

A prospective randomised-controlled pilot study for evaluating the teaching utility of interactive educational diabetes simulators¹

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ABSTRACT. AIDA is an interactive educational diabetes simulator that is useful for recreating clinically realistic diabetes situations. It is available without charge from <http://www.2aida.org> on the Web. This paper describes a prospective, clinical randomised-controlled trial (RCT) run at the Ospedale di Marino (Italy) for evaluating the educational utility of AIDA in small group teaching sessions. Twenty-four volunteers (12 male and 12 female) with Type 1 diabetes of more than 6-year duration, aged 19-48 years, who gave written informed consent, were randomly assigned to one of two study groups, each receiving different teaching interventions. Group A was exposed to the AIDA diabetes simulator, while Group B (the control group) received conventional lessons with slides and transparencies. Six lessons were held for each group (one per week). At the end of the conventional lessons, after a 'washout' period of 4 weeks, Group B entered a partial cross-over phase with the simulator during a further 6-week block of lessons. Before and after the 6 weeks of lessons, twice for Group A and 3 times for Group B, all subjects had their HbA_{1c} measured. The subjects also carefully documented the incidence of any symptomatic hypoglycaemic episodes ('hypos'), whether mild (sweating, dizziness), moderate (nausea, vomiting), or severe (requiring assistance). All data were analysed using non-parametric statistics (Wilcoxon signed rank tests). HbA_{1c} levels in Group A dropped significantly from 7.2% to 6.4% after lessons with the diabetes 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 cross-over phase lessons (6.8%). 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 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 cross-over phase ($p=0.03$ vs 6-week data). Larger trials involving more patients in more centres are clearly needed, but this proof-of-concept (pilot) study does demonstrate the feasibility of using a prospective RCT approach for the evaluation of educational diabetes simulation software such as AIDA.

Diab. Nutr. Metab. 16: 7-23, 2003.

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INTRODUCTION

The education of patients with diabetes has been the source of considerable interest (3) and controversy (4). In the past, diabetes self-management education has often been undervalued and unsupported, mostly due to an inability to document the effectiveness of teaching interventions on metabolic control. Also it has been difficult to demonstrate improvements in quality of life (5). In this respect the role of education in the well-being of patients has frequently been accepted, but not as frequently proven (6). Nevertheless, more recently there has been a surge

¹ Presented in part at the Mayo Clinic International Symposium on Computers in Diabetes Care held in Rochester, Minnesota, USA in September 2000 (1), and at the 61st American Diabetes Association Annual Scientific Meeting held in Philadelphia, Pennsylvania, USA in June 2001 (2).

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Key words: Diabetes mellitus, randomised-controlled trial, evaluation, dynamic simulation, modelling, education, computer-assisted learning.

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Received 23 June 2001; accepted 14 December 2001.

of interest in this topic (7, 8). However much of the research carried out in the field of diabetes education seems to have been centred more on traditional teaching, with or without feedback from the patient. Some attempts have been made in the past with some computer programs (9), essentially applying an on-screen presentation of a conventional textbook, with some hints at interaction, like a question and answer session (10, 11).

By contrast, a relatively novel approach to diabetes education is represented by the AIDA interactive diabetes simulator which has been made available without charge via the Internet (12-14). Among the features of AIDA that make it potentially useful as a teaching tool are its dynamic representations of the effects of insulin injections, the program ability to

display on the spot the effect of variations in the insulin dose, insulin preparation, carbohydrate ingestion, and timing of insulin injections. Furthermore, the flexibility of the software permits its use by patients on their own, or in conjunction with a teacher and others with diabetes.

AIDA BACKGROUND

AIDA is a freeware computer program which permits the interactive simulation of plasma insulin and blood glucose profiles for demonstration, teaching and self-learning purposes. It has been made freely available on the World Wide Web as a non-commercial contribution to continuing diabetes education. In the 5 years since its Internet launch, over

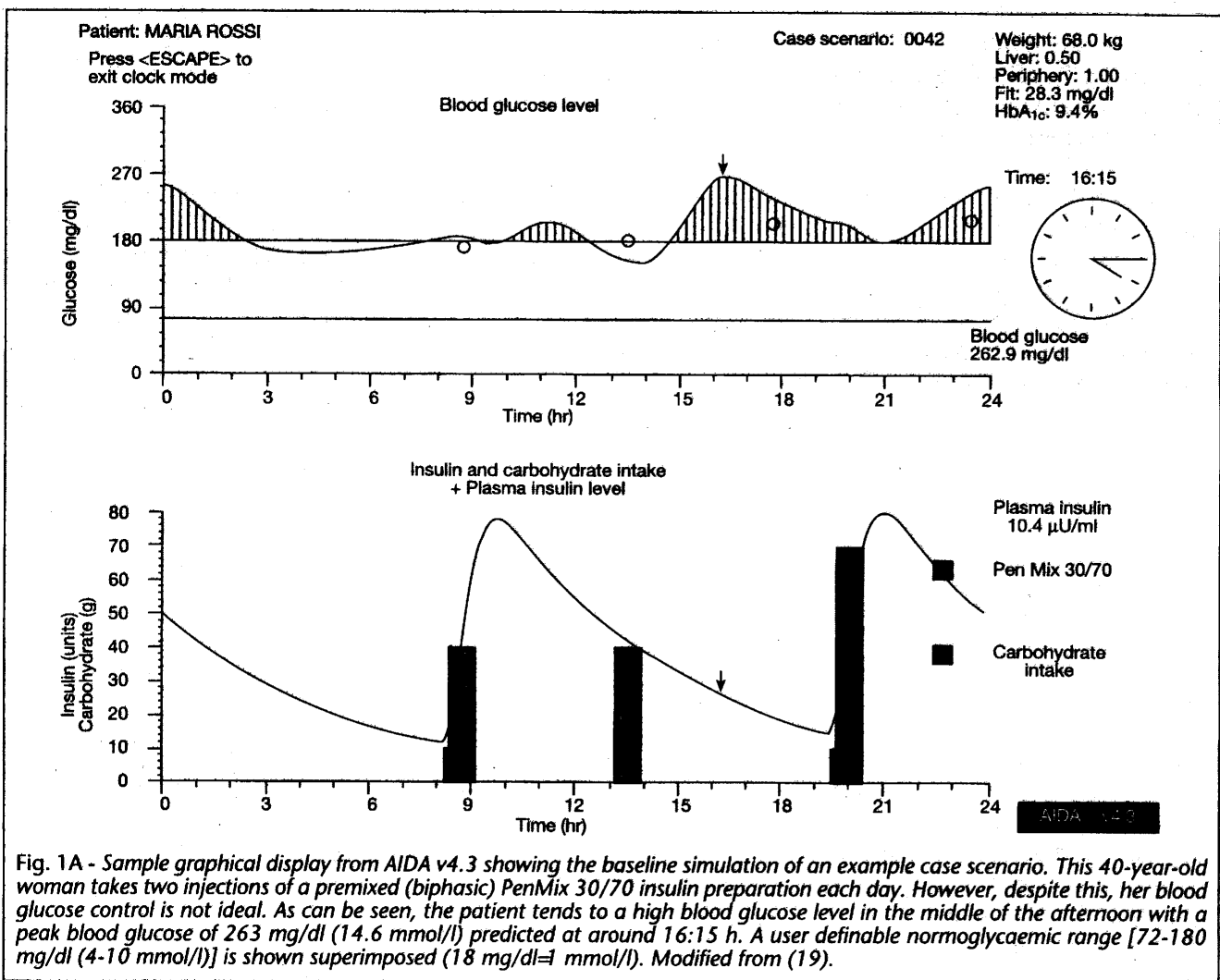


Fig. 1A - Sample graphical display from AIDA v4.3 showing the baseline simulation of an example case scenario. This 40-year-old woman takes two injections of a premixed (biphasic) PenMix 30/70 insulin preparation each day. However, despite this, her blood glucose control is not ideal. As can be seen, the patient tends to a high blood glucose level in the middle of the afternoon with a peak blood glucose of 263 mg/dl (14.6 mmol/l) predicted at around 16:15 h. A user definable normoglycaemic range [72-180 mg/dl (4-10 mmol/l)] is shown superimposed (18 mg/dl=1 mmol/l). Modified from (19).

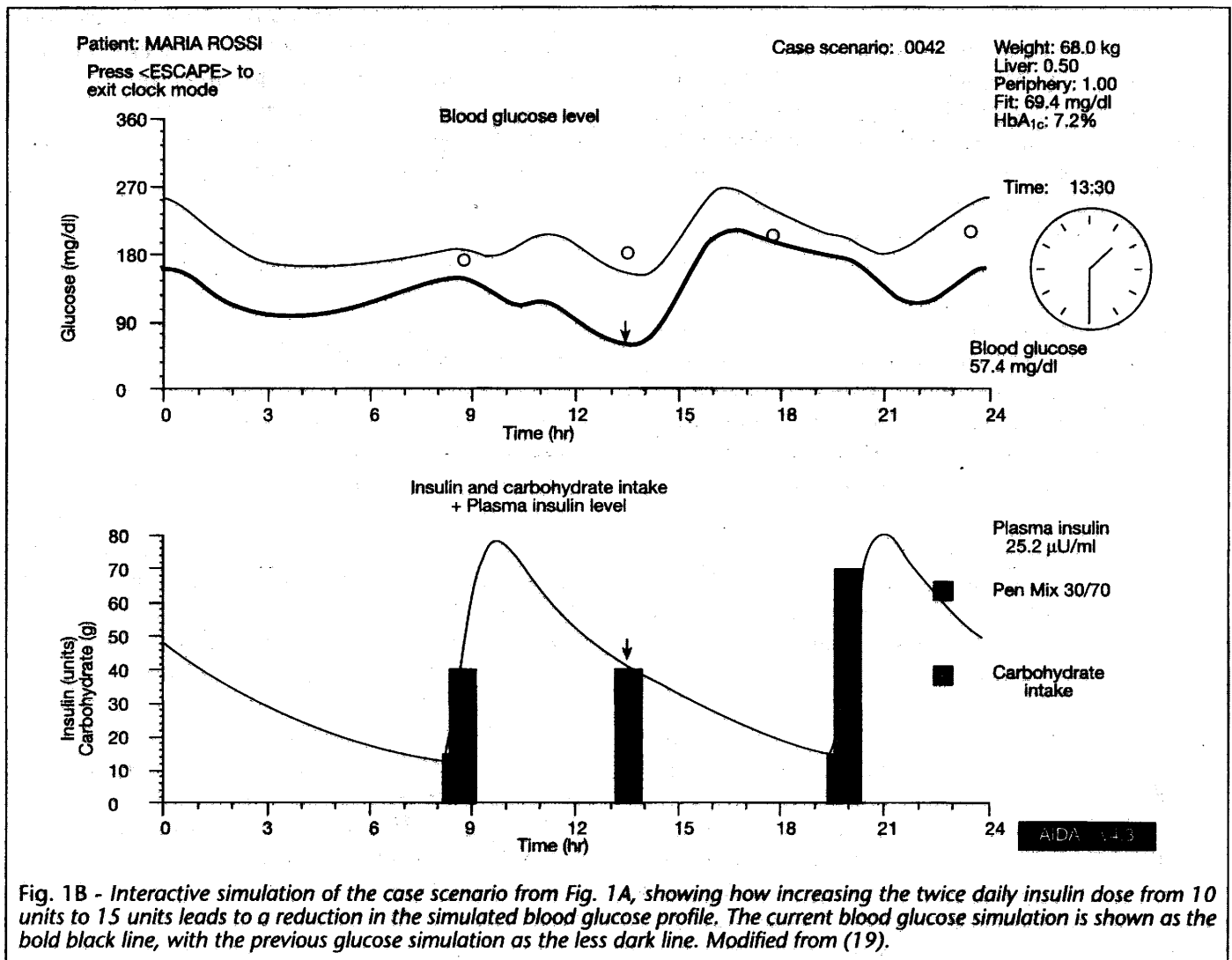


Fig. 1B - Interactive simulation of the case scenario from Fig. 1A, showing how increasing the twice daily insulin dose from 10 units to 15 units leads to a reduction in the simulated blood glucose profile. The current blood glucose simulation is shown as the bold black line, with the previous glucose simulation as the less dark line. Modified from (19).

100,000 people have visited the AIDA Website – <http://www.2aida.org> – and over 24,000 copies of the program have been downloaded, *gratis*.

The AIDA software has been overviewed in previous articles in this journal (15, 16). Briefly the program incorporates a compartmental model that describes glucose-insulin interaction in patients completely lacking endogenous insulin secretion [*ie* patients with Type 1 diabetes mellitus (T1DM)]. The model contains a single extracellular glucose compartment into which glucose enters via both intestinal absorption and hepatic glucose production. The model also contains separate compartments for plasma and 'active' insulin (17, 18), the latter being responsible for glycaemic control while insulin is removed from the former by hepatic degradation. Figure 1 demonstrates a little of what AIDA can do.

Figure 1A shows a baseline simulation of an example case scenario. Blood glucose information is given in the top graph, while insulin and carbohydrate details are given in the lower graph. A user definable normoglycaemic range [72-180 mg/dl (4-10 mmol/l)] is shown superimposed highlighting the hyperglycaemia which is expected to occur in the middle of the afternoon with a peak blood glucose of 263 mg/dl (14.6 mmol/l) at 16:15 h (19). As has been described previously elsewhere (12-16) the main utility of the AIDA diabetes simulation approach comes from being able to make changes to the regimen and then re-simulate the effect(s) of those change(s) on the blood glucose profile. Therefore, for instance, Figure 1B shows the glycaemic effect of increasing the dose of the patient's twice-daily pre-mixed (biphasic), PenMix 30/70 insulin

injections (before breakfast and supper) from 10 IU to 15 IU being simulated. As can be seen, this is predicted to lead to a substantial reduction in the simulated blood glucose profile with a minimum blood glucose level of around 57 mg/dl (3.2 mmol/l) predicted to occur at 13:30 h. If this sort of glycaemic control was maintained longer term, the AIDA v4.3 model (20) predicts that an HbA_{1c} level of around 7.2% would result, as compared with an HbA_{1c} level of 9.4% for the previous example shown in Figure 1A (19).

AIDA comes with 40 such sample case scenarios for simulation, and additional cases can be created by users. Further examples of the sort of simulations that AIDA can offer can be found elsewhere in the literature (21-23), and on the Internet at <http://www.2aida.org>

However, it is to be stressed that the simulator does not give firm or didactic 'rules' to follow, but rather only puts users into a situation and lets them experiment with it as a way of learning and hopefully gaining confidence in diabetes self-management.

AIDA usage

A substantial number of patients with T1DM (and their relatives) seem to be making use of the AIDA software on their own. For instance a recent survey at the AIDA Website (24) found that 946 of 1,360 downloads (>69%) of the AIDA v4.0 program were being made by patients or their relatives. It remains unclear how much these people have liaised first with their health-care professionals prior to using the software. However, ideally it should be possible to develop an educational approach that allows patients to benefit from whatever the program might have to offer in a supervised setting – before maybe later moving on to use the software on their own at home/work. We have described such an approach (25) – based on classes involving 6 separate diabetes

education lessons – which can be run either using AIDA, or with conventional slides/overheads/transparencies and standard lecture materials. A supplementary benefit of our design (25) is that it is amenable to formal study to evaluate the efficacy of the overall diabetes simulation approach. In this respect, while simulation software like AIDA may appear intuitively of benefit – there is still a great need for such applications to be properly evaluated.

AIDA VALIDATION STUDIES

With AIDA we have been trying to formally assess the utility of the program by conducting a variety of studies – ranging from qualitative assessments to more quantitative studies. Table 1 summarises some of the different sorts of work that can be undertaken, and the different levels of evidence that can be generated to support clinical use of such an application (24).

Level 1 studies (randomised-controlled trials, RCTs) are clearly the optimum method for rigorously assessing educational/clinical utility. Nevertheless, useful information can also be obtained from less formal studies. In the case of AIDA, under level 5 (methodological verification and validation studies), a quantitative assessment was reported in 1994 to document the accuracy of the blood glucose simulations in a cohort of 30 patients with T1DM (26). While the simulations were not shown to be accurate enough for individual patient glycaemic prediction or therapy planning, they have found widespread use for educational/demonstration/self-learning purposes where individual predictive accuracy is less critical (27, 28).

Under level 4 (anecdotal evidence – including independent user comments and reviews) various AIDA users have written for the Website, and in print, their thoughts about the software (22, 29, 30) and its sister Web-based application called 'AIDA on-line' (accessible via: <http://www.2aida.org/online>) (31-33). Some short comments/'sound bites' about the downloadable AIDA PC software have also recently appeared elsewhere (34-36).

Under level 3 observational studies (including the use of surveys and questionnaires), as highlighted above, some diabetes surveys have been undertaken about AIDA via the Internet (24). The feedback and survey responses that have been obtained so far have been very informative and useful, and general

Table 1 – Levels of evidence for clinical application. Derived from (24).

Level 1 - Formal, open, clinical randomised-controlled trials
Level 2 - Case controlled trials (comparisons made but not randomised)
Level 3 - Observational studies (including surveys and questionnaires)
Level 4 - Anecdotal evidence (including independent user comments and reviews)
Level 5 - Methodological verification and validation studies

experience with the software has been very encouraging (22, 23). However the next stage in the evaluation process, as set out in Table 1, is to undertake level 2 (case controlled) or level 1 (randomised-controlled) trials. As RCTs offer a 'gold standard' method of evaluation, for the current work we have focused on trying to evaluate the AIDA diabetes simulation software in an RCT setting.

As such the present study has aimed to explore the effectiveness of AIDA as an educational tool in small-group teaching sessions, involving patients with T1DM. The intention was to study the effects of using the program on HbA_{1c} levels and the results of self-monitoring blood glucose (SMBG) data, as well as on the number of symptomatic hypoglycaemic episodes ('hypos').

SUBJECTS AND METHODS

The study approach adopted for this work has been previously described in this journal (25). Briefly, an RCT approach was used, with a partial cross-over design, to evaluate the effect of a 6-week educational intervention with AIDA on a group of patients with T1DM.

The protocol defined *a priori* (25) required the recruitment of volunteers with T1DM of more than 6-year duration, who were using at least 0.7 IU of insulin per kilogram of body weight, with a body mass index (BMI) ≤ 26 kg/m². All subjects had to be aged between 18 and 50 years, and free of any serious diabetic complications or any other disease that might interfere with their ability to participate in the study. The study design is summarized in Table 2 and Figure 2. The current study was undertaken initially in a relatively small cohort of patients to offer a proof-of-concept for the overall evaluation approach (25) – and also to provide useful preliminary (pilot) data to be used for sample size estimations for future larger-scale, multi-centre studies.

As overviewed previously (25), 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 recorded, as was the incidence of any 'dropouts' 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 'wizard' or 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 (24) is that it is DOS-based and

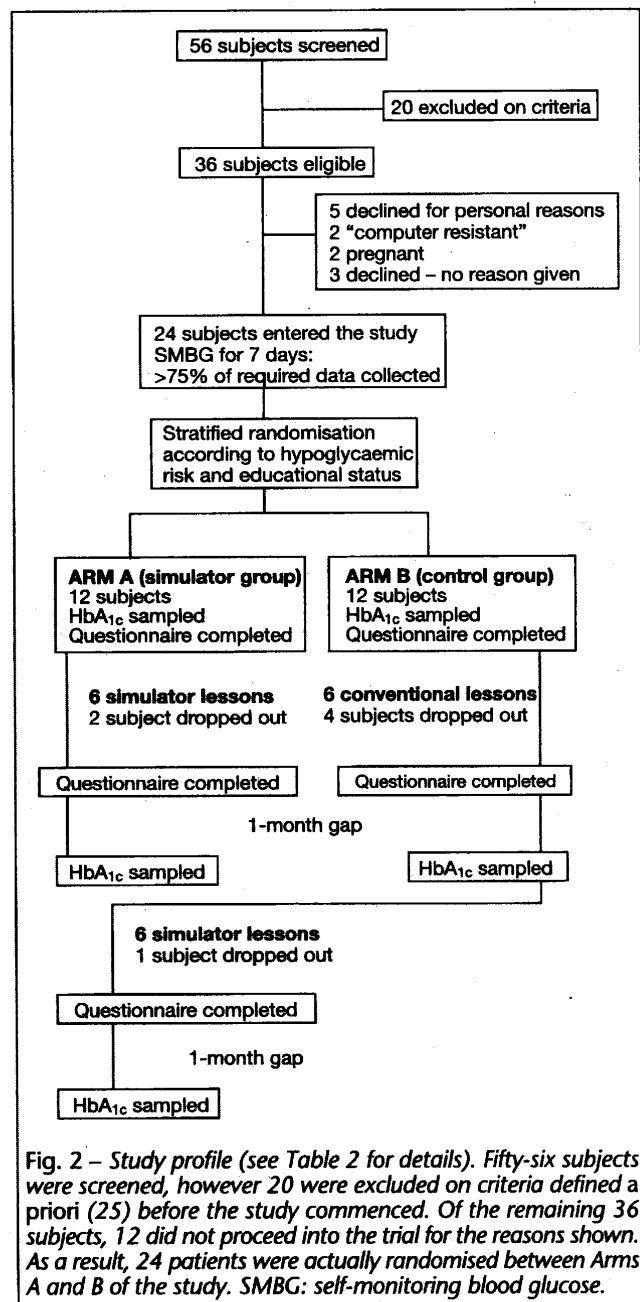


Fig. 2 – Study profile (see Table 2 for details). Fifty-six subjects were screened, however 20 were excluded on criteria defined *a priori* (25) before the study commenced. Of the remaining 36 subjects, 12 did not proceed into the trial for the reasons shown. As a result, 24 patients were actually randomised between Arms A and B of the study. SMBG: self-monitoring blood glucose.

therefore does not make use of a standard, Windows graphical user interface. Given this – provided the teacher is fully conversant with use of the software – the ‘wizard’/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 functions. Furthermore, using a ‘wizard’ approach 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 ‘wizard’ also served as a language translator.

At the beginning and end of the study SMBG data were collected, details of any hypoglycaemic episodes recorded, and assessments made of HbA_{1c}. In addition

a partial cross-over study design was used whereby subsequently the control group was exposed to the AIDA simulator during a further six-week course of lessons. This ensured that the maximum number of subjects eventually received the active intervention.

Stratified randomisation

Twenty-four patients with T1DM were recruited and assigned to one of the two study groups, Arm A (AIDA group) or Arm B (control group crossing over to AIDA), using a process of stratified randomisation according to their educational level and hypoglycaemic risk (Table 2). The numbers used for the randomisation process were obtained from a computerised pseudo-random number generator.

For the purposes of the current study, low educational status was defined as less than 10 years of school education, and high educational status as greater than or equal to 10 years of school/university education. ‘Hypo’ risk was categorised based on an initial one-week of SMBG data collection (Table 2). High ‘hypo’ risk was defined as any symptomatic hypoglycaemic episodes or recorded SMBG data <70 mg/dl (3.9 mmol/l) during that week. Low ‘hypo’ risk was defined as no symptomatic hypoglycaemic episodes or recorded SMBG data >70 mg/dl (3.9 mmol/l) during that week (25).

HbA_{1c} levels were measured using an HPLC method (Menarini, Firenze, Italy) with a normal range of 4.5-5.5%.

Subjects

All the subjects were in good health and without serious diabetic complications. None of them had hypoglycaemia unawareness, defined as an inability to recognize hypoglycaemia with blood glucose levels less than 70 mg/dl (3.9 mmol/l). None of the females were pregnant, and there was no history of cheating with SMBG in any of the cohort. None of the patients had previous experience with the simulator nor with any other diabetes computer software. None had taken part in a systematic education course during the previous two years, apart from sporadic information about new diabetes innovations (eg insulin pens, lispro, etc). All of the subjects came from the same population living in a small town (Marino, Italy) or in the surrounding area. They all had an open predisposition towards diabetes education and the innovation of the simulator, and no evident psychological problems. The

Table 2 – 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 (25), such as age, duration of disease, pregnancy, etc. Of the remaining 36 patients, 5 subjects declined for personal reasons, like being unable to attend lessons, 2 declared that they were ‘unhappy with a computer’, 2 females declined because they were planning a pregnancy, and 3 did not give any reason.
2. The 24 subjects who agreed to participate collected self-monitoring blood glucose (SMBG) data for 7 days – fasting and 2 hr post lunch and dinner (more than 75% of the required data were collected).
3. Stratified randomisation done with a pseudo-random number generator. The stratification in this proof-of-concept study was achieved using the risk of hypoglycaemia and educational status of the subjects.
4. The subjects were randomly assigned to the simulator (Group A) or the conventional (Group B) arms of the study.
5. HbA_{1c} levels were sampled and a questionnaire completed by all participants.
6. Group A followed a course of 6 lessons with the AIDA diabetes simulator. Group B followed a course of 6 conventional lessons with overhead transparencies and standard lectures.
7. After the conclusion of the course of 6 lessons the questionnaire was completed again, and one-month later the HbA_{1c} level was re-sampled. The one month period was defined *a priori* (25) as necessary to demonstrate a significant effect on the HbA_{1c} level.
8. Cross-over phase. Group B was switched over to the simulator and subsequently went through the same lessons as Group A.
9. After the conclusion of the cross-over phase lessons the questionnaire was completed again and one month later the HbA_{1c} level was sampled again.

Table 3 – Baseline characteristics of the study cohort – mean±SD values given.

	Group A (AIDA diabetes simulator group)	Group B (Control group crossing over later to AIDA lessons)
Age (years)	29±7	31±8
Duration of diabetes (years)	11±4	11±5
Body mass index (BMI) (kg/m ²)	22.7±1.4	22.7±1.2
Marital status: Married/Engaged/ Single	8/4/0	7/5/0
Educational status ¹	2=83.3% 3=16.7%	2=75% 3=25%
Number of insulin injections (/day)	3=16.7% 4=83.3%	3=8.3% 4=91.7%
Insulin dose (units/day)	48±10	49±10
Male:Female ratio	6:6	6:6
Baseline HbA _{1c} level (%)	7.2±1.0	7.1±0.9
Baseline mean SMBG (mg/dl) during data collection week	169±50	174±53
Baseline mean number of 'hypos' during data collection week	2.5±1.7	1.7±1.6

¹Educational status determined by what level (grade) subjects had previously reached at school/university (2 = High School; 3 = University). SMBG: self-monitoring blood glucose.

subjects were all regular attenders of the local hospital (Ospedale di Marino). All the subjects agreed not to use the simulator on their own for the duration of the study. The study was approved by the local Ethics Committee, and all participants gave their written informed consent.

The baseline characteristics of the study cohort are documented in Table 3.

Data collection

All subjects collected SMBG data for one week at standard times (fasting and 2 hr after lunch and din-

ner) and kept a log of any symptomatic hypoglycaemic episodes. All of the participants collected at least 75% of the baseline SMBG data requested. Throughout this study the same blood glucose metre was used (the standard one used in the Marino diabetes centre). The accuracy of the metre is routinely, independently checked and varies from 2% in the 70 mg/dl (3.9 mmol/l) to 210 mg/dl (11.7 mmol/l) range, to 5% outside these values. HbA_{1c} samples were drawn at the beginning and end of each phase of the study (*ie* twice for subjects in Group A, and 3 times for subjects in Group B).

Teaching of lessons

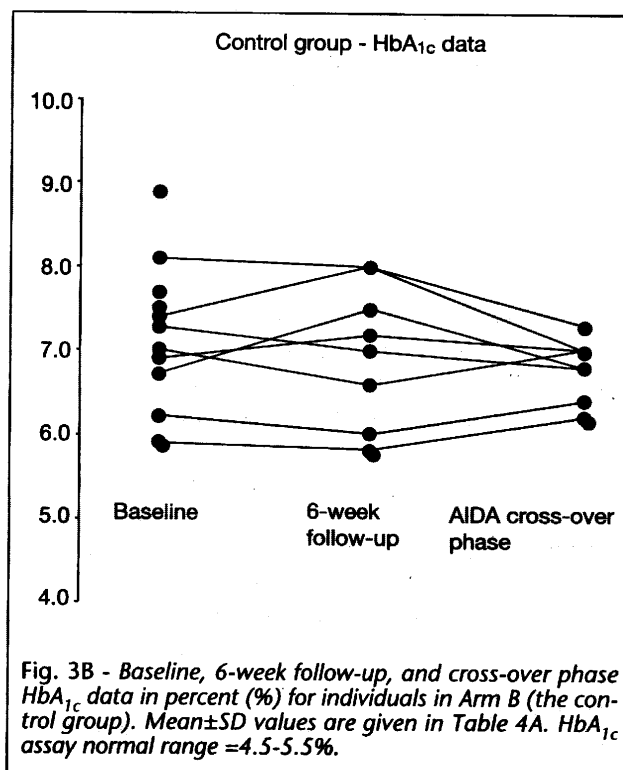
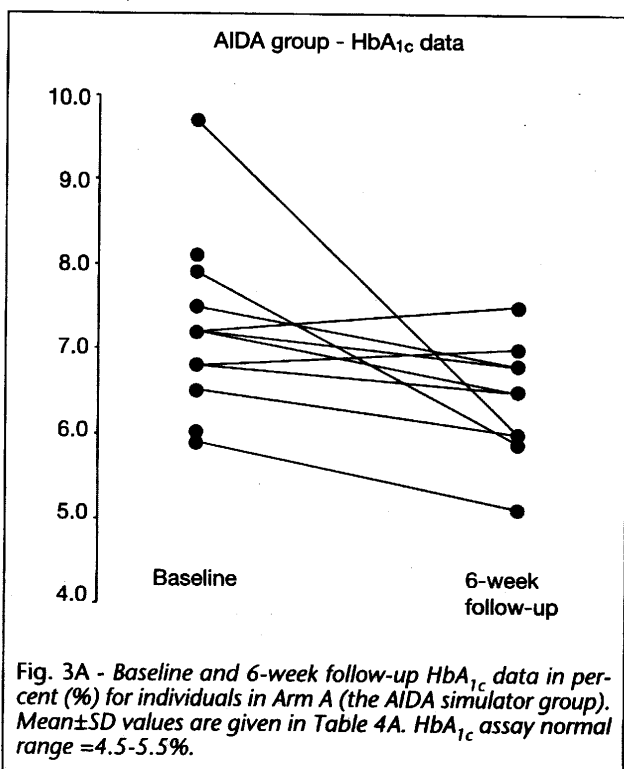
Although in the original protocol (25) it was envisaged that at least 2 teachers would be required to teach the diabetes lessons – for this initial proof-of-concept, pilot study it was decided to use only a single teacher (P.T.) in order to avoid any unnecessary influence of the teaching style, knowledge, experience or enthusiasm on the outcome.

The 24 subjects were split into 4 classes (classes 1-4), each containing 6 subjects. All lessons were given on different days, but at approximately the same time of day, and with the same material (audio-visuals, slides, transparencies – and case scenarios for the simulator). The topics for the 6 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 were: a) how to match insulin and food intake, b) overnight regulation of blood glucose levels, c) role of exercise and the renal threshold of glucose, d) avoidance and treatment of hypoglycaemia, e) shift work or travel abroad, and f) how to manage blood glucose in unforeseen circumstances.

A cross-over design was applied, as described previously (25), to increase the number of subjects exposed to the simulator, and thus increase the overall power of the study.

Simulator lessons

Photographs of typical Group A (AIDA) simulator lessons can be found elsewhere in the literature (37, 38), each simulator lesson making 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.



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.

Questionnaires

At the beginning and end of each phase of 6 lessons, subjects were requested to complete some standard questionnaires (19, 39) – freely available from <http://www.2aida.org/appendix> on the Web – to assess their degree of competence and their quality of

life. The main questionnaire (39) covered the following 7 areas: baseline demographic data, plus topics about self confidence, quality of life and metabolic control, social and emotional impact of diabetes on lifestyle, attitudes towards SMBG, prior knowledge about diabetes, and ‘what-if’ type questions and knowledge about insulin dosage calculation. Following lessons with the AIDA simulator, subjects were also asked for their opinions and feedback regarding the software (19). The results of analyses of the questionnaire data will be reported separately.

STATISTICAL ANALYSES

Given the relatively small number of patients studied in this preliminary trial, we could not be certain

Table 4A - HbA_{1c} levels – mean ±SD values given. The table shows the HbA_{1c} levels in both groups before and after the first cycle of lessons.

Group	Before the lessons	After the lessons	Wilcoxon signed rank test
A – AIDA	7.2±1.0%	6.4±0.7%	p=0.014
B – Control	7.1±0.9%	7.0±0.8%	p=0.889 (NS)

Table 4B - Hypoglycaemic events. The table shows the mean±SD and total number of hypoglycaemic episodes per week in both groups before and after the first cycle of lessons.

Group	Before the lessons	After the lessons	Wilcoxon signed rank test
A - AIDA	2.5±1.7 'hypos' (total episodes = 31)	1.4±1.2 'hypos' (total episodes = 14)	$p=0.03$
B - Control	1.7±1.6 'hypos' (total episodes = 20)	2.7±1.7 'hypos' (total episodes = 22)	$p=0.08$ (not significant rise)

that the entire data-set would conform with the assumptions required for the use of traditional (parametric) statistical methods. Therefore, for this initial study paired comparisons were made within groups with non-parametric statistics using the Wilcoxon signed ranked test. All statistical analyses were done with the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA). The level of statistical significance was set at $p<0.05$.

RESULTS

HbA_{1c} levels

The HbA_{1c} data are given in Table 4A and the results shown graphically for individual subjects in Figure 3. HbA_{1c} levels in Group A dropped significantly from 7.2% to 6.4% after lessons with the diabetes 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 cross-over phase lessons (6.8%).

Hypoglycaemic episodes ('hypos')

Data regarding the number of symptomatic hypoglycaemic episodes ('hypos') are summarised in Table 4B and shown graphically for individual subjects in Figure 4. In this study only mild (sweating, dizziness) or moderate (nausea, vomiting) hypoglycaemic episodes occurred. No 'hypo' was so severe as to require external assistance.

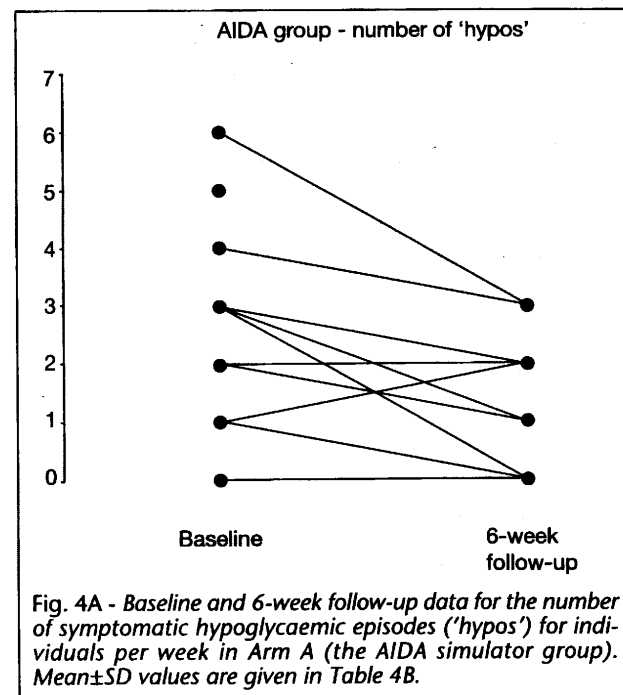
The number of hypos decreased significantly from 31 to 14 in Group A ($p=0.03$) after AIDA lessons, but did not change significantly in Group B from baseline ($n=20$) to after the control lessons ($n=22$). However, the number of hypos did decrease significantly (to $n=10$) in Group B after exposure to the simulator during the cross-over 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).

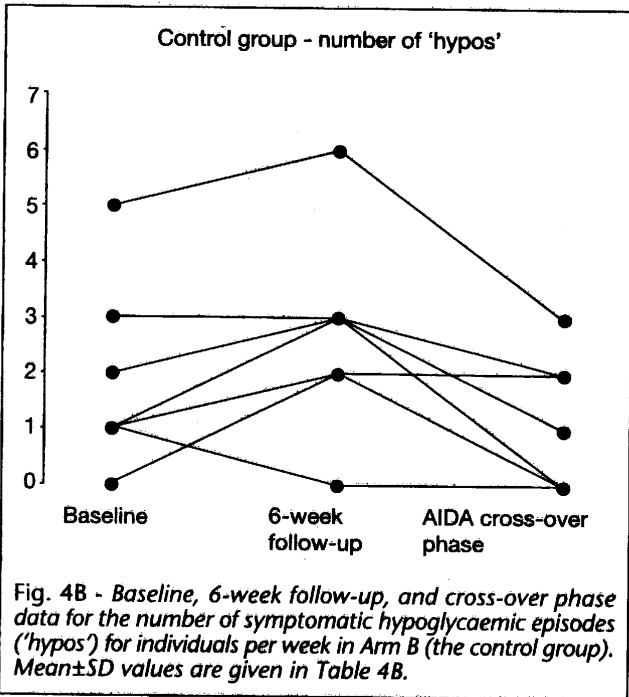
SMBG data

The SMBG data from this study are presented in Table 4C. The mean blood glucose level did not change significantly from baseline to the end of the first cycle of 6 lessons in either the simulator (A) or control (B) groups. However the mean blood glucose level did drop significantly in Group B from the end of the first cycle of standard lessons to the end of the cross-over phase with AIDA lessons, from 171 ± 47 to 156 ± 46 mg/dl (9.5 ± 2.6 to 8.7 ± 2.6 mmol/l) ($p=0.007$).

Length of lessons and 'dropouts'

Table 5 summarises the length of time spent, and the number of simulations run, per lesson in the two phases of the study. Lessons with the diabetes simulator lasted on average 104 min (range 70-140 min),





(Table 5A) as compared with the standard (control) lessons which only lasted on average 63 min (range 60-70 min), (Table 5B). Each lesson with AIDA involved on average 24 diabetes simulations, although there was a wide range (10-38 simulations per lesson). In particular, in the cross-over phase group the lessons tended to last longer, with more simulations being run (Table 5C).

There were two 'dropouts' from the study in Group A and five 'dropouts' in Group B. Therefore, overall 7 out of 24 subjects (29%) dropped out of the study.

Sample size estimations (power calculations)

With power calculations it is necessary to know the effect size that one might observe before one can apply such calculations. However, with this work – pri-

or to running this pilot study – it was difficult to be certain what the effect size would really be. However, now that the proof-of-concept study 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 pilot study. Based on a standard statistical approach (40) 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% dropout rate, in the 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.

DISCUSSION

Patient education in any chronic disease, and in T1DM in particular, has been considered one of the mainstays of long-term management. However, this tenet has not been conclusively proven. This is particularly important to clarify at times of cost containment, during which the allocation of resources must be made on a sound basis. The need to demonstrate efficacy is even more important with the introduction of new technologies. Unfortunately, at present relatively few diabetes software programs are being rigorously validated or clinically evaluated (41). We are trying to address this issue with the AIDA diabetes simulator.

While a large number of downloads of the AIDA software have been logged at the AIDA Website, up to now, apart from user testimonials about the program (22, 29, 30) – and *ad hoc* comments received by the system developers via e-mail (34-36) – there has been no formal assessment of the simulator.

The data presented in this paper are a first step towards trying to properly evaluate the program. They demonstrate a beneficial effect of the diabetes sim-

Table 4C - Self-monitoring blood glucose (SMBG) data. Mean values±SD, in mg/dl, before the lessons and after the first cycle of lessons.

Group	Before the lessons	After the lessons	Wilcoxon signed rank test
A – AIDA	169±51	167±35	p=0.47 (NS)
B – Control	174±53	171±47	p=0.55 (NS)

(18 mg/dl = 1 mmol/l)

Table 5A - Arm A (AIDA diabetes simulation group) first cycle of lessons. Time spent and the total number of simulations run per lesson in the two classes, between which the 12 subjects were divided.

Lesson	Class 1 Subjects A1-A6 Time (min)	Simulations run	Lesson	Class 2 Subjects A7-A12 Time (min)	Simulations run
1	80	16	1	90	10
2	80	22	2	90	21
3	100	25	3	100	19
4	100	24	4	70	24
5	120	26	5	120	25
6	120	21	6	140	28
Mean	100	22	Mean	102	21

ulation 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). Hypoglycaemic episodes are of great concern because they are frequent in T1DM and can be mishandled (42). Furthermore their occurrence serves to limit the intensiveness of intensive insulin therapy that can be adopted (43). As is evident from Table 4B, 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 4A). The number of 'hypos' even worsened in the control group after the first 6 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.

Ideally for use by patients with T1DM 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 services which are usually offered through a diabetes clinic/education facility. In this respect we have described a detailed evaluation protocol (25) 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.

However, as in any research trial there are a number of potential confounding factors which need to be considered in any interpretation of data from such a study.

Confounding factors

Baseline differences

In spite of the randomisation that was applied for this pilot study, differences were observed in the number of 'hypos' between Groups A and B at baseline – with there being on average 2.5 'hypos' per patient in Group A before the lessons with only 1.7 'hypos' per patient in Group B (Table 4B). These differences, although unfortunate, do not alter the findings of this study.

Firstly, no such baseline differences existed in HbA_{1c} levels – for which significant benefits from the simulation lessons were also observed. Secondly, the analyses of the data on hypoglycaemia have used paired statistical tests (generally comparing baseline data with follow-up data). In this way unpaired comparisons between groups have been avoided. Nevertheless, in future larger-scale studies it is intended to apply a more rigorous external randomisation service (*vide infra*) to try and

Table 5B - Arm B (control/standard group) first cycle of lessons (conventional lessons). Time spent per lesson in the 2 classes, between which the 12 subjects were divided.

Class 3 Subjects B1-B6		Class 4 Subjects B7-B12	
Lesson	Time (min)	Lesson	Time (min)
1	60	1	60
2	70	2	60
3	60	3	60
4	70	4	70
5	60	5	60
6	60	6	70
Mean	63	Mean	63

better control for baseline differences between the groups.

'Dropouts'/losses to follow-up

The number of 'dropouts' differed substantially between the two groups – being more than double in the conventional group compared with the simulator group. This may well represent a sign of reduced interest in the conventional/standard education sessions. In future studies it may be helpful to ask patients who 'drop out' why they did not continue with the trial. However, it is recognised that such patients are often lost to follow-up and can be the hardest subjects to contact. It is noteworthy that most of the dropouts in the control group were during the first cycle of lessons and not during the cross-over lessons with the simulator. This may indicate a greater involvement or simply the fact that those who 'survived' the first cycle of lessons were more motivated.

Length of lessons

Another possibly related observation is the fact that the simulation lessons generally lasted twice as long as the conventional lessons (Table 5). Once again this seems to reflect that patients were more interested and motivated in the simulator arm. The teacher (P.T.) was not surprised by this observation since the participants in the simulator group appeared more involved from the start. Furthermore, during the simulator lessons subjects could have a much more active role than is possible during conventional/standard

lessons. However, the length of time spent on simulation lessons was unexpected (*a priori* both study arms were anticipated to have lessons of equal length (25)). In fact all the simulator lessons had to be cut short by the teacher. Connected with this, it is interesting that the subjects wanted to continue even longer with the diabetes simulations than the (extended) time they had. Further studies will be required to establish if differences in HbA_{1c} levels and numbers of 'hypos' between the two groups might be accounted for by the different length of lessons. One way to assess this in a future study might be by extending the control group lessons – so they lasted as long as participants in Group A wanted for the AIDA lessons (*eg* say 100-110 min).

'Hawthorne'/placebo effect

There is a well-recognised phenomenon in science that the effect of investigating or measuring something can lead to a change – especially if the scientific process affects the variable being measured. In diabetes clinical trials this can manifest itself as the 'Hawthorne' or placebo effect with the process of enrolling patients into a study leading to improvements in their metabolic control (HbA_{1c}) separate from any effect of the intervention under investigation. For the current study we have sought to circumvent any such issues by introducing a control group. Furthermore, rather than just making use of a placebo group we have ensured that the control group receives as good an educational intervention

Table 5C - Cross-over phase - Arm B, second cycle of lessons (simulator). Time spent and the number of simulations run per lesson for Group B subjects (conventional group) when they were switched over to the simulator.

Classes 3 + 4 combined (minus 'dropouts')		
Lesson	Time (min)	Simulations run
1	120	18
2	90	32
3	100	34
4	140	26
5	120	29
6	100	38
Mean	112	30

(if not better) than what is currently offered as standard in routine diabetes care. However, as 'routine care' and the level of diabetes education offered vary greatly between different hospitals and clinics, especially in different countries, further studies will eventually be required to investigate the possible effects of such diabetes simulation lessons in these different educational/hospital/clinic settings.

'Ceiling effect'

Although not an absolute confounding factor – it is important to note that the patients in this study were quite well controlled at baseline with average HbA_{1c} levels of 7.2% and 7.1%, respectively, in the AIDA and control groups (Table 3). Such low values indicate quite tight glycaemic control which is in keeping with the management approach of the Marino diabetes clinic. While this can lead to a larger number of mild or moderate 'hypos' – for study purposes this also can create a 'ceiling effect' where improvements in glycaemic control generated by an intervention (in this case AIDA) might be relatively underestimated because of the tight metabolic control with which the patients entered the study. In this respect it is conceivable that larger effects on the HbA_{1c} level may be observed following lessons with such diabetes simulators in patients with poorer glycaemic control. It should however be mentioned that any such 'ceiling effect' on the HbA_{1c} level clearly will not apply to the number of symptomatic hypoglycaemic episodes, which provides an alternative useful indicator of improved metabolic control.

The role of the teacher/facilitator

It is recognised that as this evaluation methodology (25) is trialled in a larger number of centres and clinics, the enthusiasm of the teacher/facilitator ('wizard'), and their 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 Internet (24) – 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 practicable way to run such studies – maybe until it is possible to offer patients direct access to a self-learning diabetes tutorial to go with such simulations, possibly via the Internet.

There is a widely recognised phenomenon in medical-computing today of locally successful systems failing when deployed in new settings. We seem to have overcome this problem with the widespread distribution and usage of AIDA via the Internet (20). Nevertheless, there is also a well-recognised phenomenon more generally in medicine of novel applications sometimes seeming to work well locally in dedicated units, but maybe not working so well when tried perhaps by less motivated health-care professionals in less specialist centres.

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 are currently considering what methods might be applied to ensure that prospective teachers/facilitators are sufficiently experienced with the software – before using it with patients (38, 44). 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 (38, 44).

How best to apply diabetes simulations

Qualitative experience gained from running this study has highlighted various ways in which it is possible to optimise the use of the simulator for participants during lessons. Potentially these suggestions could help to improve the overall efficacy of AIDA as a teaching tool.

- a) One of the most important things seems to be to give each participant a role during the simulation lessons (*eg* monitoring a different simulation parameter on the computer screen).
- b) It seems useful to let the discussion during each lesson flow freely, but at the same time retain the focus on the chosen topic of the lesson.

- c) Applying the diabetes simulator as an interactive 'blackboard'—and thereby as a vehicle for discussion—seems to be one of the more profitable ways of making use of the simulations during lessons.
- d) Although not formally investigated in the current study – selection of patients who may benefit most from such computer-assisted teaching sessions may also be important. For instance, young, intellectually alert subjects appear to get the most out of such simulator-based lessons.

Implications for future studies

We regard our previously described protocol (25) as a useful starting point for future studies. However it is recognised that some flexibility in the approach may also be required to cater for local variations in practice between study centres. In this respect we envisage that a number of procedures might be improved in a future larger-scale study:

- a) Multiple teachers will clearly be needed to teach a larger number of patients. As outlined above, these teachers will need to undergo a period of training/interaction with the software. For an evaluation study such training will also need to ensure that the teachers impart similar information with the same emphasis in both the simulator and control groups. Teachers might also switch between the AIDA and control groups to reduce the chance of introducing any teacher 'bias' into the lessons. Figure 5 shows one way in which this might be done.

- b) Historical HbA_{1c} data, based on the average values for the preceding 12 months will be used in place of educational status for the randomisation. As highlighted (25), previous educational status does not seem to work well since the school degree obtained does not accurately represent skill or intelligence. Using this approach, in this preliminary study, the cutoff between low and high HbA_{1c} for stratified randomisation would have been set at 7.2%, the median baseline HbA_{1c} level for the cohort (Table 3).
- c) An external randomisation service has been set up at <http://www.2aida.org/random> via the AIDA Website. Data entered via this route can be automatically submitted across the Internet, via e-mail, to a co-investigator (E.D.L.) in London. Using dedicated software written specifically for this purpose, it will be possible for this co-author to independently randomise participants, randomisation codes being returned to the referring nurse/physician by e-mail. In this way the execution of the study protocol will be fully separated from the randomisation procedure.
- d) Although not done in the current study – in future RCTs it would be interesting to monitor HbA_{1c} levels a longer time after the completion of the study (eg 3 or 6 months later). The rationale for doing this is that it may be one thing to show a short-term improvement in the HbA_{1c} level – but another to actually show a longer-term benefit or improvement in metabolic control.

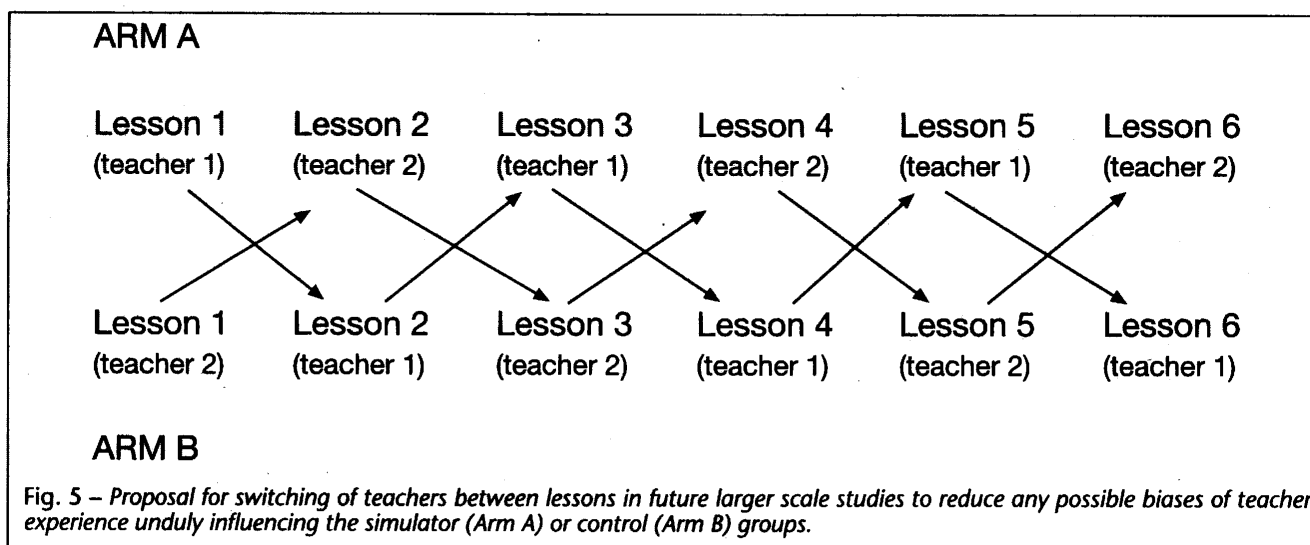


Fig. 5 – Proposal for switching of teachers between lessons in future larger scale studies to reduce any possible biases of teacher experience unduly influencing the simulator (Arm A) or control (Arm B) groups.

Longer follow up could reveal if possible benefits from lessons with a diabetes simulator can be maintained in the long-term.

- e) Related to this, all patients who completed the current study chose to continue using AIDA on their own at home/work – following the end of the study. Perhaps this can be encouraged, and combined with the longer-term HbA_{1c} monitoring proposed above, to see if 6 weeks of lessons using AIDA – with continued patient access to the program on a self-directed basis – can actually help achieve and maintain longer-term improvements in glycaemic control. In this respect, patients would not necessarily need to have a computer at home/work – but rather could access a Web-based version of AIDA (called ‘AIDA on-line’) which is available completely free-of-charge at: <http://www.2aida.org/online> on the Internet (45, 46). This version of the AIDA diabetes simulator does not actually require a computer for usage (no downloads or local installation are needed) – but in fact can be run even via an Internet-enabled television set (eg via WebTV). In this way, potentially, patients with T1DM might be able to ‘top up’ their experience using the simulator in their spare time between hospital/clinic visits.

Easy access to AIDA at: <http://www.2aida.org> via the World Wide Web, and the novel simulations that it offers, makes AIDA an interesting tool for evaluation. Furthermore, the fact that the program is being made available free-of-charge should in the long-term also support its use in less developed countries, although clearly Internet access will ideally be required for the widespread dissemination of the program. Nevertheless, it is possible that in the future AIDA may turn out to be a cost effective tool for diabetes education. However, this remains to be objectively demonstrated in cost-benefit studies, and we wish to stress that the educational efficacy of the diabetes simulation approach also still remains to be proven in larger-scale, multi-centre RCTs.

CONCLUSIONS

This current preliminary/pilot trial has been run as a proof-of-concept study to confirm a) the utility of small-group educational sessions as a way of teaching using AIDA, and b) the validity of the basic evaluation approach that has been proposed (25). In this respect we believe that the study can be considered a success.

The evaluation protocol previously described in detail in this journal (25) 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 above. 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.

In addition, the actual results obtained with the diabetes simulator have been very encouraging. This pilot study suggests that the AIDA software, if properly applied, may potentially be of use for patients with T1DM 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 very promising. However, larger-scale studies involving more patients and more teachers (in more clinics/centres) are obviously required before any firm conclusion 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 <http://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 on-line’) is also available for use at: <http://www.2aida.org/online> on the Web. People who wish to be automatically informed about future updates and enhancements to the AIDA/‘AIDA on-line’ diabetes software range can subscribe (for free) to the 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 trial protocol (25) themselves in an evaluation of AIDA in their

own unit(s) for clinician/specialist 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 <http://www.2aida.org/evaluate> on the Web.

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