Title: Study Protocol with Statistical Analysis Plan

NCT number: Pending

Document date: 12/12/2024

GENERAL STUDY INFORMATION

Study Title

Prescription antipyretics to decrease unscheduled return visits in a pediatric emergency department

1 Review Type (Choose one)

Please choose which level of review best fits your research. This is an investigator's assessment of review and does not preclude the IRB from alternate determinations. In cases where the investigator and the IRB's determination of review conflict, the IRB's determination will be considered the official determination.
***Note**: Expedited review does not refer to the timeliness of the review of your protocol, but specific categories of research defined by OHRP. If you would like help determining which type of review best fits your research study, please contact the IRB staff in the Office of Research Support & Compliance:*
https://research.utexas.edu/ors/human-subjects/get-help/

a ☐ **Full Board Review – Greater than Minimal Risk Research**
b ☒ **Expedited Review – Minimal Risk Research**

2 Research Hypotheses

Please describe the research aims and hypotheses in the box below. To input text, click in the box below and start typing. Note: Procedures will be explained in a separate section below.

The study aims to evaluate whether unscheduled return visits within one week for similar complaints are impacted by ensuring parents have access to the appropriate doses of acetaminophen and ibuprofen. We hypothesize that prescribing appropriately dosed acetaminophen and ibuprofen will decrease the rate of unscheduled return visits.

3 Study Background

Provide the rationale and the scientific or scholarly background for the proposed activity, based on existing literature (or clinical knowledge). Describe the gaps in current knowledge that the project is intended to address.

Unscheduled return visits (URV) to the Emergency Department (ED) are a burden on both the healthcare system and patients. Published literature has attempted to categorize the rate of URV and type of complaints that lead to URVs. Rate of URV is variable, but as high as 22% for children with infectious illnesses and parents often return to the ED due to unresolved fever in a child[1,2]. Unresolved fever may be due to continued progressive worsening of illness or inability to provide the appropriate amount of anti-pyretic (anti fever) medicine to the child, as pediatric medication dosing is not only age-based, but also weight-based[3]. This increased variability could lead to confusion on the part of the caregivers. There are no published studies looking at whether appropriately prescribed antipyretics decrease the rate of return visits. Further, there is no standardization for antipyretic prescribing nationally or at the research team's hospital and some providers frequently provide prescriptions for these medications while others almost never do. It is unknown if providing a prescription for an over-the-counter medication makes a difference with health outcomes. The study aims to evaluate whether

unscheduled return visits within one week for similar complaints are impacted by ensuring parents leave the ED with a prescription for appropriately dosed acetaminophen and ibuprofen.

1. Jacobstein, C. R., Alessandrini, E. A., Lavelle, J. M., & Shaw, K. N. (2005). Unscheduled revisits to a pediatric emergency department: risk factors for children with fever or infection-related complaints. *Pediatric Emergency Care*, 21(12), 816–821. https://doi.org/10.1097/01.pec.0000190228.97362.30
2. Trapani, S., Fiordelisi, A., Stinco, M., & Resti, M. (2023). Update on fever of unknown origin in children: Focus on etiologies and clinical approach. *Children* (Basel, Switzerland), 11(1), 20. https://doi.org/10.3390/children11010020
3. Section on Clinical Pharmacology and Therapeutics, Committee on Drugs, Sullivan, J. E., & Farrar, H. C. (2011). Fever and antipyretic use in children. *Pediatrics*, 127(3), 580–587. https://doi.org/10.1542/peds.2010-3852

4 Design and Methodology

Provide a brief description of the study design or data collection methodologies. Details regarding protocol specific research procedures will be discussed in a later section.

Research Design

This study will be a single center, randomized controlled trial in the pediatric emergency department (ED) at the north or central campus of Dell Children's Medical Center (DCMC). Patients meeting inclusion and exclusion criteria will be identified by research personnel during the ED visit.

Inclusion Criteria:

- Children 6 to < 36 months of age being discharged home from DCMC ED who are evaluated for fever
- Caregiver fluent in English or Spanish

Exclusion Criteria:

- Previous enrollment in this study
- Patient admitted to hospital
- Parental request for a prescription for acetaminophen and/or ibuprofen
- Trauma patient
- Orthopedic complaint
- Other painful indication for acetaminophen or ibuprofen
- Acetaminophen or ibuprofen prescribed for anything other than fever
- Allergy or another contraindication to acetaminophen or ibuprofen
- Parent and patient unlikely to follow up in the region (i.e., lives out of state)

Patients will be randomized to the intervention or control group after parental/caregiver permission is obtained for general participation in a research study. Computerized randomization functions and opaque envelopes will be used to achieve random assignment and allocation concealment. Patient care will look the same for all participants, but discharge process will differ slightly for each group. Both groups will receive standard discharge education, but the intervention group (n=220) will receive prescription with weight-based dosing for acetaminophen and ibuprofen. The control group (n=220) will also receive standardized printed discharge instructions, which includes the appropriate dose of acetaminophen and ibuprofen. As noted above, there is no standardization for antipyretic prescribing nationally or at our hospital. Some providers frequently provide prescriptions for these medications while others almost never do. It is unknown if providing a prescription for an over-the-counter medication makes a difference with patient satisfaction or health outcomes justifying the additional costs to the healthcare system.

One week after discharge, the research team will contact the child's caregiver to determine if an unscheduled return visit was made, and, if so, the reason why. We will ask about visits to EDs, urgent cares, and clinics/primary care providers, and about their satisfaction with the care they received in the ED. The primary outcome will be unscheduled revisits to the ED (binary endpoint). Secondary endpoints include total number of unscheduled return visits, return with hospital admission, and parental satisfaction with ED care. The caregiver will be debriefed on the randomization part of the study at this time and permission will be requested for continued use their child's health data and the caregiver's responses for the purposes of the research study.

5 Data Analysis

Describe the data analysis plan, including any statistical procedures or power analysis.

Data collection and analysis will be performed by the study physicians with the support from research personnel and faculty at DCMC. Summary statistics of demographic variables will be presented using means with standard deviations (normally distributed continuous data), and medians with interquartile ranges (non-normal continuous data). Categorical data will be presented as total number and percentages. The categorical primary and secondary endpoints will be analyzed using the Chi squared or Fisher's exact test. Continuous endpoints will be analyzed with the t-test for parametric data, or the Wilcoxon Rank Sum test for non-parametric data. Logistic regression will be utilized to assess the impact of the intervention on the primary endpoint if significant differences of baseline variables are observed between the groups.

STUDY ELEMENT IDENTIFICATION

6 Study Elements

Check each research procedure included in your study. A full description of all study procedures should be provided in the Procedures (Details) section below. Procedures denoted with "" below have supplemental forms. Navigate to the UTRMS-IRB Library, Templates tab to download the applicable supplemental form.*

☐	Bio-specimens*	☐	Biometrics	☐	Registry or Repository*
☐	Focus Group	☐	Genetic Analysis	☐	Genomic Data Sharing
☐	International Research*	☒	Interview/Survey	☐	MRI
☒	Protected Health Information*	☐	Observation	☐	Radioactive Material/PET/Nuc. Med
☐	Record Review	☐	Sensors (Externally Placed)	☐	Sensors (Inserted)
☐	Audio (only) Recording	☐	Video Recording	☐	X-Ray/CT/DEXA

7 Study Intervention

*Click on the check box (or double click and type an "X" if using Google Docs) if you will implement any of the following interventions. A full description of all study interventions should be provided in the Procedures (Details) section below. * Interventions denoted with "*" below have supplemental forms. Navigate to the UTRMS-IRB Library, Templates tab to download the applicable supplemental form.*

☒	Behavioral	☐	Device*	☒	Drug/Biologic*

8 Clinical Trial

Click on the following check box if the research meets the below definition of a clinical trial.

☒ **This study meets the definition of a clinical trial according to clinical trials.gov in that it involves one or more human subjects who are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.**

9 Additional Oversight

Check the box(es) below if you are implementing research procedures that require oversight from additional UT committees.

☐ **Energy introduced to the subject (electrical, magnetic, light)**

☐ **Human embryonic, human induced pluripotent, or human totipotent stem cells; or human gametes or embryos**

☐ **Radiation exposure without direct clinical benefit**

☐ **Biological Samples, Biohazards, Recombinant DNA, or Gene Transfer**

If biological samples are used and stored on UT campus UT IBC approval is needed.

a ☐ **UT IBC has (or will have) oversight.**

Provide UT IBC Number:

b ☐ **Biological samples collected will not be stored at UT Austin and another agency has responsibility for biospecimen safety.**

10 Alternatives to Participation in This Study

Provide a description of alternatives to participation in this study, as applicable.

We will obtain permission from parents/caregivers prior to randomization. Parents/caregivers will not be told specifically about being randomized to the prescription group or the over the counter (OTC) group, but they will have the option to not participate in the research at this point. If parents in the OTC arm request a prescription at discharge it will be provided to them. These subjects will remain in the study and be analyzed as both intention-to-treat and per protocol participants. Parents assigned to the intervention group also have the alternative to give their child OTC medicine and not fill the prescription.

STUDY PROCEDURE DESCRIPTION

11 Procedure Description

Describe all study procedures, including a step-by-step outline of what participants will be asked to do or how data will be used. Be sure to describe all of the following in detail, as applicable:

- *Description of all research procedures being performed and when they are performed, in sequential order.*
- *Describe/list all research measures/tests that will be used [**NOTE: upload copies of all measures, surveys, scripts, data collection forms, etc., in "Other Attachments" in UTRMS-IRB**].*
- *Secondary data or specimens that will be obtained, how they are collected, how are they used.*

- *Where research activities will take place and duration (include expected time commitment of participants).*
- *Study elements checked in #6 above should be described here.*

Note: if this is a multi-site or collaborative study include the following:

- *This is a "Multi-site Study that involves more than one site performing ALL aspects of the research procedures as outlined above." OR "This is a collaborative study that involves UT Austin researchers working with external researchers who are engaged in performing the following study activities (list activities)."*
- *For assistance with multi-site/collaborative research, download HRP-UT932 Request to Rely Assessment Form from the UTRMS-IRB Library and email irbreliance@austin.utexas.edu.*

Once eligibility is established, research personnel will approach parents/caregivers in the patient's private room in the ED about participating in a research study to improve care for febrile children who present to the ED. If a parent/caregiver agrees to participate, they will sign a permission/consent form and contact information will be obtained to conduct the follow-up call. Patients will then be randomized to the intervention or control group. Computerized randomization functions and opaque envelopes will be used to achieve random assignment and allocation concealment. Patient care will look the same for all participants, but discharge instructions will differ. Both groups will receive standard discharge education, but the intervention group (n=220) will receive prescriptions with weight-based dosing for acetaminophen and ibuprofen. The control group (n=220) will receive standardized printed discharge instructions, including the appropriate dose of acetaminophen and ibuprofen. The randomization assignment will be given to the provider.

Discharge instructions for all patients – both those in the prescription group and the standard of care group, as well as all patients who receive discharge information about medication – include weight-based dosing information. This information is provided by the medical provider at discharge and doses were created by rounding the volume to the most reasonable amount for the weight, for example, for ibuprofen (100mg/5ml): 12 – 17 lbs = 2.5ml, 18-23 lbs = 3.75ml, 24-35 lbs = 5ml, 36-47 lbs = 7.5ml. Only the 100mg/5ml dose of ibuprofen will be prescribed.

The protocol does not dictate what information providers give, and parents' questions will be answered as usual. If the participant is randomized to the prescription arm and the parent asks about using over the counter medications instead, the provider will let the parent know that that is an option and provide medication instructions as over the counter drugs may not include dosing information for children under age 2. One of the outcomes we will be looking at is whether prescriptions were filled and, if not, why not. Both arms of this study are considered standard of care and providers can answer parent or caregiver questions as they would in any case.

One week (7 days) after discharge, the research team will contact the child's caregiver to determine if an unscheduled return visit for the same illness occurred, and, if so, the reason why. We will ask about visits to EDs, urgent cares, and clinics/primary care providers. The primary outcome will be the proportion of children with any unscheduled return visit. During this call, the research team will let the parent/caregiver know about the randomization component of the study and again offer the opportunity to opt out of having their/their child's data used for study purposes.

The research team will attempt to contact the caregiver(s) up to 5 times at each phone number available. Phone calls will be made over the course of two weekdays. If, after these attempts, the caregiver is unable to be reached, the caregiver/child dyad will be considered "withdrawn" as they are unable to be reached.

SUBJECT POPULATION

12 Protected Subject Populations

Click on the check box (or double click and type an "X" if using Google Docs) each population, if they are specifically studied for this research.

☐ Active Military Personnel	☒ Children/Minors	☐ Decisionally Impaired Adults
☐ Emancipated Minors	☐ Fetuses	☒ Individuals with Limited English Proficiency
☐ Neonates (Uncertain Viability)	☐ Neonates (Non-Viable)	☐ Prisoners
☐ Pregnant Women	☐ UT Staff/Employees	☐ UT Students

13 Research Participant Information

Describe the general characteristics of the subject populations or groups including gender, health status, and any other relevant characteristics. ***If you have multiple research populations (e.g., teachers and students), clearly outline characteristics for each group.***

Children: 6 to < 36 months of age being discharged home from DCMC emergency department with a diagnosis of fever will be put into one of two groups:

1) Intervention group (n=220) will receive a prescription with weight-based dosing for 120 mL of acetaminophen (concentration 160mg/5mL) and ibuprofen (concentration 100mg/5 mL)
2) Control group (n=220) will receive standardized printed discharge instructions, including the appropriate dose of OTC acetaminophen and ibuprofen

Caregivers/parents of children as detailed above.

b Minimum Age

Include the minimum age range for target population. If you have multiple research populations ***(e.g., teachers and students), clearly state the minimum age for each group.***

Children: 6 months (both groups)
Caregivers: 18 years

c Maximum Age

Include the maximum age range for target population. If you have multiple research populations ***(e.g., teachers and students), clearly state maximum age for each group.***

Children: < 36 months (both groups)
Caregivers: 90 years

d Inclusion Criteria

Describe the specific criteria that will be used to decide who will be INCLUDED in the research from interested or potential subjects. Define technical terms in lay language, as applicable.

- Children 6 to < 36 months of age being discharged home from DCMC ED who are evaluated for fever
- Caregiver fluent in English or Spanish, over the age of 18

e Exclusion Criteria

Describe the specific criteria that will be used to decide who will be EXCLUDED from the research. Define technical terms in lay language, as applicable.

- Previous enrollment in this study
- Patient admitted to hospital
- Parental request for a prescription for acetaminophen and/or ibuprofen
- Trauma patient
- Orthopedic complaint
- Other painful indication for acetaminophen or ibuprofen
- Acetaminophen or ibuprofen prescribed for anything other than fever
- Allergy or another contraindication to acetaminophen or ibuprofen
- Parent and patient unlikely to follow up in the region (i.e., lives out of state)

14 Total Sample Size

Enter the total target sample size below.

Children: 440
Caregivers: 440
Total: 880

15 Sample size rationale

Describe your sample size rational below.

A literature review cites a current rate of URVs for patient with febrile illness at approximately 20% at 7 days after ED discharge[1]. Using a 20% baseline return rate with an α of 0.05 and an effect size of 10% (absolute), we calculated a sample size of 400 (200 per arm). Assuming a 10% loss to follow up, 440 child subjects are needed. As caregivers will also be queried as part of the study, 440 corresponding caregiver subjects are needed.

SCREENING AND RECRUITMENT

16 Identification and Screening

*Check the box below if this study involves a screening process **prior** to the informed consent process.*

☒ **This study involves obtaining information or biospecimens for the purpose of screening, recruiting or determining eligibility of prospective subjects prior to informed consent by either:**
1. Oral or written communication with the prospective subject or LAR
2. By accessing records containing identifiable private information or stored identifiable biospecimens.

17 Identification and/or Screening Procedures

Describe the identification and/or screening procedures below.

ED providers (MD, DO, APP, NP, RN) will be trained in study recruitment procedures and asked to identify potential study candidates who are under their care. Upon identification of a possible participant, a trained enrolling researcher will be contacted to review the patient's eligibility and get prospective permission/consent from the caregiver/parent. If eligible and the parent/caregiver agrees to participate, the patient will receive a randomization assignment, and this will be given to the provider.

18 Recruitment Overview

Check box indicating all recruitment methods utilized for this research.

☐	E-mail	☐	Flyer
☒	In-Person	☐	Letter
☐	Social Media	☐	Research Pool
☐	Telephone/Text	☐	Snowball Sampling
☐	Web-post	☐	Word of Mouth

19 Describe the recruitment process, including where recruitment will take place.

Describe recruitment procedures in the box below. Describe all elements checked above to provide a complete understanding of the recruitment strategies/methods.

NOTE: Upload copies of all recruitment materials to UTRMS-IRB in the "Recruitment Materials" section.

All patients with an emergency department evaluation for fever and who are being discharged will be evaluated for study enrollment. Parents/caregivers will be approached about participation directly by a member of the research team. The parent/caregiver will be approached in the patient's private room within the ED and told about the research study. The research team member, however, will not provide all the details about the study (specifically the randomization to the prescription group or the OTC group). They will be told that the study is being conducted to improve care for febrile infants who come to the ED for care and asked if they would like to participate in the study. Signed permission/consent will be obtained at this point.

OBTAINING INFORMED CONSENT

20 Consent Overview

Check the box(es) for consenting procedures that will be used.

☒	Obtaining Written Informed Consent/Parental Permission	☐	Requesting a Waiver of Documentation of Informed Consent

☐	Requesting a Waiver of Informed Consent	☒	Requesting an Alteration of the Required Elements of Informed Consent
☐	Obtaining Child Assent	☐	Obtain Consent Using a Short Form with a Witness

21 Consent and Assent Processes

Provide a detailed description of consent/assent procedures in the box below. Include: who will obtain consent, where will consent be obtained, how is consent obtained, how consent/assent is documented, and when the consent process will occur in such a manner that participants will have sufficient time for adequate consideration.

NOTE: Upload copies of all consent/assent/permission forms/scripts to UTRMS-IRB in the "Consent Forms" section. This is required for UTRMS-IRB to appropriately stamp consent forms for approval.

We are requesting an alteration of the required elements of informed consent for the research study process in the ED at the initial visit.

At the initial ED visit, a member of the research team will approach the parent/caregiver and give them an overview of the study but not about the randomization to one of the two groups. The parent/caregiver will be told that the study is being conducted to help improve care for febrile infants presenting to the ED. If the parent/caregiver agrees to participate, they will sign off on the permission/consent form at the ED encounter.

At the one-week follow-up call, a member of the research team will provide information that was not captured on the initial permission/consent form. The debriefing researcher will go through this information with the parent/caregiver over the phone and answer questions that arise during the call. If the parent/caregiver gives permission for their/their child's data to be used for the research, this will be noted by the researcher.

In the event that a parent/caregiver is upset or has a complaint about being randomized to one of the two groups, the debriefing researcher will reiterate the reasoning why this was done and how the data will not be used further for research purposes. The researcher will also remind the parent/caregiver that participating or not participating in the research did not and will not affect their or their child's relationship with Dell Children's Medical Center, Ascension Seton, or UT Austin. If the parent/caregiver would like to talk to the PI or the IRB, they will be provided with the appropriate contact information.

22 Electronic Consent

Check the box below if this study involves obtaining consent with an electronic signature. Be sure the section above is consistent. NOTE: This box should NOT be checked participants are responding "yes" or clicking "I Agree" on a consent form. ***This section should only be completed if an electronic signature is being obtained.***

☐ **This study involves documenting informed consent/parental permission using an electronic signature.**

If true, specify method for obtaining e-consent below (e.g., DocuSign):

23 Consent and Translation

Check the box below to indicate that consent documents/scripts will be translated to a language other than English.

☒ **The study population will likely include participants whose limited English speaking status requires translation of the consent form.**

Translation Process

If above is checked, complete the below information describing the translation process. Either A or B must be checked.

A ☐ **The consent documents will be translated by a certified translator.**

B ☒ **A non-certified translator will translate the consent documents.**

If selected, complete the next two items below. Section describing qualifications must be completed and backtranslation (ii) must be true.

i Describe the translator's qualifications

To input text, click in the light grey area below.

The consent form has been translated by the study coordinator Lina Palomares, RN, LMSW. Ms. Palomares is fluent in Spanish and has 20 years of experience in survey design and translation.

ii ☐ **Another individual will confirm that the translation is accurate and appropriate**

26 Waiver of Documentation of Informed Consent

*Only complete this section if a waiver of documentation of consent is requested (checked above in #21). To approve a waiver of documentation of consent, one of the following options must be appropriate and justified by the researcher. Please choose **one** waiver option and provide additional information as prompted. **Waiver option 2 is most common.***

A Waiver Option 1

Check the box below for each item (all required – #1-4) and provide protocol-specific information as to how the criteria below are met.

NOTE: This is the only applicable waiver of documentation option for greater than minimal risk research. If your study is greater than minimal risk and does not meet Option 1 criteria, you will need to obtain written consent.

1 ☐ **The only record linking the subject and the research would be the consent document.**

i Provide protocol specific information as to how this criterion is met.

2 ☐ **The principal risk would be potential harm resulting from a breach of confidentiality.**

i Provide protocol specific information as to how this criterion is met.

3 ☐ **Each subject will be asked whether the subject wants documentation**

linking the subject with the research, and the subject's wishes will govern.

i **Provide protocol specific information as to how this criterion is met.**

4 ☐ **Describe the mechanism for documenting that informed consent was obtained**

Briefly explain how the researcher will document that consent was obtained from participants.

B Waiver Option 2

Check the box below for each item (all required – 1-3) and provide protocol-specific information as to how the criteria below are met.

1 ☐ **The study is minimal risk.**

i **Provide protocol specific information as to how this criterion is met.**

2 ☐ **Written consent would not be required outside the research context.**

i **Provide protocol specific information as to how this criterion is met.**

3 ☐ **Describe the mechanism for documenting that informed consent was obtained**

Briefly explain how the researcher will document that consent was obtained from participants.

i

C Waiver Option 3

Check the box below for each item (all required – 1-4) and provide protocol-specific information as to how the criteria below are met.

1 ☐ **The subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm**

i **Describe the cultural group or community.**

2 ☐ **The research presents no more than minimal risk of harm to subjects.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

3 ☐ **There is an appropriate alternative mechanism for documenting that informed consent was obtained.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

4 **Describe mechanism for documenting that informed consent was obtained**

To input text, click in the light grey area below

27 Waiver or Alteration of Informed Consent

Only complete this section if a waiver or alteration of consent is requested. *To approve a waiver or alteration of consent, all of the following criteria must be appropriate and justified by the researcher.* ***All boxes must be checked.*** *SKIP THIS SECTION IF NOT REQUESTING A WAIVER/ALTERATION OF CONSENT*

A ☒ **The research involves no more than minimal risk to the subjects.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

We are requesting an alteration of informed consent for the initial ED visit in order to not disclose the randomization and that half of the participants will be randomized to the intervention group and half will be randomized to the control group. Parents/caregivers will be approached and asked for permission/consent, but will only be told that the study is to improve the care for febrile infants presenting to the ED.

Both arms of this study are considered the standard of care at this institution and nationally. Some providers routinely provide prescriptions for these over-the-counter medications, others rarely or never do. There are various reasons for this variability including uncertainty of the utility of the prescriptions, cost of the prescriptions to the family and/or medical system, and variable coverage by insurance companies. This study will provide valuable insight to clarify this practice in the future.

B ☒ **The waiver or alteration will not adversely affect the rights and welfare of the subjects.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below.

As both arms of this study constitute the standard of care for febrile children presenting to the ED, no family will have their rights or care adversely affected by inclusion in this study. Parents/caregivers will be asked permission to participate in the overall research and be contacted within a week. The consent form includes as much information/required consent elements as possible without disclosing the randomization design. Collection of information about return visits and use of medications before

debriefing the caregiver about the randomization design will not adversely affect the rights and welfare of the subjects as the caregiver can still refuse to have their/their child's data used as part of the research study at that point.

It is very unlikely that the prescription would cost more than the OTC version of a medication, but parents/caregivers are free to purchase either. DCMC clinicians provide prescriptions hoping that insurance will cover it but understanding that parents will likely just purchase the OTC version if insurance does not. In all cases at DCMC, if a parent/caregiver has any financial concerns about medications or their child's care, they can be referred to case management for assistance.

C ☒ **The research could not practicably be carried out without the waiver or alteration (it is impracticable to perform the research if obtaining consent is required and not just impracticable to obtain consent).**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below.

The integrity of this study would be irrecoverably compromised if families were made aware of the other arm of the study or the full study purpose. We believe that both families and providers have strong opinions about receiving prescriptions for over-the-counter medications that may or may not be supported by data. This study aims to determine the objective benefit of these prescriptions as it relates to costly follow-up visits for febrile children, which requires blinding of the parents to the study objectives.

The gold standard study design for interventional clinical research is randomized and controlled. The reason for this is because non-randomization introduces confounding that often cannot be corrected and invalidates the study. This is the most appropriate design for a study like this as determined by our expert statistician. Similarly, consenting the patients for the randomization and including the full study purpose would introduce a potential for bias that could not be corrected at the analysis phase. The rights and welfare of patients and families in this standard of care comparative study will not be affected through the alteration of consent as explained throughout this protocol. Parents/caregivers who do not want to participate in research at all will be able to refuse participation at the initial encounter.

D ☒ **If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below.

In order to track these subjects after discharge to ascertain the primary endpoint we will need to collect identifiers such as name, parent name, MRN, and phone number. This information will be kept private and confidential throughout the study (see below).

28 Deception/Incomplete Disclosure and Debriefing

Only complete the sections below if requesting an alteration of informed consent for research that involves deception/incomplete disclosure.
Deception (as applies to research) means intentionally giving research subjects false information in order to establish false beliefs during the course of a research study.
Incomplete disclosure means that the principal investigator withholds some information about the real purpose of the study or the nature of the research procedures.
See IRB Policies and Procedures Section 15 for a description of deception.
If this study does not involve deception/incomplete disclosure, skip this section.

A ☒ **It is appropriate to provide additional pertinent information to the subject after research activities are complete (e.g., the researcher needed to deceive the subject to the nature of the study).**

B ☐ **Research participants will have the opportunity to withdraw their data during the debriefing.**

C **Describe the nature of deception/incomplete disclosure and why it is necessary to conduct the research.**

We are requesting an alteration of informed consent for the purposes of blinding the participant families to ensure the scientific integrity of the study results (see above). Parents/caregivers will still be able to accept or refuse participation in the overall research at the initial ED encounter. Once the parent/caregiver is debriefed at the follow-up call, permission will be obtained for the continued use of the child's health data for the study and for the parent/caregiver responses about follow-up visits.

D **Describe debriefing procedures.**

To input text, click in the light grey area below. ***NOTE: Upload the debriefing form to UTRMS-IRB in the "Consent Forms" section.***

During the follow-up phone call the families will be informed about the randomization component of the study. They will be offered the opportunity to opt out of the study at this time. If they opt out, the data will be kept but not included in the final analysis. Only after ascertainment of the primary and secondary endpoints will families be informed about the randomization into either of the two arms (again to ensure blinding for integrity of the endpoints).

BENEFITS

29 Benefits to Society

Describe the scientific and societal benefit(s) below.

The potential benefit of this study would be the identification of a superior outpatient discharge process/instruction for pediatric fever. If the prescription does not prove beneficial then we could potentially save resources for the medical system through decreased provider time and reduced unnecessary prescribing.

30 Potential Direct Benefits to Participants

Click on the applicable check box. A or B must be checked.

A ☒ **There is no anticipated direct benefit to participants.**

B ☐ **There are anticipated benefits to participants.**

i **If applicable, describe the potential direct benefits to participants.**

RISKS

31 Describe the risks associated with each activity in this research

To input text, click in the light grey area below. Note: Risks should also be outlined in the consent form(s).

The primary risk is loss of confidentiality.

There are also potential risks of side effects related to use of acetaminophen or ibuprofen, including upset stomach. Acetaminophen may cause severe skin reactions. Symptoms may include skin reddening, blisters, rash. Severe liver damage may occur if a child takes more than 5 doses of acetaminophen in 24 hours or with other drugs that contain acetaminophen. Ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include hives, facial swelling, asthma (wheezing), shock, skin reddening, rash, blisters. Ibuprofen can also cause stomach bleeding if a child has/had stomach ulcers or bleeding problems, takes a blood thinning (anticoagulant) or steroid drug, takes other drugs containing prescription or nonprescription non-steroidal anti-inflammatory drugs (NSAIDs; aspirin, ibuprofen, naproxen, or others).

Most children given acetaminophen or ibuprofen will not have side effects, however. It is standard practice for all febrile children to be advised by their provider to take these medications.

32 Describe how each risk is mitigated/minimized.

Note: Risks mitigation should be outlined in the consent form(s), as applicable.

The parent/guardian can discontinue use of acetaminophen/ibuprofen if their child has side effects from the treatment and/or they are uncomfortable continuing with the treatment. The risk of loss of confidentiality does exist but will be minimized with previously mentioned data protection procedures and de-identification plans.

33 Data Safety Monitoring

For additional information regarding data safety monitoring boards and data safety monitoring plans, please see Section 21 of our Policies and Procedures. One of the following must be checked (A, B, or C).

A ☒ **In the investigator's opinion, this study is minimal risk and does not require a Data Safety Monitoring Plan (DSMP) or a Data Safety Monitoring Board (DMSB).**

PLEASE NOTE: The IRB may determine minimal risk studies do require data safety monitoring under certain circumstances (e.g., if there is a known risk with an expected frequency).

B ☐ **This study does not have a Data Safety Monitoring Board, but**

researchers have an internal plan to monitor for safety (Data Safety Monitoring Plan (DSMP)).

Complete Data Safety Monitoring Details

C ☐ **This study has a Data Safety Monitoring Board (DSMB).**

*Complete Data Safety Monitoring Details section below **or** upload this study's Data Safety Monitoring Board's charter that contains the information below.*

34 Data Safety Monitoring (Details)

*Complete this section if the study has a Data Safety Monitoring Plan. **SKIP this section there is not a DSMP/DSMB.** If the study has a DSMB, ensure all items below are addressed in the charter (and charted uploaded to UTRMS-IRB) or provide additional information below, as needed.*

A How is safety information collected?

B When will safety data collection start (for each participant or for the whole study, as applicable)?

C How frequently will safety data be collected?

D Who will review the data for safety?

E How frequently will data be monitored for safety concerns?

F What data will be reviewed?

G State the frequency or periodicity of the review of cumulative data.

H State any conditions that would trigger an immediate suspension of the research.

35 Early Withdrawal

***Only complete this section if there are planned conditions under which a participant will be withdrawn from the study.** If not applicable, skip to next section. Include this information in your consent form.*

A List the criteria for withdrawing individual participants from the study (e.g., safety or toxicity concerns, emotional distress, inability to comply with the protocol, or requirements from study sponsor).

Not applicable.

B Describe any necessary procedures for ensuring the safety of a participant

who has withdrawn early.

Not applicable

36 **Describe any pre-specified criteria for stopping or changing the study protocol due to safety concerns.**

Not applicable

REQUIRED DISCLOSURES

37 **Required Consent Disclosures**

Identify each element below that may require additional information to be disclosed in the consent form.

A ☐ **It is reasonable that researchers could discover or suspect child or elder abuse.**

Add appropriate disclosure in consent form(s).

B ☐ **It is reasonable that researchers could learn of an incident that could require reporting under Title IX.**

Add appropriate disclosure in consent form(s). See Title IX and Research Guidance for information and download the Title IX Reporting Form on the Special Topics page.

C ☐ **It is reasonable that researchers could discover incidental findings or other information of medical interest about a participant's previously unknown condition.**

Add appropriate language to consent form(s).

i **Articulate methods for addressing and reporting incidental findings, if applicable.**

Ensure appropriate information is in consent form(s), as applicable.

PRIVACY AND CONFIDENTIALITY

38 **Privacy**

Describe how you will protect the identity and privacy of study participants during each phase of research. Privacy focuses on the individual participants rather than data. In this section, researchers should focus on issues such as where research activities take place and how participant involvement is protected from non-participants. Describe methods to ensure participants' privacy during identification, recruitment, screening, the consent process, the conduct of the study, and dissemination of data.

Data will be stored in a secure electronic database which will be password protected and stored on a secure network. Data will be de-identified after the data preparation and collection stage. A unique ID number will be assigned to each subject included in the study. The PI will maintain a list correlating patient medical record numbers to the unique ID numbers in order to assist in quality control of the data. This file will be stored separately from the health information in the analysis file. All data will be analyzed in a de-identified format. Identifiers will be destroyed on study closure. The

data from this study may be published, but the subject identities will not be disclosed.

To protect participant privacy, all study activities, including recruitment, consent/parental permission, phone calls and chart reviews, will be conducted in private patient rooms or in locked, private, single offices at Dell Children's Medical Center. All calls and chart reviews will be conducted in a manner and location that others will not be able to hear or see what is being done.

39 Confidentiality and Data Security Plan

Provide general information below regarding confidentiality and data security plan. Provide additional details regarding how you will protect the confidentiality of data or address confidentiality concerns.
Include the following, as applicable:

- *If identifiers will be coded to protect confidentiality describe how and where identifiers are stored.*
- *Describe where and how data is stored and maintained.*
- *Include details regarding storage of consent forms, if applicable.*

Data will be de-identified after the data preparation and collection stage. A unique ID number will be assigned to each subject included in the study. The PI will maintain a list correlating patient medical record numbers to the unique ID numbers in order to assist in quality control of the data. This file will be stored separately from the health information in the analysis file.

40 Research Data/Records Destruction Details

Confirm general research data/information (including consent forms, as applicable) destruction timeline. ***One of the following must be checked.***

☐ **Research Data/Records will be retained for 3 years after study completion per UT record retention policy.**

☒ **Research Data/Records will be retained for longer than 3 years and retention information is provided below.**

Describe data retention timeline below. To input text, click in the light grey area below.

HIPAA regulations require records to be maintained for 6 years after study completion.

41 Confirm identifiable data destruction details

One of the following must be checked.

☒ **Identifiable data will be destroyed.**

If checked, ensure the below section describes identifiable data destruction plan and timeline.

All identifiable data will be destroyed upon completion of the study. Paper documents with any identifiable information will be securely shredded. Electronic files will be deleted with eraser software by Ascension IT services. Consent forms will be retained according to federal law and University of Texas policy.

☐ **Identifiable data will not be destroyed.**

If checked, explain below the rationale for retaining identifiable data indefinitely.

42 Data Access

Click on the check box (or double click and type an "X" if using Google Docs) for each group of individuals that will have access to study data. If you plan on creating a repository, complete the repository form as well (download from Library in UTRMS-IRB).

☒	**Study Team Members**	☐	**External Collaborators**	☐	**Data coordinating center**
☐	**Sponsor**	☐	**Future Sharing with other researchers**		

☐ **Others**

Describe below. To input text, click in the light grey area below.

43 **Describe data sharing plan for each group checked above and state whether researchers plan on sharing identifiable, coded, or de-identified data.**

To input text, click in the light grey area below. Ensure that data sharing and future use is addressed in the consent form(s).

Only study team members (affiliated with both Ascension Texas and UT Austin) will have access to the data.

44 **Certificate of Confidentiality**

Click on the check box to identify each element below that may require additional information to be disclosed in the consent form. ***If a Certificate of Confidentiality is not applicable for this study, skip this section.***

A ☐ **NIH has issued a Certificate of Confidentiality for this study.**

Ensure CoC language is included in the consent form(s).

B ☐ **A Certificate of Confidentiality has not been obtained, but there are plans to apply for one.**

Ensure appropriate CoC language is included in consent form(s). Apply for a CoC for non-NIH funded research here: NIH Certificate of Confidentiality System. Once CoC is granted by NIH, you must update the consent form language and ensure a copy of the CoC approval (only for non-NIH funded research) is uploaded to UTRMS-IRB.

COMPENSATION AND COSTS

45 **Compensation**

Click on the check box (or double click and type an "X" if using Google Docs). A or B must be checked.

A ☐ **Subjects receive compensation.**

I ☐ **Confirm: Amount of compensation and its form is reasonable for this population for the activities requested of them.**

ii **Total Amount of Compensation**

Include the total amount of compensation below.

iii **Type of Compensation**

☐ Cash ☐ Check ☐ Gift Card

☐ Course Credit ☐ ClinCard ☐ Tango Card

☐ Other

Describe other form of compensation below.

iv **Proration Schedule**

Describe the proration schedule for multi-visit/session studies. Skip if not applicable.

B ☒ **Subjects will not receive compensation.**

46 **Costs**

A ☐ **Participants will have no costs associated with this study**

B ☒ **Participants will have the following costs associated with this study.**

☒ **Standard of care procedures contributing to study data** ☐ **Research procedures not associated with standard of care**

☐ **Administration of drugs / devices** ☐ **Study drugs or devices**

☐ **Transportation and parking**

i **Describe all costs below.**

To input text, click in the light grey area below.

It is very unlikely that the prescription would cost more than the OTC version of a medication, but parents/caregivers are free to purchase either. DCMC clinicians provide prescriptions hoping that insurance will cover it but understanding that parents will likely just purchase the OTC version if insurance does not. In all cases at DCMC, if a parent/caregiver has any financial concerns about medications or their child's care, they can be referred to case management for assistance

CONFLICTS OF INTEREST

*This section is **required** for all studies. Please confirm that all research personnel who meet the definition of "covered individuals" are designated as such in the* Local Study Team Members *section of the SmartForm application in UTRMS-IRB.*

47 **Financial Conflicts of Interest**

Financial interest includes utilizing your licensed intellectual property in the study; serving as a paid consultant, or advisory board member, or officer/director with a related entity; and equity or business ownership in a

company that is related to this project. Additional guidance on financial conflicts of interest is available on the [COI website]

A ☐ **The PI and/or other covered individual(s) has/have a financial interest related to this study**

i **If A is checked above, please provide the name(s) of the covered individuals involved, and briefly describe the interest:**

To input text, click in the light grey area below.

B ☒ **To the best of your knowledge, no one on the study team has financial interest related to this study**

48 Non-financial Conflicts of Interest

Non-financial Interests could include such things as:
- utilizing your unlicensed intellectual property in the study,
- serving as an unpaid advisory board member or officer/director with a related entity,
- equity or business ownership in a company that has yet to make a profit and is related to this project,
- conflict of time/effort,
- personal and professional relationships/affiliations,
- intellectual passions or personal beliefs
- other factors that could create bias in the study

A ☐ **The PI and/or other covered individual(s) has/have a non-financial interest related to this study**

i **If A is checked above, please provide the name(s) of the covered individuals involved, and briefly describe the interest:**

B ☒ **To the best of your knowledge, no one on the study team has non-financial interest related to this study**