960	4.365

significant, which implied that group variances were similar enough that ANOVA was appropriately used.

The analysis suggests that the less patients knew about their diabetes treatment, the more likely they were to be anxious, depressed and frustrated. In addition, Chinese and Malays tended to have a high belief in traditional medicine, as compared with other races.

Discussion

The results imply that only a small correlation¹³ ($\rho = 0.197$) existed between reported adherence and metabolic control once the treatment regime had been standardised. As sampling was adequate and the result statistically significant, the most likely explanation was that the underlying premise was flawed. This suggests that adherence to treatment has a much smaller impact on metabolic control in diabetes mellitus than previously thought.

We found that across all grades of reported adherence, HbA1c tended to cluster at lower values. Only a few outliers (4 out of 130 subjects) strayed from this trend, and this group may have misreported adherence or had other extrinsic confounding factors like undocumented use of corticosteroids or traditional medicine. With outliers excluded, the frequency plot showed a mean HbA1c of 6.95% which was far below the national average of 8.5%.

In our practice, we normally receive referrals for specialist review only when the HbA1c exceeds 8% for an extended period after attempts at optimisation by the primary physician are unsuccessful. Frequently HbA1c exceeds 10% on the initial clinic visit, and lowering to an average of 6.95% after following the MOHCPG is a highly significant result.

While this observation may seem counterintuitive, the authors postulate that occasional lapses in treatment do not affect overall metabolic control significantly. From our own experience, minor fluctuations in HbA1c can often be compensated for by adjusting the medication regime, without causing undue hypoglycaemia.

We thus conclude that adherence to the MOHCPG for diabetes mellitus results in good metabolic control across a wide range of self-reported patient adherence, as shown by the mean study HbA1c of 6.95%. It is only a small number whose adherence is very poor or where other exogenous factors are involved, who still have poorly controlled diabetes.

We also found that feelings of frustration, anxiety, and depression were strongly associated with a lack of knowledge about diabetes treatment. This suggests that good patient education and counselling can avoid leaving patients with a negative attitude about their diabetes treatment.

In addition, belief in traditional medicine was found to be strongly associated with ethnicity. This finding reflects the high standing that practitioners of traditional medicine enjoy in both Chinese (*sinsehs*) and Malay (*bomohs*) culture.¹⁵ While Ayurvedic medicine is still used by some segments of the Indian community, the authors observe that Western medicine generally predominates.

No attempt was made to correlate factors obtained in the second analysis with patient adherence, as this was not in the original study design. However, this could be attempted in a future study with construction of an ordinal logit model to test the candidate factor groups.

A significant limitation of this study was that patients on insulin therapy were excluded, and the low HbA1c values seen reflect patients solely on oral hypoglycaemic agents. This was a compromise made in the original study design, as examining insulin use would introduce many new issues with regard to compliance, thus further complicating the study.

Another limitation is that patients were collected only from a single specialist clinic. A broader patient base would allow greater generalisation of the results obtained.

Although standardisation of the treatment regime according to the MOHCPG was attempted in all cases, deviation was sometimes unavoidable due to patient factors such as intolerance to medications or cost constraint. This reflects the real world situation in which the guidelines were intended to be used. In spite of this limitation, 60% of patients were still able to lower their HbA1c to less than 7%.

The final and most important limitation is that of reliability of self-reported adherence. While other methods of assessment do exist such as bottle counts, structured interviews, and biochemical tracers, these are laborious and time-consuming. An assessment of these methods suggests that self-reporting is as effective as the others, and is especially appropriate where resources are limited.¹⁶ As the final goal is to develop a statistically validated instrument to measure patient adherence, ease of use will be important in determining its eventual clinical utility.

Acknowledgements

We would like to thank Dr Soon Puay Cheow for his support in carrying out this study, and Mr Chan Siew Pang for technical advice relating to study design.

REFERENCES

1. National Health Survey. Singapore: Ministry of Health, 2004.
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with

- conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352:837-53. Erratum in: *Lancet* 1999;354:602.
 3. Sum CF. Improving diabetes care – can we do more? *Singapore Med J* 2001;42:498-500.
 4. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE. Psychosocial problems and barriers to improved diabetes management: results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. *Diabet Med* 2005;22:1379-85.
 5. Wee HL, Ho HK, Li SC. Public awareness of diabetes mellitus in Singapore. *Singapore Med J* 2002;43:128-34.
 6. Tan AS, Yong LS, Wan S, Wong ML. Patient education in the management of diabetes mellitus. *Singapore Med J* 1997;38:156-60.
 7. Vallis TM. Understanding diabetes nonadherence: psychosocial factors associated with poor self-care. *Can J Diabetes Care* 1998;22:13-21.
 8. Donnan PT, MacDonald TM, Morris AD. Adherence to prescribed oral hypoglycaemic medication in a population of patients with Type 2 diabetes: a retrospective cohort study. *Diabet Med* 2002;19:279-84.
 9. Clinical Practice Guidelines for Diabetes Mellitus. Singapore: Ministry of Health, 1999.
 10. Singapore Population. Singapore: Department of Statistics, 2000.
 11. Lee WR, Lim HS, Thai AC, Chew WL, Emmanuel S, Goh LG, et al. A window on the current status of diabetes mellitus in Singapore – the Diabcare-Singapore 1998 study. *Singapore Med J* 2001;42:501-7.
 12. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405-12.
 13. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. New Jersey: Lawrence Erlbaum Associates, 1988.
 14. Norman GR, Streiner DL. Biostatistics: The Bare Essentials. St. Louis: Mosby, 1994.
 15. Ho NK. Understanding traditional Chinese medicine – a doctor's viewpoint. *Singapore Med J* 2001;42:487-92.
 16. Homedes N, Ugalde A. Research on patient compliance in developing countries. *Bull Pan Am Health Organ* 1994;28:17-33.
-