Injectable Combination Therapies for the Management of Diabetes: A Guide for Health Care Decision Makers

Table of Contents

Introduction

Diabetes affects more than 29 million adult Americans and is a leading cause of disability, death, and health care resource utilization.[1] In fact, it is estimated that 1 in 5 health care dollars is spent on diabetes-related care, making it the most expensive traditional therapy category when ranked on a per-member-per-month basis.[2] Type 2 diabetes mellitus (T2DM) accounts for 90% to 95% of all diagnosed cases of diabetes in adults[1] and is characterized by high blood glucose, insulin resistance, loss of pancreatic beta cell function, abnormal hepatic glucose output and glucagon release, and decreased incretin response.[3] Consequently, management of T2DM is complex and treatment, once it begins, generally continues through the life of the patient. Multiple classes of effective and safe diabetes therapies are available, yet despite the availability of effective therapies and evidence-based treatment guidelines, only about half of patients will achieve glycemic control, defined as a HbA1c level of <7%.[4]

Treatment of patients with T2DM should include education and lifestyle changes including diet, exercise, and weight reduction when appropriate. Metformin is typically prescribed as first-line drug therapy for most patients, but due to the progressive nature of T2DM, therapeutic intensification through dose increase and/or addition of another agent with a complementary mechanism of action is often required, with insulin-based regimens often the last line of treatment. However, with intensive insulin treatment, achievement of glycemic targets is often limited by concerns about the risks of hypoglycemia and weight gain.[5]

Delayed or suboptimal treatment intensification may be caused by patient fears of hypoglycemia, weight gain, and regimen complexity as well as prescriber concerns of poor patient adherence, reluctance to increase regimen complexity, and cost.[6,7] Further treatment options for optimizing glycemic control are therefore needed, ideally without increasing complexity, the risk of hypoglycemia, or weight gain, particularly in patients with poorly controlled, long-standing T2DM.

Fixed-Dose Combinations of Insulin and Glucagon-like Peptide-1 Receptor Agonists

There is good physiological and clinical rationale to support a treatment strategy that combines glucagon-like peptide-1 receptor agonists (GLP-1 RA) and basal insulin.[8,9] This combination offers effective glucose lowering via the complementary actions of its component parts. Specifically, basal insulin targets fasting and post-absorptive glucose control and GLP-1 RAs reduce postprandial glycemic excursion through the inhibition of gastric emptying, stimulation of glucose-dependent insulin secretion, and suppression of hyperglucagonemia.[10] In addition, the low hypoglycemic potential of GLP-1 RAs suggests they are less likely than bolus insulin to cause hypoglycemia when combined with basal insulin. Furthermore, the weight-lowering effect of a GLP-1 RAs may offset the weight gain associated with insulin. Finally, this combination might allow insulin dosage to be reduced, which could further lower the risks of hypoglycemia and weight gain (Figure 1).[11]

Figure 1.[5, 11]

Basal Insulin	
Advantages	**Disadvantages**
• Effective in controlling HbA1c	• Increased risk of hypoglycemia • Weight gain
GLP-1 Receptor Agonists	
• Effective in controlling HbA1c • Low rates of hypoglycemia • Weight loss (in some patients)	• Gastrointestinal side effects (eg, nausea)

In November 2016, the FDA approved two once-daily fixed-dose combination products containing basal insulin plus a GLP-1 RA: insulin glargine plus lixisenatide (iGlarLixi) and insulin degludec plus liraglutide (IDegLira). iGlarLixi, marketed in the United States as Soliqua 100/33, combines insulin glargine (100 Units/mL) and the GLP-1 RA lixisenatide (33 mcg/mL) in a once-daily 3mL injection. Regulatory approval and indication of iGlarLixi was based on the results of the Phase 3 LixiLan-L which enrolled 736 patients with T2DM.[12,13] The safety and efficacy of IDegLira, marketed in the US as Xultophy 100/3.6, was studied in the Phase 3 DUAL (Dual Action of Liraglutide and Insulin Degludec in Type 2 Diabetes) trial program involving 1,393 adults with T2DM.[14] Based on the results of their respective Phase 3 trial programs, iGlarLixi and IDegLira were approved as adjuncts to diet and exercise to improve glycemic control in adults with T2DM inadequately controlled on basal insulin or GLP-1 RA therapy.[12,14]

iGlarLixi (Insulin Glargine and Lixisenatide Injection) Pivotal Trials

Regulatory approval of iGlarLixi was based on results of the Phase 3 randomized, 30-week, active-controlled, open-label, two-treatment arm, parallel-group, multicenter insulin intensification study. The primary outcome was change in HbA1c levels at 30 weeks.[12,13]

Patients screened had T2DM with a mean duration of diabetes of approximately 12 years. Patients had to have been receiving basal insulin for at least 6 months with the dose stable between 15 to 40 units/day for at least 2 months before the screening visit. Doses of any oral antidiabetic drugs (metformin, sulfonylurea, glinide, SGLT-2 inhibitor, DPP-4 inhibitor) had to be stable during the 3 months prior to screening. Baseline HbA1c was between 7.5% and 10% and fasting plasma glucose (FPG) was ≤180 mg/dL or ≤200 mg/dL depending on the previous antidiabetic treatment. Additional characteristics of the screened population: mean age 60 years, 46.7 percent male, 91.7% Caucasian, 5.2% African American, 17.9% Hispanic, mean BMI approximately 31 kg/m^2, and mean eGFR 80.6 mL/min/1.73 m^2 (86.1% had an eGFR ≥60 mL/min).[12,13]

Eligible patients entered a 6-week run-in phase during which any oral antidiabetic drug other than metformin was discontinued. Patients were switched to insulin glargine (100 units/mL) if they were treated with another basal insulin and the insulin glargine dose was titrated/stabilized for all patients. The mean HbA1c decreased during run-in period from 8.5 to 8.1%.

At the end of the run-in period, patients (n=736) with an HbA1c between 7% and 10%, FPG ≤140 mg/dL and insulin glargine daily dose of 20 - 50 units were randomized to either iGlarLixi (n=367) or insulin glargine 100 units/mL (n=369). iGlarLixi and insulin glargine were titrated weekly to target a FPG goal of <100 mg/dL. The mean dose of insulin glargine at baseline was 35 units.

At Week 30, there was a reduction in HbA1c from baseline of -1.1% for iGlarLixi and –0.6% for insulin glargine (100 units/mL). The mean difference (95% CI) in HbA1c reduction between iGlarLixi and insulin glargine was -0.5 [-0.6, -0.4] and statistically significant. At Week 30, a significantly greater proportion of patients treated with iGlarLixi reached HbA1c targets of <7.0% (55% vs. 30%) and ≤6.5% (34% vs. 14%) compared with insulin glargine ($p<0.0001$ in each case). The improvement in HbA1c was accompanied by a significant difference of 1.4 kg in body weight change from baseline to Week 30 favoring iGlarLixi compared with insulin glargine ($p<0.0001$).[13] At the end of the trial, the mean final doses of insulin glargine were equivalent between treatment groups.[12]

Table 1. Efficacy results at Week 30.[12]

	iGlarLixi	Insulin Glargine
Number of Subjects Randomized and Treated	365	365
HbA1c, %		
Baseline, mean, post run-in	8.1	8.1
End of study, mean	6.9	7.5
Change from baseline, mean	-1.1	-0.6
Difference vs. insulin glargine [95% CI]	-0.5* [-0.6, -0.4]	
Patients reaching HbA1c <7% at Week 30, n (%)	201 (55.1%)	108 (29.6%)
FPG, mg/mL		
Baseline, mean	132.3	132.0
End of study, mean	121.9	120.5
Change from baseline, mean	-5.7	-7.0

*p<0.01

The safety of iGlarLixi was evaluated in a pooled analysis of two 30-week Phase 3 trials (mean treatment duration: 203 days) which enrolled a total of 834 patients with T2DM [Trial A (n=469) and Trial B (n=365)]. Nausea was the most common adverse event (AE) occurring in ≥5% of iGlarLixi-treated patients. Other common AEs are shown in Table 2. Hypoglycemia was the most commonly observed AE in patients using insulin and insulin containing products including iGlarLixi. Severe symptomatic hypoglycemia, defined as an event requiring assistance of another person to actively administer resuscitative actions, was observed in 1.1% of patients enrolled in Trial B. Documented symptomatic hypoglycemia, defined as an event with symptoms of hypoglycemia accompanied by self-monitored plasma glucose of ≤70 mg/dL, was observed in 25.6% of patients in Trial A and 40% of those in Trial B.[12]

Table 2. Adverse reactions occurring in ≥5% of iGlarlixi-treated patients observed in two pooled phase 3 clinical trials.[12]

	iGlarLixi (n=834)
Nausea, %	10.0
Nasopharyngitis, %	7.0
Diarrhea, %	7.0
Upper respiratory tract infection, %	5.5
Headache, %	5.4

IDegLira (Insulin Degludec and Liraglutide) Pivotal Trials

FDA approval of IDegLira was based on the results of three Phase 3 trials involving 1,393 adults with T2DM. Study A was conducted in subjects converting from liraglutide up to 1.8 mg; Study B was conducted in patients converting from any basal insulin, and Study C was conducted in patients converting from insulin glargine U-100. IDegLira (Studies A, B and C) and basal insulin comparators (Studies B and C) were titrated to target twice weekly by increments or decrements of 2 units IDegLira (2 units insulin degludec/0.072 mg liraglutide) or 2 units basal insulin, respectively, to achieve a pre-specified FPG target of 72-90 mg/dL. In Study B, titration in the comparator arm was limited by a maximum dose of 50 units of insulin degludec.[14]

Converting to IDegLira From Liraglutide

Study A was designed to compare once-daily IdegLira to liraglutide in a 26-week randomized, open-label, treat-to-target (FPG goal: 72-90 mg/dL) trial. The primary endpoint, change in HbA1c, was tested for superiority of IDegLira to unchanged liraglutide therapy. Study A enrolled 348 patients inadequately controlled on liraglutide and metformin alone or in combination with pioglitazone, sulfonylurea or both. Oral anti-diabetic drugs were continued throughout the trial and 21.8% of patients were treated with sulfonylureas in combination with metformin with or without pioglitazone. The mean age of the population was 58.1 years; mean duration of diabetes was 10.0 years; 49.1% were male; 90.8% were white, 7.5% were African American, 10.6% were Hispanic; 5.7% of patients had eGFR <60 mL/min/1.73m^2; no patient had eGFR <30 mL/min/1.73m^2; and the mean BMI was 33.1 kg/m^2.[14] The starting dose of IDegLira was 16 units (16 units insulin degludec/0.58 mg liraglutide) and the average starting dose of liraglutide was 1.7 mg. IDegLira was titrated twice weekly to target a FPG goal of <90 mg/dL. The end of trial dose of IDegLira was 44 units (44 units insulin degludec/1.58 mg liraglutide). As shown in Table 3, at the end of 26 weeks, there was a reduction in HbA1c from baseline of 1.31% for IDegLira and 0.36% for liraglutide.[14]

Table 3. Results of a 26-week trial with IDegLira in patients with T2DM inadequately controlled on liraglutide (Study A).[14]

	IDegLira + Metformin ± Pioglitazone ± SU	Liraglutide 1.8 mg + Metformin ± Pioglitazone ± SU
Total, n	232	116
HbA1c, %		
Baseline	7.8	7.8
End of trial, mean	6.4	7.4
Change from baseline, mean	-1.31	-0.36
Estimated treatment difference [95% CI]	-0.95 [-1.15; – 0.75]*	
Patients achieving HbA1c <7%, %	74.6	30.2
FPG, mg/dL		
Baseline	161	169
End of trial, mean	112	153
Change from baseline, mean	-51.1	-10.9

*p<0.0001

Converting From Basal Insulin: Safety and Efficacy of IDegLira vs. Insulin Degludec and Metformin

Study B was a 26-week randomized, double-blind trial which compared IDegLira to insulin degludec. Patients (n=398) inadequately controlled on basal insulin and metformin alone or in combination with sulfonylurea and glinides were enrolled in the trial. Mean age of the trial population was 57.2 years; mean duration of diabetes was 10.6 years; 54.8% were male; 77.4% were white, 4.8% African American, 10.1% were Hispanic; 6.8% had eGFR <60 mL/min/1.73m^2; no patient had eGFR <30 mL/min/1.73m^2; and the mean BMI was 33.7 kg/m^2.[14]

The trial was designed to show the contribution of the liraglutide component to glycemic lowering and the insulin degludec dosing algorithm was selected to isolate the effect of the GLP-1 component. Basal insulin and sulfonylurea and glinides were discontinued at randomization. IDegLira and insulin degludec were titrated twice weekly to target a FPG goal of <90 mg/dL. The starting dose of IDegLira was 16 units insulin degludec/0.58 mg liraglutide and 16 units of insulin degludec. Patients could not increase their dose by more than 4 units per week; the prespecified maximum dose of insulin degludec was 50 units. The targeted FPG goal was achieved in 24.0% of patients randomized to insulin degludec and 31.6% of the patients randomized to IDegLira at 26 weeks.[14]

At the end of 26 weeks, reductions in HbA1c from baseline of 1.94% for IDegLira and 1.05% for insulin degludec were observed (Table 4). The mean difference (95% CI) in HbA1c reduction between IDegLira and insulin degludec was -0.89 [-1.10; -0.68; p<0.01]. At the end of the trial, the doses of insulin degludec were equivalent between treatment groups.[14]

Table 4. Results of a 26-week trial with IDegLira in patients with T2DM inadequately controlled on basal insulin (Study B).[14]

	IDegLira + Metformin	Insulin Degludec + Metformin
Total, n	199	199
HbA1c, %		
Baseline	8.7	8.8
End of trial, mean	6.9	7.7
Change from baseline, mean	-1.94	-1.05
Estimated treatment difference [95% CI]	-0.89 [-1.10; – 0.68]*	
Patients achieving HbA1c <7%, %	57.3	22.6
FPG, mg/dL		
Baseline	175	172
End of trial, mean	110	118
Change from baseline, mean	-63.5	-55.5

*p<0.01

Converting From Basal Insulin: Safety and Efficacy of IDegLira vs. Insulin Glargine U-100 and Metformin

The efficacy and safety of IDegLira compared to insulin glargine U-100 was studied in a 26-week randomized, open-label, two-arm parallel trial in 557 patients inadequately controlled on insulin glargine U-100 and metformin (Study C). Mean age of the trial population was 58.8 years; mean duration of diabetes was 11.5 years; 50.3% were male; 94.6% were white, 2% African American, 43.1% were Hispanic; 6.3% of patients had eGFR <60 mL/min/1.73m^2; one patient had eGFR <30 mL/min/1.73m^2; and mean BMI was 31.7 kg/m^2. The mean dose of insulin glargine U-100 in patients entering the trial was 32 units.[14]

IDegLira and insulin glargine were titrated twice weekly with a target a FPG goal of <90 mg/dL. The starting dose of IDegLira was 16 units (16 units insulin degludec/0.58 mg liraglutide). The average starting dose of insulin glargine U-100 was 32 units. Patients could not increase the dose of the two products by more than 4 units per week. There was no maximum allowed dose of insulin glargine. The targeted FPG goal was achieved in 39.6% of patients randomized to insulin glargine and 32.9% of the patients randomized to IDegLira at 26 weeks.[14]

At the end of 26 weeks, mean HbA1c reduction from baseline in patients treated with IDegLira (-1.67) was shown to be non-inferior to that elicited by insulin glargine U-100 (-1.16; Table 5). At the end of the trial, the average dose of IDegLira was 41 units (41 units insulin degludec/1.48 mg liraglutide) and the dose of glargine was 66 units, although it is unclear that these observed differences in insulin doses are clinically important.[14]

Table 5. Results of a 26-week trial with IDegLira in patients with T2DM inadequately controlled on insulin glargine U-100 (Study C).[14]

	IDegLira + Metformin	Insulin Glargine U-100 + Metformin
Total, n	278	279
HbA1c, %		
Baseline	8.4	8.2
End of trial, mean	6.6	7.1
Change from baseline, mean	-1.67	-1.16
Estimated treatment difference [95% CI]	-0.51 [-0.67; – 0.34]*	
Patients achieving HbA1c <7%, %	68.3	46.2
FPG, mg/dL		
Baseline	161	160
End of trial, mean	110	110
Change from baseline, mean	-49.9	-49.6

*p<0.01

Treatment with IDegLira has been shown to favorably impact body weight in patients with T2DM. This was confirmed by data from the recently completed Phase randomized, 26-week, open-label, multicenter DUAL VII trial designed to investigate the safety and efficacy of IDegLira vs basal-bolus therapy in adults (n=506) with T2DM previously treated with insulin glargine U100 and metformin. IDegLira elicited an 89% reduction in confirmed symptomatic hypoglycemic episodes compared to the combination of insulin glargine U100 and insulin. Patients receiving IDegLira also experienced weight loss of 0.9 kg compared with weight gain of 2.6 kg for people treated with the basal-bolus regimen; a superior weight difference of -3.6 kg.[15]

Safety of IDegLira was evaluated in 1,881 patients over a mean duration of exposure of 33 weeks. The most common AE was nasopharyngitis, which occurred in 9.6% of patients treated with IDegLira (Table 6). In the Phase 3 trials, events of severe hypoglycemia were defined as an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions. No clinically important differences in risk of severe hypoglycemia between IDegLira and comparators were observed in the IDegLira trials (Table 7). Gastrointestinal adverse reactions including nausea, diarrhea, vomiting, constipation, dyspepsia, gastritis, abdominal pain, flatulence, eructation, gastroesophageal reflux disease, abdominal distension and decreased appetite have been reported in patients treated with IDegLira. Gastrointestinal adverse reactions may occur more frequently at the beginning of IDegLira therapy and diminish within a few days or weeks on continued treatment.[14]

Table 6. Adverse reactions occurring in ≥5% of IDegLira-treated patients observed phase 3 clinical trials.[14]

	IDegLira (n=1881)
Nasopharyngitis, %	9.6
Headache %	9.1
Nausea, %	7.8
Diarrhea, %	7.5
Increased lipase,%	6.7
Upper respiratory tract infection, %	5.7

Table 7. Severe hypoglycemia episodes reported in IDegLira-treated patients.[14]

	Study A	**Study B**	**Study C**
	IDegLira	**IDegLira**	**IDegLira**
Total patients, N	291	199	278
Percent of patients with severe hypoglycemia, n/total N	0.3	0.5	0.0

Summary: iGlarLixi and IDegLira

iGlarLixi and IDegLira are the first injectable combination products that contain both a basal insulin and a GLP-1 RA (Table 8). These novel products elicit substantial HbA1c lowering while minimizing or eliminating AEs that often cause treatment failure or limit tolerability, particularly when patients are taking one or more diabetes medications. Thus, approval of these two products provides patients who are not achieving adequate glucose control or who cannot tolerate their current treatment options additional options to choose from. For patients currently on dual therapy, treatment with either agent may also mean one less injection per day and one less copay per month.

Table 8. Summary of iGlarLixi and IDegLira efficacy and safety.[12,14]

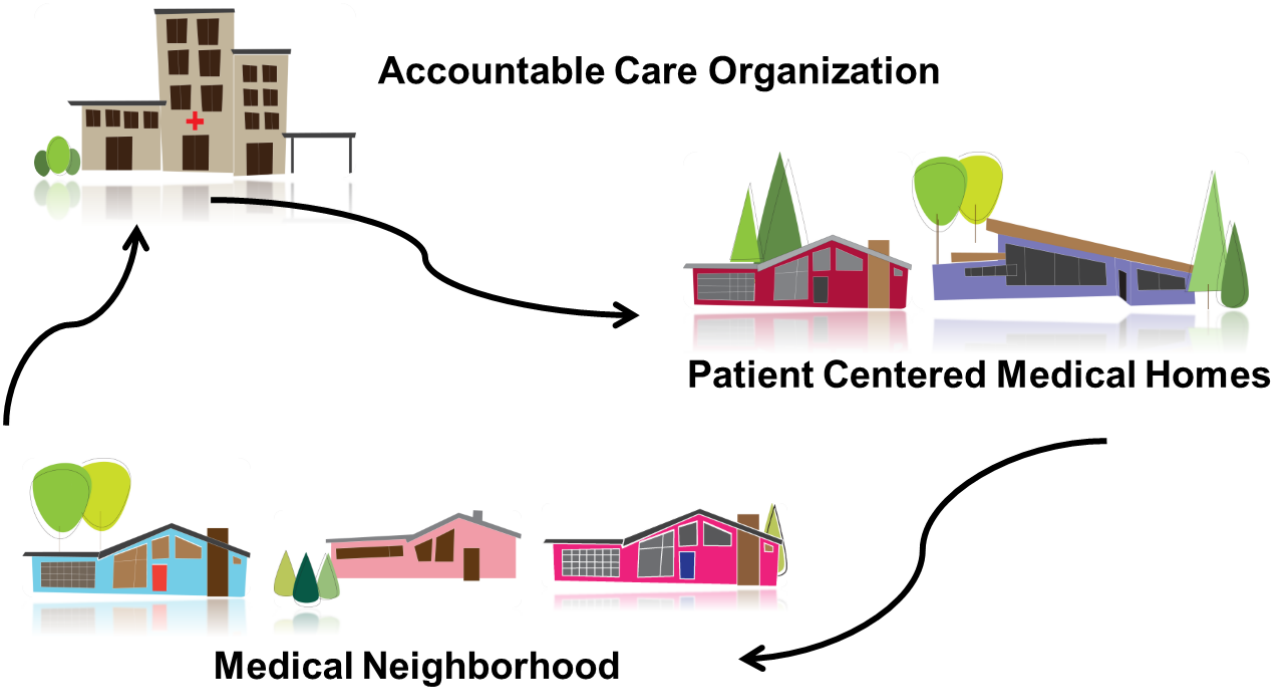
	Efficacy	Safety
iGlarLixi	• Superior HbA1c reduction vs. lixisenatide and insulin glargine • Greater number of patients achieving treatment success with iGlarLixi • Body weight loss / mitigation of body weight gain	• Mild to moderate GI events; lessened with iGlarLixi • Limited risk for hypoglycemia • Maximum daily dosage is 60 units (60 units of insulin glargine and 20 mcg of lixisenatide) • Use an alternative antidiabetic product if patients require a IGlarLixi daily dosage below 15 units or over 60 units

IDegLira	• Significantly greater HbA1c reduction vs. all comparators
	• 60% -80% of patients achieved HbA1c target <7%
	• Mitigated weight gain seen with basal insulin
		• Safety profile consistent with individual components
		• Confirmed hypoglycemia rates with IDegLira consistently lower than with basal insulin
		• GI AEs
		  ○ Lower than with GLP-1 RAs
		  ○ Higher than with basal insulin alone

Patient-Centered Diabetes Care

Diabetes care is often fragmented with no single entity effectively coordinating different aspects of care.[16, 17] Initiatives such as the Patient-Centered Medical Home (PCMH), the Medical Neighborhood, and Accountable Care Organizations (ACOs) are designed to reduce fragmentation by incentivizing coordination of care (Figure 2). Improved health and cost savings will not be achieved unless incidence rates of chronic diseases such as diabetes are reduced. New comprehensive models of care that engage patients in health promotion and disease prevention must be implemented to improve health outcomes and reduce health care costs.[17]

Figure 2.



The Patient-Centered Medical Home (PCMH)

The Patient-Centered Medical Home (PCMH) is a care delivery model providing comprehensive and continuous diabetes care based on personal, collaborative relationships between patients, physicians, members of patients' families, and a multidisciplinary health care team.[18] The goal is to provide a centralized "home" for each patient that enables delivery of coordinated, multidisciplinary, efficient, safe, and cost-effective collaboration between patients and individual physicians, specialists, and health care agencies (eg, payers, community organizations, etc.) providing diabetes services. The interdisciplinary team often includes nurses, pharmacists, physician specialists, nutritionists, mental health practitioners, social workers, case managers, diabetes educators, and community partners. Within the PCMH, the primary clinician caring for the patient may be a physician, nurse practitioner, or physician assistant. This clinician is designated to lead the PCMH care team by coordinating diabetes care delivery activities across all practice settings including acute care, chronic care, preventive services, and end-of life care.[17,18] Routine use of patient registries, electronic medical records, and other information technology platforms enables timely communication across the care team.[18]

Primary care providers within the PCMH are advocates for their patients and work to achieve clearly defined health outcomes through a structured diabetes care planning process. Decision making is guided by evidence-based medicine and clinical support tools that harness the power of information technology to measure performance against predetermined objectives in order to reduce treatment variability, improve health outcomes, and reduce health care expenditures.[17,18] Patient education is also a priority to ensure patients have the knowledge to actively participate in treatment decision making. High levels of patient engagement in their care can lead to greater adherence to treatment[4], improved glycemic control[6], greater satisfaction with care[5], and increased loyalty to their providers.[17] Payers frequently use incentives to encourage primary providers to practice coordinated, multidisciplinary care. Thus, novel payment strategies have been designed to incentivize adoption of practice patterns that drive innovative approaches to quality improvement.[17]

Many payers and providers are devising innovative approaches to care to manage costs and improve the quality of care delivered. The trend toward using interventional approaches to care coordination is one example of such an innovation. In this model, payers proactively screen claims databases and/or patient registries using algorithms to identify patients at risk for increased cost or adverse health events. Once identified, these patients are targeted for integrated (medical and/or pharmacy) care management. Triggers used to identify patients at risk include those with poor adherence to their prescribed medication, those frequently missing appointments or labs, and patients with specific comorbidities (eg, hypertension, dyslipidemia, history of coronary heart disease, etc.).[19] Working closely with patients and their health care providers allows for rapidly and effectively responding to patient needs improve care and reduce the need for expensive services.

The Medical Neighborhood

Achieving the goals of the PCMH requires a high-functioning "medical neighborhood" that encourages communication and coordination between and across diabetes care providers, institutions, and patients as well as establishes some level of accountability to ensure that all stakeholders readily participate in that information exchange.[17] Due to its focus on providing primary—not specialty—care, the PCMH relies on specialists, hospitals, other providers, health plans, and others to create an integrated medical neighborhood.[17] The medical neighborhood is rarely a geographic construct with all health care services provided under a single roof. Rather, it is a set of relationships between the PCMH and a tightly coordinated team of health care providers. Most medical neighborhood clinicians are likely to be in close proximity to the patient and his or her medical home.[17]

The "collaborative care agreement" forms the foundation of the medical neighborhood. This agreement outlines expectations for both the referring physician and the consultant when a patient's care requires the services of multiple health care providers.[20] At a minimum, a medical neighborhood requires three levels of communication and coordination to be functional: 1) the preconsult exchange, 2) the consult, and 3) co-management (Table 9).[20,21]

Table 9. Communication and coordination within a medical neighborhood.[20,21]

	Referring Physician	Specialist
Preconsult exchange	• Clearly state clinical question • Use common referral platform to communicate request • Triage urgency of consult requests	• Have a single point of access • Respond to requests within a specified time using common referral platform
Consult	• Clearly state reasons for consult • Explain to patient purpose of consult • Order appropriate tests prior to consultation	• Use a standardized method for obtaining consultation that is consistent across all departments • Adhere to access time frame • Send consult note to referring physician within a specified number of days
Co-management	• Agree explicitly on who manages medications, monitors laboratory test results, and handles related issues • Notify each other of major interventions, emergency department visits, and hospitalizations • Offer urgent visits to patients within 1-2 days • Send all visit notes to each other within a specified number of days, or sooner if urgent issues have arisen • Confer with each other prior to ordering additional referrals related to the patient's condition	

Accountable Care Organizations

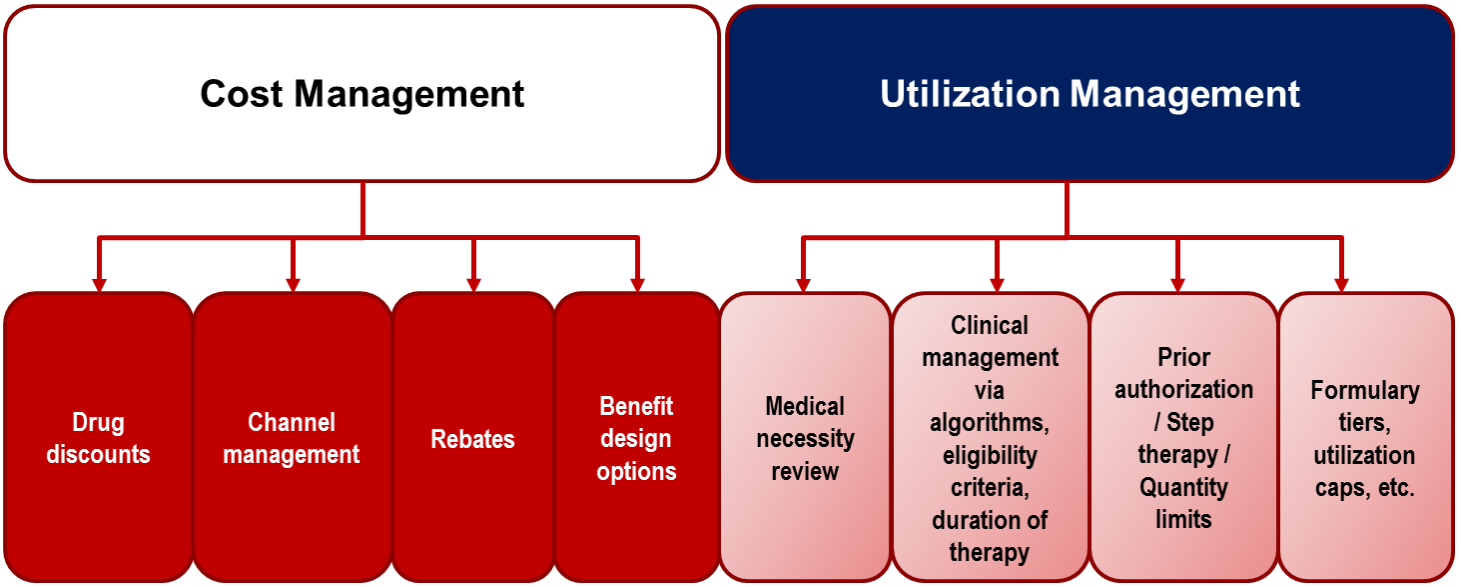
Embedded in the Affordable Care Act are programs designed to improve quality of care and reduce costs by encouraging Medicare providers to form networks to coordinate patient care.[22] These networks are referred to as Accountable Care Organizations (ACOs) and include physicians and professionals in group practices or networks of practices; partnerships or joint venture arrangements between hospitals and physicians/professionals; and hospitals employing physicians/professionals who work together to coordinate across all patients in the network.[23] The ACO negotiates a range of payment models with health insurers (ie, capitation, bundled payments, and fee-for-service) and strives to meet and report requisite quality measures on assigned beneficiary panels with diabetes and other common chronic conditions in order to be reimbursed a portion of the Medicare savings it generates. Thus, the ACO is accountable to all patients—even those who are not cooperative or engaged as their results count in the world of accountable care.[23]

There are now over 700 ACOs in operation, covering 23 million lives making them one of the largest health care payment and delivery reform efforts currently underway.[24] In an ACO practice, provider attention is incented to shift to the management of health risks in all patients across the entire spectrum of health, from those who are well to those with complex conditions such as diabetes. The health risks in a practice population are often much greater than is readily apparent. It is this health risk which is incorporated into the health benefits packages of many employers and third-party insurers.[25]

Benefit Design Strategies to Improve Clinical Outcomes and the Overall Value of Diabetes Care

According to the American Diabetes Association (ADA), more than 29 million Americans have been diagnosed with diabetes. In addition, it's estimated that diabetes goes undetected in almost one of four Americans.[1] As diabetes continues to remain one of the top leading causes of death in the United States, the ADA estimates that the total cost of diabetes in the United States stands at $245 billion, which means one in five health care dollars is spent treating diabetes and its complications.[5] Most patients with diabetes will take medication for the rest of their lives. An analysis of per capita health care spending in 2014 for people with diabetes found average costs were $16,021, roughly $11,000 higher than the average $4,396 in per capita spending for people without the disease.[25] As utilization of drugs to treat diabetes continues to rise, implementing appropriate strategies to control cost trend while maximizing patient outcomes is critical for successful long-term management.[27] Among the many cost management strategies employed are drug discounts, channel management, and rebates (Figure 3).[27]

Figure 3.



Utilization management strategies focus on provider medical necessity reviews, clinical management via algorithms, eligibility criteria, prior authorization, step therapy, quantity limits, formulary tiers, and utilization caps.[28] Payers are also passing a greater percentage of the cost of care onto patients. While this strategy may have a favorable impact on costs in the short term, it is becoming evident that increased out of pocket expenses leads to decreased patient adherence to their prescribed therapy.[29] Therefore, providers must find a balance between shifting the cost toward preference for generic drugs while giving patients the option to pay for name brands if they desire. Studies have shown treatment adherence increases when high risk patients are enrolled in more generous plans (defined as plans that offer mail order distribution, disease management and/or wellness programs, and lower out of pocket expense).[30]

Summary

Diabetes is one of the most common chronic conditions, yet despite significant expenditures on diabetes care, relatively few patients achieve evidence-based treatment goals, often due to patient confusion caused by treatment complexity and poor adherence due to fears of hypoglycemia and weight gain. Recently, the FDA approved iGlarLixi and IDegLira, combination products containing basal insulin plus a GLP-1 RA. Both products are administered as a single daily injection. Clinical trial evidence suggests that despite a lower dose of both the insulin and GLP-1 components than if each product were used individually, the efficacy of the combined products does not appear to be impacted. Furthermore, rates of hypoglycemia, weight gain (both associated with insulin use) and GI-related side effects (associated with GLP-1 receptor agonists) are lower than those typically reported with use of the individual components.

Diabetes is an example of a high cost prevalent chronic illness where a significant quality chasm exists. In recent years, several initiatives have been introduced to strengthen delivery of chronic care. Diabetes care stands to gain from the introduction of novel care delivery models as they emphasize a coordinated, patient-centered, team-based multidisciplinary approach in which the provider, payer and patient are held accountable for achieving improved health outcomes.

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