Insul-In This Together Program: Optimizing Family-based Interventions for Adolescents With Type 1 Diabetes and Their Parents

NCT04589689

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1. PURPOSE OF THE STUDY

a. Brief Summary

The current study seeks to evaluate an evidence-based family intervention for teens with type 1 diabetes and their parents to offset the psychosocial and diabetes self-management risks during this period. This study will collect survey and biomedical data to assess this program in a randomized controlled trial. 165 families (including an adolescent and parent) will be enrolled, complete surveys, provide biomedical data via glucose monitors and receive the intervention. The results of this study will inform future intervention redesign to provide more judicious interventions to be disseminated across diabetes care.

b. Objectives

This study will evaluate the relative efficacy of each of the individual intervention components and also identify the mechanisms of actions (mediators) that are most impacted by these types of interventions as well as most linked to long-term outcomes for adolescents. This information will provide a more in-depth understanding of family-based program efficacy for teens with adolescents and provide more judicious and streamlined intervention options to be offered in diabetes clinics in the future.

c. Rationale for Research in Humans

In order to optimize family-based interventions, we need to evaluate adolescent and parent outcomes.

2. STUDY PROCEDURES

a. Procedures

Recruitment and enrollment: Informed parental consent and adolescent assent (for ages 12-17) or consent (for ages 18-19) will be secured prior to enrollment. The recruitment phase will span 3 years. Participants will be recruited based on A1C results in charts or shared reports that fall within 4 weeks of baseline data collection.

Randomization and assignment: After enrollment, each family will be randomly assigned to either the intervention condition (50%) or the waitlisted control condition (50%), regardless of all other characteristics or variables. Once randomized, instructions for scheduling and accessing the

intervention will be immediately provided to the intervention group. The intervention group will also be offered to participate in a voluntary monthly parent group with other parent participants to discuss the intervention. The waitlisted control group will receive the intervention after 6-month follow-up.
Intervention: The intervention will be conducted by the PI or an interventionist (clinically trained research staff) via Zoom, an easy to use, accessible, and HIPAA- compliant software. Participants and facilitators can interact and screen- share to simultaneously view materials and videos of each other.
Data collection: Data collection: Online surveys (adolescent and parent report on demographics, parent-adolescent relationship, diabetes, and family issues) and glucose monitoring data will be captured at baseline and 3-month (proximal endpoint), 6-month (primary endpoint), and 12-month (distal endpoint) follow-ups.
Glucose monitoring data will be collected via glucose monitors that are already in use, among participants already using these devices at the time of enrollment, with data being shared by the participant with the research team via secure online portals created and run by their corresponding device company. For participants who are not already using glucose monitors at the time of enrollment, Libre 2 glucose monitor devices will be provided by study staff, as well as training on use following FDA-approved self-start guides that are available online. Research staff will also provide support throughout use, and will be used to collect 2 weeks of data at each time point.
A smaller set of surveys will also be conducted at approximately 2-, 4-, and 6-week follow-ups (after every 2 sessions for the intervention group and at corresponding time points for the control group). Participants will be asked to report their A1Cs (or gathered from medical records) at baseline and 6-month and 12-month follow-ups. If participants do not have an A1c result from the target period, they will be sent via mail a blood collection kit that can be completed at home and returned via mail to a laboratory where the specimen will be tested for HbA1c.

b. Procedure Risks

The above procedures present minimal risk. Engaging in the intervention modules carries minimal risk for emotional discomfort or stress. Subjects will have the option of not participating in conversations or exercises in the intervention modules that cause them any discomfort. They will also be free to withdraw from participating in the intervention and/or overall study at any time. All intervention modules will be carried out by Dr. Wong, a licensed clinical psychologist (license #29814) or a clinically trained interventionist who will be consistently supervised by Dr. Wong. Survey measures are non-invasive and present minimal risk. Glucose monitors are minimally invasive and provide no added level of risk or discomfort beyond routine diabetes management tasks. A1C home test kits present minimal risk as long as participants practice safe hygiene practices and follow the instructions provided. Finger lancing is part of the usual care for people with diabetes and should not be a significant contributor to risks in this study. A small drop of blood will be obtained by finger stick to measure blood glucose and HbA1c. This is a standard method to obtain blood for routine hospital laboratory tests. Pain is common at the time of lancing. In about 1 in 10 cases, a small amount of bleeding under the skin will produce a bruise. A small scar may persist for several weeks. The risk of local infection is less than 1 in 1000. Nevertheless, our staff (including Dr. Rayhan Lal who has extensive experience with diabetes devices) will be available to address any potential discomfort or adverse responses to these procedures that might arise and will connect families with additional mental health or medical services if needed. Adolescent and caregiver participants will be advised of their rights to withdraw from the intervention at any time without penalty or consequence on their receipt of future health care services at Stanford University's Lucile Packard Children's Hospital or affiliated clinics.

c. Use of Deception in the Study

No deception will be used.

d. Use of Audio and Video Recordings

Video recordings of intervention sessions led by interventionists will be collected for clinical supervision and quality assurance purposes. These recordings will be destroyed once no longer needed for clinical supervision/ongoing training purposes. All recordings will be destroyed before the study ends.

e. Alternative Procedures or Courses of Treatment

The procedures and treatment offered by this study are additive the current services and no alternative are currently available.

f. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Therapy options (in the form of behavioral or psychosocial interventions) will be offered to participants at the conclusion of the study, if indicated, including referrals to both in-clinic and external services.

g. Study Endpoint(s)

3-month (proximal endpoint), 6-month (primary endpoint), and 12-month (distal endpoint) follow-ups. Endpoints were selected based on prior evaluations of similar interventions for youth with T1D showed effects at 6-month follow-up and maintained thereafter. Given the wait-listed control group design, we will be able to test pre-post differences as well as group differences to evaluate efficacy.

3. BACKGROUND

a. Past Experimental and/or Clinical Findings

Less than 1 out of every 4 adolescents with type 1 diabetes (T1D) meets the American Diabetes Association (ADA) guidelines for target hemoglobin A1c, a common indicator of glycemic control. These deteriorations in glycemic control during adolescence can persist into adulthood. Family-based interventions are empirically supported to offset this adolescent risk, although behavioral health services are rarely included in diabetes care. Despite the ADA recommendation for integrated care, a minority of diabetes clinics offer any behavioral health services and less than 1 in 5 include a psychologist. Lack of behavioral health providers who specialize in diabetes as well as institutional/economic constraints serve as barriers toward more integrated models of care, enhancing the need for intervention options that require limited resources. The current study seeks to address that need by evaluating an evidence-based family intervention to be optimized and integrated within real-world clinic care for adolescents with T1D and their parents.

b. Findings from Past Animal Experiments

None.

4. PARTICIPANT POPULATION

a. Planned Enrollment

The target enrollment will be 165 families (165 adolescents and 165 caregivers). Potential participants will be recruited through the Division of Pediatric Endocrinology and Diabetes at Stanford, the Stanford Diabetes Research Center's clinical registry, and online email listervs. Inclusion criteria are: 1) T1D diagnosis according to ADA criteria for at least 6 months, 2) ages 12-19, and 3) participation of at least one cohabitating parent/caregiver. The age range was chosen due to evidence that diabetes management problems first arise between the ages of 11 and 18 years. Exclusion criteria will be lack of access to a smartphone or Wi-Fi via computer, restricted English proficiency, and pervasive developmental, data collection or intervention modules.
Glucose monitoring data will be collected via glucose monitors that are already in use, among participants already using these devices at the time of enrollment, with data being shared by the participant with the research team via secure online portals created and run by their corresponding device company. For participants who are not already using glucose monitors at the time of enrollment, Libre 2 glucose monitor devices will be provided by study staff, including training on use and support throughout use, and will be born to collect 2 weeks of data at each time point.

b. Age, Gender, and Ethnic Background

Adolescents ages 12-19 and at least one caregiver will be recruited to participate across genders and ethnic backgrounds.

c. Vulnerable Populations

165 adolescents will be enrolled. Normative adolescent shifts in cognitive and affective development and transitions from parental dependence toward greater autonomy can compromise self-management and glycemic control among adolescents with T1D. Less than 1 out of every 4 adolescents with type 1 diabetes (T1D) meets the American Diabetes Association (ADA) guidelines for target hemoglobin A1c, a common indicator of glycemic control. These deteriorations in glycemic control during adolescence can persist into adulthood. Family-based interventions are empirically supported to offset this adolescent risk, although behavioral health services are rarely included in diabetes care. The current study seeks to identify ways to offset risks among adolescents.

d. Rationale for Exclusion of Certain Populations

Women, minorities, and children will be included.

e. Stanford Populations

None.

f. Healthy Volunteers

None.

g. Recruitment Details

Potential participants will be recruited through the Stanford Pediatric outpatient diabetes clinics of the Division of Pediatric Endocrinology and Diabetes at Stanford, the Stanford Diabetes Research Center's clinical registry and similar IRB approved email lists compromised of individuals who requested to be contacted about potential research participation, as well as online email listervs, and social media.
In-clinic recruitment will consist of posting flyers in clinic, including exam rooms, waiting room, and hallways. The research team will recruit with the flyers and provide assistance with completing the online screening and informed consent when possible. Clinic staff will also be provided with copies of the flyers to distribute to potential participants. Stanford pediatric diabetes clinics are a common venue for research and patients are made aware that they participation or decision not to participate in research will in no way compromise the services they receive there and that participation can be withdrawn at any time without any penalty or negative impact to the services that they receive.
Potential participants will also be contacted through our endocrine and IRB approved patient recruitment lists, including the Stanford Diabetes Research Center's clinical registry (in which subjects have already consented to be recruited for research studies). Stanford Diabetes Research Center's clinical registry is compromised of individuals who have expressed interest in participating in research and have voluntarily included their name in the registry to be contacted for potential participation in studies. More information on the SDRC registry can be found at: https://sdrc.stanford.edu/clinical-research-registry. Participants will also be recruited through online flyers sent out through established diabetes-related listervs run by diabetes organizations. If/when eligibility criteria are revised, a re-send recruitment email (see Section 16) will be sent to again across listervs to clarify that interested potential participants who were previously ineligible have an opportunity to complete the screening again as they may now be eligible.
The IRB-approved recruitment flyer and email will also be circulated through online websites, forums newsletters, emails listervs, and social media pages (primarily run by diabetes organizations such as DYF and JDRF) and shared with diabetes providers and clinics within and outside of Stanford. These online avenues are often used to disseminate information to families of youth with type 1 diabetes offering various information and resources, including opportunities to participate in studies similar to the current study.

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h. Eligibility Criteria

i. Inclusion Criteria

Inclusion criteria are: 1) type 1 diabetes (T1D) diagnosis according to ADA criteria for at least 6 months, 2) ages 12-19, and 3) participation of at least one cohabitating parent/caregiver. The age range was chosen due to evidence that diabetes management problems first arise between the ages of 11 and 18 years.

ii. Exclusion Criteria

Exclusion criteria will be lack of access to a smartphone or Wi-Fi via computer, restricted English proficiency, and pervasive developmental, cognitive, or psychiatric limitations that compromise participation in the intervention sessions and study. Glucose monitors will be provided to

participants who are not already using these devices such that device use will not be a criterion of eligibility or exclusion.

i. Screening Procedures

Eligibility will be determined based on a screening survey completed through RedCap prior to informed consent and enrollment.

j. Participation in Multiple Protocols

Both verbal and written information on consent (and assent) will be obtained by the research staff and/or PI to assess understanding of consent during interactions with potential participants. Individuals who are not proficient in English or have any impairment in communication that might compromise informed consent/assent will be excluded from the study.

k. Payments to Participants

We will enroll 330 participants (165 adolescents with type 1 diabetes and their 165 caregivers). Participants will be asked to participate in a 6-session family-based intervention delivered via the internet, complete online surveys, provide glucose monitoring data either via continuous glucose monitors (CGMs) that the have already been using prior to enrollment or blinded CGMs provided by the study, and provide A1C test results that will be collected via chart review or from participants sharing their test results at baseline, 6-month, and 12-month follow-up. We will compensate each parent and each adolescent participant with a total of $[redacted] worth of gift cards for complete data collection. Graduated incentives are provided at each time point:

- Baseline = $[redacted]
- First intermediate survey = $[redacted]
- Second intermediate survey = $[redacted]
- Third intermediate survey = $[redacted]
- 3-month follow-up = $[redacted]
- 6-month follow-up = $[redacted]
- 12-month follow-up = $[redacted]

l. Costs to Participants

None.

m. Planned Duration of the Study

The probable duration of the entire study is 4.5 years. We anticipate screening will require 5 minutes, recruitment of all 165 participants can take up to 3 years, and activate participation in the study will require approximately 12 months. Each participant will spend 8 hours total on study participation and analysis of participant data will require approximately 1 year. Surveys will require approximately 30 minutes each to complete and each intervention sessions for the intervention group will require approximately 10-20 minutes each.

5. RISKS

a. Potential Risks

i. Investigational devices

None.

ii. Investigational drugs

None.

iii. Commercially available drugs, biologics, reagents or chemicals

None.

iv. Procedures

Data Collection: Self-reported survey will be kept confidential and collected online via secure REDCap database system. There are no known psychological risks to subjects completing self-report subjective rating scales or participating in the intervention sessions. However, the survey and intervention may contain items or questions that make the subjects feel uncomfortable in that they ask about their physical and psychological health and feelings/emotions. Subjects will be informed that any items on questionnaires or topics discussed in the intervention modules that produce these effects may be skipped or ignored. Further, Dr. Wong (PI) is a licensed psychologist who will be available to participants to address any potential discomfort or risks that may arise, assess, and triage as appropriate. If any discomfort or adverse events arise with continuous glucose monitor use, our research staff including Dr. Rayhan Lal will be available to assist and assure that the appropriate medical services are received to address the issue, as well as minimize risk in general.

Intervention: Engaging in the intervention modules carries minimal risk for emotional discomfort or stress. Subjects will have the option of not participating in conversations or exercises in the intervention modules that cause them any discomfort. They will also be free to withdraw from participating in the intervention and/or overall study at any time. All intervention modules will be carried out by Dr. Wong, a licensed clinical psychologist (license #29814) or a clinically trained interventionist who will be trained and supervised by Dr. Wong. Adolescent and caregiver participants will be advised of their rights to withdraw from the intervention at any time without penalty or consequence on their receipt of future health care services at Stanford University's Lucile Packard Children's Hospital of affiliated clinics.

Protections Against Risk. Dr. Wong and all research staff have completed rigorous training in the protection of human subjects, including CITI training. The plan for protecting privacy and confidentiality recognizes that the protection of privacy in studies involving sensitive data is of utmost importance. We will attempt to do this in several ways. The PI will introduce the study to eligible participants and explain the purposes, benefits, and risks of the project to the subjects, and offer them an opportunity to ask questions and/or decline participation. The voluntary and confidential nature of the research, as well as limits to confidentiality, will be highlighted during informed consent process. Study participation will not interfere with clinical care and all patients have standard access to the treatment team on a routine (clinical care) and emergency basis. All responses to interview items will be given by subjects in private. Survey data collection will only occur through tools and resources that have acceptable security features. We will minimize all communications that involve names or other identifying information. All clinically-relevant and study information will be kept in locked files in locked offices or password protected files. Our research staff including Dr. Rayhan Lal will be available to assist and assure that the appropriate medical services are received to address any issues with glucose monitoring, as well as minimize risk of issues related to device use.

The participants will send the A1c test kits with their samples to the Advanced Research and Diagnostic Laboratory (ARDL) at the University of Minnesota where it will be processed and the results will be sent securely without any identifiers to the study team.

All recordings of intervention sessions will be saved on a password-protected secure server. Information about subjects will not be accessible to any nonauthorized study personnel without the written consent of the subject. In all datasets we will use ID numbers only. A separate dataset linking names with ID numbers will be accessible only to authorized study personnel under the direction of the PI.

v. Radioisotopes/radiation-producing machines

None.

vi. Physical well-being

None.

vii. Psychological well-being

Data Collection: Self-reported survey will be kept confidential and collected online via secure REDCap database system. There are no known psychological risks to subjects completing self-report subjective rating scales or participating in intervention sessions. However, the surveys and intervention topics may contain items or questions that make the subjects feel uncomfortable in that they ask about their physical and psychological health and feelings/emotions. Subjects will be informed that any items on questionnaires or topics discussed in the intervention modules that produce these effects may be skipped or ignored. Further, Dr. Wong (PI) is a licensed psychologist who will be available to participants during data collection and will be facilitated the intervention in order to address any potential discomfort or risks that may arise, assess, and triage as appropriate.

Intervention: Engaging in the intervention modules carries minimal risk for emotional discomfort or stress. Subjects will have the option of not participating in conversations or exercises in the intervention modules that cause them any discomfort. They will also be free to withdraw from participating in the intervention and/or overall study at any time. All intervention modules will be carried out by Dr. Wong, a licensed clinical psychologist (license #29814). Adolescent and caregiver participants will be advised of their rights to withdraw from the intervention at any time without penalty or consequence on their receipt of future health care services at Stanford University's Lucile Packard Children's Hospital of affiliated clinics. Protections Against Risk. Dr. Wong has completed and will maintain rigorous training in the protection of human subjects, including CITI training. The plan for protecting privacy and confidentiality recognizes that the protection of privacy in studies involving sensitive data is of utmost importance. We will attempt to do this in several ways. The PI will introduce the study to eligible participants and explain the purposes, benefits, and risks of the project to the subjects, and offer them an opportunity to ask questions and/or decline participation. The voluntary and confidential nature of the research, as well as limits to confidentiality, will be highlighted during informed consent process. Study participation will not interfere with clinical care and all patients have standard access to the treatment team on a routine (clinical care) and emergency basis. All responses to interview items will be given by subjects in private. Survey data collection will only occur through tools and resources that have acceptable security features. We will minimize all communications that involve names or other identifying information. All clinically-relevant and study information will be kept in locked files in locked offices or password protected files.

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viii. Economic well-being

None.

ix. Social well-being

None.

x. Overall evaluation of risk

NA.

b. International Research Risk Procedures

NA.

c. Procedures to Minimize Risk

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All recordings of intervention sessions will be saved on a password-protected secure server. Information about subjects will not be accessible to any nonauthorized study personnel without the written consent of the subject. In all datasets we will use ID numbers only. A separate dataset linking names with ID numbers will be accessible only to authorized study personnel under the direction of the PI.

d. Study Conclusion

The study will end after 4.5 years. Participation will end one year after baseline data collection completion. No adverse events are anticipated.

e. Data Safety Monitoring Plan (DSMC)

i. Data and/or events subject to review

We will review CGM data for wide and dangerous fluctuations in glucose levels, and report to the study participant and clinical team (if acceptable to study participant).

ii. Person(s) responsible for Data and Safety Monitoring

Dr. Jessie Wong is responsible for ongoing monitoring and Dr. Laura Nally will serve as Safety Monitor.

iii. Frequency of DSMB meetings

During the course of the trial, data will be reviewed monthly for completeness and accuracy (all data points fall within the possible range for each measure), with guidance from the mentorship team. In addition, bi-weekly reviews will examine occurrence of adverse events and whether participants are satisfied with their participation.
Because this study involves randomization and interventions associated with diabetes management, but because the study itself is not masked and is low risk, the PI will be involved with the oversight in conjunction with an external Safety Monitor (rather than a Data Safety and Monitoring Board). The Safety Monitor will be informed of all serious adverse events and any unanticipated adverse device events that occur during the study and will review compiled adverse event data at the completion of the study.

iv. Specific triggers or stopping rules

The PI will be responsible for evaluating each unanticipated problem and determining whether it affects the risk/benefit ratio of the study and whether modifications to the protocol and consent forms are required. Specific triggers include any indication through data collection or participant interactions that indicate severe risk, such as indications of diabetic ketoacidosis or suicidality. These issues are rare but our team will be trained in identifying early signs to immediately inform PI to determine whether reporting, stopping, and/or other actions must be taken.

v. DSMB Reporting

The PI will be responsible for reporting unexpected problematic events involving any aspect of the study to the NIH and local IRB per institutional guidelines. The Safety Monitor will be informed of all serious adverse events and any unanticipated adverse device events that occur during the study and will review compiled adverse event data at the completion of the study. Unanticipated problems to be assessed include adverse events, deviations from the study protocol, problems with informed consent, and confidentiality violations.

vi. Will the Protocol Director be the only monitoring entity? (No)

Dr. Jessie Wong (PI) will primarily be responsible for monitoring though the project research coordinator will be trained in monitoring and Dr. Hood will be consulted as needed.

vii. Will a board, committee, or safety monitor be responsible for study monitoring? (No)

The Safety Monitor will be involved, as needed, in monitoring but will not be responsible for monitoring.

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f. Risks to Special Populations

Benefits a) Describe the potential benefit(s) to be gained by the participants or by the acquisition of important knowledge which may benefit future participants, etc. This study presents no greater than minimal risk, given that all the procedures are no more invasive or risky than standard

practices within diabetes management. Further, research staff will be available to prevent, address, and resolve any potential risks that may arise.

6. BENEFITS

The potential benefit of this study is the provision of new knowledge and skills about methods of improving glycemic control among adolescents with type 1 diabetes. Participants may find intervention sessions interesting and relevant.
Collection of the psychosocial and clinical data may provide information for diabetes clinicians and other stakeholders to help optimize the way that new beneficial technology is introduced to their patients.

7. PRIVACY AND CONFIDENTIALITY

All participant information and specimens are handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and privacy policies of Stanford University, Stanford Health Care, and Stanford Children's Health.