Correlates of Insulin Injection Omission

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OBJECTIVE — The purpose of this study was to assess factors associated with patient frequency of intentionally skipping insulin injections.

RESEARCH DESIGN AND METHODS — Data were obtained through an Internet survey of 502 U.S. adults self-identified as taking insulin by injection to treat type 1 or type 2 diabetes. Multiple regression analysis assessed independent associations of various demographic, disease, and injection-specific factors with insulin omission.

RESULTS — Intentional insulin omission was reported by more than half of respondents; regular omission was reported by 20%. Significant independent risk factors for insulin omission were younger age, lower income and higher education, type 2 diabetes, not following a healthy diet, taking more daily injections, interference of injections with daily activities, and injection pain and embarrassment. Risk factors differed between type 1 and type 2 diabetic patients, with diet nonadherence more prominent in type 1 diabetes and age, education, income, pain, and embarrassment more prominent in type 2 diabetes.

CONCLUSIONS — Whereas most patients did not report regular intentional omission of insulin injections, a substantial number did. Our findings suggest that it is important to identify patients who intentionally omit insulin and be aware of the potential risk factors identified here. For patients who report injection-related problems (interference with daily activities, injection pain, and embarrassment), providers should consider recommending strategies and tools for addressing these problems to increase adherence to prescribed insulin regimens. This could improve clinical outcomes.

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M ore than 25% of people with diabetes take insulin (1). The American Diabetes Association and the European Association for the Study of Diabetes recently issued a consensus algorithm for management of type 2 diabetes identifying insulin as the most effective glucose-lowering agent (2). Lower compliance with insulin regimens is associated with higher A1C levels (3,4) and with higher rates of hospital admissions for diabetes-related complications (3).

Despite the importance of adhering to prescribed insulin regimens, little is known about the degree to which patients are adherent or about factors associated with adherence. In a study using a Department of Veterans Affairs database, insulin use was 77% of prescribed amounts (3). In this population, two-thirds of whom were ≥65 years of age, age did not predict insulin regimen adherence, and adherence was nearly identical for men and women, but non-Hispanic white patients were more adherent than patients who were African American or Hispanic. In another study of patients who switched from using a syringe to deliver insulin to using a pen, 36% of the patients had medication possession rates of >80% while using a syringe, but this rose to 55% after switching to a pen (5).

A recent review identified factors associated with adherence to any diabetes medication (6). These factors include medication costs, regimen complexity, the patient's emotional well-being, and the patient's perceptions of medication side effects and medication-related intrusions on activities of daily living.

Medication costs can affect adherence. In a U.S. survey of adults with type 2 diabetes using glucose-lowering agents, 11% reported that they had cut back on their medication in the past year (7). Adherence rates are also affected by regimen complexity. Rates of adherence for oral diabetes medication decline with the number of times each day the medication should be taken (8), but we could find no report on the association between insulin injection frequency and insulin omission. Depression also has been associated with diabetes medication nonadherence (9) and with insulin omission among adolescent females (10).

Several researchers have developed questionnaires to assess patient perceptions of insulin therapy that could affect regimen adherence (11–16). These questionnaires assess factors such as *1*) interference with eating, exercise, and activities of daily living; *2*) dissatisfaction with the amount of time required to administer insulin and with injection-related pain, bruising, and embarrassment; *3*) worries about insulin-related side effects such as hypoglycemia; and *4*) negative affect associated with administering insulin. Unfortunately, none of these studies formally assessed the association between any of these factors and intentional insulin omission. However, a recent publication did find that insulin adherence is lower among young women who are concerned about their weight (17).

The current study is designed to address questions about intentional insulin omission, including the frequency of this behavior and factors hypothesized to be associated with this behavior, in a large sample of patients weighted to be representative of all adult diabetic patients in the U.S. who take insulin. In a previous report, we found that most insulin-treated patients wanted to reduce the number of insulin injections they take each day, and some reported that injection-related problems affect the number of injections they are willing to take (18). Here we formally assess the impact of a broad range of factors that might be expected to influence intentional insulin omission, including demographic and

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disease factors, as well as perceived burden of insulin therapy (i.e., interference with activities of daily living), the injection experience (e.g., pain and embarrassment), and negative emotions (e.g., dread) associated with insulin injections.

RESEARCH DESIGN AND METHODS
— Data were obtained through an Internet survey of U.S. adults self-identified as taking insulin to treat type 1 or type 2 diabetes; the survey was conducted 13 June to 7 July 2008 by Harris Interactive, a contract research organization. The sample was drawn from the Harris Interactive Chronic Illness Panel. Patients were recruited by email if they had diabetes and currently used a syringe or insulin pen to deliver insulin. The recruitment quota was 500 participants.

Institutional review board approval for the study protocol was obtained from the Human Subject Research Committee of Loyola University Maryland.

Measures
Data collected from participants included the following: *1*) basic demographic information; *2*) disease type, duration, complications, and treatment; *3*) perceived burden of insulin injections; *4*) the experience of injections; *5*) negative affect toward insulin injections; and *6*) frequency of skipping insulin injections. Respondents reported whether they had ever been diagnosed with type 1 or type 2 diabetes, depression, obesity, or cardiovascular disease ("high blood pressure" or "heart disease") and whether they treat their diabetes with diet, exercise, and medications. Other measures are described below.

Burden of injections. Interference with eating and exercise was measured as the mean of two items asking, "How much does the way you inject insulin interfere with eating/exercising when you want?" (response options: 1 = not at all, 2 = a little, 3 = a moderate amount, 4 = a great deal). The reliability of this scale was moderate ($\alpha = 0.80$). Interference with activities of daily living was measured as a count of the affirmative responses to the question, "Do your insulin injections have a negative effect on: social activities, recreational activities, sexual activity, work/career, family care-giving?" (possible range = 0–5). Another measure of interference was whether the respondent plans daily activities around insulin injections (1 = yes, 0 = no).

Experience of injections. There were five measures—dissatisfaction with injection time needed, ease of use, pain, inflammation/bruising, and embarrassment—each measured by a single item (response options: 1 = very satisfied, 2 = satisfied, 3 = somewhat satisfied, 4 = not at all satisfied).

Negative affect toward insulin injections was measured as the mean of three items: "I dread insulin injections"; "Injecting myself with insulin is the hardest part of managing my diabetes"; "I have to mentally prepare myself before each injection" (response options: 1 = strongly disagree, 2 = somewhat disagree, 3 = somewhat agree, 4 = strongly agree). The reliability of this scale was moderate ($\alpha = 0.85$). Worry about hypoglycemia was measured by a single item (response options: 1 = never, 2 = rarely, 3 = sometimes, 4 = often).

Frequency of intentional insulin omission. The dependent variable in this study was the response to the question, "How often do you skip insulin injections that you know you should take?" (response options: 1 = never, 2 = rarely, 3 = sometimes, 4 = often).

Statistical analysis
The sample was weighted to be representative of the U.S. population of people with diabetes. Multiple regression analysis was used to assess independent relationships with frequency of skipping insulin injections. Control variables (demographic and disease characteristics) were entered first, and then injection-related experience and attitudes were entered using stepwise criteria ($P < 0.05$). Separate analyses were performed in the type 1 and type 2 diabetic populations to see whether associations differed between populations.

RESULTS

Sample profile
The sample ($n = 502$) was 55% male, 73% white, 11% Hispanic, 11% African American, and 5% other race/ethnicity, with a mean age of 55 years (Table 1). About half (51%) had attended college. Only about one-third (38%) were presently employed, and those who were not employed included 8% students and 8% disabled; the remainder were mostly retired or nonworking spouses. Median annual income of the sample was about $35,000.

Approximately one-third (32%) reported having been diagnosed by a health care professional as having depression. A total of 77% of the sample said they had type 2 diabetes, and the rest said they had type 1 diabetes; patients reported having diabetes for an average of almost 15 years. A total of 61% of the patient sample identified a primary care physician as their primary diabetes health care provider, whereas 28% named an endocrinologist and 11% named another (nonphysician) health care provider. Of the sample, 39% reported engaging in physical activity and 55% said they followed a healthy diet. A total of 70% of patients surveyed said they took insulin using a syringe and 30% said they used a pen; most (56%) changed their needle with each injection. Patients reported taking an average of 2.7 injections a day (maximum of five recorded).

A substantial minority of respondents (22%) said they planned their daily activities around their insulin injections, and similar proportions reported that insulin injections interfered with their lives: 23% said insulin injections interfered with their eating/exercising schedule more than a little, and 25% said that insulin injections had a negative effect on one or more activity of daily living. Further, a substantial minority of respondents (22%) reported they had to mentally prepare themselves before each injection, and 33% identified they had some level of dread associated with taking their daily injections.

Attitudinal measures tended to fall below the halfway point of the response options (i.e., <2.5). Respondents reported moderate levels of satisfaction with the pain and the inflammation and bruising associated with insulin injections (the scores for pain and inflammation/bruising were significantly higher than those for embarrassment, time needed, and ease of use, $P < 0.001$). A quarter (24%) of respondents had a score representing negative affect toward injections (they scored above the midpoint on the scale), and 21% reported "often" worrying about hypoglycemia.

Regression analysis
Over half (57%) of respondents reported skipping insulin injections they knew they should take; 20% report skipping them sometimes or often. Table 2 shows the results of the regression analysis of intentional insulin omission frequency. Control variables (demographic and diabetes characteristics) accounted for 26% of the variance in intentional insulin omission. Older respondents, those who

Table 1—Sample profile

	All respondents	Type 1 diabetes	Type 2 diabetes
N	502	114	388
Sex			
M	55	41%	59%
F	45	59%	41%
Race/ethnicity			
White	73	70%	74%
Hispanic	11	19%	9%
African American	11	8%	12%
Other	5	3	5
Current age (years)	54.9 ± 13.9	46.9 ± 15.6	57.5 ± 12.2
Education			
No college	49	24	44
Some college	28	38	26
College graduate	14	17	13
Graduate school	9	21	17
Employment			
Full-time employment	28	33	27
Part-time employment	10	16	8
Not employed (student)	8	14	7
Not employed (disabled)	8	2	10
Other	46	35	48
Household income ($)			
<15,000	23	23	23
15,000–24,999	11	5	12
25,000–34,999	10	10	10
35,000–49,999	13	11	14
50,000–74,999	16	12	17
≥75,000	13	25	10
No answer	14	14	14
History of depression	32	30	33
History of cardiovascular disease	71	58	75
History of obesity	36	20	41
Duration of diabetes (years)	14.8 ± 10.2	21.4 ± 13.0	12.8 ± 8.3
Diabetes care provider			
Primary care physician	61	46	66
Endocrinologist	28	48	22
Nonphysician	11	6	12
Engage in physical activity	39	55	34
Follow healthy diet	55	65	52
Insulin injection device			
Pen	30	33	29
Syringe	70	67	71
Change needle each use	56	50	58
Daily injection frequency	2.7 ± 1.4	3.5 ± 1.3	2.5 ± 1.3
Plan daily activities around insulin injections	22	32	19
Interference with eating and exercise*	1.7 ± 0.8	1.9 ± 0.8	1.6 ± 0.8
Interference with activity of daily living*	0.5 ± 1.0	0.7 ± 1.3	0.5 ± 1.0
Dissatisfaction with time needed for injection†	2.0 ± 0.9	1.9 ± 0.9	2.1 ± 0.9
Dissatisfaction with injection ease of use†	2.0 ± 0.9	1.9 ± 0.9	2.0 ± 0.9
Dissatisfaction with injection pain†	2.3 ± 0.9	2.2 ± 0.9	2.3 ± 0.9
Dissatisfaction with injection inflammation/bruising†	2.4 ± 1.0	2.4 ± 0.9	2.5 ± 1.0
Dissatisfaction with injection embarrassment†	2.0 ± 0.9	2.1 ± 0.9	2.0 ± 0.9
Negative affect toward injections‡	1.8 ± 0.9	1.6 ± 0.7	1.9 ± 0.9
Worry about hypoglycemia*	2.7 ± 0.9	2.8 ± 1.0	2.7 ± 0.9
Skip insulin injections§	1.8 ± 0.8	1.7 ± 0.7	1.8 ± 0.8

Data are % or means ± SD, unless otherwise stated. *1 = not at all, 2 = a little, 3 = a moderate amount, 4 = a great deal. †1 = very satisfied, 2 = satisfied, 3 = somewhat satisfied, 4 = not at all satisfied. ‡1 = strongly disagree, 2 = somewhat disagree, 3 = somewhat agree, 4 = strongly agree. §1 = never, 2 = rarely, 3 = sometimes, 4 = often.

Table 2—*Multiple regression analysis of frequency of insulin injection omission*

	B	SE	β	Significance
Female sex*	−0.045	0.067	−0.028	0.499
White race/ethnicity†	−0.006	0.073	−0.003	0.936
Current age (years)	−0.015	0.003	−0.256	<0.001
Education‡				
Some college	−0.001	0.076	−0.001	0.990
College graduate	−0.023	0.100	−0.010	0.818
Graduate school	0.305	0.121	0.109	0.012
Employment§				
Not employed (student)	0.273	0.125	0.094	0.030
Not employed (disabled)	−0.317	0.120	−0.107	0.009
Part-time employment	−0.136	0.104	−0.051	0.192
Full-time employment	−0.108	0.078	−0.061	0.166
Household income ($)	−0.068	0.017	−0.176	<0.001
History of depression	0.048	0.072	0.028	0.504
History of cardiovascular disease	−0.028	0.072	−0.016	0.699
History of obesity	−0.062	0.070	−0.038	0.371
Type 2 diabetes‖	0.428	0.092	0.226	<0.001
Duration of diabetes	0.001	0.004	0.019	0.686
Diabetes care provider¶				
Endocrinologist	−0.085	0.077	−0.048	0.270
Nonphysician	−0.169	0.102	−0.066	0.096
Engage in physical activity	−0.093	0.071	−0.057	0.186
Follow healthy diet	−0.157	0.069	−0.098	0.023
Use insulin pen#	−0.001	0.074	−0.001	0.989
Needle change frequency	−0.049	0.070	−0.031	0.479
Daily injection frequency	0.118	0.025	0.205	<0.001
Plan daily activities around insulin injections	0.247	0.079	0.129	0.002
Interference with activity of daily living	0.112	0.033	0.146	0.001
Dissatisfaction with injection pain	0.130	0.042	0.149	0.002
Dissatisfaction with injection embarrassment	0.146	0.041	0.169	<0.001

*Reference category = male. †Reference category = nonwhite. ‡Reference category = no college. §Reference category = other not employed. ‖Reference category = type 1 diabetes. ¶Reference category = primary care physician. #Reference category = use syringe.

were disabled, those with higher household income, and those who followed a healthy diet were significantly less likely to skip injections, whereas subjects who were students and had the highest education or type 2 diabetes and subjects who took more injections were significantly more likely to skip injections.

Four measures of injection burden and experience had significant independent associations with higher levels of intentional insulin omission and accounted for an additional 10% of the variance. These included two aspects of interference (planning one's activities around insulin injections and injections interfering with activities of daily living) and two aspects of the injection process itself (pain and embarrassment). Respondents who planned daily activities around insulin injections, those who said that taking injections interfered with activities of daily living, and those who reported injection-related pain or embarrassment intentionally skipped insulin injections more often.

Separate analyses using the variables listed in Table 2 were performed among subjects with type 1 diabetes and subjects with type 2 diabetes (results not shown). Because there were more participants with type 2 diabetes, the overall model most closely resembled that for type 2 diabetes. Only two variables significant in the overall model were not significant in the type 2 model—being a student and following a healthy diet. Only three variables were significant in the type 1 model—following a healthy diet, number of daily insulin injections, and interference with activities of daily living (being a student had a *P* value of 0.056).

CONCLUSIONS — This study suggests that intentional omission of insulin injections that should be taken occurs in the majority of adults using insulin to treat their diabetes and is common in ∼20% of these individuals. Intentional insulin omission among adults varies with a number of demographic and disease characteristics. It also is associated with indicators of perceived burden and the experience of injections as painful and embarrassing.

Demographic and disease factors
We found that respondents with higher household income, but not individuals with more education, were less likely to skip insulin injections they knew they should take. This may reflect easier access to medications and supplies among individuals with higher income, but it is also likely that higher socioeconomic status is associated with more access to diabetes education, higher health literacy, greater control over one's daily routines, and better problem-solving skills (19). Our study appears to be among the first to identify an association between socioeconomic status and insulin omission. Future research should seek to identify potential mediators of this relationship, i.e., what links lower socioeconomic status to insulin omission.

Contrary to earlier reports (3,4), we found no racial/ethnic differences in intentional insulin omission. This may be because we did not have enough nonwhite respondents to examine the different racial/ethnic groups separately. Alternatively, this may be due to our controlling for income and education in the analysis, thereby eliminating the confounding of race/ethnicity with socioeconomic status.

Much prior research has suggested that intentional insulin omission is common among female adolescents with type 1 diabetes, serving as a weight control strategy and sometimes linked to eating disorders (10). We found that students (who were younger than nonstudents) were more likely to skip injections they knew they should take, but this behavior was not more common among women than it was among men. We found no overall association between age and intentional insulin injection omission among patients with type 1 diabetes, suggesting that patients with type 1 diabetes "age-out" of this behavior by early adulthood, when they complete their education. Ascertaining the validity of this interpretation would require following youth with type 1 diabetes as they age into adulthood to determine change in rate of insulin omission.

Our finding that, among individuals with type 2 diabetes, older respondents were less likely to skip insulin injections is consistent with earlier studies (3,4). This

suggests that there are parallel aging-out processes among individuals with type 1 and type 2 diabetes, but in type 2 diabetes, this process takes place later in the life course (almost all people with type 2 diabetes are diagnosed as adults). Ascertaining the validity of this interpretation would require following adults with type 2 diabetes as they age to determine change in rate of insulin omission.

Having type 2 diabetes was itself associated with higher levels of intentional omission of insulin injections. The beta for this variable (0.226) was approximately twice the size of the unadjusted eta (0.095), reflecting the fact that controlling for confounding factors (such as age and number of daily injections) revealed a stronger underlying association. The independent association of type 2 diabetes with increased insulin omission may reflect the fact that patients with type 2 diabetes have a residual insulin response, reducing the immediate consequences of omitting an injection. Thus, these individuals may feel less vulnerable to the effects of skipping insulin injections they know they should take. Interestingly, whereas duration of diabetes was associated with the frequency of insulin injection omission, regression analysis revealed that duration of diabetes did not make an independent contribution to this behavior. That is, although insulin omission may be less common among individuals with longer duration of diabetes, this is likely a function of other factors such as age and type of diabetes rather than of duration per se.

The associations of insulin injection omission with other health conditions were examined. Surprisingly, history of depression was not associated with insulin omission; this contradicts findings from studies of general adherence (9,20) and of insulin omission among adolescents (10). However, because current depression was not assessed, any concurrent association was likely to be lost. Others have shown that depression symptom scores fluctuate substantially over relatively short periods of time; individuals with elevated depression symptoms at a given point in time are likely to not report elevated symptoms 6 months later (21,22). In addition, depression symptoms across the whole range of severity symptoms have been shown to predict regimen adherence more powerfully than diagnosed depression (23). Being disabled was associated with less insulin omission; this may be due to a variety of

reasons, including their receiving more assistance with care, or making a greater effort to compensate for poor health.

Two aspects of patients' treatment regimens were associated with increased insulin omission—respondents who took more injections each day and those who did not follow a healthy diet were more likely to skip injections. That dietary nonadherence is associated with insulin nonadherence is not surprising. More frequent injection omission among individuals taking more injections could reflect the frequently reported finding that more complex regimens are associated with lower levels of adherence (6). It might also be that the impact of skipping a shot is reduced among individuals who take more shots.

Insulin and injection-related factors

Our study suggests that insulin omission is affected by the perceived burden of insulin therapy (i.e., having to plan one's life around insulin injections and feeling that the insulin regimen interferes with activities of daily living such as social activities, work-related activities, and family care-giving responsibilities). We offer one caveat regarding our findings; we do not believe that the behavior of planning one's day around insulin injections actually increases the level of insulin injection omission, but we do believe that feeling that one has to plan around one's injections is associated with higher frequency of skipping insulin injections one should take. That is, when there is a conflict between scheduling of treatment and life activities, one can either plan one's activities in a way that reduces this conflict or deal with the conflict by ignoring treatment needs. Reducing the perceived burden of insulin injections may require more effort from health care providers. As we have suggested elsewhere, providers must find out what the specific issues are for each patient and work with that patient to develop solutions that will work for him or her (24).

We note that the measure of interference with eating and exercise was significantly associated with insulin injection omission until interference with activities of daily living was entered into the model (results not shown). Thus, while interference with eating and exercise might be part of the burden of insulin therapy, interference with other aspects of daily living had a more substantial association with insulin omission.

Our study suggests that insulin omission may be affected by the immediate

experience of injecting insulin as painful and embarrassing (but not dissatisfaction with time needed, ease of use, or skin inflammation/bruising). There are numerous device-related strategies for reducing pain and embarrassment, including insulin pens, finer gauge needles, injection ports, needleless injectors, and other injection assistance devices. However, we have found that patients do not feel that their health care providers are giving them adequate assistance in managing these problems, even when they raise the issue with their providers (18).

We note that the measure of negative affect toward injections was significantly associated with insulin omission until dissatisfaction with injection embarrassment and pain were entered into the model (results not shown). This suggests that addressing pain and embarrassment may reduce not only insulin omission, but also the emotional burden of injections, thereby enhancing psychological well-being. It is interesting that worry about hypoglycemia did not predict intentional omission of insulin injections, even though worry about hypoglycemia was high in the study population. This suggests that patients may address this worry by eating more or lowering insulin doses rather than by skipping injections altogether.

Study strengths and limitations

Strengths of the study include the large sample of diabetic patients drawn from a general population and the fact that the sample was weighted to be nationally representative. However, patients volunteer for the panel from which respondents were drawn and may not be representative of all patients (e.g., they may be more adherent with their treatment regimens).

Limitations of the study include the fact that there was no objective measure of insulin use (e.g., pharmacy records). Moreover, while our measure of insulin omission was very specific (i.e., skipping injections that respondents knew they should take), it is possible that some respondents included injections they did not skip intentionally, but rather simply forgot to take. Respondents might also have included scheduled injections that were appropriately skipped because a meal was not eaten or blood glucose levels were very low. This could explain (at least in part) the association between following a healthy diet and fewer skipped injections. More disciplined eating behavior reduces meal skipping, which is an often-cited reason for skipping insulin injections. This is

consistent with the fact that the relationship between our diet measure and insulin omission is present only among individuals with type 1 diabetes where closer matching of food and insulin is required.

Finally, our study probably underestimated the level of insulin nonadherence in this population because it did not capture instances in which patients took an injection but gave less than the amount of insulin they knew was needed for optimal glucose control.

Clinical implications

Our findings make clear that while most patients did not report regular omission of insulin injections, a substantial number did. Thus, our findings suggest that it is important to identify patients who omit insulin and to be aware of the potential risk factors identified here. Lack of personal resources (especially income) is one potential warning sign. Although much attention has been focused on insulin omission among adolescents with type 1 diabetes, our findings suggest that among adults, individuals with type 2 diabetes are at higher risk. Patients who are not adhering to other elements of the treatment regimen, especially diet, also may be at risk for insulin omission. For patients who report injection-related problems (interference with daily activities, injection pain, and embarrassment), providers should consider recommending strategies and tools for addressing these problems to prevent insulin omission. This may contribute to improved treatment adherence and consequent clinical outcomes.

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