Comprehensive approach to the management of diabetes: offering improved outcomes for diabetics and the healthcare system

Riccardo Perfetti*

- Although treatment guidelines are in place for diabetes, many people do not achieve optimal glycemic control.
- There are a number of barriers to optimal glycemic control, including poor adherence to treatment, clinical inertia and misalignment of resources, resulting from a fragmented approach to care.
- Diabetes care should be individualized and all aspects of care (glycemic control, management/prevention of complications, and psychological, emotional and behavioral well-being) should be included in the treatment plan.
- In addition, it is essential that people with diabetes are educated about their condition and encouraged to play an active role in its management.
- Patient and physician education is key to improving outcomes in people with diabetes, and should stress the synergy between medications and disease management tools.
- Newer classes of drugs have been developed, including incretin-based therapies (GLP-1RAs and DPP-4 inhibitors), islet amyloid polypeptide analogs and SGLT-2 inhibitors. These agents act on different systems to reduce hyperglycemia and their successful integration into the treatment landscape should be considered to ensure their optimal use.
- Drug delivery systems, treatment algorithms and self-monitoring blood glucose devices, as well as innovations in medication, may provide the tools needed for a patient-centered multidisciplinary integrated care system, and it is vital that all these tools are used in the best possible combination.
- Furthermore, a more comprehensive, multidisciplinary approach to treatment might overcome the misalignment of resources, enabling more people to attain and maintain optimal glycemic control.
- This comprehensive approach, which allows the coordinated use of all available tools, has the potential to revolutionize diabetes care, which is often delivered in a fragmented manner.
- Integrated diabetes care models will need to be validated to assess their economic sustainability.

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SUMMARY  The incidence of diabetes is increasing globally, resulting in an ever-increasing social and economic burden. Despite advances in treatment options, metabolic control often remains suboptimal, resulting in high levels of morbidity and mortality, and increased healthcare expenditure. Current guidelines advocate individualized treatment and a multidisciplinary approach to disease management. For these recommendations to be realized, a comprehensive system of care could be beneficial. In the proposed system, patients would be at the center of a multidisciplinary approach, being provided with the necessary tools, education and support to take responsibility for their condition. Drug delivery systems, treatment algorithms and self-monitoring blood glucose devices, as well as innovations in medication, may provide the tools needed for a patient-centered multidisciplinary integrated care system. Such an integrated approach needs to be economically sustainable and flexible so that it can be scaled up or down to adapt to different healthcare systems.

The incidence of both Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) is increasing throughout the world, with the incidence of T2DM increasing in parallel with obesity. The International Diabetes Federation (IDF) estimates that 552 million people will be affected by diabetes globally by 2030 [1]. The true burden of the disease is likely to be even greater, as a large number of people remain undiagnosed; the IDF estimates that as many as 183 million people globally, or half of those who have diabetes, are unaware of their condition [20]. In sub-Saharan Africa, the proportion of people with diabetes who are undiagnosed can reach up to 90% in some countries [2]. Even in high-income countries, approximately a third of people with diabetes have not been diagnosed [20]. Notably, the relationship between T2DM and cardiovascular disease is now well established, with cardiovascular disease being a major cause of death in people with T2DM [3–6].

Due to the complex nature of the disease, treatment guidelines recommend that diabetes is best managed in an individualized manner by a multidisciplinary approach. When and where possible, such an integrated care team should include primary care physicians, nurse practitioners, social and case workers, dieticians, physician assistants, diabetes educators, pharmacists and care managers [7–10]. However, even when such a multidisciplinary approach is available and affordable, it can be difficult for patients to achieve treatment goals necessary to minimize the risk of diabetic complications [7,8]. Results from the cross-sectional PANORAMA study, which provided an update on glycemic control in European people with T2DM, reported that 37.4% of those enrolled had not achieved glycemic goals (HbA1c < 7%) [11]. Likewise, results from a General Electric EMR Database (2005–2010) in the USA, which assessed people with T2DM who were initiated on basal insulin between February 2006 and August 2009, demonstrated that a high proportion of people did not achieve adequate glycemic control (HbA1c ≤ 7%); only 44% of people reached this target within 1 year, rising to 58% during the approximately 2.5-year follow-up. Among those who reached the HbA1c ≤ 7% target, 57.6% were unable to sustain this treatment goal [12]. Notably, in other parts of the world, such as Asia and Latin America, even lower rates of glycemic control have been reported. For example, results from a recent study that evaluated diabetes care in Malaysia in 1670 patients reported deteriorating glycemic control, with only 22% of patients achieving a HbA1c target of < 7% [13]. In a cross-sectional, population-based study of 11,550 adults in seven urban Latin America populations, only 16.3% of people receiving pharmacologic treatment attained good glycemic control (fasting glucose < 6.1 mmol/l) [14]. The long-term consequences of ineffective metabolic control, including microvascular complications and premature death, have been described in various studies, including DCCT, UKPDS and DECODE [15–17].

A number of barriers affect the delivery of high-quality diabetes management, ultimately resulting in poor glycemic control and impaired quality of life (QoL). Barriers may be system oriented (e.g., fragmentation of the care delivery system), resulting in misalignment of treatment goals, lack of coordination and inefficient allocation of resources [18]. Other barriers are attributed to the behavioral aspects of patients (e.g., diet, energy expenditure, family eating patterns, medication taking, lack of education and ongoing self-management, psychosocial/behavioral and clinical support, and fears over side effects) and healthcare providers (e.g., lack of awareness of guidelines, inappropriate use of existing medications, delayed initiation and intensification of...
A comprehensive approach to diabetes management must be selected based on each individual’s needs [7,8]. Although essential, glycemic control is not the only therapeutic goal for the majority of people with diabetes [20,21]. Risk factors such as obesity, hypertension and dyslipidemia need to be managed appropriately, while screening for complications should be regularly performed [20,21,23]. Although diabetes can be effectively managed by a primary care physician, the complexity of the disease and its associated complications mean that a multidisciplinary team approach should be the standard of care in all settings and appropriate management techniques should be adopted to ensure that a comprehensive approach towards diabetes management is taken [9]. This individualized, multidisciplinary approach should enable all aspects of care (e.g., glycemic control, complications of diabetes, cardiovascular risk factors, and psychological, emotional and behavioral well-being) to be addressed at the highest possible level. Effective collaboration among the different members of the multidisciplinary team is critical to the success of this concept to ensure that people with diabetes are provided with consistent guidance, as fragmentation of care will adversely impact treatment outcomes and cost of therapy [18,22,23]. The healthcare provider and patient need to fully understand the complexity of diabetes, which requires an integrated management approach encompassing all medical, physiological, educational, technical, social and economic aspects of the disease. While an integrated approach is an efficient way to improve diabetes care continuously, it is essential that such an approach is economically sustainable. In addition, to effectively adapt to different healthcare systems, integrated care systems need to be flexible so that they can be scaled up or down as required.

A comprehensive approach to care has been shown to be an effective strategy for those conditions that require involvement of different disciplines, improving both patient management and treatment outcomes [9,24,25]; this is achieved by breaking down barriers between disciplines, enabling optimal sharing of ideas and resources, and spreading the burden of care [9,19,26,27]. It can also help to eliminate regional variations in diabetes management by standardizing care [26]. Integration of all providers into a single, wider care team may decrease the economic burden on a single clinic [9,19]. An integrated care system could be used to ensure that clinical guidelines and recommendations are correctly followed, and one way to achieve this is to build healthcare systems around the guidelines [28]. For example, clinical guidelines could be incorporated into computer systems or flow sheets that accompany patient notes [28]. Indeed, one study reported that the use of flow sheets was associated with better...
mean guideline adherence scores for the assessment (55.4 vs 50.1%; p = 0.02) and treatment of diabetes (79.6 vs 74.7%; p = 0.004) [29].

A number of integrated care models already exist and their benefits have been clearly demonstrated. A study by Rothe et al. evaluated the Saxon Diabetes Management Program (SDMP) in the German state of Saxony, which was based on integrated practice guidelines, shared care and integrated quality management, between the years 2000 and 2002. The state-wide implementation of the SDMP, which was applied to diabetes contracts between health insurance providers, general practitioners and diabetes-specialized practitioners, resulted in a change in therapeutic practice and better cooperation. Median HbA1c at the time of referral to diabetes-specialized practitioners decreased from 8.5 to 7.5%, as did the overall mean HbA1c. Moreover, at study end, 78% of people achieved the guideline therapeutic target (HbA1c ≤7%), compared with 69% of people at baseline. These findings demonstrate that an integrated care disease management system, based on practice guidelines implemented into the care structure, is an innovative way to improve diabetes care continuously throughout a country [26].

Evidence suggests that integrated systems, if properly implemented and coordinated, have the potential to reduce costs. Results from studies in The Netherlands have found implementation of diabetes guidelines to be cost effective, with the level of cost–effectiveness varying between different aspects of care [30,31]. Likewise, results from a study that assessed the cost–effectiveness of an integrated approach to assist general practitioners with diabetes management reported that the program was estimated to reduce treatment costs [32]. In addition, the program led to projected improvements in expected life years and quality-adjusted life expectancy, with an incremental cost–effectiveness of AU$8106 per life-year saved and AU$9730 per year of quality-adjusted life expectancy gained [32].

**Patient education & empowerment**

The management of diabetes is complex, involving lifestyle and behavioral changes, as well as ensuring adherence to medication [7]. As such, it is essential that people with diabetes are educated about their condition and encouraged to take an active role in their treatment [33]. This may be particularly beneficial in overcoming ‘psychological insulin resistance’, a phenomenon in which patients may refuse insulin therapy once it is prescribed, due to concerns over injections and increased risk of hypoglycemia, feelings of personal failure, and skepticism about the effectiveness of insulin [34]. Patient education will also help to overcome clinical inertia, which may be simply defined as failure to intensify treatment of a patient who is not at their evidence-based HbA1c goal [28]. To prevent diabetes-related morbidity and mortality, evidence-based guidelines have expressed the need for dedicated self-care behaviors in multiple domains, including food choices, physical activity, proper medication intake and blood glucose monitoring [7,35]. Interestingly, the American Association of Diabetes Educators has identified seven self-care behaviors that should form an integral part of any educational program: healthy eating; being active; blood glucose monitoring; taking medication; problem-solving; healthy coping; and reducing risks [36].

The effectiveness of patient education in diabetes has been well documented, with numerous studies highlighting its positive effects on glycemic control and frequency and accuracy of self-monitoring of blood glucose (SMBG) [37,38]. Importantly, patient education can be undertaken in groups, reducing the time and cost of its implementation [39]. Other recent innovations include the use of remote learning programs. A randomized, controlled trial in 415 people with uncontrolled T2DM reported that, compared with usual care, people receiving online education had a significantly reduced HbA1c at 6 months (-1.3 vs -0.7%; p < 0.001), although the differences were not significant at 12 months (-1.1 vs -0.9%; p = 0.133) [40]. Educational programs should be tailored to the individual to obtain the best possible outcomes [41]. Consistent with this observation, in a randomized trial in 623 patients with T2DM, mean HbA1c levels decreased in all three groups, but the decrease was significantly greater with individual education (-0.5%) than with group education (-0.3%) and usual care (-0.2%; p = 0.01 vs both groups) [37].

It is also paramount that patient education is targeted to facilitate healthy coping and to improve the QoL and emotional status of people with diabetes [33]. Psychosocial issues, such as depression, anxiety and diabetes-related distress, are prevalent in persons with diabetes and have been associated with lower levels of self-management behaviors. This was clearly demonstrated in the
Comprehensive approach to the management of diabetes  REVIEW

**Long-acting insulin analogs**

Long-acting insulin analogs (insulins glargine and detemir) are increasingly used in the treatment of diabetes, and have been developed to address many of the limitations of earlier intermediate-acting insulins, such as neutral protamine Hagedorn (NPH) insulin. Basal insulin analogs have flatter pharmacodynamic profiles, with a much lower peak of action, and their prolonged duration of action more closely mimics endogenous insulin secretion [48]. Consequently, they have been shown to provide consistent glycemic control, with a lower incidence of hypoglycemia compared with conventional insulin treatments, including NPH insulin (Figure 1) [49]. These agents have also been shown to reduce within-subject variability in plasma glucose levels, which has been strongly associated with a reduced incidence of nocturnal hypoglycemia in the clinical setting [50,51]. Long-acting analogs also provide the possibility of once-daily administration of basal insulin, which is more convenient than twice-daily injections, and may improve both patient QoL and adherence to therapy.

**Rapid-acting insulin analogs**

Rapid-acting insulin analogs (insulins glulisine, aspart and lispro) were developed to have a rapid onset of action and duration of activity to more closely coincide with the postprandial blood glucose peak. Onset of action occurs in approximately 10–20 min, with maximal serum concentrations being reached in approximately 45 min. Rapid-acting analogs also provide individuals with the convenience of an insulin injection immediately before their meals.

**Patient-directed titration algorithms**

The ADA/EASD guidelines recommend that insulin is initiated at a low dose (0.1–0.2 U/kg/day; or 0.3–0.4 U/kg/day in more severely hyperglycemic people) and intensified gradually until blood glucose targets are reached, with this intensification process being supervised by a healthcare professional [7]. Notably, insulin titration can be successfully initiated in a group setting, with results from the INITIATE study demonstrating that total time (visits and phone calls) spent initiating insulin in the patients in groups was 48% less than in those treated individually (2.2 ± 0.1 vs 4.2 ± 0.2 h, respectively) [52]. The ADA/EASD have developed a treatment algorithm for T2DM that details potential intensification strategies;

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**Advance in the development & use of insulin analogs**

All individuals with T1DM require permanent insulin treatment from diagnosis, whereas many people with T2DM try and fail to sustain adequate glycemic control through lifestyle modifications or oral antidiabetic drugs over the long term, and will eventually require insulin therapy. Significant improvements have been made to insulin preparations over the years, including the development of insulin analogs that are designed to overcome the limitations of traditional human insulins.
this guidance allows for individualization of treatment and details a number of factors that should be taken into consideration during intensification (Figure 2) [7]. When intensifying insulin therapy, these guidelines recommend a stepwise approach with basal insulin, followed by the addition of one, two and finally three daily injections of a rapid-acting insulin (Figure 3) [7].

Historically, insulin titration has been guided by physicians, with evidence suggesting that insulin therapy is often initiated too late [53] and that many people do not have insulin doses titrated sufficiently to achieve target levels of glucose control [54]. Indeed, results from a randomized controlled trial by van Bruggen et al. in The Netherlands reported that 45% of people did not receive appropriate intensification of diabetes therapy due to clinical inertia [55]. In line with the patient-centered approach advocated by the ADA/EASD, it has, therefore, become apparent that patient empowerment and ongoing education and support is essential for enabling patients to reach treatment targets, and several patient-directed titration algorithms have now been developed that can be easily implemented and managed by the person with diabetes [54,56]. The ATLANTUS study group demonstrated that a patient-administered titration algorithm was more effective than titration led by a healthcare professional (HbA1c change: -1.2 vs -1.1%; \( p < 0.001 \)) [54]; similar findings were reported by the TITRATE study group, in which patient-directed titration effectively lowered fasting plasma glucose and increased the likelihood of individuals achieving HbA1c <7% [56]. Other recent developments include the use of telecare, in which blood glucose readings are monitored remotely and advice on titration provided over the telephone [57]. This has been shown to be an effective strategy, with results from a randomized, multi-center, parallel-group study demonstrating that there was no difference between telecare and conventional support for titrating the addition of one bolus injection of insulin glulisine in people with T2DM in terms of HbA1c reduction (-0.7 vs -0.7%, respectively) [57].

**Advances in insulin delivery devices**

- **Insulin pens**

The introduction of insulin pens in the 1980s greatly increased the flexibility and convenience of insulin administration [58]. Furthermore, these pens address many of the mechanical barriers associated with the traditional vial-and-syringe method, thereby enhancing treatment adherence [59] and improving glycemic control [60]. Insulin pens are available in two types: reusable insulin pens; and prefilled, disposable insulin pens. With the insulin cartridge and syringe combined in a single unit, pen devices have been reported to improve dosing accuracy [61,62].

Prefilled insulin pens are associated with improved insulin adherence compared with the
vial-and-syringe method. Results from a study in 1156 people with T2DM reported that a switch from administration of insulin therapy by vial and syringe to a prefilled analog pen device improved medication adherence (from 62 to 69%; \( p < 0.01 \)), increasing the proportion of people considered adherent following conversion (from 36.1 to 54.6%; \( p < 0.01 \)) [60]. Compared with the vial-and-syringe method, the pen device was also associated with a 50% reduction in hypoglycemic events, reduced emergency and physician visits, and lower annual treatment costs [60]. Similarly, results from a literature review reported that there was improved adherence with insulin pen devices compared with insulin vials and syringes, and healthcare resource utilization and associated costs were found to decrease with the use of pen devices compared with vials and syringes [63]. Treatment compliance may also be enhanced with insulin pen devices, as they can be modified with colored bodies, lids and labels, enabling people to easily identify the type of insulin contained within [64]. This is particularly beneficial

<table>
<thead>
<tr>
<th>Healthy eating, weight control and increased physical activity</th>
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<tbody>
<tr>
<td><strong>Metformin</strong></td>
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<tr>
<td>- High</td>
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<tr>
<td>- Low risk</td>
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<tr>
<td>- Neutral/loss</td>
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<tr>
<td>- GI/lactic acidosis</td>
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<tr>
<td>- Low</td>
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If needed to reach individualized HbA1c target after \(~3\) months, proceed to two-drug combination (order not meant to denote any specific preference):

<table>
<thead>
<tr>
<th>Metformin</th>
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**Two-drug combinations**

<table>
<thead>
<tr>
<th>Efficacy (+HbA1c)</th>
<th>Hypoglycemia</th>
<th>Weight</th>
<th>Major side effects</th>
<th>Costs</th>
</tr>
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<tbody>
<tr>
<td>High</td>
<td>Moderate risk</td>
<td>Low</td>
<td>Gain</td>
<td>Hypoglycemia Low</td>
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**Three-drug combinations**

<table>
<thead>
<tr>
<th>Efficacy (+HbA1c)</th>
<th>Hypoglycemia</th>
<th>Weight</th>
<th>Major side effects</th>
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<td>Moderate risk</td>
<td>Low</td>
<td>Gain</td>
<td>Hypoglycemia Low</td>
</tr>
</tbody>
</table>

If combination therapy that includes basal insulin had failed to achieve HbA1c target after 3–6 months, proceed to a more complex insulin strategy, usually in combination with one or two noninsulin agents:

<table>
<thead>
<tr>
<th>Insulin (usually basal)</th>
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<th>Insulin (usually basal)</th>
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<tr>
<td>+</td>
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**More complex insulin strategies**

<table>
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<th>Insulin (multiple daily doses)</th>
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Figure 2. American Diabetes Association/European Association for the Study of Diabetes treatment algorithm for Type 2 diabetes mellitus.

↓: Decreased; DPP-4i: DPP-4 inhibitor; Fx: Fracture; GI: Gastrointestinal; HF: Heart failure; SU: Sulfonylurea; TZD: Thiazolidinedione. Reproduced with permission from [7].
for people with T1DM who routinely manage their disease using a multi-insulin regimen.

Additional benefits of insulin pens include easy portability, discretion of use, ease of training, greater stability of the device during injection and improved user confidence. They are also perceived as being more socially acceptable by users. Notably, insulin pens reduce the fear associated with needles and minimize injection-site pain as they enable the use of short, fine (5–6 mm/31 or 32 gauge) needles, thereby improving patient’s QoL [65]. Insulin pens can be adapted for use by children; for example, half-unit pens are particularly well suited for children on low doses of insulin, and removable ‘skins’ are available to enable children to personalize their pens. Insulin pen devices may be particularly advantageous for those with physical disabilities, such as visual impairment or dexterity issues [66]. Emperra® GmbH E-Health Technologies (Bernau bei Berlin, Germany) has developed a pen-based system for mobile communication and a web-based medical management system for patients with diabetes. The pen collects information on dosing, time of injection and daily behavioral activities, and makes this data accessible via the internet [204].

Despite the obvious advantages of insulin pen devices over vial and syringe, their use in several markets, including the USA, is limited. While approximately two-thirds of insulin prescriptions in Europe and approximately three-quarters in Japan are for pen devices [67], only 15% of people in the USA are thought to use insulin pens [68]. A possible reason for the low adoption rates in the USA is a lack of awareness among healthcare professionals regarding the advantages of insulin pens [69], highlighting that there is a need to increase physician awareness of the potential benefits of insulin pens through targeted education. A lack of insurance coverage may also account for the low uptake of pen devices in the USA. Indeed, according to the US Census Bureau, there were 49.9 million people in the USA (16.3% of the population) who were without health insurance in 2010 [205].

**Continuous subcutaneous insulin infusion**

Rapid-acting insulin analogs can also be used for continuous subcutaneous insulin infusion (CSII;
sometimes referred to as ‘insulin pump therapy’) in some people with diabetes [70–72]. CSII more closely mimics physiological insulin secretion, with smaller, more frequent insulin dose adjustments than can be achieved using multiple daily injections [72]. It also delivers larger prandial doses of insulin at mealtimes to prevent hyperglycemia [70]. The potential advantages and disadvantages of CSII are shown in Box 1 [70,72,73]. To overcome some of the current limitations of CSII pumps, CSII sets have now been developed with continuous glucose monitoring to alert the user to hypo- or hyper-glycemia; tubeless sets that reduce the number of components are also now available [70]. Although such technological developments will enhance the functional capabilities of modern insulin pumps, careful patient selection for insulin pump therapy is crucial to optimize its benefits and lessen the associated risks [70]. Furthermore, experience with CSII indicates that candidate patients should be thoroughly educated and actively motivated to improve their blood glucose control [74].

**Innovation in blood glucose monitoring devices**

SMBG is an integral component of intensive diabetes therapy that allows patients and clinicians to detect high or low blood glucose levels, thereby facilitating therapeutic adjustments to achieve long-term HbA1c treatment goals and reducing hypoglycemia in people with both T1DM and T2DM using insulin. Importantly, there is now strong evidence from a number of trials that SMBG is an effective method for monitoring overall glycemic control in people with T2DM who are not on insulin [75,76].

Modern handheld systems for home use are small and easy to use, and require very little blood (typically <5 µl). Furthermore, recent technological advances have led to improved analytical parameters, such as increased test result accuracy and sensitivity, as well as enhanced user experience (e.g., via faster test time) [77]. Several other recent advances – alternative site testing (testing blood glucose on parts of the body other than the fingertip), codeless systems to minimize user errors and dynamic electrochemistry (an innovative technology that uses varying electrical signals to extract a spectrum of information from the blood that is inaccessible with traditional fixed-signal electrochemical methods) – have also improved treatment outcomes [77]. Some blood glucose monitoring devices enable recording of results (e.g., via applications [apps]) [78], which can aid diabetes management by facilitating the discussion of the results between the person with diabetes and their physicians. These apps can also record other values of interest, including calorie...

**Box 1. Potential advantages and disadvantages of continuous subcutaneous insulin infusion.**

**Advantages**
- Improved control of blood glucose levels, as measured by improvements in HbA1c, particularly in those with higher baseline HbA1c
- Reduction in blood glucose fluctuations
- Fewer episodes of severe hypoglycemia
- Reductions in total daily insulin dose (partly offsetting the additional costs of continuous subcutaneous insulin infusion)
- Flexibility and accuracy of insulin dosing
- Reduces needle insertions
- Improves portability
- Higher treatment satisfaction
- Improved quality of life, through reduced fear of hypoglycemia and improved lifestyle flexibility

**Disadvantages**
- Costs of therapy
- User dependent
- Risk of incidental insulin nondelivery
- Frequent monitoring of blood glucose needed to ensure appropriate basal rate
- Risk of diabetic ketoacidosis; can occur rapidly if delivery of insulin is interrupted
- Need to be attached to the system
- Risk of catheter-site infection

Data taken from [70,72,73].
intake and insulin dose. Some new and innovative glucose monitoring devices are overviewed in Table 1.

The introduction of continuous glucose monitors (CGMs) over the past decade was a major breakthrough in diabetes care. These devices measure interstitial fluid and use predefined algorithms to calculate current blood glucose values. CGMs provide a wealth of information about the patient’s glucose control compared with SMBG, which only provides a single measurement [78]. However, a potential disadvantage of CGM is the proposed time lag between the blood glucose value and the interstitial glucose value. A number of randomized clinical trials have confirmed the role of CGMs in diabetes clinical care, suggesting significant benefits for glycemic control, particularly in those with a higher baseline HbA1c [79,80]. Notably, results from a comparative analysis of 14 randomized controlled trials reported that, compared with SMBG, the use of CGMs was associated with a greater reduction in HbA1c (-0.3%; p < 0.0001) [81]. Although the number of hypoglycemic events was not significantly different between the CGM and SMBG groups (p = 0.5), the duration of hypoglycemia was shorter for the CGM group (75 vs 89 min/day), with an incremental reduction of hypoglycemia duration of 15.2 min/day (p < 0.0001) [81].

Blood glucose monitoring devices can facilitate patient education by giving patients more information about their condition. The impact of blood monitoring devices on patient education was highlighted by the results from an ongoing, 5-year, multinational, observational study in patients with T1DM in Latin America and the Middle East. The 5-year study reported that a significantly higher proportion of patients in both regions achieved glycemic control (HbA1c <7%) if they were self-managing their diabetes (defined as both SMBG and insulin self-adjustment) compared with those who were not (Figure 4). These findings highlight that specific effort should be made to empower adults with diabetes to improve their quality of care and treatment outcomes [38]. However, to effectively use SMBG and CGMs, patients must be able to successfully interpret readings to make appropriate changes in their therapy or activity based on the results. As such, it is essential that physicians are able to educate patients on glucose self-monitoring. The importance of patient education was highlighted in a multicenter, open, randomized, parallel-group study that compared insulin glargine plus metformin with NPH insulin plus metformin in people with T2DM, who were taught how to self-adjust their insulin dose and use a modem to send the results of home glucose monitoring to treatment centers. Results reported highly significant differences between the participating centers regarding achieved fasting glucose and HbA1c values, insulin doses, and weight gain during insulin therapy, suggesting that the teaching skills of the diabetes care provider contribute to the success of insulin therapy [82].

The ADA recommends that people receiving insulin therapy should check their blood glucose levels regularly before meals and snacks, while the Global Consensus Conference on Glucose Monitoring Panel recommends that blood glucose levels are tested at least three times a day [8,83]. However, despite these recommendations, many people do not monitor their blood glucose as regularly as advised [84], which negatively impacts on long-term health outcomes. Indeed, results from an epidemiologic, nonrandomized, retrospective study in Germany that followed 3268 people over a median of 6.5 years reported that those who performed SMBG had lower levels of nonfatal (7.2 vs 10.4%; p = 0.002) and fatal (2.7 vs 4.6%; p = 0.004) events than those who did not (Figure 5) [85].

Development of new therapies

Newer classes of drugs are now available for the management of diabetes, including incretin-based therapies, such as the GLP-1RAs, DPP-4 inhibitors, islet amyloid polypeptide (amylin) analogs and SGLT-2 inhibitors. The development of the incretin-based therapy drugs followed the recognition that this system is pivotal to the regulation of blood glucose homeostasis [86].

- GLP-1RAs

Four GLP-1RA preparations are currently approved for the treatment of T2DM – exenatide (twice-daily injection and once-weekly injection), liraglutide (once-daily injection) and lixisenatide (a once-daily prandial GLP-1RA). Results from a number of studies have demonstrated that GLP-1RAs provide significant reductions in HbA1c, postprandial glucose and fasting plasma glucose, with a low risk of hypoglycemia and beneficial effects on weight, making them good candidates for combination with treatments such as sulfonylureas and basal insulin [87–90]. Indeed, results from a 24-week,
### Table 1. New and innovative glucose monitoring devices.

<table>
<thead>
<tr>
<th>Name</th>
<th>Approval</th>
<th>Minimum blood required</th>
<th>Time to reading</th>
<th>Key features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Invasive monitors</strong></td>
<td></td>
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</tr>
<tr>
<td>iBGStar®</td>
<td>US FDA: Yes</td>
<td>0.5 µl</td>
<td>6 s</td>
<td>Small device that can be used alone or attached to an iPhone® for easier display and management of information. Various applications allow management and sharing of data with healthcare provider.</td>
</tr>
<tr>
<td>Telcare BGM®</td>
<td>FDA: Yes</td>
<td>0.8 µl</td>
<td>6 s</td>
<td>Uploads data to computer automatically via integrated wireless system. Caregiver can access results online. Optional autosync with iPhone.</td>
</tr>
<tr>
<td>MyGlucoHealth®</td>
<td>FDA: Yes</td>
<td>0.3 µl</td>
<td>3 s</td>
<td>Uploads data to computer automatically via integrated wireless system. Caregiver can access results online. Optional autosync with iPhone.</td>
</tr>
<tr>
<td>Freestyle InsuLinx®</td>
<td>FDA: Yes</td>
<td>0.3 µl</td>
<td>5 s</td>
<td>Uploads data to computer (via USB). Large easy-to-read touch screen.</td>
</tr>
<tr>
<td>One Touch® Verio® IQ</td>
<td>FDA: Yes</td>
<td>0.4 µl</td>
<td>5 s</td>
<td>Sends data via integrated wireless to iPhone. PatternAlert™ technology allows easy monitoring of glucose patterns and alerts user.</td>
</tr>
<tr>
<td><strong>Noninvasive monitors</strong></td>
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<tr>
<td>GlucoTrack™</td>
<td>FDA: No</td>
<td>NA</td>
<td>Not available</td>
<td>Ultrasonic, electromagnetic and thermal technologies measure glucose via sensor attached to the earlobe. Main monitor includes USB for uploading data to computer and can be used by up to three patients with diabetes at once.</td>
</tr>
<tr>
<td>I-SugarX</td>
<td>FDA: No</td>
<td>NA</td>
<td>4 min</td>
<td>Handheld device providing polarimetric-based measurements of glucose by reading eye aqueous solution. Data can be uploaded onto computer.</td>
</tr>
</tbody>
</table>

NA: Not applicable.

iBGStar® image reprinted with permission from [212]. Telcare BGM® image reprinted with permission from [213]. MyGlucoHealth® image reprinted with permission from [214]. Freestyle InsuLinx® image reprinted with permission from [215]. One Touch® Verio® IQ image reprinted with permission from [216]. GlucoTrack™ image reprinted with permission from [217]. I-SugarX image reprinted with permission from [218]. Grove Glucometer image reprinted with permission from [219]. Symphony® tCGM System image reprinted with permission from [220].
randomized, double-blind, placebo-controlled study in Asian patients reported that lixisenatide as an add-on treatment to basal insulin, with or without a sulfonylurea, significantly improved HbA1c versus placebo (p < 0.0001), and allowed more patients to achieve HbA1c <7.0 and ≤6.5% (Figure 6) [87]. Lixisenatide had a beneficial effect on weight (least squares mean change: -0.38 kg), with no events of severe hypoglycemia being reported [87]. Similar results have been reported with both exenatide and liraglutide [91,92]. All GLP-1RAs are available in prefilled pens. A recent interview-based pilot study examined the use of lixisenatide, liraglutide and exenatide pens in GLP-1RA-naive patients with T2DM, including the elderly and those with manual dexterity or visual impairments [93]. Overall, patients reported that all three pens were easy to use, as assessed using three important practical

<table>
<thead>
<tr>
<th>Name</th>
<th>Approval</th>
<th>Minimum blood required</th>
<th>Time to reading</th>
<th>Key features</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noninvasive monitors (cont.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grove Instruments noninvasive glucometer</td>
<td>FDA: No EU: No</td>
<td>NA</td>
<td>&lt;20 s</td>
<td>Handheld device that uses light to measure glucose via the earlobe or fingertip</td>
<td></td>
</tr>
<tr>
<td>HGI-c</td>
<td>FDA: No EU: Yes</td>
<td>NA</td>
<td>Continuous</td>
<td>Small sensor attached to the skin that uses monochromatic light to detect glucose Readings sent via wireless to iPhone and alerts sent when glucose levels deviate from pre-set levels</td>
<td></td>
</tr>
<tr>
<td>Symphony® tCGM System</td>
<td>FDA: No EU: No</td>
<td>NA</td>
<td>Continuous</td>
<td>Small sensor attached to the skin that measures interstitial fluid via transdermal skin permeation Readings sent to wireless handheld device and alerts sent when glucose levels deviate from pre-set levels</td>
<td></td>
</tr>
</tbody>
</table>

NA: Not applicable.

Table 1. New and innovative glucose monitoring devices (cont.).

---

Figure 4. Proportion of patients achieving target HbA1c (≤7%).

ISA: Insulin dose self-adjustment; NS: Not significant; SMBG: Self-monitoring blood glucose.

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aspects: time taken to use the device; usage error (successful performance); and user satisfaction (user rating) [93].

**DPP-4 inhibitors**

DPP-4 is the main enzyme that degrades GLP-1 and GIP [94]. Inhibiting DPP-4 increases the half-life of GLP-1 and GIP, resulting in higher circulating concentrations, which – as with GLP-1RAs – improves postprandial glucose control and reduces the risk of hypoglycemia [95,96]. A number of DPP-4 inhibitors are currently available, including sitagliptin, saxagliptin, linagliptin and vildagliptin; results from a recent meta-analysis of these four DDP-4 inhibitors reported that they lowered HbA1c significantly more than placebo, with comparable safety profiles to placebo [97].

**Amylin analogs**

Amylin is a hormone that is secreted by pancreatic β-cells in response to nutrient intake. It suppresses postprandial glucagon secretion and regulates gastric emptying and appetite, and is deficient in people with diabetes [98,99]. Although amylin replacement could possibly improve glycemic control, it is unsuitable for therapeutic use as it exhibits physicochemical properties that predispose the peptide hormone to aggregate and form amyloid fibers, making it relatively insoluble in many diluents [98]. An amylin analog (pramlintide) has, therefore, been developed, and has been shown to improve postprandial glucose control, while reducing the risk of both hypoglycemia and weight gain [98].

**SGLT-2 inhibitors**

SGLT-2 inhibitors are a new class of oral drugs developed for the treatment of T2DM. They lower blood glucose insulin independently by inhibiting glucose reabsorption in the proximal renal tubules. In optimal conditions, all of the glucose filtered by the kidneys is reabsorbed, and this is mediated by SGLT-1 and -2 [100]. It is only when the plasma glucose load saturates these transporters that glucose normally appears in the urine. SGLT-2 accounts for 90% of glucose reabsorbed by the kidney, while SGLT-1 accounts for only 10% at this site, playing an important role in glucose absorption from the intestine [100]. Therefore, by inhibiting SGLT-2, increased renal glucose excretion is promoted, which results in improved glycemic control and weight loss in an insulin-independent manner. Dapagliflozin was the first SGLT-2 inhibitor approved in Europe in November 2012, with trials demonstrating its beneficial effect on weight loss and blood pressure, as well as its low risk for hypoglycemia [100,206]. However, owing to the glycosuria caused by these agents, there is an increased risk for genital and urinary tract infections, and there are concerns over the increased incidence of breast and bladder cancer observed in the
In March 2013, canagliflozin became the first SGLT-2 inhibitor to be approved in the USA and empagliflozin is currently being investigated in clinical trials for the treatment of T2DM [102–104].

Integrating patient care, diabetes tools & therapies into a comprehensive approach

For an integrated and comprehensive approach to diabetes management to be successful,

healthcare professionals and the person with diabetes must act as partners in order to reach a consensus on the therapeutic course of action. Indeed, results from a large, multinational survey, SHARED, of people with T2DM (n = 1609), general practitioners (n = 818) and diabetes specialists (n = 697) from eight countries highlighted the importance of patient involvement and shared decision-making. Patients generally perceived diabetes as a serious condition and reported moderate distress. By contrast, physicians tended to underestimate patients’ perceived seriousness of disease and overestimate their level of distress. Physicians experienced difficulty estimating which diabetes complications most concerned their patients and what their patients required to feel more confident about their condition. Notably, patients did not wish for more consultation time, but rather active involvement, information and easy access to their physician, underscoring the fact that diabetes management requires teamwork [105].

Importantly, an understanding and successful implementation of a multidisciplinary approach is vital to ensure that therapies, devices and techniques are used in the best combination to optimize patient outcomes. Integral to this approach is patient and physician education to stress the benefits of the combination of medications and disease management tools (e.g., insulin pens and blood glucose monitors) (Figure 7).

A number of governments have implemented programs for the comprehensive management of diabetes. For example, The National Service Framework for Diabetes was developed by the UK government to tackle variations in care for patients with diabetes [106]. In Australia, the government has launched the Medicare Enhanced Primary Care initiative for chronic disease management to support integrated allied health and general medical practitioner care. Results from the pilot program in people with T2DM demonstrated that integrated allied health/general practitioner guideline-based care, provided in general practitioner clinics, has the potential to improve patient access to allied healthcare, promote the role of integrated care in the management of T2DM, and improve patient education and self-management [107]. The role of government is particularly crucial in poor and developing regions and countries. In India, a project has been initiated to improve diabetes awareness and care for those living below the poverty line in rural Assam, by creating a scalable and replicable platform for T2DM prevention, screening and management [207]. Likewise, in Pakistan, a project has been initiated to establish comprehensive management of T1DM to prevent acute and chronic complications [208].

Nongovernmental organizations, including charities and patients’ rights bodies, also play an important role in the provision of diabetes education, including patient-based education programs. The ADA works with communities throughout the USA to create awareness, prevent diabetes among at-risk populations and ensure that all people with diabetes receive the best care, treatment and information about how to manage their condition. The ADA provides both general and population-specific programs; for example, as American Indians and Alaska Natives have the highest age-adjusted prevalence of diabetes among all US racial and ethnic groups, the ADA have developed a number of programs that are specifically targeted at the Native American community (e.g., Awakening the Spirit) [209]. Other community programs run by the ADA include diabetes camps for children and ‘The Stop Diabetes @ Work’ initiative that can help people take charge of their health and reduce their risk of developing diabetes. The National Diabetes Education Program (NDEP) is a partnership of the NIH, CDC and more than 200 public and private organizations working together to reduce the burden of diabetes and prediabetes by facilitating the adoption of proven approaches to prevent or delay the onset of diabetes and its complications [210]. To help meet these goals, NDEP provides free diabetes education information to the public through a number of resources, including fact sheets, posters, videos, podcasts, webinars, press releases and radio and television public service announcements [210]. Diabetes UK is a British-based patient, healthcare professional and research charity that cares for, connects with and campaigns on behalf of all people affected by and at risk of diabetes. Diabetes UK runs a website that includes information about diabetes for healthcare professionals and people living with the disease, and also operates a careline that offers support to people with diabetes, as well as their friends and family members. Diabetes UK also trains Diabetes Community Champions to help educate and raise awareness of diabetes, and provides speaker scheme volunteers who are given training and promotional materials.
to enable them to talk on behalf of Diabetes UK to groups in their local communities [211].

The shift towards a more comprehensive disease management model requires manufacturers of drugs and devices to adjust to a different business model. Pharmaceutical companies could explore the possibility of providing comprehensive treatment packages— including antidiabetic drugs, pen devices, blood glucose monitoring systems and apps—as part of a comprehensive, yet individualized, disease management plan. It is anticipated that such a comprehensive treatment approach may enhance adherence to therapy, improve long-term outcomes and reduce healthcare costs; it is likely that the reduction in costs will be a key driver in the implementation of comprehensive, integrated care packages. Although the cost-effectiveness of many diabetes treatments has been assessed [108,109], there has been little assessment of the value of an integrated approach to diabetes, and such an evaluation is, therefore, urgently required. While such a data set will need to be generated, it is envisaged that the integration of patient care, diabetes tools and therapies into a comprehensive approach will provide value for money. Another approach to comprehensive disease management is the use of chronic care management models. However, it is essential that stakeholders (professional organizations, patients, charities, politicians and disease management partners) are involved in the development and endorsement of these models. Furthermore, society as a whole will play a key role in determining their value and uptake.

**Conclusion**

Current treatment guidelines for diabetes advocate individualized treatment and a
multidisciplinary approach to disease management to enable all aspects of diabetes care to be addressed. In the proposed system, patients would be at the center of a multidisciplinary approach, being educated about their condition and encouraged to take an active role in their treatment. Advances in drug delivery systems, development of new therapies, patient-directed titration algorithms and innovations in SMBG devices provide the tools required for a patient-centered integrated care system. The integration of these tools in an optimal manner should improve care, as well as long-term outcomes. It is essential that this approach is scalable, as well as economically sustainable, so that it can be adapted to different healthcare systems worldwide. In some settings, an integrated approach to diabetes management could be implemented by a team of healthcare professionals with various skills. However, this can be costly and would be suitable only in certain settings and socioeconomic situations. This comprehensive approach, which allows the coordinated use of all available tools, has the potential to revolutionize diabetes care, which is currently often delivered in a fragmented or incomplete manner. In the future, the widespread adoption of chronic care management models could potentially transform diabetes care.

**Future perspective**

Despite recent developments, the natural course of diabetes cannot be altered with current treatments, resulting in progressive deterioration of glycemic control over time. In the future, improved management of diabetes is likely to come from three different sources: molecular innovation; technological advances and the integration of existing therapies with educational tools; and the means to foster adherence and compliance. As the treatment landscape becomes ever more crowded, it will be crucial to determine which therapy, or combinations of therapies, will be most suited to which individuals, and which therapies work best in combination with each other. This understanding will probably come from clinical experience and the development of detailed treatment algorithms. In the future, the creation of improved titration algorithms, coupled with a greater understanding of how different combinations of agents interact to produce subtly different glycemic outcomes, will ensure that current agents are used to their optimal advantage. Improved use of existing therapies will be of paramount importance in lower-income countries, where people are less likely to have access to newer therapies and are likely be more dependent on generic agents. To this end, current research and treatment paradigms need to be carefully examined and revised where appropriate.

As the promotion of healthy eating and weight loss are key to the management of diabetes, drugs that can change patient behavior are of particular interest. As such, there has been increasing research into the potential of GLP-1RAs to reduce food intake and body weight, with investigators hypothesizing that GLP-1RAs affect central reward and satiety circuits, and that this may contribute to weight loss. More than a dozen human studies, in both normal subjects and those with obesity or T2DM, have examined the relationship between GLP-1 infusion and food intake [100], with the majority demonstrating a significant inhibition of short-term food intake with concurrent GLP-1 infusion [111]. Furthermore, results from a recent pilot study demonstrated that short-term use of the GLP-1RA liraglutide improved visceral fat adiposity, appetite, food preference and the urge to consume fat in obese Japanese patients with T2DM [112]. Studies that, in the future, will increase our understanding of the role of GLP-1 in the central regulation of feeding behaviors and appetite control are currently ongoing. SGLT-2 inhibitors, the first of which was approved in Europe in November 2012, have also demonstrated a beneficial effect on weight, promoting weight loss through increased excretion of glucose from the body. In addition, greater emphasis should be placed on the prevention of T2DM through a number of lifestyle interventions that are designed to impact on individuals’ food intake and physical activity levels [113]. Medical nutrition therapy is important for both the prevention of diabetes and the management of prediabetes [113]. Among individuals at high risk of developing T2DM, structured programs emphasizing lifestyle changes that include moderate weight loss (7% body weight) and regular physical exercise (150 min/week), as well as dietary strategies, including reduced calories and reduced intake of dietary fat, can reduce the risk of developing diabetes [113].

It is anticipated that more widespread adoption of telemedicine will help to improve glycemic management. Indeed, 7-year results from
the Svendborg Telemedicine Diabetes Project demonstrated that telemedicine consultations for remote outpatients to assist with diabetes control is feasible, achieving high-quality results in essential diabetes treatment parameters [114]. In addition, the telemedicine setup was associated with improved cost-effectiveness and patient satisfaction [114]. Recently, efforts have been made to develop a closed-loop artificial pancreas system that includes three essential parts: a pump for insulin delivery; a CGM system to keep continuous track of blood glucose; and an algorithm (device based or eventually integrated as part of the pump) that determines insulin delivery amounts and rates (Figure 8) [115,116]. This system eliminates the possibility of human error as patients do not have to administer insulin themselves. In addition, it removes the need to frequently test blood glucose levels by SMBG. Preliminary studies have demonstrated that closed-loop control is feasible and can be applied to improve glucose control in people with T1DM, although the algorithm needs to be further improved to achieve better glycemic control, and concerns remain about the possibility of severe hypoglycemic episodes due to a closed-loop system [117]. It is anticipated that this CGM system, along with other recent technological advances in the management of diabetes (insulin pumps, CGMs and improved computer algorithms), will improve the acceptance of intensive therapy, adherence and QoL in people with diabetes.

Further development and adoption of new disease management structures, such as chronic care management models, will help to improve the care of people with diabetes. Indeed, one such chronic care model, which uses a systematic approach to restructure medical care to create partnerships between health care providers and patients, has been shown to improve outcomes and reduce costs [118].

In summary, telemedicine and closed-loop systems offer promising avenues for improving diabetes care. However, further research is needed to refine the algorithms and ensure patient safety and satisfaction.
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Review

systems and communities, is being used for diabetes care in US primary care settings, with positive outcomes being reported [118]. Results from a systematic review recommended that future research on integration of chronic care models into primary care settings for diabetes management should measure diabetes process indicators, such as self-efficacy for disease management and clinical decision-making. In addition, restructuring of the delivery of healthcare services and the development of quantification models to assess the quality of diabetes care may improve treatment outcomes in the future [118].

In an ever-changing treatment landscape in which a number of new investigational agents for the treatment of T2DM are currently underdeveloped (Table 2) [119], it is important that any new disease management model will include an economic sustainability plan that can be scaled and adapted to different socioeconomic environments. As with any aspect of healthcare, this new comprehensive approach to diabetes management will need to be supported by real-world outcomes data to demonstrate that this concept translates into clinical benefits.

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### Table 2. Comparison of investigational agents for the treatment of Type 2 diabetes.

<table>
<thead>
<tr>
<th>Class</th>
<th>Mechanism(s)</th>
<th>Potential advantages</th>
<th>Potential disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGLT-2 inhibitors</td>
<td>Inhibit renal SGLT-2 Increase glucosuria</td>
<td>Insulin-independent effects</td>
<td>No hypoglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight loss</td>
<td>Reduces blood pressure</td>
</tr>
<tr>
<td>FFAR1 (GPR-40 agonists)</td>
<td>Activate FFAR1 in β cells Increase insulin secretion</td>
<td>No hypoglycemia</td>
<td></td>
</tr>
<tr>
<td>Dual PPAR agonists</td>
<td>Activate PPAR-α and γ Decrease insulin resistance</td>
<td>No hypoglycemia</td>
<td>Edema/heart failure Weight gain Bone effects</td>
</tr>
<tr>
<td>11-β-HSD1 inhibitors</td>
<td>Inhibit 11-β-HSD1 in liver/adipose Decrease insulin resistance</td>
<td>No hypoglycemia</td>
<td>Elevated androgens (women) Effects on HPA axis</td>
</tr>
<tr>
<td>GK activators</td>
<td>Activate GK in liver/β cells Increase insulin secretion Decrease hepatic glucose production</td>
<td>Combined actions on liver and β cells with one drug</td>
<td>Hypoglycemia Hypertiglyceridemia Hepatic steatosis†</td>
</tr>
<tr>
<td>Salicylates</td>
<td>Inhibit NF-κB, reducing inflammation Decrease insulin resistance</td>
<td>No hypoglycemia</td>
<td>Increased albuminuria</td>
</tr>
<tr>
<td>Ranolazine</td>
<td>Inhibits late cardiac sodium currents Promotes glucose-stimulated insulin secretion</td>
<td>No hypoglycemia</td>
<td>Edema Dizziness</td>
</tr>
<tr>
<td>Glucagon receptor</td>
<td>Decrease hepatic glucose production</td>
<td>hypoglycemia</td>
<td></td>
</tr>
<tr>
<td>antagonists</td>
<td></td>
<td>Hepatic steatosis†</td>
<td></td>
</tr>
<tr>
<td>Fructose-1,6-biphosphatase inhibitors</td>
<td>Decrease hepatic glucose production</td>
<td>hypoglycemia</td>
<td>Lactic acidosis†</td>
</tr>
<tr>
<td>PTP1B inhibitors</td>
<td>Inhibit insulin receptor deactivation Decrease insulin resistance</td>
<td>Weight loss</td>
<td>Effects on PTPs other than PTP1B</td>
</tr>
<tr>
<td>Liver-specific CPT-1</td>
<td>Inhibit hepatic fatty acid oxidation Decrease hepatic glucose production</td>
<td>–</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>inhibitors</td>
<td></td>
<td></td>
<td>Hepatic steatosis†</td>
</tr>
</tbody>
</table>

Information on the potential advantages and disadvantages was not available for all investigational agents.

†Based on animal data.

‡Based on human mutation data.

11-β-HSD1: 11-β-hydroxysteroid dehydrogenase type 1; GK: Glucokinase; HPA: Hypothalamic–pituitary–adrenal; PTP: Protein tyrosine phosphatase.

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Highlights how specialized diabetes care centers that utilize a multidisciplinary diabetes team to provide patients with highly individualized care result in improved patient outcomes and reduced overall costs.


Evaluation of the Saxon Diabetes Management Program, which demonstrated that integrated care disease management with integrated quality management, including collaboration between general practitioners and specialist services, is a significant innovation in chronic care management and an efficient way to improve diabetes care continuously.


Consensus report highlighting the importance of clinicians understanding the individual characteristics of their patients and their perspectives in developing mutually accepted treatment goals.


Update to the National Standards for Diabetes by a task force that was jointly convened by the American Association of Diabetes Educators and the American Diabetes Association. The task force made the decision to change the name of the standards from the ‘National Standards for Diabetes Self-Management Education’ to the ‘National Standards for Diabetes Self-Management Education and Support’ to emphasize the significance of ongoing support for people with diabetes and those at risk of developing the disease, particularly to encourage behavior change, the maintenance of healthy diabetes-related behaviors and to address psychosocial concerns.


Daley G. Optimum management of Type 2 diabetes – timely introduction, optimization and intensification of basal insulin. Diabetes Obes. Metab. 10(Suppl. 2), S5–S13 (2008).


Results from a prospective, multicenter, multinational, open-label, 24-week randomized trial demonstrating that a simple subject-administered titration algorithm conferred significantly improved glycemic control, with a low incidence of severe hypoglycemia compared with physician-managed titration.


87 Seino Y, Min KW, Niemoeller E, Takami A; on behalf of the EFC/0887 GetGoal-L Asia Study Investigators. Randomized, double-blind, placebo-controlled trial of the once-daily GLP-1 receptor agonist lixisenatide in Asian patients with Type 2 diabetes insufficiently controlled on basal insulin with or without a sulfonylurea (GetGoal-L-Asia). Diabetes Obes Metab. 14(10), 910–917 (2012).


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111 Results from a double-blind, placebo-controlled, crossover study that demonstrated a marked effect of GLP-1 on appetite by showing enhanced satiety and reduced energy intake in patients with Type 2 diabetes mellitus.
119 Literature review demonstrating that a chronic care model that uses a systematic approach to restructuring medical care to create partnerships between health systems and communities is effective in managing diabetes in US primary care settings.
121 Overview of a number of new agents that are currently being developed to better address the pathogenesis of Type 2 diabetes mellitus and to overcome the limitations of current therapies. Agents that are advancing through clinical trials are reviewed and the rationale behind their use, mechanisms of action and potential for glucose lowering, as well as what is known of their limitations, is described.

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211 Diabetes UK. www.diabetes.org.uk

212 BGStar and iBGStar. www.ibgstar.com


214 MyGlucoHealth®. www.myglucohealth.net

215 Freestyle InsuLinx®. www.abbottdiabetescare.co.uk/your-products/freestyle-insulin

216 One Touch®/Verio® IQ. www.onetouch.ca/verioiq

217 GlucoTrack™. www.integrity-app.com


219 Grove Instruments noninvasive glucometer. www.groveinstruments.com

220 Symphony®tCGM System. www.echorx.com