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Safe and Efficacious Use of Automated Bolus Advisors in Individuals Treated With Multiple Daily Insulin Injection (MDI) Therapy: Lessons Learned From the Automated Bolus Advisor Control and Usability Study (ABACUS)

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Abstract

Numerous studies have shown that use of integrated automated bolus advisors (BAs) provides significant benefits to individuals using insulin pump devices, including improved glycemic control and greater treatment satisfaction. Within the past few years, BA devices have been developed specifically for individuals treated with multiple daily insulin injection (MDI) therapy; however, many clinicians who treat these individuals may be unfamiliar with insulin pump therapy and, thus, BA use. Findings from the Automated Bolus Advisor Control and Usability Study (ABACUS) revealed that BA use can be efficacious and clinically meaningful in MDI therapy, and that most patients are willing and able to use this technology appropriately when adequate clinical support is provided. The purpose of this article is to review key learnings from ABACUS and provide practical advice for initiating BA use and monitoring therapy.

Keywords

bolus advisor, MDI, multiple daily insulin injection, type 1 diabetes, type 2 diabetes, ABACUS

A key challenge for many patients with diabetes who are treated with intensive insulin therapy is calculating accurate bolus insulin dosages.[1,2] Bolus insulin calculation requires individuals to utilize several factors, including insulin-to-carbohydrate (I:CHO) ratios, insulin sensitivity factors (ISFs), target blood glucose (BG) range, current BG values, anticipated physical activity, and general health status.[3] Making these calculations is especially problematic in individuals with deficits in literacy and numeracy, which are common in many societies and, thus, among individuals with diabetes.[4] Another obstacle is lack of competency in carbohydrate counting; several studies have shown that inaccuracy in carbohydrate counting is widespread among children and adults.[3,5-7] Because these dosage calculations can be both complex and time-consuming, individuals often rely on empirical estimates of their insulin needs, which can limit their ability to achieve optimal glycemic control.[8]

Many current insulin pump systems feature bolus advisor capability, which automatically calculates insulin boluses to address carbohydrate intake and out-of-range BG levels. Use of an automated bolus advisor (BA) can address many of the obstacles associated with intensive insulin therapy by reducing the burden of intensive insulin regimens,increasing treatment satisfaction,[3,9,10] addressing deficits in numeracy and carbohydrate counting,[1,3,9,11] and improving glycemic outcomes.[8,12,13] However, because insulin pump use has not been widely adopted due to perceived complexity of insulin pumps and the extensive training required,[14,15] individuals treated with multiple daily insulin injections (MDIs) do not benefit from automated BA technology in their self-management regimens.

Although a growing number of smartphone apps and devices with BA technology are in development, none of the apps are FDA-approved, and only 2 stand-alone devices with integrated BG monitoring capability are commercially

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available today: the FreeStyle® InsuLinx system (Abbott Diabetes, Alameda, CA, USA) and Accu-Chek® Aviva Expert system (Roche Diagnostics, Indianapolis, IN, USA). These devices have been formally evaluated in observational and/or clinical studies.[1,3,9,10,16-18] The InsuLinx system is available in Europe only, whereas the Aviva Expert system is available in Europe and the United States.

Because many clinicians who provide care to individuals treated with MDI therapy may be unfamiliar with the use of BA devices, it is important that they understand the requisite criteria for safe, efficacious initiation and use of these devices. In 2013, we reported results from the Automated Bolus Advisor Control and Usability Study (ABACUS), a 26-week, multicenter, multinational, prospective randomized controlled trial that assessed the impact of using a BA (Aviva Expert) on glycemic control and treatment satisfaction in 218 adults with type 1 or type 2 diabetes treated with MDI therapy.[3] In this article, we review key learnings from ABACUS and provide practical advice for initiating BA use and monitoring therapy.

Findings From the Automated Bolus Advisor Control and Usability Study (ABACUS)

In the ABACUS trial, we hypothesized that use of an automated BA would enable more MDI-treated participants to achieve clinically significant improvements in glycemic control compared with participants who calculated their bolus insulin doses manually. The goal of the trial was to achieve >0.5% HbA1c reductions in most participants. Changes in HbA1c, hypoglycemia, glycemic variability (magnitude of glycemic excursions [MAGE]), carbohydrate counting competency, and treatment satisfaction (as measured by the Diabetes Treatment Satisfaction Questionnaire [DTSQ]) were assessed.

Among the 218 participants (n = 202 type 1, n = 16 type 2) who were recruited for the study, 105 (n = 98 type 1, n = 7 type 2) were randomized to the experimental group (EXP). EXP participants used a BA device (Aviva Expert) in conjunction with enhanced usual care, which included clinic visits that focused specifically on diabetes management. The 113 participants (n = 104 type 1, n = 9 type 2) who were randomized to the control group (CNL) received enhanced usual care and manually calculated bolus insulin dosages according to individualized parameters. Eligibility for the trial specified that all participants must have completed a diabetes education program (standardized within their home countries) within 2 years of study enrollment. The only additional training provided to EXP patients was instruction in operating the BA device.

An important component of the study was use of structured self-monitoring of blood glucose (SMBG) in both study groups. All participants were instructed to generate 7-point BG profiles (preprandial and 2-hour postprandial at all main meals and bedtime) over the course of 3 consecutive days and to document their results on the standardized form that was provided prior to study visits. Participants also used the form to document meals, physical exercise, basal insulin doses, prandial bolus doses, and correction bolus doses over the 3-day testing period. At study visits, investigators uploaded the meter data, collected and reviewed the participant diaries, and adjusted therapy parameters as needed.

Among the 193 participants (CNL, n = 93; EXP, n = 100) who completed the study, significantly more EXP (50.0%) than CNL (34.4%) patients achieved >0.5% HbA1c reductions ($P < .01$) with no significant between-group differences in hypoglycemia (<50 mg/dL). Only EXP participants showed significant reductions in mean amplitude of glycemic excursions ($P < .01$) and showed significant improvements in carbohydrate estimation variability ($P < .01$). Improvements in mean treatment satisfaction scores were also significantly greater in EXP participants than CNL participants ($P < .01$). Moreover, these improvements were achieved without increased glucose test strip utilization.[18] EXP participants used their BA for a significant percentage (73.5%) of all possible bolus opportunities. Additional analyses revealed that BA use was associated with earlier, more frequent changes in key insulin parameters, specifically the ISF.[18] Interestingly, CNL participants calculated their insulin bolus dosages an average of 4.0 times per day, yet the average frequency of *correct* use of their insulin-to-carbohydrate ratios (I:CHO) and ISFs was only 1.6 times per day.

Lessons Learned From ABACUS

Overall, the ABACUS trial showed that use of an automated BA can be efficacious and clinically meaningful in MDI therapy when adequate clinical support is provided. Although it is gratifying for us, as investigators, to discover that our hypothesis was correct, even more gratifying is the important, clinically relevant lessons learned from study.

Many Individuals Treated With MDI Therapy Are Both Willing and Able to Effectively Use an Automated BA

As reported in the ABACUS trial, EXP participants used their BA for almost three-fourths of their bolus calculations.[3] In addition, older patients tended to use the BA more often than younger patients ($P < .05$).[3] In essence, the ABACUS findings suggest that use of a BA device was not burdensome or too complex, regardless of age, and that participants trusted the bolus advice they received. Interestingly, most of CNL participants who withdrew from the study indicated to investigators that they discontinued because they were *not* randomized to the EXP group.

Accurately Establishing, Monitoring, and Adjusting Insulin Parameters, as Needed, Is Critical to Accurate Bolus Calculation

Because BA devices base their dosage calculations on numerous factors, including current glucose level, ISF settings,

I:CHO ratios, and since these factors can change over time as patients' physiologic and lifestyle needs change, it is important that both clinicians and their patients periodically perform comprehensive assessments to ensure the accuracy of insulin parameters and make adjustments when needed. An earlier study that looked at BA use in 24 individuals on insulin pumps found that most of the enrolled participants had been using inappropriate basal rates and inaccurate insulin therapy parameter settings (eg, ISF, I:CHO).[12] Assuming that most of the individuals on insulin pumps are treated by clinicians who are experienced in intensive insulin management, it would be reasonable to question the accuracy and appropriateness of the insulin parameters used by MDI-treated individuals who may be managed by less experienced clinicians. Regarding frequency of insulin parameter adjustments, a subsequent analysis of the ABACUS findings found that more EXP than CNL participants received adjustments to their insulin therapy parameters during the study, and that these adjustments occurred earlier and more frequently.[18] We believe that this may have contributed to the glycemic improvements seen in the EXP group. Moreover, the increased frequency in insulin parameter adjustments could be attributed to clinicians' response to their patients' BA use. Feedback from ABACUS investigators at the conclusion of the study suggest that many clinicians may have presumed that the ability to program insulin parameters into the meter at clinic visits supported their patients' ability to more accurately and consistently use their revised parameters.[18]

Collaboration Between Patients and Their Health Care Team Facilitates Success

Strong collaboration between patients and their health care providers is an essential component of effective diabetes management,[19,20] and was a significant success factor in the ABACUS trial. While it is up to the clinician to provide the expertise in diabetes management, it is important to remember that the average individual with diabetes spends approximately 9000 hours per year managing their diabetes on their own,[21] and thus should be encouraged to participate both in analyzing and interpreting their SMBG data and in determining treatment goals and regimens. Through this collaborative relationship, clinicians strengthen patients' involvement in their treatment and identify any knowledge/skill deficits or psychosocial issues that are impacting treatment adherence and quality of life. For example, in the ABACUS trial, we found that many control participants who achieved >0.5% reductions in HbA1c (study goal) *incorrectly* used their ISF setting more frequently than those participants who did not achieve these reductions. We speculated that this may have occurred because the "goal-achieving" participants found their prescribed ISFs to be inadequate and subsequently used different ISFs but did not communicate this with their clinician. Greater clinician-patient collaboration may have identified this "disconnect" between what clinicians thought participants were doing and what the participants were actually doing. Another consideration is how collaboration impacts patient attitudes and concerns about their diabetes management. Individuals with diabetes often become frustrated with their self-management efforts, which can lead nonadherence to treatment.[22] By focusing on their patients' progress and successes (even small ones), clinicians can help patients overcome their frustrations and sense of hopelessness and develop a sense of self-efficacy.[23]

Structured SMBG Is the Central Component to Effective Diabetes Management

Structured SMBG is a formal approach in which BG data are obtained according to a defined regimen, interpreted and then utilized to make appropriate treatment adjustments.[24] As discussed, all ABACUS participants obtained 3-day, 7-point glucose profiles (before/2 hours after meals and at bedtime), which were reviewed at clinic visits and acted on accordingly. As the central component to BA use, structured SMBG use appears to have contributed to diabetes management in 3 ways. First, it facilitated identification of problematic glucose patterns that indicated the need to adjust therapy parameters. Second, it provided immediate feedback to patients about their self-management behaviors. Third, structured SMBG provided a basis for meaningful discussion with patients, which not only supported clinician-patient collaboration but also improved practice efficiencies (as reported by study investigators) because the time spent with patients is more productive. It was suspected that use of structured SMBG by all ABACUS participants may partially explain why so many CNL participants achieved the >0.5% HbA1c reductions.

Application of Evidence in Clinical Practice

As part of the health care team, diabetes educators can play an important role in helping their patients realize the benefits of BA use as a key component of diabetes management. However, it is important that patients fully understand how to use their BA devices safely and effectively, as with any new tool or technology, and that their clinicians are persistent in monitoring their patients' glycemic status and adjust insulin parameters as needed.

1. Determine patient competency in utilizing MDI therapy and self-management skills, such as carbohydrate counting/calorie counting, sick day management and hypoglycemia treatment. The checklist presented in Table 1 was adapted from the tool utilized in the ABACUS trial to assess patient knowledge and skills relevant to MDI therapy and carbohydrate counting. Any deficits identified should be addressed before initiating BA use.

Table 1. Checklist for Assessing MDI/Carbohydrate Counting (CHO) Knowledge and Skills.

GLUCOSE TARGETS
___ Can state his/her HbA1c target
___ Can state his/her fasting/preprandial glucose target
___ Can state his/her postprandial glucose target
KEY CONCEPTS/PRINCIPLES OF MDI
___ Can explain the concept and rationale for MDI therapy
___ Can explain the purpose of basal insulin
___ Can explain the purpose of mealtime bolus insulin
___ Can explain the purpose of correction bolus insulin
INSULIN-TO-CARBOHYDRATE RATIO (I:CHO)
___ Can explain the purpose of his/her I:CHO for calculating a mealtime bolus dose
___ Can state his/her I:CHO
___ Can explain the calculation of and process for using his/her I:CHO to calculate a mealtime bolus dose
___ Can explain how he/she adjusts his/her I:CHO
INSULIN SENSITIVITY FACTOR (ISF)
___ Can explain the purpose of his/her ISF/Correction Factor for correcting out-of-range BG
___ Can state his/her ISF/Correction Factor
___ Can explain the calculation of and process for using his/her ISF/Correction Factor to calculate a bolus dose prior to a meal
___ Can explain the calculation of and process for using his/her ISF/Correction Factor to calculate a bolus doses to correct high BG following a meal
___ Can explain how he/she adjusts his/her ISF/Correction Factor
SAFETY
___ Can list the potential causes of hypoglycemia
___ Can list and describe his/her symptoms of hypoglycemia
___ Can explain how to prevent hypoglycemia
___ Can explain how he/she should treat hypoglycemia if it occurs
___ Can list the potential causes of hyperglycemia
___ Can list and describe his/her symptoms of hyperglycemia
___ Can explain how to prevent hyperglycemia
___ Can explain how he/she should treat hyperglycemia if it occurs
___ Can list/explain his/her instructions for managing BG during illness
CARBOHYDRATE COUNTING
___ Can explain the concept and rationale for carbohydrate counting
___ Can explain the role of carbohydrates in providing energy and nutrition
___ Can identify the foods/food groups that contain carbohydrates
___ Can identify the food groups that do not contain carbohydrates
___ Can differentiate between simple carbohydrate foods and complex carbohydrate foods
___ Can describe a well-balanced meal—carbohydrates, protein, healthy fats
___ Can accurately estimate the number of carbohydrates in common foods
___ Can state the carbohydrate content of their chosen foods
___ Can explain what happens to BG when he/she underestimates number of carbohydrates to be eaten when calculating mealtime bolus dose
___ Can explain what happens to BG when he/she overestimates number of carbohydrates to be eaten when calculating mealtime bolus dose

Source: Adapted from assessment tools used in the ABACUS trial.[3]

2. Check the appropriateness of each patient's basal dose and key insulin parameters: ISF and I:CHO (during all time periods), BG targets, and prescribed dosage adjustments (±%) for exercise and changing health status (eg, physical activity, illness, menstruation).
3. Utilize structured SMBG with patients. Although it is neither necessary nor realistic to ask patients to obtain 7-point glucose profiles on a daily basis, periodic use of these profiles (e.g., before clinic visits) is advised.
4. Monitor patient therapy persistently. Also, discuss with patients how often they accept bolus advice or override it. What is driving this action?
5. Ensure that "practice devices" are available for patients (if possible), and that clinicians and educators receive adequate training in BA device use.

Summary

The goals of diabetes management are to safely and effectively achieve optimal glycemic control, prevent/reduce the development of diabetes-related complications, while minimizing the emotional burden of diabetes and optimizing independence and quality of life. Use of BA devices can help patients achieve these goals. BA use facilitates improvements in glycemic control without increasing hypoglycemia[3,9,10] or cost.[3] Moreover, it can improve treatment satisfaction,[3,9,10] reduce dosage errors,[1] assist in improving carbohydrate counting competency,[3,11,17] and reduce fear of hypoglycemia.[16] In addition, many ABACUS investigators believe that BA use in MDI-treated patients could assist in their transition to insulin pump therapy. However, it is important that clinicians work closely with their patients to establish correct insulin parameters and regularly monitor and adjust these parameters as needed. Clinicians now have another tool that is less complicated and costly than insulin pumps to help patients who do not choose insulin pump therapy improve their effectiveness and confidence in managing their diabetes.

Abbreviations

ABACUS, Automated Bolus Advisor Control and Usability Study; BA, bolus advisor; BG, blood glucose; CHO, carbohydrate; CNL, control; DTSQ, Diabetes Treatment Satisfaction Questionnaire; EXP, experimental; FDA, US Food and Drug Administration; I:CHO, insulin-to-carbohydrate ratio; ISF, insulin sensitivity factor; MAGE, magnitude of glycemic excursions; MDI, multiple daily insulin injection; SD, standard deviation; SMBG, self-monitoring of blood glucose.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: CGP has received consulting fees from Roche Diagnostics, DexCom, Intuity, CeQur, and Boston Therapeutics. KB has received consulting fees from Roche Diagnostics. DAH has received consulting fees from Roche, Intuity, Lilly/BI, Sanofi, and AZ/BMS and serves on advisory boards for Jannsen, Intuity, Lilly/BI, and Sanofi.

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References

1. Sussman A, Taylor EJ, Patel M, et al. Performance of a glucose meter with a built-in automated bolus calculator versus manual bolus calculation in insulin-using subjects. *J Diabetes Sci Technol*. 2012;6:339-344.
2. Ahola AJ, Makimattila S, Saraheimo M, et al. Many patients with type 1 diabetes estimate their prandial insulin need inappropriately. *J Diabetes*. 2010;2:194-202.
3. Ziegler R, Cavan DA, Cranston I, et al. Use of an insulin bolus advisor improves glycemic control in multiple daily insulin injection (MDI) therapy patients with suboptimal glycemic control: first results from the ABACUS trial. *Diabetes Care*. 2013;36:3613-3619.
4. Cavanaugh K, Huizinga MM, Wallston KA, et al. Association of numeracy and diabetes control. *Ann Intern Med*. 2008;148:737-746.
5. Mehta SN, Quinn N, Volkening LK, Laffel LM. Impact of carbohydrate counting on glycemic control in children with type 1 diabetes. *Diabetes Care*. 2009;32:1014-1016.
6. Bishop FK, Maahs DM, Spiegel G, et al. The Carbohydrate Counting in Adolescents With Type 1 Diabetes (CCAT) study. *Diabetes Spectrum*. 2009;22:56-62.
7. Huizinga MM, Carlisle AJ, Cavanaugh KL, et al. Literacy, numeracy, and portion-size estimation skills. *Am J Prev Med*. 2009;36:324-328.
8. Gross TM, Kayne D, King A, Rother C, Juth S. A bolus calculator is an effective means of controlling postprandial glycemia in patients on insulin pump therapy. *Diabetes Technol Ther*. 2003;5:365-369.
9. Schmidt S, Meldgaard M, Serifovski N, et al. Use of an automated bolus calculator in MDI-treated type 1 diabetes: the BolusCal Study, a randomized controlled pilot study. *Diabetes Care*. 2012;35:984-990.
10. Maurizi AR, Lauria A, Maggi D, et al. A novel insulin unit calculator for the management of type 1 diabetes. *Diabetes Technol Ther*. 2011;13:425-428.
11. Rabbone I, Scaramuzza AE, Ignaccolo MG, et al. Carbohydrate counting with an automated bolus calculator helps to improve glycaemic control in children with type 1 diabetes using multiple daily injection therapy: an 18-month observational study. *Diabetes Res Clin Pract*. 2014;103:388-394.
12. Zisser H, Wagner R, Pleus S, et al. Clinical performance of three bolus calculators in subjects with type 1 diabetes mellitus: a head-to-head-to-head comparison. *Diabetes Technol Ther*. 2010;12:955-961.
13. Klupa T, Benbenek-Klupa T, Malecki M, Szalecki M, Sieradzki J. Clinical usefulness of a bolus calculator in maintaining normoglycaemia in active professional patients with type 1 diabetes treated with continuous subcutaneous insulin infusion. *J Int Med Res*. 2008;36:1112-1116.
14. Bode BW. Insulin pump use in type 2 diabetes. *Diabetes Technol Ther*. 2010;12(suppl 1):S17-S21.
15. Skyler JS, Ponder S, Kruger DF, Matheson D, Parkin CG. Is there a place for insulin pump therapy in your practice? *Clin Diabetes*. 2007;25:50-56.
16. Barnard K, Parkin CG, Young A, Ashraf M. Use of an automated bolus calculator reduces fear of hypoglycemia and improves confidence in dosage accuracy in patients with type 1 diabetes mellitus treated with multiple daily insulin injections. *J Diabetes Sci Technol*. 2012;6:144-149.
17. Mitchell H, Greene S, Alexander V, et al. Insulin adjustment for blood glucose and carbohydrate content of meals from day 1 of diagnosis in children and adolescents with Type 1 diabetes improves glycaemic control by 3 months in a home based education programme. *Diabet Med*. 2014;31:23, A62.
18. Cavan DA, Ziegler R, Cranston I, et al. Use of an insulin bolus advisor facilitates earlier and more frequent changes in insulin therapy parameters in suboptimally controlled patients with diabetes treated with multiple daily insulin injection therapy: results of the ABACUS trial. *Diabetes Technol Ther*. 2014;16:310-316.
19. Mast O, Polonsky WH, Fisher L, et al. Structured blood glucose monitoring reduces HbA1c levels and annual test strip consumption in poorly controlled, non-insulin treated type 2 diabetes: Results from the STeP Study. *Diabetologia*. 2011;53:1.
20. Polonsky WH, Fisher L, Schikman CH, et al. A structured self-monitoring of blood glucose approach in type 2 diabetes encourages more frequent, intensive, and effective physician interventions: results from the STeP study. *Diabetes Technol Ther*. 2011;13:797-802.
21. Lange K. Therapieadhärenz bei Typ 1 Diabetes. Herausforderung, Barrieren und Chancen. *Der Diabetologe*. 2012;1:1-10.
22. Barnard KD, Lloyd CE, Dyson PA, et al. Kaleidoscope model of diabetes care: time for a rethink? *Diabet Med*. 2014;31:522-530.
23. Bandura A. *Self-Efficacy: The Exercise of Control*. New York, NY: Freeman; 1997.
24. Parkin CG, Buskirk A, Hinnen DA, Axel-Schweitzer M. Results that matter: structured vs. unstructured self-monitoring of blood glucose in type 2 diabetes. *Diabetes Res Clin Pract*. 2012;97:6-15.