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An on-line support tool to reduce exercise-related hypoglycaemia and improve confidence to exercise in type 1 diabetes

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ABSTRACT

Objective: Hypoglycaemia related to exercise and lack of confidence to exercise, are common in T1DM. An online educational exercise tool (ExT1D) was tested to determine whether these parameters can be improved.
Research design and methods: Thirty two adults with T1DM (50%M, age 35.8 ± 9.5 yr diabetes duration 12.3 ± 9.9 yr, median HbA1c 7.1%[ICR 6.4–7.7] NGSPU) exercising ≥ 60 min/week enrolled in a RCT utilising ExT1D, with partial cross-over design. The primary end-point was Exercise-related hypoglycaemia (ErH) number corrected for exercise session number, with ErH defined as CGM episodes < 4.0 mM occurring within 24 h of exercise. Secondary RCT endpoints were total ErH duration, and ErH duration/episode. A pre-defined longitudinal analysis with each subject compared with their baseline was also undertaken, for the three ErH parameters, and using fear of hypoglycaemia questionnaires.
Research: In the RCT a 50% lower median ErH number (P = 0.6) (37% lower ErH number per exercise session (P = 0.06, NS primary endpoint) occurred in the Intervention vs Control group. A 49% lower ErH duration per episode (P = 0.2), and 80% less ErH duration (P = 0.3), were also observed in the Intervention vs Control group. In the longitudinal study, ErH number reduced by 43% (P = 0.088), ErH duration per episode by 52% (P = 0.157) and total duration of ErH fell by 71% (P = 0.015). Confidence to prevent glucose lowering by exercise also improved (P = 0.039). Post-hoc analysis showed those with the greatest ErH events at baseline benefited most. Fructosamine and HbA1c levels were unchanged from baseline.
Conclusions: ExT1D can reduce exercise-related hypoglycaemia and provide greater confidence to exercise.

1. Introduction

As in people who do not have diabetes, exercise is recommended for people with diabetes, as it may help reduce cardiovascular risk, and improve physical fitness and sense of wellbeing.[1] However for many people with type 1 diabetes, preventing exercise-related hypoglycaemia and maintaining safe blood glucose levels during and following physical activity can be problematic.[2,3] Available guidelines have provided a limited evidence base for recommendations in managing glycaemia around the time of exercise.[4,5]

To prevent hypoglycaemia related to exercise various laboratory and field studies have focused on adequate carbohydrate supplementation,[6–10] reduction in insulin at meal bolus dosing[11,12] or the longer acting[13] or basal insulin,[14] and by combining aerobic exercise of moderate intensity with short bursts of high intensity exercise such as brief sprints,[15–20] or resistance training.[21,22] These findings in combination have not been found to be widely adapted for the benefit of people with type 1 diabetes who either wish to start or continue with exercise.[23–25] Currently, notwithstanding some recent educational programs,[26] there are limited evidence-based tools that focus on preventing exercise-related hypoglycaemia and that are also readily accessible by people with type 1 diabetes. This is important as even mild hypoglycaemia has been associated with fear of hypoglycaemia,[27] which is a recognised barrier to physical activity[28] and inactive lifestyle is more prevalent in people living with type 1 diabetes than in the general population.[29] Furthermore, the importance of prevention of delayed, including nocturnal, hypoglycaemia following exercise has been recognised.[9,30,31]

Considering the need to support evidence-based, practical interventions in exercise and type 1 diabetes, we undertook a randomised

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controlled trial in adults with type 1 diabetes to determine if an established on-line support tool, ExT1D, is able to help to reduce exercise-related hypoglycemia and improve confidence to exercise.

1.1. Research design and methods

The T1Ex study was conducted at the Diabetes Centre, at Royal Prince Alfred Hospital, Sydney, following approval by the RPAH Zone Ethics Committee and the University of Sydney Human Research Ethics Committee. The clinical trial was registered with the ANZ Clinical Trials registry number ACTRN12617001651370. Participants were adults with type 1 diabetes voluntarily recruited from the Diabetes Centre as well as local endocrinologist private practices. Eligible participants were above 16 years of age with type 1 diabetes duration of at least 12 months, who undertook regular structured exercise of at least 60 min per week prior to enrolment, were utilising insulin to carbohydrate ratios, and receiving continuous subcutaneous insulin infusion or intensive basal-bolus insulin therapy, and were willing to undertake regular multiple times (at least 4 or more) daily fingerpick blood glucose level monitoring. Exclusion Criteria were HbA1c level > 9.0% (NGSP units), receiving premixed insulin therapy regimen, having experienced one or more episodes of severe hypoglycaemia within the previous 6 months, unstable cardiovascular disease, untreated vision-threatening diabetic retinopathy, active foot ulcer, or current pregnancy. Previous access and utilisation of the online ExT1D tool was also an exclusion criterion.

The study design was a prospective randomised controlled trial with crossover of the Control group into the Intervention arm (Fig. 1). At the Baseline visit, participants were informed of the aims of the study as well as potential risks and provided written informed consent. Participant demographics and medical history were obtained and a comprehensive physical examination was undertaken, including to assess for microvascular and macrovascular complications of diabetes: diabetic retinopathy, chronic kidney disease, and peripheral neuropathy, as well as macrovascular disease. Similar to other studies in type 1 diabetes, continuous glucose monitoring (CGM) was used to determine the presence of hypoglycaemia and hypoglycaemia duration.[32–35] Following a baseline CGM Study Period (CGM1) participants underwent computer randomisation and were assigned to either the Control or the Intervention arm. During the following 5-week period participants in the Intervention arm accessed the website and the Control arm continued with usual care. Subsequently, all participants underwent a second CGM Study Period (CGM2). This was followed by the second 5-week period during which the Intervention arm continued with the website review and the Control arm gained access to the website, in the partial crossover design. The second five-week period concluded the trial with CGM Study Period (CGM3). CGM3 enabled the ability of ExT1D to affect outcomes in the original Control Group, as well as for the sustainability of the Intervention, to be tested in the Intervention group (Fig. 1).

In addition to the cross over study, all participants were included in a longitudinal study which compared their own baseline with final outcomes following access to ExT1D.

The CONSORT diagram of study subject flow is shown in Table 1. A total of 90 study subjects (~3 times those who were randomised) were invited to participate. Most did not participate as either they declined to partake due to study protocol demands (the majority), or their exercise regimen was not at least 60 min weekly. The two subjects who did not complete the study run-in chose not to continue in the study due to the study protocol intensity and their own lack of time to commit to the study. Following completion of the study run-in, n = 32 were (non-block) randomised into the study, as n = 15 in the Control group and n = 17 into the Intervention group.

Study procedures: Each CGM Study Period (CGM) lasted approximately 6 days, during which participants wore CGM devices under free living conditions, monitored capillary blood glucose levels, undertook usual exercise recorded with a HR monitor, and documented food and insulin in the provided contemporaneous diary. The continuous glucose monitoring system iPro2 (Medtronic Minimed, Northridge, CA) was used to evaluate glucose level fluctuation including hypoglycemia. The Enlite sensor was inserted into the subcutaneous tissue of the lateral abdominal region or in the upper gluteal area, depending on the participant's personal preference. Participants were blinded to their CGMS glucose readings. For calibration purposes participants were instructed to monitor glucose levels in steady state pre-meals and prebed with readings within at least 12 h of each other. They were also encouraged to self-monitor capillary glucose levels as per their usual care. To standardise glucose measurements each participant was provided with a memory glucose meter (OneTouch Verio, Johnson & Johnson) and test strips for capillary glucose measurements.

To objectively document each exercise session duration and intensity, participants were encouraged to use a wrist watch and chest strap for heart rate telemetry (Suunto, Vantaa, Finland). Participants were instructed in its use and were asked to commence recording their exercise session at the beginning of a warm up and to then cease recording at the end of cooling down period. The data were downloaded into the online software (Suunto, Vantaa, Finland). Each participant's resting heart rate and estimated maximum HR,[40] were obtained to estimate individual maximum heart rate.

For the follow-up visit, on the seventh day participants returned to the Diabetes Centre for CGM sensor removal. Data were downloaded and processed using CareLink iPro™ Therapy Management Software for Diabetes. Each individual's fitness level was assessed via a graded treadmill test to volitional fatigue (Bruce protocol). During the test information regarding baseline, incremental and maximal heart rate, METS and estimated VO_2max (from time-based normative data) were obtained. Capillary glucose levels were obtained prior to and up to 15 min post exercise test completion.

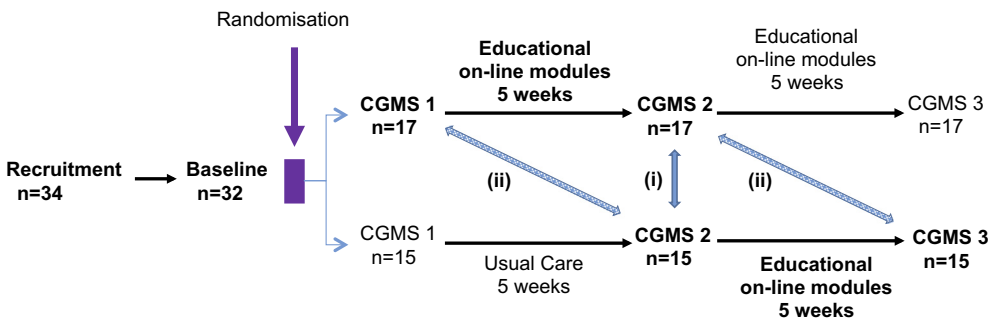
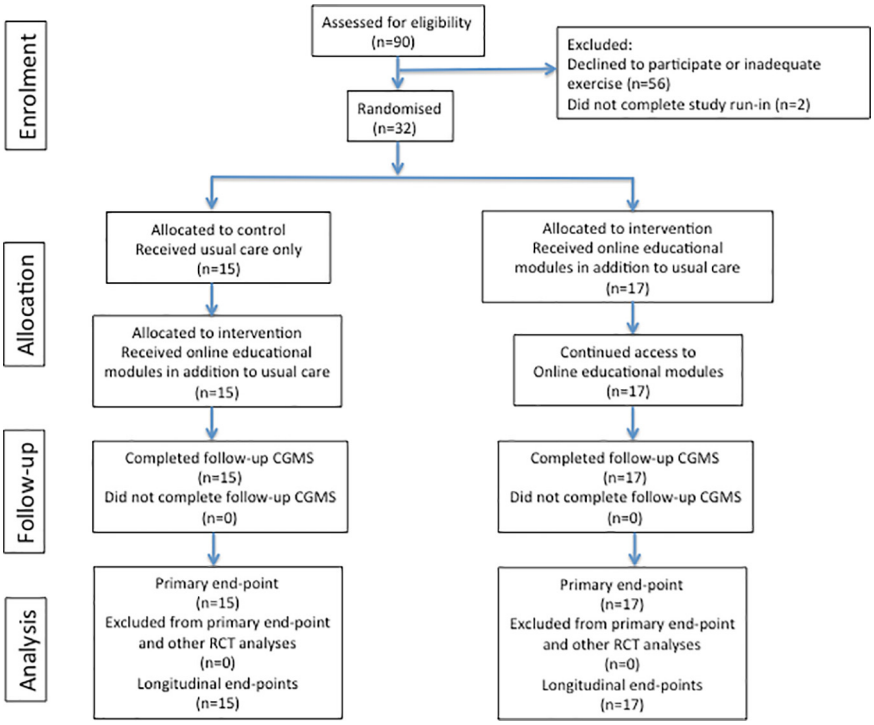


Fig. 1. The randomised partial crossover study design utilised: (i) the RCT comparing Exercise-related Hypoglycemia Number between the Intervention and the Control group at CGM 2 as a Primary Endpoint; Duration (min) per episode and Total Duration(min) of Exercise-related Hypoglycemia between the Intervention and the Control group at CGM 2 as Secondary Endpoints; (ii) the Longitudinal Study comparing Exercise-related Hypoglycemia Number, Duration per episode(min) and Total Duration(min) from baseline and following Intervention for each participant in the Intervention Group (CGM 1 and CGM 2) and the Control group (CGM2 and CGM 3) as pre-defined Secondary Endpoints.

Table 1
CONSORT diagram of study subject flow.



Participants completed 4 questionnaires: the modified Stanford survey to document the amount and type of their physical activity, Clarkes questionnaire to document the degree of impaired awareness of hypoglycaemia, and two fear of hypoglycaemia scales: HFS-II (Hypoglycaemia Fear Questionnaire-II) and FH-15 depicting the degree of fear of hypoglycaemia.

Blood sampling involved laboratory electrolytes and renal function, liver enzymes and function, lipid profile, full blood count, HbA1c, C-peptide, TSH and 25OH vitamin D levels, as well as BHCG in female subjects to exclude pregnancy.

For the study intervention, participants accessed the online educational tool (www.ext1d.com.au), which is a pre-existing commercial website developed for people with type 1 diabetes. Participants were asked to review the learning modules on glucose management in type 1 diabetes in relation to exercise. Included topics were: dose reduction and timing of meal bolus and/or temporary basal insulin for a given exercise, additional carbohydrate type and amount in relation to exercise, and glucose monitoring. It was pre-determined that it would require ~3 to 5 h to review the 6 modules. In brief, Module 1 contains an overview of the topics to be reviewed, and the baseline knowledge quiz consisting of 40 questions. Modules 2–6 contain educational content and short knowledge quizzes. Module 2 covers basic exercise physiology in type 1 diabetes and especially focuses on increase in insulin sensitivity, increased risk of exercise-related hypoglycaemia and glycogen storage and utilisation. Module 3 discusses insulin management with a focus on timing of insulin bolus in relation to onset of exercise as well as reduction of both short acting, including temporary basal rate in continuous insulin infusion, and long acting insulin dose for exercise. Module 4 reviews the type and amount of carbohydrate supplementation as a method of prevention of exercise-induced hypoglycaemia during exercise as well as following late onset hypoglycaemia including nocturnal episodes. Module 5 summarises the key points in previous modules and provides examples in how to plan for a given exercise by appropriate timing exercise during the day, reducing meal insulin bolus and/or long acting insulin and supplementing with carbohydrates. Module 6 discusses basic hypoglycaemia information including lack of hypoglycaemia awareness as well as management. Participants were asked to choose recommendations related to exercise and stabilising glucose that best suited them and to incorporate those recommendations into their exercise routine. Participants were encouraged to utilise the online tool 'dashboard' which suggests possible individualised insulin dose tailoring, typically an exercise-related reduction, as well as carbohydrate supplementation amount for a given exercise regimen.

For statistical analysis, hypoglycaemia and hyperglycaemia were based on CGMS and defined as glucose levels below 4.0 mmol/L and above 10 mmol/L, respectively. Any reading below 4.0 mmol/L by CGM was classified as a hypoglycaemia episode, with events completing when the glucose level had risen to at least 4.0 mmol/L. The time period as well as hypoglycaemia and hyperglycaemia occurring within 24 h of onset of exercise were defined as being exercise-related, as per Moser et al.[19] Nocturnal hypoglycaemia was defined as hypoglycaemia occurring between midnight and 6 am, as per the USFDA definition.[36]

The primary study endpoint was a proportionate reduction in exercise-related hypoglycaemia number corrected for the number of exercise sessions in the Intervention vs Control subjects in the RCT (Fig. 1). We pre-determined 87% power to detect a 50% reduction in the number of ex-related hypoglycaemic events proportionally corrected for exercise number using non-parametric statistics.

Predefined secondary endpoints were: total hypoglycaemia number in the Intervention vs Control subjects in the RCT; exercise-related and total hypoglycaemia duration in the Intervention vs Control subjects in the RCT; exercise-related hypoglycaemia number and exercise-related hypoglycaemia duration from baseline following intervention of the entire cohort in the longitudinal study; confidence to exercise by self-report in the Intervention vs Control subjects in the RCT and also from baseline following intervention of the entire cohort in the longitudinal study.

Tertiary exploratory endpoints included retrospective CGMS glucose variability markers, including low blood glucose (LBGI) and high blood glucose (HBGI) indices,[4,37,38] plus other defined parameters of MAGE and CONGA.[2,34]

Statistical analysis was performed using IBM SPSS Statistics 22 and NCSS 9 software packages. A modified intention to treat analysis was undertaken, where each study participant included was randomised and undertook at least one exercise session in the study. As the hypoglycemia data in number of episodes and duration were each non-normally distributed data, the results are presented as median (Interquartile range). Unpaired Mann-Whitney-Wilcoxon test was used to compare exercise-related data including hypoglycaemia and questionnaire data between the Intervention and Control arms in the RCT Study; a paired Mann-Whitney-Wilcoxon test was used to compare exercise-related data including hypoglycaemia and questionnaire data from baseline following Intervention in each participant in the Longitudinal Study. A two tail test with $P < 0.05$ was considered statistically significant.

2. Results

Data from the 32 participants that were randomised (CONSORT diagram, Table 1) were included in further analysis. There was no difference in baseline characteristics between the Intervention group (n = 17) or Control group (n = 15) (Table 2). Participants were 35.8 ± 9.5 years of age, had long-standing diabetes of 12.3 ± 9.9 years, and were on average not overweight with BMI 24.2 ± 2.6 kg/m^2. Participants were classified as having good cardiorespiratory fitness with exercise capacity at 11.0 ± 1.9 METS or 38.5 ± 3.5 mL/kg/min at baseline, and overall good glycaemic control with a median HbA1c level of 7.1 [6.4–7.7]% NGSP Units (54 mmol/mol IFCC units). More than half of the subjects (63%), were on CSII therapy. The remaining participants were using an intensive regimen with multiple daily injections. Groups were not different in study subject baseline exercise number or in exercise-related hypoglycemia number (Table 2).

For the primary outcome, the median number of exercise-related hypoglycemia events was 4 in the Control group and 2 in the Intervention group (P = 0.6, NS) (Fig. 1) (Table 3a), and the proportionate change in number of exercise-related hypoglycaemia events per episode of exercise was 37% less in the Intervention group compared with the Control group (primary end-point P = 0.06, NS). In the RCT secondary outcomes, compared with the Control group, in the Intervention group there was 49% (P = 0.2, NS) less hypoglycemia duration per episode of hypoglycaemia, and 80% less total hypoglycaemia duration in the Intervention group compared with the Control group (P = 0.3, NS) (Table 3a).

Pre-defined longitudinal analysis of all subjects compared with their own baseline following intervention, showed a non-significant reduction in the exercise-related number of hypoglycaemic events of 43% (P = 0.088, NS) (Table 3b). Duration of hypoglycaemia per episode was non-significantly reduced (52%; P = 0.16, NS) and total hypoglycaemia duration was significantly reduced (71%; P = 0.030) (Table 3b) following Intervention. Corresponding HbA1c and fructosamine levels remained similar from baseline and did not change following intervention (P = NS) (Table 3b).

When the exercise-related hypoglycaemia events of at least 20 min duration were examined using a sensitivity analysis (Supplementary Table 1), data were found to be similar to that for all exercise-related hypoglycaemia events (Tables 3a, 3b), generally showing a trend that favoured the exercise intervention, but with non-statistically significant outcomes. The exercise-related hypoglycaemia events of at least 20 min duration at n = 30, compared with n = 125 in the total ErH number. In these at least 20 min episodes of ErH events there was a 14% reduction in the primary proportionate ErH number corrected for exercise number (P = 0.7, NS). The duration of ErH per episode of exercise was statistically significant in the longitudinal study at P = 0.029 (40% reduction) (Supplementary Table 1).

Individual data demonstrated that most participants experienced a reduction in the exercise-related hypoglycaemia number and duration from baseline following intervention, but a small minority, n = 5, experienced an increase in hypoglycaemia number related to exercise (Fig. 2). Of note, nine subjects across the 32 experienced no baseline exercise-related hypoglycaemia (Supp. Fig. 1).

In the Intervention group CGM1, the reduced % of time spent in hypoglycaemia in the Study appeared to be maintained in the Study Period CGM3 (1.94% compared to 1.96% (period CGM2), (Supp. Table 2)).

Confidence to undertake exercise was unchanged for the total cohort. The total overall diabetes self-management Questionnaire score following Intervention was 7.9 ± 1.2 (mean ± SD) compared with baseline 8.0 ± 1.6 (P = NS). There was an increase (improvement) in the score for the item: 'How confident are you that you can do something to prevent blood glucose levels from dropping when you exercise?' (baseline: 7.4 ± 2.1 versus Intervention: 8.3 ± 1.3; P = 0.039) (Fig. 2).

For tertiary endpoints of glycaemic variability there was a mean 16% reduction in exercise-related LBGI score from baseline following intervention (P = NS). Combining LBGI with the clinically important parameter of hypoglycaemia duration showed a 43% reduction following intervention (P = 0.030). The other CGM parameters studied are also given in Supp. Table 2.

In *post-hoc* analysis, the 50% of participants with the highest number of exercise-related hypoglycaemia events at baseline, had greater reductions in the number of exercise-related hypoglycaemia events at Intervention, with median (IQR) baseline 7.5 (5–12) vs following intervention 4 (2–7), at P = 0.002. Similarly, those same 50% of participants with the highest baseline number of exercise-related hypoglycaemia, had a significant reduction in the number of exercise-related hypoglycaemia events lasting at least 20 min in duration at Intervention, median (IQR) baseline 6.0 (4.0–9.8) vs following Intervention 3.0 (1.0–6.0), P = 0.004. These participants also had a 30% reduction in total fear of hypoglycemia score (P = 0.041) and a 14% score reduction for the item referring to 'fear of hypoglycaemia that interferes with leisure activity' (P = 0.019).

In terms of study subject website access, the average ± SD time spent accessing the website per participant was 264.2 ± 170.3 min, SE

Table 2
Baseline clinical characteristics of study participants.

Characteristics	Total cohort n = 32	Intervention (I) group n = 17	Control (C) group n = 15
Gender M	50%	50%	50%
Age (years)	35.8 ± 9.5	36.8 ± 8.7	34.7 ± 10.5
Diabetes duration (years)	12.3 ± 9.9	14.6 ± 10.7	9.6 ± 8.1
BMI (kg/m^2)	24.2 ± 2.6	24.5 ± 2.6	24.1 ± 2.8
Insulin type (MDI%)	63	53	73
Cardiorespiratory Fitness (mL/kg/min)	38.5 ± 3.5	39.9 ± 4.6	37.5 ± 8.1
Exercise number	5.8 ± 3.6	5.5 ± 3.3	6.1 ± 4.0
	5 (3–7)	5 (3–6.5)	5 (3–8)
Exercise-related hypoglycaemia number per 6 days	4.1	3.9	4.2
HbA1c (mmol/mol) %	7.1 (6.4–7.7)	7.3 (6.3–7.7)	7.0 (6.5–7.8)
	54(46–61)	56(45–61)	53 (48–62)
Fructosamine (μM)	347 (297–438)	354 (299–424)	346 (296–442)

Data are mean ± SD, median (IQR), or frequency;

Table 3a
RCT study, exercise-related hypoglycaemia, primary and secondary endpoints.

RCT study	Primary endpoint	Secondary endpoints	
Study group	Number of episodes/6 days	Duration (min) per episode	Total duration (min) of hypoglycemia
Control n = 15	4.0	58.3	225.0
	(1.0–5.0)	(10.0–87.5)	(10.0–700.0)
Intervention n = 17	2.0	30.0	45.0
	(1.0–5.5)	(5.0–54.4)	(5.0–265.0)
	50% reduction	49% reduction	80% reduction
	p = 0.6	p = 0.2	p = 0.3

Data are presented as median (IQR), Mann Whitney U, 2 tailed, unpaired for control vs intervention.

30.1, range (0–618). Amongst the 32 participants 3 spent zero time accessing the website. Excluding those who spent no time accessing the website, the average time was 291.5 ± 154.5 min, SE 28.7 min, range (58–560 min). Amongst the 32 participants module 2 was reviewed by 24 participants, module 3 by 21, module 4 by 19 and module 6 by 16 participants. Knowledge scores assessed at the end of individual modules showed significant improvement in knowledge compared with the baseline quiz ($P < 0.01$).

The total number of reviewed modules had a negative correlation at study completion, with total score of fear of hypoglycaemia FH-15 $r = -0.52$, $P = 0.004$ as well as the item score for nocturnal fear of hypoglycaemia derived from FH-15 $r = -0.43$, $P = 0.020$, and a positive correlation with confidence in managing glycaemia around exercise $r = 0.40$, $P = 0.032$. The total time spent accessing the website per participant had a negative correlation with the item score for fear of nocturnal hypoglycaemia derived from FH-15 $r = -0.56$, $P = 0.001$ and a positive correlation with confidence in managing glycaemia around exercise $r = 0.41$, $P = 0.026$ following Intervention.

3. Discussion

The American Diabetes Association Workgroup on Hypoglycemia reached a consensus, where a satisfactory outcome following any 'drug, device or management strategy' in diabetes care, was a reduction in documented non-severe hypoglycaemia rate by 30%, that was also not associated with an increase in HbA1c.[39] In the current study we aimed to assess the efficacy of an online tool for improving exercise-related hypoglycaemia and exercise confidence. The total cohort exceeded the goal described by the ADAWH, by having a reduction in exercise-related hypoglycaemia number and duration of 43% and 71% from baseline, respectively, following a 5-week exposure to the Intervention. The improvement in hypoglycaemia was associated with unchanged markers from baseline in metabolic control (HbA1c and fructosamine levels), indicating no overall worsening of metabolic control.

The benefits in reduction in exercise-related hypoglycaemia were demonstrated despite 28% (9 out of 32 participants Supp. Fig. 1) having no exercise-related hypoglycaemia at baseline. However, possibly as this had reduced our baseline hypoglycaemia sample size, statistical significance was not reached in the RCT primary end-point. While a 50% reduction in the number of hypoglycaemia events was demonstrated between the Control and Intervention arm, it was not statistically significant, with a wide IQR. For exercise-related hypoglycaemia duration and hypoglycaemia duration per episode there was similar wide IQR, contributing to a non-significant result, despite 48% and 80% reduction in hypoglycaemia, respectively.

For the majority of participants following Intervention compared with their baseline, there was a significant improvement in hypoglycaemia number and duration. Those improvements in exercise related hypoglycaemia were associated with improved confidence in managing glycaemia around exercise. For the total cohort at baseline in these people with type 1 diabetes who undertake regular exercise, the mean total score of Self-Efficacy Stanford Questionnaire was already quite high at 7.9, and was unchanged following Intervention. In contrast, there was an improvement in the item score pertaining to confidence in preventing glucose from falling with exercise. This implies that while participants considered other aspects of their diabetes self-care at baseline as satisfactory, this was not the case in self-management of glycaemia around exercise.

As *post-hoc* exploratory outcomes, we also examined which participants may have benefitted most from accessing the online tool. We examined those 50% of participants with the highest number of hypoglycaemia at baseline. At baseline these participants were found to have experienced 4 or more exercise-related hypoglycaemia events (Supp. Fig. 1). These participants had significant reductions in exercise-related hypoglycaemia and also a reduction in fear of hypoglycaemia.

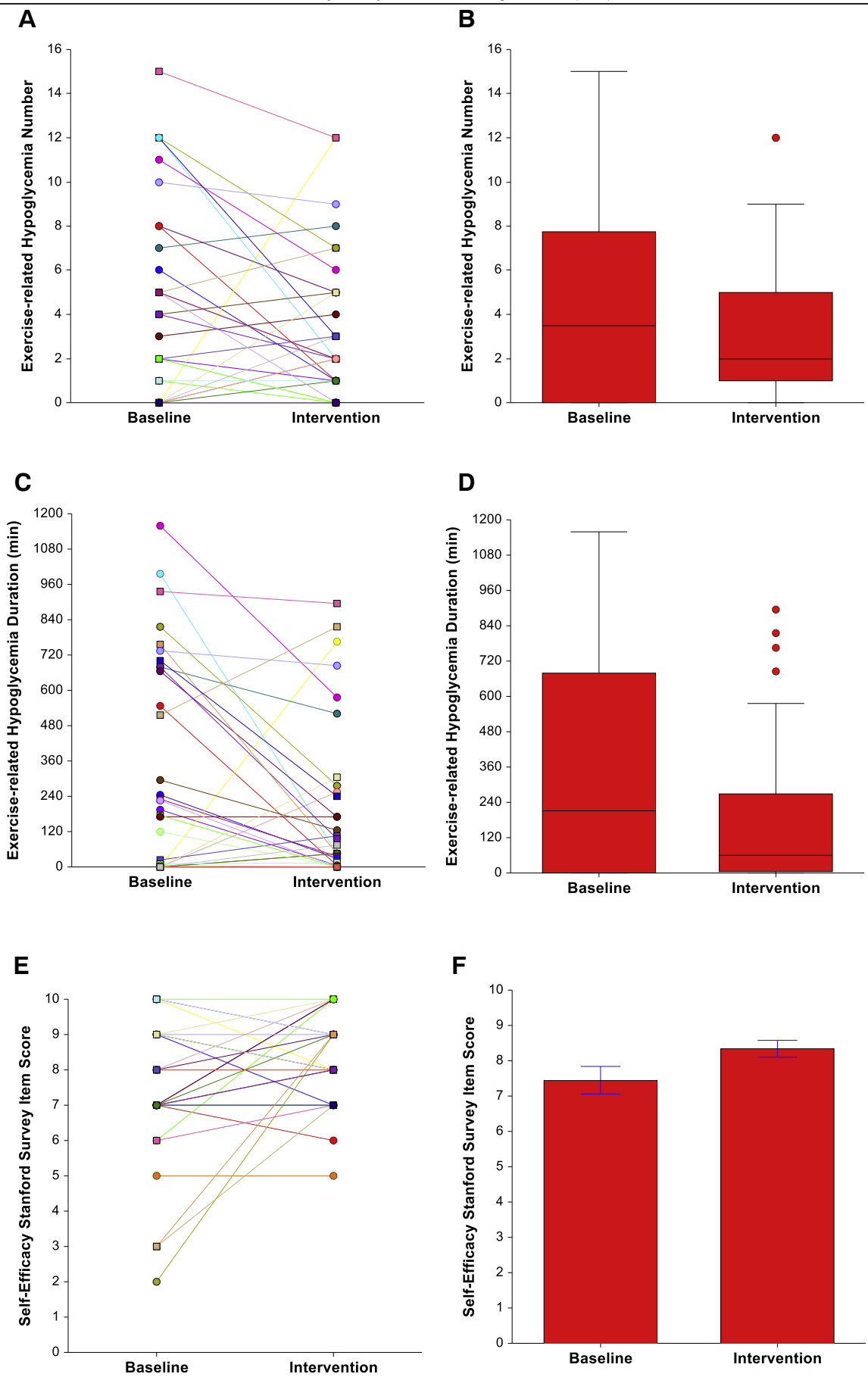
We have shown that a reduction in exercise-related hypoglycaemia is possible for people with type 1 diabetes who undertake exercise, utilising a behaviourally based system. The Intervention was an online based educational e-tool (www.ext1d.com.au). Participants accessed the website according to their randomisation. They were asked to review the content, consisting of 6 modules and a dashboard. The post module quiz scores showed significant improvement from baseline, implying an improvement in knowledge base. The strength of the study is that the benefits seen were achieved under normal living conditions, in a reasonably short period of time of 6 weeks, with the majority of patients continuing with their work and social lifestyle, and regular exercise. *Post-hoc*, people who were most likely to benefit were those who had experienced 4 or more exercise-related hypoglycaemic events at baseline, despite being under regular diabetes specialist team care.

Relative study weaknesses were that a minimum number of exercise-related hypoglycaemia events at baseline was not required for study entry. While that approach aids generalizability of the study,

Table 3b
Longitudinal study, exercise-related hypoglycaemia, secondary endpoints.

Longitudinal study	Secondary Endpoints			Glycaemic parameters	
Study group	No. of episodes/6 d	Duration (min) per episode	Total duration (min) of hypoglycaemia	HbA1c % mmol/mol	Fructosamine μM
Baseline n = 32	3.5	57.5	210.0	53 (46–61),	342
	(0.0–7.8)	(0.0–83.1)	(0.0–680.0)	7.0 (6.4–7.7)	(300–407)
Intervention n = 32	2.0	27.5	60.0	54 (49–62) 7.1% (6.6–7.8)	352
	(1.0–5.0)	(5.0–63.1)	(5.0–270.0)		(309–410)
	43% reduction	52% reduction	71% reduction	NS	NS
	P = 0.088	P = 0.157	P = 0.030		

Data are presented as median (IQR) Mann Whitney U, 2 tailed, unpaired for control vs intervention.


A
Exercise-related Hypoglycemia Number
16
14
12
10
8
6
4
2
0
Baseline
Intervention
B
Exercise-related Hypoglycemia Number
16
14
12
10
8
6
4
2
0
Baseline
Intervention
C
Exercise-related Hypoglycemia Duration (min)
1200
1080
960
840
720
600
480
360
240
120
0
Baseline
Intervention
D
Exercise-related Hypoglycemia Duration (min)
1200
1080
960
840
720
600
480
360
240
120
0
Baseline
Intervention
E
Self-Efficacy Stanford Survey Item Score
10
9
8
7
6
5
4
3
2
1
0
Baseline
Intervention
F
Self-Efficacy Stanford Survey Item Score
10
9
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3
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1
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Baseline
Intervention

it limited study power by increasing the interquartile range of the primary end-point. In addition, while all study subjects were under routine type 1 diabetes specialist physician care, they had not received specific counselling about exercise before study commencement. Further, studies potentially with larger sample size could concentrate on people with type 1 diabetes who experience 4 or more exercise-related events per week. Our sample population had good cardiorespiratory fitness, regularly exercised and tight overall glycaemic control based on HbA1c levels. Subsequent studies could also focus on people with type 1 diabetes who are younger than 16 years of age and those who do not undertake regular and/or structured physical activity.

The novelty of this intervention provides an ease of access of information related to self-managing glycaemia around exercise. This is important as people living with type 1 diabetes and who exercise, may experience varying support through their healthcare providers. Healthcare access to groups such as DAFNE[18,23] may be infrequent and may prove costly and is more focused on caloric intake rather than exercise per se. This educational tool ExT1D can also be accessed via the internet at any time and prospective patients may choose the recommendations that best suit their exercise routine.

Technological advances in closed loop artificial pancreas systems and, in time, further trials with smart insulins will predictably be helpful in safe exercise in type 1 diabetes. However, they may not be available for several years. Even then, closed loop systems may not be acceptable by some people with type 1 diabetes, or may not be possible due to financial constraints. Furthermore, behavioural interventions in type 1 diabetes that stabilise glycaemia and help to prevent hypoglycaemia are a main component of safe blood glucose care. Therefore, this readily accessible educational online tool with behavioural impact, is a viable and long-term option for those people with type 1 diabetes who wish to exercise with confidence with minimisation of hypoglycaemia.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jdiacomp.2019.05.011.

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Fig. 2. The Longitudinal Study demonstrates change from baseline for the combined cohort of the Intervention and Control groups. For the Individual data each line represents single participant's direction of change in hypoglycaemia or Self-Efficacy Stanford Questionnaire score following 5 weeks of exposure to the ext1d website. Median (IQR) demonstrates total cohort data at baseline and following 5 weeks of exposure to the ext1d website. Panel a. Exercise-related Hypoglycemia Number, Individual data panel b. Exercise-related Hypoglycemia Number, median (IQR) panel c. Exercise-related Hypoglycemia Duration, Individual data panel d. Exercise-related Hypoglycemia Duration, median (IQR) panel e. Self-Efficacy Stanford Questionnaire Item Score, 'How confident are you that you can do something to prevent blood glucose levels from dropping when you exercise?' Individual data panel f. Self-Efficacy Stanford Questionnaire Item Score, 'How confident are you that you can do something to prevent blood glucose levels from dropping when you exercise?', mean (SEM), outliers presented as dots.

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