Barriers to Insulin Progression Among Patients With Type 2 Diabetes
A Systematic Review

Purpose

Treatment guidelines recommend insulin progression (switching from basal to a premixed insulin regimen, adding bolus doses, and/or increasing dosing frequency) to achieve HbA1C targets as type 2 diabetes progresses, but fewer patients are being progressed than would be indicated based on their disease status. This systematic review proposes 2 questions regarding insulin progression among patients with type 2 diabetes: (1) What are the patient, provider, and health system barriers to insulin progression? (2) Do insulin progression barriers differ between insulin-naive and insulin-experienced patients?

Methods

We conducted a systematic review in the MEDLINE, EMBASE, Science Citation Index, PsycINFO, CINAHL, and Cochrane Library databases through July 2011.

Results

Of 745 potentially relevant articles, 10 met inclusion criteria: 7 evaluated patient and 2 evaluated provider barriers, and 1 was an intervention to reduce barriers among physicians. Patients with prior insulin experience had fewer barriers arising from injection-related concerns and worries about the burden of insulin progression than did insulin-naive patients. Physician barriers included concerns about patients’ ability to follow more complicated regimens as well as physicians’ own inexperience with insulin and progression algorithms. The cross-sectional nature, narrow scope, and failure of all studies
In recognition that appropriate insulin progression can prevent or delay type 2 diabetes–related complications and reduce unnecessary health expenditures, researchers, clinicians, and policy makers have an interest in understanding and addressing barriers to progression among patients with type 2 diabetes. In this systematic review, we evaluate the peer-reviewed literature through July 2011 to answer 2 questions regarding insulin progression among patients with type 2 diabetes: (1) What are the patient, provider, and health system barriers to insulin progression? (2) Do insulin progression barriers differ between insulin-naïve and insulin-experienced patients, and how? By enumerating the multiple sources of potential barriers to insulin progression and the challenges of patients with different insulin treatment experiences, this review summarizes the best available evidence regarding obstacles to insulin progression, highlights opportunities for overcoming those barriers, and identifies knowledge gaps.

**Research Design and Method**

We followed PRISMA guidelines for the conduct and reporting of systematic reviews.12

**Data Sources**

We limited initial searches to articles published in MEDLINE, EMBASE, Science Citation Index (ISI Web of Science), PsycINFO, CINAHL, or the Cochrane Library on or before July 15, 2011. Our search strategy focused on terms related to type 2 diabetes mellitus, insulin, and treatment progression (eg, in Medline: [Diabetes Mellitus, Type 2][Mesh] AND “Insulin”[Mesh] AND “Therapeutics”[Mesh] AND (intens* OR escalat* OR increas* OR progres*) AND (barrier* OR obstacle* OR challeng* OR disincentiv* OR impediment* OR diffi-cult* OR limitation*)]. Search strategies specific to each database can be found in the online appendix. After eliminating duplicates across search databases, articles meeting search criteria were included in the review and were reference mined for related articles. No language restriction was imposed.

**Study Selection**

Final articles were included if they reported original data regarding barriers to insulin treatment progression among patients with type 2 diabetes, whether data were...
drawn from self-report surveys, interviews, clinical trials, and/or observational studies. Both patient and physician data were included. Articles reporting only barriers to insulin initiation were excluded, as were case studies and case series. Five reviewers (J.P., B.S., B.C., J.S., J.C.) participated in the study selection process, with at least 2 reviewers evaluating each title and abstract to identify potentially relevant articles. At least 2 reviewers then assessed complete articles for inclusion, noting 1 or more reasons for exclusion if the article was removed from consideration. Disagreement at these 2 stages of the review process was resolved by the judgment of a third reviewer (J.P., B.S., or J.C). All 5 reviewers assessed the final group of selected articles for inclusion.

Data Extraction

Two reviewers extracted data from selected articles (B.S., J.P.), including the key research questions, data sources, characteristics of the study population, study design, survey/questionnaire used or outcomes measured, results, and conclusions. J.P. and B.S. evaluated the methodological quality of all cross-sectional study analyses using a 9-point, modified assessment checklist that assigned 1 point for each of the following: representativeness of the study population (external validity); participation rate of 60% or more; description of subject attrition/data completeness; and assessment of or adjustment for type 2 diabetes disease duration, weight or body mass index, age, gender, insulin dose/type, and/or A1C when comparing 2 or more groups.

Results

Of 745 potentially relevant abstracts and titles screened, 73 were evaluated in full, and 10 met all inclusion criteria (Figure 1). Nine articles were pertinent to our goal of identifying patient, provider, and health system barriers to insulin progression: 7 articles examined patient barriers whereas 2 explored provider barriers. Relevant to our second question regarding whether barriers to insulin progression differed between insulin-naive and insulin-experienced patients (Table 1). Methodological rigor across studies was generally low, with 4 studies receiving a score of 3 or less on the 9-point scale, often due to lack of assessment of or control for potential confounders.

The first study ranked 274 patients’ willingness to pay for different benefits and costs associated with insulin use, including improved glucose control, weight gain, hypoglycemic episodes, and route of insulin administration. Patients with type 2 diabetes (N = 227) were willing to pay the most ($114) for optimal fasting glucose control, followed by $58 for 2 kg of weight gain per year as opposed to 6 or 10 kg, and $49 for no hypoglycemic episodes. Route of insulin administration was the least
# Table 1

## Studies That Explore Patient-Related Barriers to Insulin Progression

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<td>Casciano et al (2011)</td>
<td>What are patient preferences and perceptions of diabetes therapies?</td>
<td>11,883 individuals with type 2 diabetes diagnosis, age ≥ 18 y; 18 countries in Africa, Middle East, Asia, Eastern Europe, Latin America</td>
<td>Cross-sectional study</td>
<td>Self-report data from patients</td>
<td>IDMPS questionnaire included direct and indirect discrete choice scenario questions requiring patients to consider criteria in order to choose between 2 treatment options.</td>
<td>Relative attribute importance ratings, insulin-treated vs non-insulin-treated type 2 diabetes patients: Administration (oral vs injected): 3.09% vs 47.48% (P &lt; .0001); training decreased importance of administration from 33.68% to 28.21%; Presence of side effects: 31.59% vs 13.75% (P &lt; .0001); Maintenance of blood sugar levels: 27.80% vs 13.09% (P &lt; .0001); Risk of hypoglycemia: 22.47% vs 16.98% (P &lt; .0001).</td>
<td>Patient-perceived barriers to insulin therapy influenced by experience with insulin treatment, self-metabolic control, and negative side effects. Patients who receive type 2 diabetes education place less emphasis on administration route, suggesting that education regarding treatment may influence insulin use.</td>
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<p>| Guimaraes et al (2009)   | What are patients willing to pay for insulin-delivery systems, and what are the attributes of insulin therapy that best meet their preferences? | 378 Canadian patients with type 1 or type 2 diabetes at Vancouver General Hospital and St. Paul’s Hospital in Vancouver | Cross-sectional DCE | Self-report questionnaire data from patients | WTP for different attributes of insulin therapy. Discrete choice experiment. Questionnaire with 15 hypothetical choice sets in which patients must choose between 2 treatment options. Attributes included: 1. FBG control: optimal (&lt;4 mmol/L), suboptimal (4-7 mmol/L), poor (&gt; 7 mmol/L). 2. Hypoglycemic events/month: 0, 4, 8. 3. Weight gain in first year: low (2 kg), moderate (6 kg), high (10 kg). 4. Route of administration for basal dose: oral, subcutaneous, inhaled. 5. Route of administration for 3× prandial doses: oral, subcutaneous, inhaled. 6. Out-of-pocket costs/month: $0, $50, $100, $200. | Type 2 Diabetics WTP (CI) ($ Canadian): Optimal fasting glucose control: 193.95 (98.32-218.78); No hypoglycemic events/month: 48.65 (34.94-62.36); 2-kg weight gain in first year: 58.07 (44.72-71.42). Subcutaneous route for long-acting insulin: pay 16.17 (7.72-24.62) to avoid it, whereas type 1 diabetes patients willing to pay 16.02 for it. Subcutaneous route for short-acting insulin: pay 47.23 to avoid it, whereas type 1 patients willing to pay 11.53 for it. Insulin users WTP (CI) ($ Canadian): Optimal fasting glucose control: 193.95 (98.32-218.78); No hypoglycemic events/month: 48.65 (34.94-62.36); 2-kg weight gain in first year: 58.07 (44.72-71.42). Subcutaneous route for long-acting insulin, willing to pay 9.23 compared with insulin naive users' WTP 32 to avoid it. Subcutaneous route for short-acting insulin: willing to pay 0.36 compared to insulin naive diabetics. Type 2 diabetes patients willing to pay the most for better glucose control, avoidance of weight gain and hypoglycemic events. Type 1 patients and all insulin users willing to pay more for increased control and fewer adverse events relative to type 2 and insulin naive diabetics. Findings support hypothesis of a psychological barrier to initiating insulin therapy, but once barrier has been broken, diabetic patients accept injectable therapy as a treatment option. | 3 |</p>
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<td>Martinez et al (2007)</td>
<td>How well does the SHP questionnaire capture patients’ motivation, fears, and barriers toward insulin injection or intensifying insulin therapy?</td>
<td>SHP Premix study (questions focused on intensification): 1,130 patients (1,150 respondents) 75.2% of these are type 2 diabetes patients, treated with insulin ≥5 y on average</td>
<td>Cross-sectional study</td>
<td>Self-report questionnaire data from patients</td>
<td>SHP questionnaire (piloted): developed with focus groups of diabetics. 3 fields of analysis on 0-100 scale: acceptance and motivation, constraints and fears, restraints and barriers.</td>
<td>Statements in “fears and constraints” category: Feeling restricted because of self-surveillance; Constraint because of dependency, liberty loss; Upset diabetes is getting worse; Fear of having more hypoglycemia crises; Fear that treatment gets more complicated. Statements in “restraints and barriers” category: Bothered by being seen while injecting insulin; Fear that people notice I’m diabetic; Bothered by risk being marked at injection site; Stressed because injections can be painful. SHP survey’s ability to predict insulin intensification is fair to good for patients already on insulin: c-statistics 0.65 for restraints and barriers, 0.78 for fears and constraints, 0.86 for acceptance and motivation. Higher proportion of patients already treated by insulin injections underwent insulin intensification compared with patients orally treated who did not initiate insulin injection, regardless the time of the study. 57 vs 61 “fears and constraints,” 21 vs 27 “restraints and barriers” (P &lt; .05) scores increased for patients who talked about insulin therapy with their physicians. P = .016 for “acceptance and motivation” score difference between patients whose physicians did or did not talk to them about insulin therapy. 70% vs 37%—patients already receiving insulin injections less reluctant to increase number of injections vs patients receiving treatment orally. 63% of patients quite motivated to highly motivated to increase number of insulin injections. 81% would have been motivated to increase insulin therapy if inhaled insulin were available. “Acceptance and motivation” scores lower in young and did (≤40 or &gt;70 y, scores of 59 and 60, respectively) (P = .023). “Restrains and barriers” scores significantly lower in older patients (P &lt; .001). “Fears and constraints” scores—no significant difference by age.</td>
<td>Patients already receiving insulin had fewer barriers to additional injections compared with those initiating insulin; still, many have concerns about disease progression and hypoglycemia. SHP confirms importance of patient-physician communication in treatment decision in diabetes.</td>
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<td>Peyrot et al (2010)</td>
<td>Is quality of life affected by adding mealtime PRAM or RAIA to basal insulin therapy in patients with inadequately controlled type 2 diabetes?</td>
<td>56 (48 completed) type 2 diabetes patients in 120-µg fixed-dose PRAM arm 56 (50 completed) type 2 diabetes patients in titrated RAIA arm</td>
<td>Randomized clinical trial; open-label, multicenter, parallel group for 24 wk across 29 centers</td>
<td>Self-report questionnaire data from patients</td>
<td>Diabetes Distress Scale; average scores across 17 items, each with 1 (extremely bothersome) to 6 (not a problem) scale. Pittsburgh Sleep Quality Index; 19 items, score of 0 (most positive) to 21 (most negative). Diabetes Treatment Satisfaction Questionnaire (8 items, score 0-36, higher score = greater treatment satisfaction). PRAM-TSQ (14 items, 1-6 Likert-type, higher score = high agreement with statement).</td>
<td>Change in scores from baseline to 24 wk (intensification started at 4 wk) for basal insulin + rapid-acting insulin group—least squares mean change (standard error or standard deviation), P value. Mealtime therapy with RAIA in addition to basal insulin was associated with a number of favorable patient-reported outcomes during a period of 20 wk.</td>
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<td>Snoek et al (2007)</td>
<td>How reliable and valid is the ITAS in measuring the positive and negative appraisal of insulin therapy in persons with type 2 diabetes?</td>
<td>282 type 2 diabetes patients (29% response rate) 148 insulin-naive 136 insulin-treated</td>
<td>Cross-sectional study</td>
<td>Self-report questionnaire data from patients</td>
<td>ITAS: developed and piloted. 5-point Likert scale, higher score = stronger agreement. To measure concurrent validity: WHO-5 PAID Survey. WHO-5 is the World Health Organization - 5 scale. PAID: 0-100 score, higher score = higher emotional distress. WHO-5: 0-100 score, higher score = better emotional well-being.</td>
<td>Comparing insulin-treated with insulin-naive, proportion who agree or strongly agree with statement: 27% vs 54%; insulin signifies failure with pre-insulin therapy 37% vs 73%; insulin signifies diabetes has worsened. 20% vs 41%; insulin will make others perceive greater sickness. 6% vs 47%; fear of needle injection. 40% vs 52%; insulin will increase the risk of hypoglycemia. 54% vs 23%; insulin will cause weight gain. 29% vs 61%; insulin will be demanding to administer. 10% vs 19%; insulin means I have to give up activities I enjoy. 10% vs 23%; injecting insulin is embarrassing. 38% vs 43%; injecting insulin is painful. 35% vs 40%; insulin makes me more dependent on my doctor. 10% vs 23%; injecting insulin is painful and &gt;50% associate insulin use with weight gain. Social stigma is dramatically reduced in insulin-treated vs insulin-naive patients, suggesting that experience with insulin improves attitudes about using it. Fear of insulin injection decreases dramatically with experience, but still nearly 40% report injection as painful and &gt;50% associate insulin use with weight gain.</td>
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<td>Vijan et al (2005)</td>
<td>What are patients' views of the burdens of diabetes therapy, and what is the impact of those views on self-management?</td>
<td>1653 veterans with type 2 diabetes (67% response rate) Recruited from 2 VA hospitals 44% treated with insulin Exclusion: age &lt;30 y (assumed to have type 1 diabetes)</td>
<td>Cross-sectional study</td>
<td>Self-report questionnaire data from patients</td>
<td>Author-designed instrument (mailed survey) to assess burdens of various hypoglycemic treatments including insulin. 7-point scale, higher score = more dislike of activity or less adherence to treatment.</td>
<td>Ratings of treatment burden—selected results from rating with experience column (mean): 3.1: combination bedtime insulin and daytime oral agents. 2.4: insulin twice a day. 3.5: insulin twice a day + self-monitoring of blood glucose 3 x per day. 4.1: insulin 3-4 x per day. Compared with patients with experience with all treatments, patients without experience with the treatment perceived it as significantly more burdensome (P &lt; .001). Multivariate analyses: prior experience with insulin remained a significant predictor of ratings of burden, with differences ranging from 1.2 to 2.8 points lower on the 0-6 scale (P &lt; .001 for all differences). Patient rating of burden: only significant predictor of acceptance of insulin therapy (odds ratio of acceptance = 0.58 per 1-unit increase in rating of burden; 95% CI, 0.48-0.69).</td>
<td>In insulin users compared with the insulin naive, the rating of insulin burden was lower, but ratings still increased dramatically based on the frequency of injections. Patients are adaptable to new treatments and experience helps, but only to a point: 13% refused insulin initiation because of perceived burden.</td>
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<td>Zambanini et al (1999)</td>
<td>Does the presence of injection-related anxiety and phobia influence compliance, glycemic control, and quality of life in patients with insulin-treated diabetes?</td>
<td>115 consecutive insulin-treated diabetic patients attending a teaching hospital diabetes outpatient clinic for routine follow-up 35 with type 2 diabetes (30%) Exclusions: age &gt;18 y, able to give verbal consent, able to complete questionnaire unaided or with interpreter</td>
<td>Cross-sectional study</td>
<td>Self-report questionnaire data from patients</td>
<td>IAS and GAS. For IAS, author-designed instrument derived from DSM-IV criteria for specific phobia. 0-3 scale (higher = more fear). 1-4 scale corresponding to number of symptoms of panic attack. Total IAS scores range from 0 to 14 (higher score = more fear). For GAS, anxiety subscale of Hospital Anxiety and Depression Scale used. A1C laboratory value measured on day of survey.</td>
<td>14% of type 2 diabetes patients avoided injections secondary to anxiety, but 29% troubled by the prospect of more injections. 25 low IAS patients unconcerned with more frequent injections vs 23 patients with high IAS expressed concern with more frequent injections (P &lt; .001). -0.17 (-0.27 to -0.07) correlation between IAS and number of daily insulin injections (P= .001). Proportion of patients avoiding injections in the high general anxiety group significantly greater (38%) compared with the low general anxiety group (9%) (P &lt; .05). Poisson regression analysis: mean GAS for injection avoiders almost twice that for nonavoiders—mean GAS ratio 1.96 (95% CI, 1.44-2.66), P &lt; .001. 33% in GAS &lt;8 group and 62% GAS ≥ 8 group expressed concern at more frequent injections (P &lt; .01). Poisson regression analysis: mean GAS significantly higher for patients expressing concern at having to inject more frequently than patients who did not (mean GAS ratio 1.62 (95% CI, 1.21-2.18), P &lt; .001). A1C control was not different between high vs low GAS score patients, nor was there a significant correlation between A1C and GAS.</td>
<td>Approximately one-quarter of patients in this study have a psychological problem with injecting insulin, and this was associated with a high injection anxiety or GAS.</td>
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Abbreviations: BMI, body mass index; CI, confidence interval; DCE, discrete choice experiment; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DTSQ, Diabetes Treatment Satisfaction Questionnaire; FBG, fasting blood glucose; GAS, general anxiety score; IAS, injection anxiety score; IDMPS, International Diabetes Management Practices Study; ITAS, insulin treatment appraisal scale; OAD, oral antidiabetes agent; RAD, Well-being index and Problem Areas in Diabetes; PRAM, pramlintide; PRAM-TSQ, Pramlintide Treatment Satisfaction Questionnaire; RAIA, rapid-acting insulin analog; SHIP, Studying the Hurdles of Insulin Prescription; WHO-5, World Health Organization - 5 scale; WTP, willingness to pay.
PCPs less involved than specialists in insulin intensification, differences in beliefs about who is responsible for intensification. More physician education and training needed for PCPs (and even specialists). Ancillary support from nurses, dieticians could alleviate time and effort concerns, worries about abilities of patients.

Main barriers to insulin intensification for type 2 diabetes:
- 49%: doctors lack experience with the available types of insulin.
- 49%: doctors feel that educating patients about insulin intensification will take too much time.
- 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy.
- 38%: doctors lack belief that insulin intensification is necessary.
- 38%: there is a lack of guidance about insulin intensification.
- 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy.
- 37%: there is a lack of concordance between physician and nurse provider on management.

Therapy most likely to be intensified in patients taking:
- Sulfonylureas, 30% with insulin, 10% with insulin + sulfonylureas.
- 55% poorly controlled patients intensified before the questionnaire period, 64% during questionnaire period, 63% post-questionnaire period.

Table 2

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<td>Cuddihy et al (2011)</td>
<td>How do primary care physicians and diabetes specialists perceive their role in treating type II diabetes and the challenges of insulin management, particularly insulin intensification?</td>
<td>Convenience sample of 600 physician-diabetes specialists from Germany, Japan, Spain, Turkey, UK, and US. PCPs seeing ≥5 type 2 diabetes patients/week, specialists seeing ≥10 type 2 diabetes patients/week. All other countries: physicians seeing ≥2 type 2 diabetes patients/week. All countries: insulin prescribers, practicing 3-30 y. First 50 qualifying PCPs and 50 specialists who took the survey from each country were included; survey closed immediately after country-quotas reached. 74% male, 30-45 y old.</td>
<td>Cross-sectional study</td>
<td>Self-report questionnaire data from physicians</td>
<td>Management of Diabetes in Future Years survey—new 15-min online descriptive survey of insulin prescribers (not validated).</td>
<td>Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country.</td>
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Abbreviation: PCP, primary care physician.

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| el-Kebbi et al (2005)     | How do primary care physicians and diabetes specialists perceive their role in treating type II diabetes and the challenges of insulin management, particularly insulin intensification? | Convenience sample of 600 physician-diabetes specialists from Germany, Japan, Spain, Turkey, UK, and US. PCPs seeing ≥5 type 2 diabetes patients/week, specialists seeing ≥10 type 2 diabetes patients/week. All other countries: physicians seeing ≥2 type 2 diabetes patients/week. All countries: insulin prescribers, practicing 3-30 y. First 50 qualifying PCPs and 50 specialists who took the survey from each country were included; survey closed immediately after country-quotas reached. 74% male, 30-45 y old. | Cross-sectional study | Self-report questionnaire data from physicians | Management of Diabetes in Future Years survey—new 15-min online descriptive survey of insulin prescribers (not validated). | Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. | PCPs less involved than specialists in insulin intensification; differences in beliefs about who is responsible for intensification. More physician education and training needed for PCPs (and even specialists). Ancillary support from nurses, dieticians could alleviate time and effort concerns, worries about abilities of patients. | 2

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| Cuddihy et al (2011)      | How do primary care physicians and diabetes specialists perceive their role in treating type II diabetes and the challenges of insulin management, particularly insulin intensification? | Convenience sample of 600 physician-diabetes specialists from Germany, Japan, Spain, Turkey, UK, and US. PCPs seeing ≥5 type 2 diabetes patients/week, specialists seeing ≥10 type 2 diabetes patients/week. All other countries: physicians seeing ≥2 type 2 diabetes patients/week. All countries: insulin prescribers, practicing 3-30 y. First 50 qualifying PCPs and 50 specialists who took the survey from each country were included; survey closed immediately after country-quotas reached. 74% male, 30-45 y old. | Cross-sectional study | Self-report questionnaire data from physicians | Management of Diabetes in Future Years survey—new 15-min online descriptive survey of insulin prescribers (not validated). | Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. Main barriers to insulin intensification for type 2 diabetes: 49%: doctors lack experience with the available types of insulin. 49%: doctors feel that educating patients about insulin intensification will take too much time. 39%: doctors do not believe that patients will be able to cope with intensified insulin therapy. 38%: there is a lack of guidance about insulin intensification. 38%: there is a lack of patient monitoring to show when type 2 patients require intensified therapy. 21%: doctors lack belief that insulin intensification is necessary. 10%: there are no barriers to insulin intensification in my country. | PCPs less involved than specialists in insulin intensification; differences in beliefs about who is responsible for intensification. More physician education and training needed for PCPs (and even specialists). Ancillary support from nurses, dieticians could alleviate time and effort concerns, worries about abilities of patients. | 2

Abbreviation: PCP, primary care physician.
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<th>Author (Publication Year)</th>
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<td>Ena et al (2009)</td>
<td>How were prescribing habits and glucose control affected by the implementation of an educational strategy for inpatients in medical wards?</td>
<td>33 internal medicine and emergency room physicians surveyed (48% response rate) Patients discharged from the internal medicine department of Hospital Marina Baixa (Spain), 54 in each period: before the intervention, 3 mo post intervention, and 9 mo post intervention—138 patients total Patient inclusion criteria: &gt;18 y old, type 2 diabetes or glycemia (&gt;200 mg/dL), hospitalization for 24-72 h Patient exclusion criteria: type 1 diabetes, pregnancy, hyperglycemia (&lt;120 mg/dL), diabetic ketoacidosis, hyperglycemic hyperosmolar syndrome</td>
<td>Quasi-experimental: before and after education intervention study. Intervention in a 20-min face-to-face educational seminar, pocket guides and posters distributed to physicians. Quasi-experimental: patient discharge records. Intervention survey: self-report questionnaire data from physicians.</td>
<td>Author-designed instrument (questionnaire) assessing provider attitudes, facilitators, and barriers regarding use of basal-bolus insulin therapy (5-point Likert scale).</td>
<td>From patients' medical record: inpatient diabetes therapy administered (adherence to practice recommendations), glycemic control, insulin dose, proportion of patients with insulin intensification at discharge.</td>
<td>17% patients treated with basal-bolus correction dose before intervention; 85% at 3 mo post intervention; 93% at 9 mo post intervention. Basal-bolus-correction insulin dosage was associated with an increase in the total amount of insulin administered per day. 20% of patients with A1C &gt;7% at discharge left with intensified insulin therapy in preintervention period; 55% at 3 mo post; 25% at 9 mo post intervention. Use of oral antidiabetic agents decreased from 44% of patients in the preintervention period to 9% at 3 mo post and 4% at 9 mo post intervention. Physician survey, no effect measure modification by age. Median 5; IQR, 5-5: willingness to use insulin as basal-bolus-correction dosage. Median 4; IQR, 4-5: perception of better glycemic control with basal-bolus correction insulin dosage. Median 4; IQR, 2.5-4: concerns about the greater risk of hyperglycemia with basal-bolus correction insulin dosage. Median 3; IQR, 2-4: simplicity of the proposed insulin algorithm as basal-bolus-correction. Median 5; IQR, 4-5: usefulness of pocket guides and poster displays.</td>
<td>Standardized educational approach addressed to physicians and nurses in internal medicine and emergency wards was safely associated with a better adherence to standards and lower glycemia in hospitalized patients with diabetes. Impact was not sustained: regression to preintervention values at 9 mo—Hawthorne effect? Concern about simplicity of dosing algorithm, even after educational intervention.</td>
<td>Cross-sectional intervention survey: 2 (patient data not assessed).</td>
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Abbreviation: IQR, interquartile range.
important attribute in a regimen for both insulin-naive and insulin-experienced patients, but experience with insulin mattered: Experienced insulin users were willing to pay only up to $9 to avoid injecting insulin, whereas insulin-naive patients were willing to pay up to $75. These data suggest that once patients were familiar with insulin injection, its importance as a barrier to treatment and insulin progression was minimized.

Injection experience was also important in a survey of 11,883 patients with type 2 diabetes: Only 3% of insulin-experienced patients ranked administration route (oral vs injected) as the most important attribute of a treatment regimen.14 Patients who had received diabetes training placed less importance on administration route than those who had not, 28% versus 34% (P < .0001). The presence of side effects (32% vs 14%), maintenance of blood sugar levels (28% vs 13%), and avoidance of hypoglycemia (22% vs 17%) were more important attributes for insulin-treated patients than for insulin-naive patients. In a validation study for a new insulin treatment appraisal scale (ITAS), insulin experience was again associated with more favorable appraisals of insulin among 282 patients with type 2 diabetes.18 When insulin-treated patients were compared with insulin-naive patients, fewer believed that insulin was demanding to administer (28% vs 61%) or that insulin would make others perceive greater sickness (20% vs 41%). However, more agreed that insulin use would cause weight gain (54% vs 23%). Although fear of needle injection was dramatically lower (6% vs 47%), 38% of insulin-treated patients still agreed that injection was painful.

Among 1653 veterans responding to a survey, insulin experience was associated with lower perceived treatment burden by 1.2 to 2.8 points on a 7-point scale.19 In a multivariate analysis of adherence to therapy, the veterans’ ratings of burden were the only significant predictor of adherence to insulin and of willingness to accept insulin therapy. One study occurred in the context of an open-label randomized controlled trial.17 Among 50 patients randomized to receive basal insulin plus a rapid-acting insulin analog for 20 weeks, patients reported on a 6-point scale (with higher ratings indicating more favorable opinion) that the regimen made it harder to control their weight (mean score = 2.83 ± 1.85). That said, these same patients agreed that the regimen’s overall benefit outweighed the need to administer additional injections (mean score = 4.70 ± 1.38), made it easier to avoid hypoglycemia (mean score = 4.00 ± 1.46), and made it easier to control appetite (mean score = 4.00 ± 1.46). The study also compared the new regimen to a basal insulin plus pramlintide regimen, but the follow-up periods on treatment were unequal, making the comparison between regimens invalid.

Two studies did not break out results by diabetes type. A questionnaire validation study found that 70% of insulin-treated patients versus 30% of insulin-naive patients were willing to increase the frequency of insulin injection.16 In a study that explored injection-related anxiety among 80 patients with type 1 and 35 with type 2 diabetes, nearly 30% of patients injecting insulin reported being troubled by the prospect of additional injections, and 14% reported avoiding injections altogether.20 There was a slight negative correlation between number of daily injections and insulin anxiety score, −0.17 (95% confidence interval, −0.27 to −0.07). Patients with high insulin anxiety scores also reported high generalized anxiety scores; however, generalized anxiety score was not associated with A1C control.

**Provider Barriers**

A cross-sectional study performed in an outpatient clinic surveyed 5 physicians and 8 nurses regarding their treatment progression decisions during 1416 patient visits for type 2 diabetes (Table 2).22 Although study results described barriers to any diabetes treatment progression, 40% of patients were already taking insulin. When providers could not agree on a treatment plan, physicians more often endorsed progression whereas nurses favored delayed action due to perceptions of glycemic control or patient noncompliance. Among 146 patients with poor glycemic control whose treatment was not progressed, providers most often reported that control was improving (34%), patients were noncompliant with medications (16%) or diet (10%), or there was an acute intervening illness (8%), or provided no reason (18%).

In a second study, a Web-based survey was administered to 600 physicians across 6 countries to explore barriers to insulin progression.24 Nearly 40% of primary care physicians and 30% of specialists found administration of progressed insulin therapy difficult and wanted more support staff and resources to assist them. About one-half (49%) reported that doctors lack experience with available types of insulin and that educating patients regarding progression would take too much time. Almost 40% agreed that patients cannot cope with progressed
regimens, there is a lack of guidance about insulin progression, and there is a lack of patient monitoring to show when patients with type 2 diabetes require progression. In the United Kingdom, Germany, and Turkey, 6% cited strict national guidelines as barriers to progression. In the United States, Spain, and Japan, 10% cited reimbursement difficulties as a barrier. Both provider-focused studies had poor methodological quality, with scores of 3 and 2, respectively, on the 9-point scale.

**An Intervention to Address Barriers**

In an inpatient setting, 33 physicians (representing a 46% response) responded to a survey regarding inpatient insulin use after they attended a 20-minute educational lecture to introduce and promote the use of a new standardized basal-bolus treatment protocol in place of a sliding scale approach (Table 3). On a 5-point Likert scale, physicians indicated great willingness to prescribe the new basal-bolus therapy (median [interquartile range] = 5 [5-5]). Most (4 [4-5]) agreed that standardized basal-bolus insulin therapy would provide better control than the former sliding scale protocol, but most also had concerns about a greater risk of hypoglycemia (4 [2.5-5]). Providers were divided about the simplicity of administering the new protocol (3 [2-4]) but did adopt it. Patient discharge records showed that 17% of inpatients were treated with basal-bolus therapy before the educational intervention, 85% at 3 months post intervention, and 93% at 9 months post intervention.

**Conclusions**

This systematic review identified 10 studies that examined barriers to insulin progression. Many compared barriers to insulin use among insulin-naive versus insulin-experienced patients. Studies that examined patient barriers to progression were most common, followed by 2 studies of provider barriers and 1 study describing an educational intervention to improve progression rates. Overall, both patient and provider experience with insulin and education about progression appeared to mitigate barriers to progression. However, the small number of studies available, along with existing studies' methodological limitations, narrow focus on only a few potential barriers, and grouping of patients with type 1 and type 2 diabetes, makes a comprehensive assessment of barriers to insulin progression difficult.

Of the 7 studies describing patient barriers to insulin progression, 6 compared the perceptions and beliefs of insulin-treated patients with insulin-naive patients. Across all 6 studies, injection-related concerns were less prominent and perceptions of insulin progression and burden of insulin therapy were more favorable among insulin-treated versus insulin-naive patients. Insulin-treated patients were less likely to believe that insulin was hard to administer, injection was painful, progression would limit their daily activities, or progression would result in greater perceptions of sickness by others. As compared with insulin-naive patients, insulin-treated patients were more concerned with side effects, glycemic control, weight gain, and hypoglycemic events than with the need for injections. These results suggest that experience with insulin and/or diabetes education can minimize barriers to insulin progression, and the results highlight the potential of educational interventions to address injection and burden of disease-related barriers. Indeed, one study found that lower perceived burden of treatment regimen was the only consistent predictor of willingness to progress and of adherence to progressed treatment, and the authors suggested that barriers to treatment progression might be reduced if patients were offered insulin as a “temporary trial.” This approach allows patients to gain experience and reassess their perceptions of insulin therapy but relieves the pressure of all-or-nothing long-term use.

However, even patients’ experience and education did not eliminate all barriers evaluated. Nearly 40% of insulin-treated patients still reported that injection was painful and 30% expressed concern about the need for additional injections. Insulin-treated patients also reported weight gain concerns. Engaging patients in a shared decision-making process to compare the benefits of treatment with potential drawbacks may improve patients’ willingness to progress their therapy and their adherence to it. In one study, patients agreed that the progressed regimen “provided enough benefit to outweigh the extra injections.” For the most part, the patient-focused studies examined barriers that have previously been identified as important predictors of insulin initiation and assessed their presence in the context of insulin progression. Few studies examined barriers that might be progression-specific, leaving a gap in our understanding of barriers that might be unique to insulin progression.

Provider-related barriers to insulin progression often derived from providers’ concerns about their patients’
abilities or willingness to adopt a progressed regimen. Barriers cited by providers in 2 studies included patients’ noncompliance with the existing pharmacological treatment regimen or diet,22 patients’ inability to cope with a progressed regimen,21 and lack of time to educate patients about progression.21 Physicians also described their own lack of experience with and knowledge of types of insulin and progression protocols,21 even those who had just participated in an educational intervention to improve progression rates in the inpatient setting.23 However, the proportion of patients in whom insulin therapy was progressed was increased following the educational intervention, suggesting that education represents an opportunity to reduce barriers to progression.

A full exploration of barriers to insulin progression was limited by the cross-sectional design of the available studies, generally low methodological quality, and narrow focus. Included studies largely relied on self-reported data assessed at a single point in time, so that they did not evaluate which barriers affected subsequent progression of therapy or the occurrence of health outcomes related to diabetes. Although 2 provider-based studies supplemented their cross-sectional data with prospective or retrospective assessment of insulin progression over time, none accounted for time-varying factors that might confound the association between intervention/survey and progression, nor did they quantify the association between barriers and progression.22,23 In their analyses, only 2 studies controlled for factors that might confound exposure-outcome associations.19,22 Few studies examined social stigma, access to pharmacies, or adherence to progressed therapy. Several studies failed to distinguish between patients with type 1 and type 2 diabetes or between patients who progressed to more frequent insulin administration versus those who progressed to other therapies.16,19,20 Despite our extensive search, we found no studies that examined health system–based barriers concurrently to explore their impact on the likelihood of insulin progression. Because treatment decisions involve all 3 levels of influence, such comprehensive studies are needed.

This systematic review suggests that both patients and physicians who have experience with insulin or who have received diabetes or insulin-specific education have fewer barriers to insulin progression compared with those who are insulin-naive. Interventions that introduce patients and physicians to insulin use and/or educate them about it may be effective in reducing barriers that can impede insulin progression, such as injection-related aversion, perceived burden of disease, and perceived inability of patients to handle progressed regimens. However, studies in large part failed to identify novel barriers that might additionally explain incomplete application of insulin progression where indicated. Novel barriers such as cost, access, social stigma, social support, and health system–based factors must be proposed and studied among insulin-experienced patients whose disease status merits progression. Cross-sectional data need to be supplemented with longitudinal data, and investigators need to use study designs that address confounding factors and the clustering of patients within providers and within health care environments. The most helpful future studies will be both multifactorial and longitudinal in nature, examining the relative contributions of patient, provider, and health system factors on progression rates and type 2 diabetes–related health outcomes. At present, enhanced education is a promising strategy, and future studies will both furnish researchers and clinicians with improved data to develop educational interventions and provide guidance on additional efforts that may be needed.

**Implications/Relevance for Diabetes Educators**

- Interventions that introduce patients and physicians to insulin use and/or educate them about it may be effective in reducing barriers that can impede insulin progression, such as injection-related aversion, perceived burden of disease, and perceived inability of patients to handle progressed regimens. Therefore, enhanced education for patients and providers is a promising strategy to improve insulin progression rates.
- Longitudinal data are needed to study the link between barriers to insulin progression and A1C and health outcomes.

**References**