APPENDIX 1: CONSORT Statement Checklist

		Reporting Item	Page Number
Title and Abstract			
Title	#1a	Identification as a randomized trial in the title.	1
Abstract	#1b	Structured summary of trial design, methods, results, and conclusions	3
Introduction			
Background and objectives	#2a	Scientific background and explanation of rationale	5-6
Background and objectives	#2b	Specific objectives or hypothesis	6
Methods			
Trial design	#3a	Description of trial design (such as parallel, factorial) including allocation ratio.	6
Trial design	#3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	#4a	Eligibility criteria for participants	7
Participants	#4b	Settings and locations where the data were collected	6-7
Interventions	#5	The experimental and control interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8
Outcomes	#6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	9-10
Outcomes	#6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	#7a	How sample size was determined.	10-11
Sample size	#7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomization - Sequence generation	#8a	Method used to generate the random allocation sequence.	8
Randomization - Sequence generation	#8b	Type of randomization; details of any restriction (such as blocking and block size)	8
Randomization - Allocation concealment mechanism	#9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	8

Randomization - Implementation	#10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to interventions	8
Blinding	#11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	9
Blinding	#11b	If relevant, description of the similarity of interventions	8
Statistical methods	#12a	Statistical methods used to compare groups for primary and secondary outcomes	N/A
Statistical methods	#12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow diagram (strongly recommended)	#13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Figure 1
Participant flow	#13b	For each group, losses and exclusions after randomization, together with reason	Figure 1
Recruitment	#14a	Dates defining the periods of recruitment and follow-up	12
Recruitment	#14b	Why the trial ended or was stopped	N/A
Baseline data	#15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	#16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Figure 1
Outcomes and estimation	#17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12-13
Outcomes and estimation	#17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	12-13
Ancillary analyses	#18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	#19	All important harms or unintended effects in each group (For specific guidance see CONSORT for harms)	12
Discussion			
Limitations	#20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16-17
Generalisability	#21	Generalisability (external validity, applicability) of the trial findings	14-16

Interpretation	#22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	14-16
Registration	#23	Registration number and name of trial registry	6
Other information			
Interpretation	#22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	14-16
Registration	#23	Registration number and name of trial registry	6
Protocol	#24	Where the full trial protocol can be accessed, if available	7
Funding	#25	Sources of funding and other support (such as supply of drugs), role of funders	1

Appendix 2: Sample Size Calculation

The full-scale multi-centre trial will include 516 participants (258 per arm), assuming α=0.05, power=80%, 1:1 allocation, a 40% (6.76 hours) minimal clinically important reduction in DKA resolution time, and 10% attrition rate. This trial will be conducted at 6 ED sites over 2 years. Based on this, the sample size for this local pilot RCT is 52 participants (26 per arm).

Sample size for Full-Scale Trial

The sample size calculation for this trial was based on a study of Clinical Effects of Balanced Crystalloids vs Saline in Adults with Diabetic Ketoacidosis(10) which compared the clinical effects of balanced crystalloids with the clinical effects of saline for the acute treatment in DKA in two clinical trials (Isotonic Solutions and Major Adverse Renal Events Trial [SMART](12) and the Saline Against Lactated Ringer's or Plasma-Lyte in the Emergency Department [SALT-ED](13_). The primary outcome for this comparison was the time between ED presentation and DKA resolution, measured in hours. Self et al. (2020) found an absolute reduction in time to DKA resolution of 3.9 hours. In the balanced crystalloids group (n=94), the median time to resolution of DKA was 13.0 hrs [IQR: 9.5-18.8], while in the saline group (n=78) the median time to resolution was 16.9 hrs [IQR: 11.9-34.5]. The IQR was used to calculate the standard deviation for each group based on the following assumption for normally distributed data: SD=IQR/1.35. The pooled standard deviation was then calculated based on the sample size and standard deviation of each group from the Self et al. (2020) study [$\sqrt{((n1-1)*SD12 + (n2-1)*SD22)/(n1+n2-2))}$] and was determined to be 12.37. To establish superiority of balanced crystalloids versus saline in the time to resolution of DKA, a superiority margin for a clinically significant difference was chosen to be a 40% (=6.76 hours) reduction in time to resolution of DKA based on expert consensus and patient partner feedback. A conservative attrition rate of 10% was selected for the sample size calculation, as loss to follow-up rates should be low given the nature of the intervention (IV fluids) and follow-up period (<24 hours). The actual attrition rate determined by this pilot study will inform the sample size calculation for the full-scale multicentre study. Therefore, to achieve 80% power at the 5% level of significance with equal allocation, the sample size for the balanced crystalloids (Ringer's lactate) group and the saline group, while accounting for a 10% loss to follow up and a 40% reduction in time to DKA resolution, is 516 participants (258 per group). The sample size was calculated using Wang and Ji's (2020) method for common clinical study designs available at http://riskcalc.org:3838/samplesize/.

We plan to conduct the full-scale trial at 6 ED sites over 2 years, which would require an average minimum recruitment of 86 participants per site (43 per site per year). Our research group has established relationships with these other Canadian EDs where we have previously conducted successful studies. If further sites are needed for recruitment, we will leverage the Network of Canadian Emergency Researchers (NCER).

Sample size for Pilot Trial

For the full-scale trial, a minimum of 43 participants must be recruited annually per site on average. The LHSC Victoria Campus ED treats approximately 130 patients with DKA annually, based on our hospital's Decision Support data from the most recent fiscal year prior to protocol development (Mar 1 2019 – Feb 29 2020).

DKA by Site	Patients
Victoria Hospital	130
(E1010) Type 1 DM with ketoacidosis	70
(E1110) Type 2 DM with ketoacidosis	51
(E1112) Type 2 DM with keto & lactic acidosis	1
(E1410) Unspecified DM with ketoacidosis	8

Based on our research team hours of coverage and past data from ED presentation time of potentially eligible patients, we expect to approach at least 104 (80%) of eligible patients in the one-year pilot study period, and a minimum of 43 approached participants (41.3%) must be recruited to meet the feasibility target. According to data from similar past trials, we anticipate being able to recruit at least 50% of approached patients (target sample size of 52 patients, 26 in each arm). With 104 patients approached per year, a 90% two-sided confidence interval around the anticipated recruitment rate will have a total width of 0.17, i.e. a lower limit of 0.415 and an upper limit of 0.585. Because the lower limit excludes the minimum feasibility target of 41.3%, we can be 90% confident that the future trial is feasible.