

When a Unit of Insulin Is Not a Unit: Detemir Dosing and Insulin Cost in Type 2 Diabetes Mellitus

Christopher K. Johnson, BS

Columbia University College of Physicians and Surgeons, New York, New York

Mona Shimshi, MD

Mount Sinai Medical Center, New York, New York

ABSTRACT

Background: Increasing acceptance of basal-bolus insulin therapy for the control of diabetes mellitus (DM) has led to newer formulations of basal insulin analogues. The newest one is detemir.

Objectives: Clinical evidence suggests that patients with type 2 DM require higher doses of detemir than other basal insulins to achieve equivalent glycemic control. This study examines evidence for greater dosing requirements and the implications of higher doses on the cost of insulin treatment.

Methods: We performed a MEDLINE search for randomized, prospective studies comparing detemir with other basal insulins in patients with type 2 DM that were published in English between January 2000 and November 2008. The mean daily doses of basal and bolus insulin and the mean total daily insulin doses were determined. Overall weighted mean doses of the insulins were used to estimate the mean total daily insulin doses required for a 100-kg patient, and published 2008 US retail prices were used to estimate the retail costs of basal-bolus and basal-only insulin regimens.

Results: Seven trials involving 3311 patients were identified in the literature search. The mean total daily insulin dose was 0.80 unit/kg for detemir-based regimens and 0.58 unit/kg for comparison regimens. For basal-bolus regimens, the estimated retail cost of the mean total daily insulin dose was \$11.24 for detemir-based regimens compared with \$8.99 for glargine-based regimens and \$6.41 for neutral protamine Hagedorn (NPH)-based insulins. For basal-only regimens, the estimated retail cost of the mean total daily insulin dose was \$8.23 for detemir compared with \$5.19 for glargine and \$2.35 for NPH.

Conclusions: It is important for health care providers and patients to know that patients with type 2 DM may require substantially higher doses of detemir than other basal insulins. This should be considered when titrating the dose as well as in cost-benefit analyses of detemir versus other insulins. (*Insulin*. 2009;4:87-93) © 2009 Excerpta Medica Inc.

Key words: detemir, glargine, aspart, NPH insulin, type 2 diabetes, equivalence, cost.

INTRODUCTION

The global prevalence of type 2 diabetes mellitus (DM) in 2000 was estimated to be 2.8% (ie, >170 million people).¹ By the year 2030, the prevalence is expected to jump by >50% to 4.4% of the world population.¹ The prevalence of type 2 DM is considerably higher in patients with a body mass index >30 kg/m².^{2,3}

This growing epidemic has major implications in terms of economic burden, particularly when dealing with the soaring costs of microvascular and macrovascular complications of DM. The association between improved glycemic control in patients with either type 1 or type 2 DM and the subsequent reduction in disease-related complications creates the framework for more frequent use of insulin. In the UK Prospective Diabetes Study,⁴ 53% of the 339 patients with newly diagnosed type 2 DM who were randomized to treatment with oral sulfonylurea medications required addi-

tional insulin therapy after 6 years. Another important reason for the increased use of insulin was the revelation of "metabolic memory."⁵ The implication of this theory is that control of diabetes should be initiated as soon as possible after diagnosis to reduce the risk of developing complications years later.⁶ With increasing age and duration of disease, tight control of blood glucose levels becomes more difficult to maintain.⁷ The cost of intensive glycemic control increases the costs of diabetes management. However, this initial investment in tight control is more than offset by the prevention of complications.⁸

A major consequence of improving glycemic control is an increase in the frequency of hypoglycemic reactions. Although patients with type 1 DM have more frequent severe hypoglycemic reactions than do patients with type 2 DM, most of the patients hospitalized with severe hypoglycemia are patients with type 2 DM because they represent the

majority of the patients taking insulin.⁹ In a community-based study conducted in Tayside, Scotland,⁹ 91 patients with type 2 DM and 69 patients with type 1 DM (11% of the patients in each group) required hospitalization for hypoglycemia.

In studies addressing psychological resistance to insulin therapy, 2 issues surfaced in terms of increasing patient adherence: fear of injections and fear of hypoglycemia.¹⁰ Insulin pens, although initially more costly than standard insulin therapy, have been found to significantly reduce the number of hospitalizations and time lost from work because of nonadherence. The savings from reduced hospitalization and time lost from work far exceeded the costs of insulin pen therapy.¹¹

The newer premeal insulin analogues, as well as the insulin analogues used for basal control, have also been shown to markedly reduce the incidence of and hospitalizations for hypoglycemia.^{8,11-13} The savings gained from the reduction in hypoglycemic reactions and the reduced utilization of both outpatient and inpatient health care services more than offset the cost of the insulin analogues.¹³

The newer premeal insulin analogues, as well as the insulin analogues used for basal control, have been shown to markedly reduce the incidence of and hospitalizations for hypoglycemia.

The earliest benefits were shown in comparisons of premeal insulin analogues and regular insulin.¹⁴ More recently, with the increased acceptance of the basal-bolus concept of treating diabetes, fewer hypoglycemic reactions have occurred with basal insulin analogue therapy than with conventional neutral protamine Hagedorn (NPH) insulin using similar target glycosylated hemoglobin (A1C) levels.⁸ Treatment with short-duration insulin analogues reduced emergency department visits by 26% and hospitalizations by 7%.¹⁵ Glargine reduced the cost of hospitalizations in a study of patients with type 2 DM by 9% for every 100 patients treated.¹⁶ This reduction more than offset the cost of the analogue. One study¹⁷ reported an estimated mean reduction of 17 episodes of hypoglycemia for every 100 patients treated with short-acting insulin analogues (lispart, aspart, and glulisine). The potential for cost savings resulting from reduced hypoglycemia and improved glycemic control is enormous.

This potential for cost savings provides the rationale for the introduction of the newest basal insulin to the market—detemir.* Detemir not only causes fewer hypoglycemic reactions, but also may cause less weight gain than other insulins, providing further clinical and economic benefits.¹⁸ However, clinical evidence indicates that higher doses of

insulin are required for patients with type 2 DM when using detemir than when using other basal insulins.¹⁹ This may be particularly true for obese patients, who represent the majority of the patients with type 2 DM in the United States.

The potential for cost savings from reduced hypoglycemia and improved glycemic control is enormous.

In this study, we compared the dosing requirements for detemir with those for other insulins in patients with type 2 DM. We also compared the cost of detemir with that of other basal insulins based on the requirements of a 100-kg patient.

Higher doses of insulin are required for patients with type 2 DM when using detemir than when using other basal insulins.

METHODS

We performed a MEDLINE search for randomized, prospective studies comparing detemir with other basal insulins in patients with type 2 DM that were published in English between January 2000 and November 2008. The identified trials were reviewed, and the mean daily doses of basal and bolus insulin and the mean total daily insulin doses (in units per kilogram of body weight) were determined. Overall weighted mean doses of the insulins and published 2008 US retail prices (NPH insulin,[†] \$49.99 for 10 mL; glargine,[‡] \$176.99 for five 3-mL syringes; detemir, \$181.72 for five 3-mL syringes; and aspart,[§] \$205.12 for five 3-mL syringes)²⁰ were used to compare the costs of both basal-bolus and basal-only insulin regimens based on the requirements of a 100-kg patient.

RESULTS

Seven randomized, prospective trials comparing detemir with other basal insulins in patients with type 2 DM were identified in the literature search.^{19,21-26} Four of these studies^{21-23,26} compared basal-bolus regimens; the remaining 3 studies^{19,24,25} compared basal-only regimens in insulin-naïve patients.

[†]Trademark: Humulin® N Pen (Eli Lilly and Company, Indianapolis, Indiana).

[‡]Trademark: Lantus® SoloStar® Pen (sanofi-aventis US, LLC, Bridgewater, New Jersey).

[§]Trademark: NovoLog® FlexPen® (Novo Nordisk Inc.).

*Trademark: Levemir® (Novo Nordisk Inc., Princeton, New Jersey).

In the 7 trials, 3311 patients were randomized to treatment (Table I). Treatment duration was 22 to 52 weeks in the 6 outpatient studies^{19,21–25} and ~1 week in the inpatient study.²⁶ Although all 4 studies of basal-bolus regimens^{21–23,26} used detemir/aspart for one arm, the comparison regimens were NPH/regular (2 studies),^{21,26} NPH/aspart,²² and biphasic aspart 30.²³ Of the 3 studies of basal-only regimens, 1 compared detemir with NPH¹⁹; 1 compared detemir with glargine²⁴; and 1 compared detemir administered in the morning, detemir administered in the evening, and NPH administered in the evening.²⁵ In the study comparing detemir AM, detemir PM, and NPH PM,²⁵ the mean daily doses were 47 units, 37 units, and 33 units in the 3 arms, respectively (only the detemir PM dose was used to calculate mean doses).

Across the 7 identified studies, the weighted mean total daily insulin dose was greater for detemir-based regimens than for other regimens (0.80 and 0.58 unit/kg, respectively) (Table II).^{19,21–26} In all 7 studies, the mean daily basal dose was greater for detemir-based regimens than for other regimens, although the differences in the individual studies were generally not statistically significant.

No significant differences in mean A1C values were observed between arms in any of the studies except the one conducted by Liebl et al²³ (Table III), which reported that detemir was superior overall and in patients who were previously treated with insulin ($P = 0.005$), but not in insulin-naive patients. In the study conducted by Philis-Tsimikas et

al,²⁵ which reported nearly identical dosing for detemir and NPH, the patients in the NPH arm had a larger, although not statistically significant, decrease in mean A1C.

Rates of hypoglycemia varied across the studies (Table III), but the differences between detemir and the comparison insulins were generally not statistically significant. Patients who took detemir in the study conducted by Philis-Tsimikas et al²⁵ had significantly less hypoglycemia than did patients in the comparison arm ($P = 0.019$), but they also had worse glycemic control. Patients gained less weight on detemir regimens than on comparison regimens in each study except the one conducted by Liebl et al,²³ which reported the largest trend toward better glycemic control in the detemir arm (Table III).

The weighted mean total daily insulin dose was 0.80 unit/kg for patients on detemir regimens and 0.58 unit/kg for patients on the comparison regimens (Table II). For the detemir-based, basal-bolus regimens, the mean daily basal (detemir) dose was 0.42 unit/kg and the mean daily bolus (aspart) dose was 0.45 unit/kg (Table IV).^{20–23,26} For the comparison regimens, the mean daily basal (glargine or NPH) dose was 0.38 unit/kg and the mean daily bolus (aspart) dose was 0.33 unit/kg. For the basal-only regimens, the mean daily dose was 0.68 unit/kg for detemir, 0.47 unit/kg for NPH, and 0.44 unit/kg for glargine (Table V).^{19,20,24,25}

Greater insulin requirements led to higher projected insulin costs. The estimated retail cost of the mean total daily

Table I. Design and baseline patient characteristics from published studies comparing detemir-based regimens with other basal insulin regimens in patients with type 2 diabetes mellitus.

Author, Year	N	Study Length, wk	Population	Insulin Regimens	Mean Age, y	Mean BMI, kg/m ²	Mean Duration of Diabetes, y
Raslová et al, ²¹ 2004	395	22	On insulin previously	Detemir/aspart NPH/regular	58	29	14
Haak et al, ²² 2005	505	26	On insulin previously	Detemir/aspart NPH/aspart	61	31	13
Hermansen et al, ¹⁹ 2006	476	24	Insulin naive	Detemir BID NPH BID	61	29	10
Philis-Tsimikas et al, ²⁵ 2006	504	20	Insulin naive	Detemir AM Detemir PM NPH PM	58	30	11
Rosenstock et al, ²⁴ 2008	582	52	Insulin naive	Detemir Glargine	59	31	9
Liebl et al, ²³ 2009	719	26	~28% On insulin	Detemir/aspart Biphasic aspart 30	61	31	9
Umpierrez et al, ²⁶ 2009	130	~1	Hospitalized, any regimen	Detemir/aspart NPH/regular	59	33	NA

BMI = body mass index; NPH = neutral protamine Hagedorn; NA = not applicable.

Table II. Mean basal and bolus doses of detemir and comparison insulins, mean total daily insulin doses, and weighted mean total insulin doses across studies (units/kg).

Author, Year	Detemir Regimen			Comparison Regimen		
	Mean Daily Basal Dose	Mean Daily Bolus Dose	Mean Total Daily Insulin Dose	Mean Daily Basal Dose	Mean Daily Bolus Dose	Mean Total Daily Insulin Dose
Raslová et al, ²¹ 2004	0.58	0.37	0.95	0.46	0.33	0.79
Haak et al, ²² 2005	0.42	0.47	0.89	0.40	0.40	0.80
Hermansen et al, ¹⁹ 2006	0.77	NA	0.77	0.52	NA	0.52
Philis-Tsimikas et al, ²⁵ 2006	0.4*	NA	0.4	0.4	NA	0.4
Rosenstock et al, ²⁴ 2008	0.78	NA	0.78	0.44	NA	0.44
Liebl et al, ²³ 2009	0.38	0.48	0.86	0.32	0.32	0.63
Umpierrez et al, ²⁶ 2009	0.33	0.30	0.63	0.27	0.18	0.45
Weighted mean			0.80			0.58

NA = not applicable.
 *Detemir PM arm only.

Table III. Glycemic control and adverse effects in studies comparing detemir-based regimens with other basal insulin regimens in patients with type 2 diabetes mellitus.

Author, Year	Insulin Regimens	Mean Starting A1C	Mean Ending A1C	Mean Change in A1C	Patients With Hypoglycemia, %	Mean Weight Gain, kg
Raslová et al, ²¹ 2004	Detemir	8.16	7.51	-0.65	35	0.5
	NPH	8.08	7.50	-0.58	36	1.1
Haak et al, ²² 2005	Detemir	7.9	7.6	-0.3	46	1.0
	NPH	7.8	7.5	-0.3	50	1.8
Hermansen et al, ¹⁹ 2006	Detemir	8.61	6.8	-1.8	64	1.2
	NPH	8.51	6.6	-1.9	80	2.8
Philis-Tsimikas et al, ²⁵ 2006	Detemir _{AM}	9.08	7.50	-1.58	19	1.2
	Detemir _{PM}	8.88	7.40	-1.48	16	0.7
	NPH _{PM}	9.15	7.35	-1.74	32	1.6
Rosenstock et al, ²⁴ 2008	Detemir	8.64	7.16	-1.48	63	3.0
	Glargine	8.62	7.12	-1.50	66	3.9
Liebl et al, ²³ 2009	Detemir	8.52	6.96	-1.56	31	2.4
	Biphasic aspart 30	8.40	7.17	-1.23	28	2.1
Umpierrez et al, ²⁶ 2009	Detemir	NA	NA	NA	33	NA
	NPH				25	

A1C = glycosylated hemoglobin; NPH = neutral protamine Hagedorn; NA = not applicable.

Table IV. Estimated retail costs of insulin used in detemir-based and comparison basal-bolus regimens for a 100-kg patient using published 2008 US retail prices.^{20–23,26}

Insulin	Mean Daily Basal Dose, Units/kg	Mean Daily Basal Cost, US \$	Mean Daily Bolus Dose, Units/kg	Mean Daily Bolus Cost, US \$	Mean Total Daily Insulin Cost, US \$
Detemir	0.42	5.09	0.45	6.15	11.24
Glargine	0.38	4.48	0.33	4.51	8.99
NPH	0.38	1.90	0.33	4.51	6.41

NPH = neutral protamine Hagedorn.

Table V. Estimated retail costs of insulin in basal-only regimens for a 100-kg patient using published 2008 US retail prices.^{19,20,24,25}

Insulin	Mean Daily Basal Dose, Units/kg	Mean Daily Basal Cost, US \$
Detemir	0.68	8.23
NPH	0.47	2.35
Glargine	0.44	5.19

NPH = neutral protamine Hagedorn.

insulin dose for a basal-bolus regimen was \$11.24 for detemir-based regimens compared with \$8.99 for glargine-based regimens and \$6.41 for NPH-based regimens (Table IV). The estimated retail cost of the mean total daily insulin dose for basal-only regimens was \$8.23 for detemir compared with \$5.19 for glargine and \$2.35 for NPH (Table V).

DISCUSSION

Results of these 7 studies suggest that higher doses of insulin are required for patients with type 2 DM when using detemir than when using other basal insulins. This is true for basal-bolus regimens as well as basal-only regimens. The largest increase in dose was found in the head-to-head comparison of detemir and glargine.²⁴

The reasons for the increased dose requirement for detemir are not clear, but the increase is likely related to the unique pharmacologic properties of the analogue. Unlike all other insulins, detemir is bound to albumin in the blood, giving it a protracted period of action. The modification used to make detemir bind to albumin (ie, attachment of myristic acid [C14 fatty acid chain]) may have resulted in decreased affinity for the insulin receptor. The first clinical trials of detemir found it to be less potent than other insulins on a mole-to-mole basis.²⁷ Consequently, detemir is prepared in a formulation 4 times more concentrated (2400 vs 600 nmol/mL) than other available insulins.²⁷ This adjust-

ment was done empirically after studies in patients with type 1 DM required detemir doses ~3.8 times greater than those required with comparison insulins.²⁸ For unknown reasons, this adjustment may be inadequate in patients with type 2 DM, where a molar ratio closer to 6:1 may be more appropriate.²⁷

The present analysis is limited by the available data. Only a few prospective, randomized trials have compared detemir with other insulins in patients with type 2 DM. The data presented here come from only a few thousand patients. Furthermore, the costs of the insulin regimens in this analysis are derived from US retail prices and may not be applicable to other regions or health care systems. However, the general analysis would be valid in any system in which detemir and glargine are priced similarly and significantly higher than generic NPH insulin.

The full cost of the insulin regimens includes more than the insulin itself. The cost of supplies, including insulin delivery devices, would likely increase in concert with the insulin dose. The costs associated with hypoglycemic reactions and other complications are not accounted for in this analysis. One retrospective analysis conducted in the United Kingdom²⁸ examined a broader range of insulin costs associated with detemir and glargine. That study reported significantly higher costs for detemir-based regimens than for glargine-based regimens ($P < 0.001$), primarily because of the higher doses of detemir.²⁹

CONCLUSIONS

Patients with type 2 DM may require substantially higher doses of detemir than other basal insulins. Higher doses translate into higher insulin costs, which must be taken into account in cost-benefit analyses comparing detemir with other basal insulins. This information is also important for health care providers who are considering switching their patients with type 2 DM from NPH or glargine to detemir for reasons such as hypoglycemia or weight gain. The provider and the patient should understand that significantly greater doses (as well as costs) will likely be necessary, and that those higher doses do not represent treatment failure or disease progression, but rather the intrinsic properties of the insulin itself.

REFERENCES

1. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047–1053.
2. Bays HE, Chapman RH, Grandy S, for the SHIELD Investigators' Group. The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: Comparison of data from two national surveys [published correction appears in *Int J Clin Pract*. 2007;61:1777–1778]. *Int J Clin Pract*. 2007;61:737–747.
3. Narayan KM, Boyle JP, Thompson TJ, et al. Effect of BMI on lifetime risk for diabetes in the U.S. *Diabetes Care*. 2007;30:1562–1566.
4. Wright A, Burden AC, Paisey RB, et al, for the U.K. Prospective Diabetes Study Group. Sulfonylurea inadequacy: Efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the U.K. Prospective Diabetes Study (UKPDS 57) [published correction appears in *Diabetes Care*. 2002;25:1268]. *Diabetes Care*. 2002;25:330–336.
5. Ihnat MA, Thorpe JE, Ceriello A. Hypothesis: The 'metabolic memory', the new challenge of diabetes. *Diabet Med*. 2007;24:582–586.
6. Kahn SE. Clinical review 135: The importance of beta-cell failure in the development and progression of type 2 diabetes. *J Clin Endocrinol Metab*. 2001;86:4047–4058.
7. Levy J, Atkinson AB, Bell PM, et al. Beta-cell deterioration determines the onset and rate of progression of secondary dietary failure in type 2 diabetes mellitus: The 10-year follow-up of the Belfast Diet Study. *Diabet Med*. 1998;15:290–296.
8. Meece J. Pharmacoeconomic advantages of insulin analogs. *US Pharm*. 2006;31:HS42–HS50.
9. Zammit NN, Frier BM. Hypoglycemia in type 2 diabetes: Pathophysiology, frequency, and effects of different treatment modalities. *Diabetes Care*. 2005;28:2948–2961.
10. Polonsky WH, Jackson RA. What's so tough about taking insulin? Addressing the problem of psychological insulin resistance in type 2 diabetes. *Clin Diabetes*. 2004;22:147–150.
11. Lee WC, Balu S, Cobden D, et al. Medication adherence and the associated health-economic impact among patients with type 2 diabetes mellitus converting to insulin pen therapy: An analysis of third-party managed care claims data [published correction appears in *Clin Ther*. 2006;28:1968–1969]. *Clin Ther*. 2006;28:1712–1725; discussion 1710–1711.
12. Leese GP, Wang J, Broomhall J, et al, for the DARTS/MEMO Collaboration. Frequency of severe hypoglycemia requiring emergency treatment in type 1 and type 2 diabetes: A population-based study of health service resource use. *Diabetes Care*. 2003;26:1176–1180.
13. Tran K, Banerjee S, Li H, et al. Long-acting insulin analogues for diabetes mellitus: Meta-analysis of clinical outcomes and assessment of cost-effectiveness [Technology Report number 92]. Ottawa, Canadian Agency for Drugs and Technologies in Health; 2007.
14. Hirsch IB. Insulin analogues. *N Engl J Med*. 2005;352:174–183.
15. Mahoney JJ. Reducing patient drug acquisition costs can lower diabetes health claims. *Am J Manag Care*. 2005;11(Suppl 5):S170–S176.
16. Warren E, Weatherley-Jones E, Chilcott J, Beverley C. Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine. *Health Technol Assess*. 2004;8:iii, 1–57.
17. Siebenhofer A, Plank J, Berghold A, et al. Short acting insulin analogues versus regular human insulin in patients with diabetes mellitus. *Cochrane Database Syst Rev*. 2006;CD003287.
18. Rosenstock J, Dailey G, Massi-Benedetti M, et al. Reduced hypoglycemia risk with insulin glargine: A meta-analysis comparing insulin glargine with human NPH insulin in type 2 diabetes. *Diabetes Care*. 2005;28:950–955.
19. Hermansen K, Davies M, Derezinski T, et al. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naive people with type 2 diabetes [published correction appears in *Diabetes Care*. 2007;30:1035]. *Diabetes Care*. 2006;29:1269–1274.
20. Drugstore.com. <http://www.drugstore.com>. Accessed December 8, 2008.
21. Raslová K, Bogoev M, Raz I, et al. Insulin detemir and insulin aspart: A promising basal-bolus regimen for type 2 diabetes [published correction appears in *Diabetes Res Clin Pract*. 2006;72:112]. *Diabetes Res Clin Pract*. 2004;66:193–201.
22. Haak T, Tiengo A, Draeger E, et al. Lower within-subject variability of fasting blood glucose and reduced weight gain with insulin detemir compared to NPH insulin in patients with type 2 diabetes. *Diabetes Obes Metab*. 2005;7:56–64.
23. Liebl A, Prager R, Binz K, et al, for the PREFER Study Group. Comparison of insulin analogue regimens in people with type 2 diabetes mellitus in the PREFER Study: A randomized controlled trial. *Diabetes Obes Metab*. 2009;11:45–52.
24. Rosenstock J, Davies M, Home PD, et al. A randomised, 52-week, treat-to-target trial comparing insulin detemir with insulin glargine when administered as add-on to glucose-lowering drugs in insulin-naive people with type 2 diabetes. *Diabetologia*. 2008;51:408–416.
25. Philis-Tsimikas A, Charpentier G, Clauson P, et al. Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes [published correction appears in *Clin Ther*. 2006;28:1967]. *Clin Ther*. 2006;28:1569–1581.
26. Umpierrez GE, Hor T, Smiley D, et al. Comparison of inpatient insulin regimens with detemir plus aspart versus NPH plus regular in medical patients with type 2 diabetes. *J Clin Endocrinol Metab*. 2009;94:564–569.
27. Misbin RI. Medical Officer Review NDA 21536. Washington, DC, US Food and Drug Administration, Center for Drug Evaluation and Research, 2005.
28. Vague P, Selam JL, Skeie S, et al. Insulin detemir is associated with more predictable glycemic control and reduced risk of hypoglycemia than NPH insulin in patients with type 1 diabetes on a basal-bolus regimen with premeal insulin aspart. *Diabetes Care*. 2003;26:590–596.

29. Poole CD, Tetlow T, McEwan P, et al. The prescription cost of managing people with type 1 and type 2 diabetes following initiation of treatment with either insulin glargine or insulin detemir in routine general practice in the UK: A retrospective database analysis. *Curr Med Res Opin.* 2007;23(Suppl): S41–S48.

Address correspondence to: Mona Shimshi, MD, Department of Endocrinology (Atran 4), Mount Sinai Medical Center, One Gustave Levy Place, New York, NY 10029. E-mail: mshimshimd@aol.com