

Letter to the Editor

Response to Biermann: Pilot Randomised Controlled Trial Results for Evaluating the Teaching Utility of the AIDA Diabetes Software Simulator—An Overview

Dear Editor:

In a recent issue of the journal, Dr. Biermann¹ raised various issues regarding the randomised controlled trial (RCT) assessment of diabetes simulation programs. As the results of a pilot RCT have recently been published,² making use of our proposed protocol,^{3,4} we thought it might be helpful to overview here the key study findings.

AIDA is a freeware computer program that permits the interactive simulation of plasma insulin and blood glucose profiles for demonstration, teaching, self-learning, and research purposes. It has been made freely available on the World Wide Web as a non-commercial contribution to continuing diabetes education. In the 8 years since its Internet launch in March/April 1996, over 400,000 visits have been logged to the AIDA Web pages and over 80,000 copies of the program have been downloaded, *gratis*. The software has been described in detail previously elsewhere in the literature,^{5,6} as well as in this journal.⁷⁻¹⁰ Independent reviews of AIDA and its Web-based sister application, AIDA online, can be found elsewhere in the literature.¹¹⁻¹⁷

With AIDA our attention recently has been focused on evaluating the program, and we have been trying to formally assess the utility of the software by conducting a variety of studies—ranging from qualitative assessments to more quantitative studies. Some issues surrounding the use of RCTs for evaluating diabetes simulators have been discussed recently by us in a previous issue of this journal.¹⁸

SUBJECTS AND METHODS

The study protocol adopted for the current work has been overviewed elsewhere.^{3,4} Briefly, an RCT approach was used, with a partial crossover design to evaluate the effect of a 6-week educational intervention with AIDA on a group of patients with insulin-dependent (type 1) diabetes mellitus. The protocol defined *a priori*^{3,4} required the recruitment of volunteers with type 1 diabetes of more than 6 years' duration, who were using at least 0.7 units of insulin/kg of body weight, with a body mass index ≤ 26 kg/m². All subjects were between 18 and 50 years old, and were free of any serious complications of diabetes or any other disease that might interfere with their ability to participate in the study.

The study design is summarised in Table 1 and Figure 1. The current trial was undertaken initially in a relatively small cohort of patients to offer a pilot study for the overall evaluation approach^{3,4}—and also to provide useful preliminary data to be used for sample size estimations for future larger-scale, multi-centre studies.

The RCT made use of two study arms—each receiving different educational interventions. During lessons, Arm A was exposed to the AIDA simulator (the active intervention), while Arm B (the control group) benefited from conventional educational methods using standard presentations with slides and transparencies. Six lessons were held for each study arm (one per week). Attendance at each lesson was

TABLE 1. STRUCTURE OF THE STUDY: SUMMARY OF KEY STEPS

1. Recruitment held at the Ospedale di Marino, Marino, Rome, Italy—36 youths were selected out of a cohort of 56 attending the institution. The other 20 were considered not eligible for various of the previously documented exclusion criteria,^{3,4} such as age, duration of disease, pregnancy, etc. Of the remaining 36 patients, five subjects declined for personal reasons, like being unable to attend lessons, two declared that they were “unhappy with a computer,” two females declined because they were planning a pregnancy, and three did not give any reason.
2. Stratified randomisation done with a pseudo-random number generator. The stratification in this initial study was achieved using the risk of hypoglycaemia and educational status of the subjects.²
3. The subjects were randomly assigned to the simulator (Group A) or the conventional (Group B) arms of the study.
4. HbA_{1c} levels were sampled.
5. Group A followed a course of six lessons with the AIDA diabetes simulator. Group B followed a course of six conventional lessons with overhead transparencies and standard lectures.
6. One month after the conclusion of the course of six lessons the HbA_{1c} level was resampled. The 1-month period was defined *a priori*^{3,4} as necessary to demonstrate a significant effect on the HbA_{1c} level.
7. Crossover phase. Group B was switched over to the simulator and subsequently went through the same lessons as Group A.
8. One month after the conclusion of the crossover phase lessons the HbA_{1c} level was sampled again.

Derived from Tatti and Lehmann.²

recorded, as was the incidence of any “drop outs” from the study.

A novel aspect of this research was the fact that the participants did not interact directly with the computer—rather the teacher served as a facilitator undertaking all interactions with the computer. This circumvented any problems if the participants were not fully computer-literate or confident to use a computer themselves. Connected with this, a perceived limitation of the current version of the AIDA software is that it is DOS-based and therefore does not make use of a standard, Windows graphical user interface.¹⁹ Given this—provided the teacher is fully conversant with use of the software—the facilitator approach should help to avoid any “learning curve” effect where it takes the study participants a number of lessons simply to become fully familiar with the program’s functions. Furthermore, using a facilitator should avoid any language difficulties as the software is written in English, while the participants’ mother tongue for this initial pilot study was Italian. In this respect, where required, the facilitator also served as a language translator.

At the beginning and end of the study details of any hypoglycaemic episodes were recorded, and assessments were made of glycosylated haemoglobin (HbA_{1c}) levels. In addition a partial crossover study design was

used whereby subsequently the control group was exposed to the AIDA simulator during a further 6-week course of lessons. This ensured that the maximum number of subjects eventually received the active intervention. The stratified randomisation approach adopted, and subject demographics have been described in detail elsewhere.² HbA_{1c} samples were drawn at the beginning and end of each phase of the study (i.e., twice for subjects in Group A and three times for subjects in Group B).

Teaching of lessons

In the original protocol^{3,4} it was envisaged that at least two teachers would be required to teach the diabetes lessons. However, for this initial study it was decided to use only a single teacher (P.T.) in order to avoid any unnecessary influence of the teaching style, knowledge, experience, or enthusiasm on the outcome.

The 24 subjects were split into four classes, each containing six subjects. All lessons were given on different days, but at approximately the same time of day, and with the same material (audiovisuals, slides, transparencies—and case scenarios for the simulator).

The topics for the six lessons were identical for the simulator (Arm A) and control (Arm B) groups and were delivered in the same order for both arms of the study. The topics covered

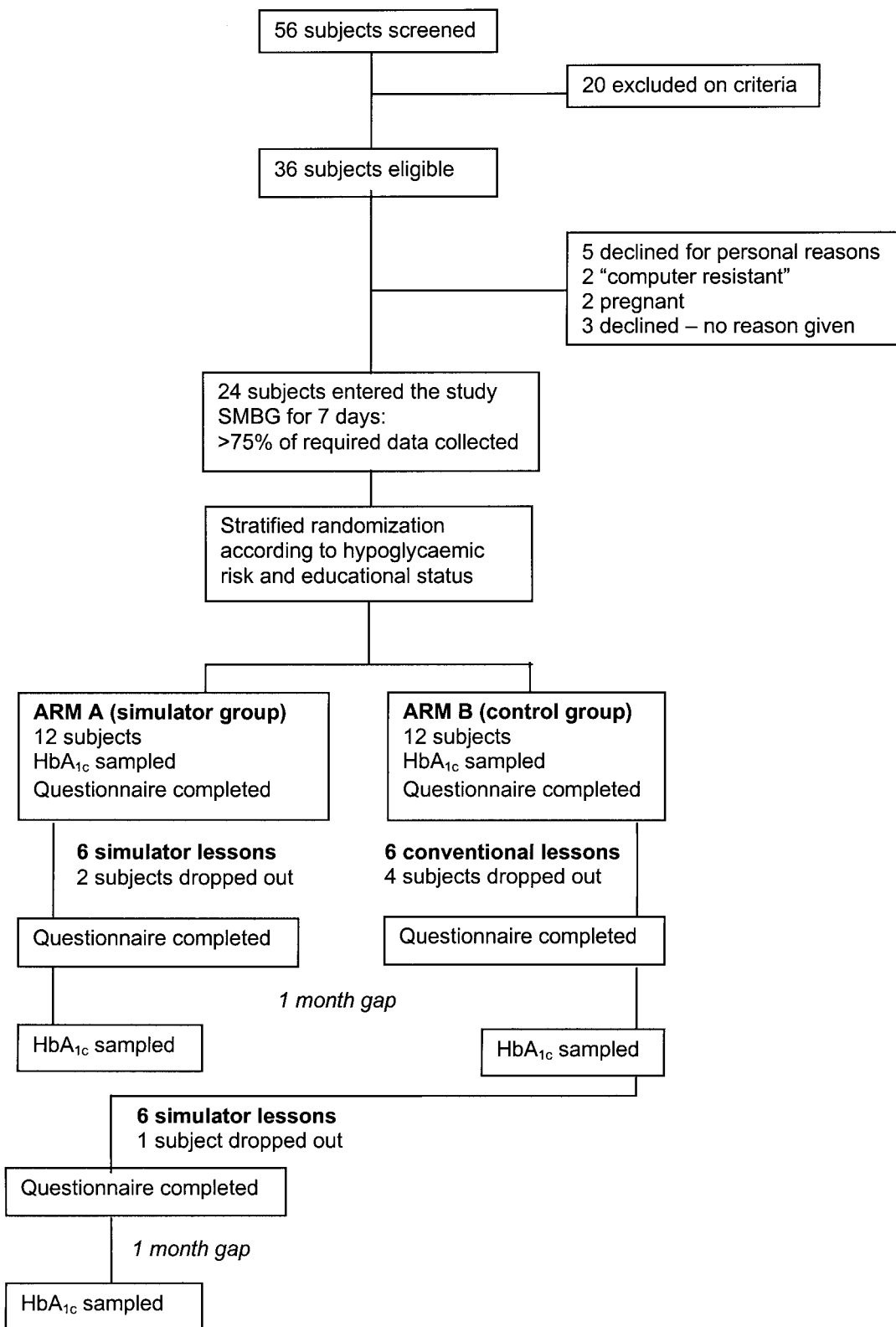


FIG. 1. Study profile (see Table 1 for details). Fifty-six subjects were screened; however, 20 were excluded on criteria defined *a priori*^{3,4} before the study commenced. Of the remaining 36 subjects, 12 did not proceed into the trial for the reasons shown. As a result 24 patients were actually randomised between Arms A and B of the study. Derived from Tatti and Lehmann.²

were (i) how to match insulin and food intake, (ii) overnight regulation of blood glucose levels, (iii) role of exercise and the renal threshold of glucose, (iv) avoidance and treatment of hypoglycaemia, (v) shift work or travel abroad, and (vi) how to manage blood glucose in unforeseen circumstances.

A crossover study design was applied to increase the number of subjects exposed to the simulator, and thus increase the overall power of the RCT.^{3,4}

For this pilot study, simulator-based and control group lessons were run from November 1999 to June 2000, inclusive.

Simulator lessons

Each simulator lesson made use of a computer connected to two monitors. The participants were arranged around a table, three of them facing each computer screen, ensuring that all study participants had a good view of the simulation graphs. Photographs of typical Group A (AIDA) simulator lessons can be found elsewhere in this journal.^{18,20}

After a brief introduction during the first lesson, each subject in Group A was put in charge of monitoring one aspect of the simulation. For instance, subject 1 had to follow the HbA_{1c} level, subject 2 had to follow the blood glucose level, subject 3 had to follow the plasma insulin level, etc. All subjects were asked to give their suggestions as to how the blood glucose profile might be improved—and cooperate in achieving a final proposal for simulation.

RESULTS

Details of the RCT, statistical analyses used, and the results obtained have been published in full elsewhere.² In the section below only an overview of the main findings is provided. Readers who are interested in a complete description of the results are referred to Tatti and Lehmann.²

HbA_{1c} levels

The HbA_{1c} data are shown in Table 2, and the results demonstrated graphically for individual subjects in Figure 2. HbA_{1c} levels in Group A dropped significantly from 7.2% to 6.4% after lessons with the AIDA simulator ($P = 0.01$). No significant changes in HbA_{1c} were observed in Group B between baseline (7.1%) and the end of the control lessons (7.0%), or the end of the crossover phase lessons (6.8%).

Hypoglycaemic episodes ("hypos")

Data regarding the number of symptomatic hypoglycaemic episodes ("hypos") are summarised in Table 2 and shown graphically for individual subjects in Figure 3. In this study only mild (sweating, dizziness) or moderate (nausea, vomiting) hypoglycaemic episodes occurred. No "hypo" was so severe as to require external assistance.

The number of hypos decreased significantly from 31 to 14 in Group A ($P = 0.03$) after AIDA lessons, but did not change significantly in Group B from baseline ($n = 20$) to after the con-

TABLE 2. HbA_{1c} LEVELS AND NUMBER OF HYPOGLYCAEMIC EVENTS ("HYPOS")

| Group | Mean \pm SD | | Wilcoxon signed rank test |
|----------------------|--------------------|--------------------|---------------------------|
| | Before the lessons | After the lessons | |
| HbA _{1c} | | | |
| A—AIDA | 7.2% \pm 1.0% | 6.4% \pm 0.7% | $P = 0.014$ |
| B—control | 7.1% \pm 0.9% | 7.0% \pm 0.8% | $P = 0.889^a$ |
| "Hypos" ^b | | | |
| A—AIDA | 2.5 \pm 1.7 (31) | 1.4 \pm 1.2 (14) | $P = 0.03$ |
| B—control | 1.7 \pm 1.6 (20) | 2.7 \pm 1.7 (22) | $P = 0.08^a$ |

Data are shown from both groups before and after the first cycle of lessons. Derived from Tatti and Lehmann.²

^aDifference not significant.

^bTotal number of episodes in parentheses.

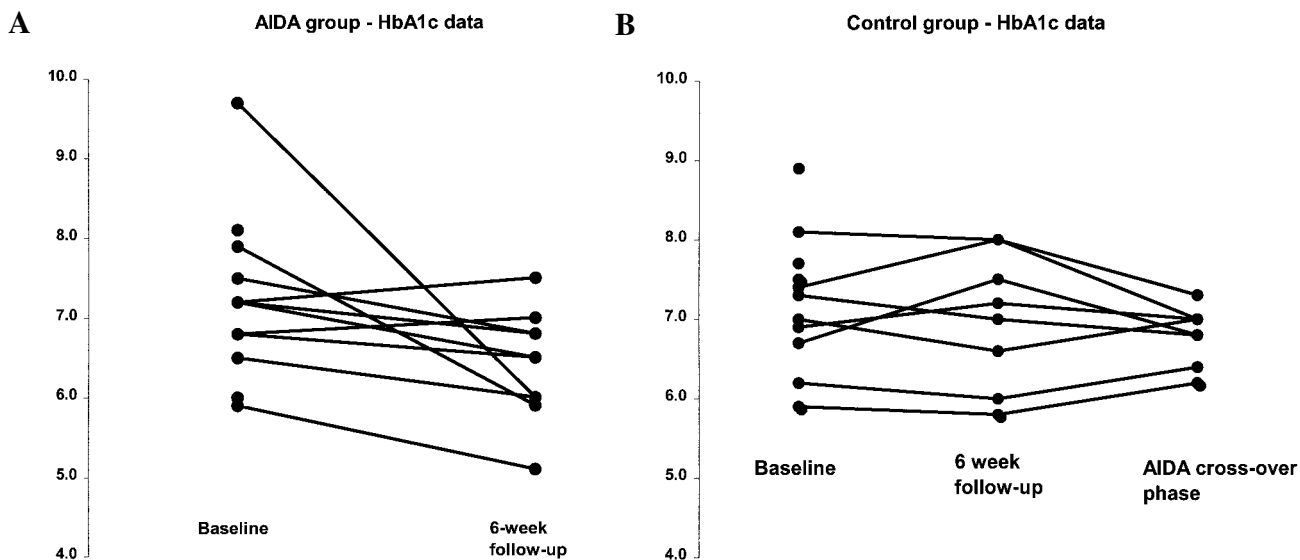


FIG. 2. **A:** Baseline and 6-week follow-up HbA_{1c} data (in %) for individuals in Arm A (the AIDA simulator group). **B:** Baseline, 6-week follow-up, and crossover-phase HbA_{1c} data (in %) for individuals in Arm B (the control group). For A and B, mean and standard deviation (SD) values are given in Table 2. HbA_{1c} assay normal range = 4.5–5.5%. Derived from Tatti and Lehmann.²

control lessons ($n = 22$). However, the number of hypos did decrease significantly (to $n = 10$) in Group B after exposure to the simulator during the crossover phase ($P = 0.03$ vs. 6-week data), although the changes did not reach statistical significance when compared with the baseline values ($P = 0.12$, not significant).

Length of lessons and “drop outs”

Lessons with the diabetes simulator lasted on average 104 min (range 70–140 min) as compared with the standard (control) lessons, which only lasted on average 63 min (range 60–70 min). Each lesson with AIDA involved

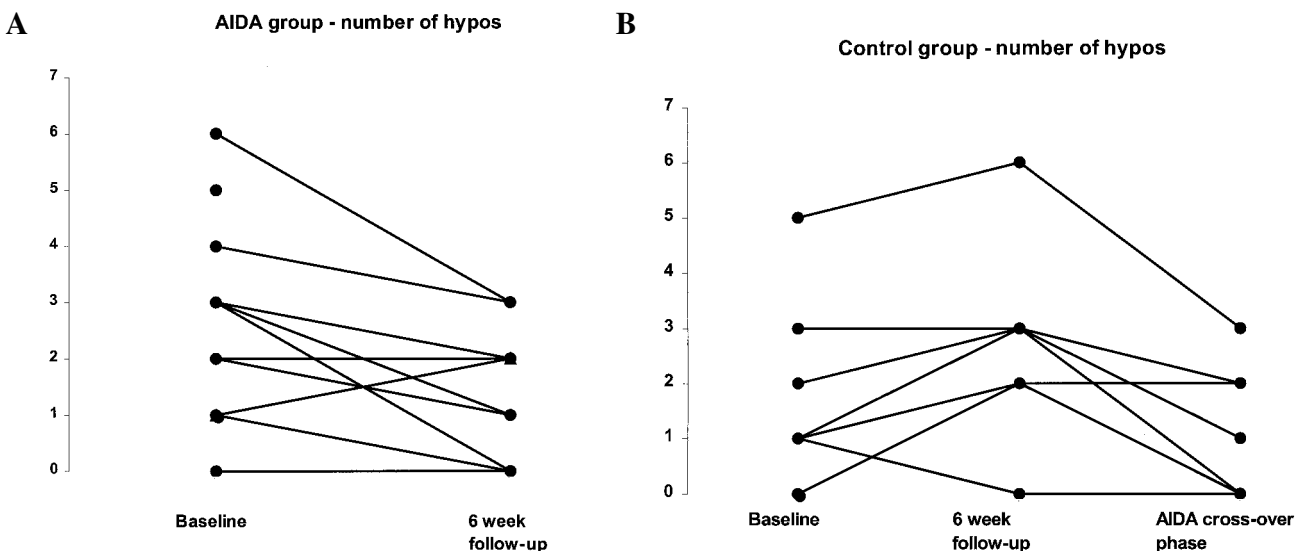


FIG. 3. **A:** Baseline and 6-week follow-up data for the number of symptomatic hypoglycaemic episodes (“hypos”) for individuals in Arm A (the AIDA simulator group). **B:** Baseline, 6-week follow-up, and crossover-phase data for the number of symptomatic “hypos” for individuals in Arm B (the control group). For A and B, mean and standard deviation (SD) values are given in Table 2. Derived from Tatti and Lehmann.²

on average 24 diabetes simulations, although there was a wide range (10–38 simulations per lesson). In particular, in the crossover phase group the lessons tended to last longer, with more simulations being run [mean lesson length = 112 min, with on average 30 simulations run (range 18–38 simulations per crossover group lesson)]. There were two “drop outs” from the study in Group A and five “drop outs” in Group B. Therefore, overall seven out of 24 subjects (29%) dropped out of the study.

DISCUSSION

The data overviewed in this letter demonstrate a beneficial effect of the diabetes simulation lessons on HbA_{1c} levels and the number of symptomatic hypoglycaemic episodes in the AIDA-treated group (Group A) that was not achieved in the control group (Group B). In the AIDA group there was a significant decrease in the number of symptomatic hypoglycaemic episodes without an increase in mean blood glucose or HbA_{1c} levels. Rather the HbA_{1c} actually decreased significantly (Table 2).

The number of “hypos” even worsened in the control group after the first six conventional lessons and improved when the subjects were crossed-over to the diabetes simulator. We cannot be definitely certain as to the reason for this. However, perhaps during the control lessons the patients realised the need to do something different to improve their blood glucose control—and therefore tried to change things—but did not quite know exactly what to do. Maybe they learnt what practical things actually to try with the diabetes simulation lessons. Further studies will be required to clarify this.²

Ideally, for use by insulin-dependent (type 1) diabetic patients on their own, it would be helpful if the program could—at least initially—form part of a process that includes the involvement of a teacher or facilitator. In this way patients might be able to learn more about what the simulations can offer—as well as possibly learn more about diabetes from the facilitator. Also this approach might perhaps allow such diabetes simulations to become better integrated with the sort of ser-

vices that are usually offered through a diabetes clinic/education facility. In this respect we have described a detailed evaluation protocol,^{3,4} which can also serve as a useful “blue print” for how to make use of the diabetes simulations in small-group diabetes clinic teaching sessions.

Nevertheless, as in any research trial there are a number of potential confounding factors that need to be considered in the interpretation of data from such a study. These have been discussed in detail elsewhere.² Other issues of interest are considered here.

The role of the teacher/facilitator

It is recognised that as the evaluation approach^{3,4} is trialled in a larger number of centres and clinics, the enthusiasm of the teacher/facilitator, and his or her own experience with the AIDA software, may well prove to be important—possibly critical—factors in the apparent overall efficacy of the program.

In this respect, ultimately the only way to remove any possible teacher “bias” or influence from the lessons would be to have patients use the software on their own, without a teacher present. While this is how many patients seem to be applying the software, after downloading it directly from the Internet¹⁹—and while this may possibly appear a methodologically more “pure” approach—in a clinical trial setting this would raise issues about patient learning curves and the time required for patients to become fully familiar with how to use the software. Furthermore, a whole series of logistical and financial issues would also need to be addressed to arrange for patients to have access to multiple computers in a diabetes clinic setting. For all these reasons the small-group teaching sessions appear the most practical way to run such studies—maybe until it is feasible to offer patients direct access to a self-learning diabetes tutorial to go with such simulations, possibly via the Internet.

If such diabetes simulations are to be successfully applied in less specialist units, then teacher training regarding how to best use the software will become of particular importance. We have been considering what methods might be applied to ensure that prospective

teachers/facilitators are sufficiently experienced with the software—before using it with patients.^{20,21} Such a “credentialling process” possibly leading to some sort of “accreditation” to teach with the simulator should establish a range of example diabetes case scenarios and a realistic number of simulations with which prospective teachers/facilitators should have practised before embarking on proper lessons with patients.^{20,21}

Power calculations

With power calculations it is necessary to know the effect size that might be observed before it is possible to apply such computations. With this work, prior to running this initial study, it was difficult to be certain what the effect size would really be. However, now that a pilot RCT has been done, some power calculation estimates of sample sizes have been carried out based on the HbA_{1c} data observed in this $n = 24$ study. Based on a standard statistical approach²² these estimates suggest that a sample size of at least 36 subjects would be required in future studies to be confident of showing a statistically significant effect on HbA_{1c} levels. However, as there was a 29% drop out rate in this study, in future at least 52 subjects would need to be recruited—on the basis of the current experience—in order to have data at the end of the study for analysis from at least 36 patients.

CONCLUSIONS

This current preliminary trial has been run as a pilot study to confirm (i) the utility of small-group educational sessions as a way of teaching using AIDA, and (ii) the validity of the basic evaluation approach that has been proposed.^{3,4} In this respect we believe that the study can be considered a success.

The evaluation protocol previously described in this journal⁴ and elsewhere³ has been demonstrated—with some minor modifications—to be fully workable in practice, in a busy clinic setting. Some further possible small changes to the protocol have been considered.² Further minor modifications—particularly with

study logistics—may be required as this approach is scaled up to be run in multiple clinics/centres involving larger numbers of patients with multiple teachers/facilitators. Nevertheless, the basic evaluation concept involving small-group teaching sessions does seem to be appropriate, and manageable. Furthermore, this current study has yielded useful data for sample size estimations for future larger-scale studies.²

In addition, the actual results obtained with the diabetes simulator have been encouraging. This pilot study suggests that the AIDA software, if properly applied, may potentially be of use for patients with insulin-dependent (type 1) diabetes as a way of educating them to improve their glycaemic control. In this respect the preliminary observations in the AIDA group of decreases in HbA_{1c} levels—with reductions in the number of symptomatic “hypos”—are clearly promising. However, larger-scale studies involving more patients and more teachers (in more clinics/centres) are obviously required before any firm conclusions can be drawn regarding the educational efficacy of the overall diabetes simulation approach.

SYSTEM AVAILABILITY

The latest release of AIDA (v4.3a) can be downloaded, without charge, from www.2aida.org on the Internet. The program runs on IBM PC or compatible 80386/80486/Pentium-based machines and requires approximately 3 Mb of hard disk storage space. The software can also be used on Apple Macintosh computers running PC emulators such as Virtual PC or SoftWindows. A free Web-based version of the diabetes simulator (called AIDA online) is also available for use at www.2aida.net on the Web. People who wish to be automatically informed about future updates and enhancements to the AIDA/AIDA online diabetes software range can subscribe (for free) to the very low volume AIDA diabetes simulator announcement list by sending a blank email note to subscribe@2aida.org

Any readers who might be interested in collaborating by applying the standardised RCT protocol^{3,4} themselves in an evaluation of AIDA in their own unit(s) for clinician/spe-

cialist nurse/educator-led patient teaching sessions are invited to contact one of the authors. Further information about the evaluation of AIDA for patient use can be found at www.2aida.org/evaluate on the Web.

REFERENCES

- Biermann E: Comment on Lehmann and Tatti: proposed controlled trial on simulators in diabetes education [letter]. *Diabetes Technol Ther* 2002;4:255-257.
- Tatti P, Lehmann ED: A prospective randomised-controlled pilot study for evaluating the teaching utility of interactive educational diabetes simulators. *Diabetes Nutr Metab* 2003;16:7-23.
- Tatti P, Lehmann ED: A randomised-controlled clinical trial methodology for evaluating the teaching utility of interactive educational diabetes simulators. *Diabetes Nutr Metab* 2001;17:1-17.
- Lehmann ED, Tatti P: Questionnaires for a randomized controlled trial methodology to evaluate the teaching utility of diabetes simulation programs. *Diabetes Technol Ther* 2001;3:293-305.
- Lehmann ED, Deutsch T: A physiological model of glucose-insulin interaction. In: *IEEE EMBS Proceedings, 13th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*. New York: IEEE Press, 1991;2274-2275.
- Lehmann ED, Deutsch T: A physiological model of glucose-insulin interaction in type I diabetes mellitus. *J Biomed Eng* 1992;14:235-242.
- Lehmann ED: Experience with the Internet release of AIDA v4—an interactive educational diabetes simulator. *Diabetes Technol Ther* 1999;1:41-54.
- Lehmann ED: User experience with the AIDA interactive educational virtual diabetes patient simulator. *Diabetes Technol Ther* 2000;2:165-171.
- Tatti P, Lehmann ED: Utility of the AIDA diabetes simulator as an interactive educational teaching tool for general practitioners (primary care physicians). *Diabetes Technol Ther* 2001;3:133-140.
- Tatti P, Lehmann ED: Use of the AIDA diabetes simulation software—www.2aida.org—as an interactive educational tool for teaching student nurses. *Diabetes Technol Ther* 2001;3:655-664.
- Wilson DM: Diabetes simulators: ready for prime time? *Diabetes Technol Ther* 1999;1:55-56.
- Anon: The virtual diabetic patient: AIDA online. *Diabetes Metab Res Rev* 1999;15:226.
- Lehmann ED: User reviews of AIDA online: a web-based interactive educational diabetes simulator. *Diabetes Technol Ther* 2000;2:329-342.
- Chausmer AB: Diabetes management tools for patients and physicians. *Med Software Rev (CRI Health Care Publications)* 2002;11(5):1-16.
- Mendosa R: AIDA On-line [review]. Formerly available from the American Diabetes Association Website. Now accessible at: <http://www.mendosa.com/aida.htm> Accessed 7 December 2003.
- Tatti P: Il training con i simulatori. Un sistema per migliorare la qualità di vita ed il controllo glicemico nei soggetti diabetici [in Italian]. *il giornale A.I.D.I.D.* 2003;IX(3):4-5.
- Dreval AB: Mass insulinphobia [in Russian]. Moscow: Prof Dreval Publications, 2003;207-283.
- Lehmann ED, Tatti P: Randomized controlled trial design for simulator use in diabetes education: some issues for consideration [letter]. *Diabetes Technol Ther* 2002;4:258-269.
- Lehmann ED: The freeware AIDA interactive educational diabetes simulator—<http://www.2aida.org>—(1) A download survey for AIDA v4.0. *Med Sci Monit* 2001;7:504-515.
- Tatti P, Lehmann ED: Using the AIDA—www.2aida.org—diabetes simulator. Part 1: Recommended guidelines for health-carers planning to teach with the software. *Diabetes Technol Ther* 2002;4:401-414.
- Lehmann ED, Tatti P: Using the AIDA—www.2aida.org—diabetes simulator. Part 2: Recommended training requirements for health-carers planning to teach with the software. *Diabetes Technol Ther* 2002;4:717-732.
- Hulley BS, Cummings SR: Sample size required per group when using the t test. In: *Designing Clinical Research*. Baltimore: Williams & Wilkins, 1988.

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