PROTOCOL TITLE:

Decreasing Antibiotic Duration for Skin and Soft Tissue Infections in Pediatric Primary Care Using Behavioral Economics Methods, A Cluster Randomized Trial

PRINCIPAL INVESTIGATOR:

Name: Joshua Watson, MD

Co-I: Kali Broussard, MD (Person of contact)
Department/Center: Pediatrics, Infectious Diseases
Telephone Number: 614-722-4450
Email Address: kali.broussard@nationwidechildrens.org
Joshua.watson@nationwidechildrens.org

VERSION NUMBER/DATE:

V2.0 9-2-2021

Revision History

Revision #	Version Date	Summary of Changes	Consent Change?
1	7/27/21	Education	n
2	9/2/21	Subjects	n

1.0 Study Summary

Study Title	Decreasing Antibiotic Duration for Skin and Soft Tissue Infections in Pediatric Primary Care Using Behavioral Economics Methods, A Cluster Randomized Trial
Study Design	Cluster, Randomized, Control
Primary Objective	Study the efficacy of a package of behavioral economics strategies (versus an education-only control condition) in altering clinician behavior regarding antibiotic prescription duration for skin and soft tissue infection (SSTI).
Secondary Objective(s)	Analyze patient and prescriber characteristics which affect long vs short duration of antibiotics for uncomplicated SSTI
Research Intervention(s)/ Investigational Agent(s)	Behavioral economics package of Epic order panel with default treatment duration, plus accountable justification
IND/IDE #	n/a
Study Population	Primary care patients with diagnosis of SSTI and prescription for enteral antibiotics, NCH primary care providers, henceforth referred to as "clinician prescribers"
Sample Size	1000 patients (with SSTI encounters including 600 antibiotic prescriptions), 98 clinician prescribers
Study Duration for individual participants	12-16 months
Study Specific Abbreviations/ Definitions	SSTI (skin and soft tissue infection), BE (behavioral economics), PCC (primary care clinics)

2.0 Methods

2.1 The 14 NCH primary care clinics will be distributed into five geographic "regions." Regions will be randomly assigned to the intervention condition or control condition. A region refers to a localized geographical zone within the greater Columbus area in which a NCH primary care pediatrician restricts her/his practice to a small number of clinics. All clinics (intervention and control) will receive baseline education regarding prescribing guidelines and release of a new Epic order panel. All 14 clinics will receive baseline education (control condition) about common infections and local and national guidelines for antibiotic choice and duration of treatment. Clinician prescribers will also be instructed about the presence of a new Epic order panel. The SSTI order panel will present itself when a clinician prescriber types in either a

preferred drug name (cephalexin, clindamycin, TMP-SMX) or diagnosis (cellulitis, impetigo, etc). All clinician prescribers within primary care clinics will have access to these order panels, however the order panel will vary in functionality based on control vs intervention clinic. For control clinics, the order panel will include diagnosis and drug name only- antibiotic duration must be then determined by the clinician prescriber at the time of the visit. Within intervention clinics, the Epic order panel will include prepopulated default "short" duration antibiotic days based on diagnosis chosen. Short antibiotic duration is defined as 5 days or fewer for cellulitis or drained abscess and 7 days for impetigo or undrained abscess. This- full functionality, default short duration- order panel will only be released to intervention clinics. We hypothesize that clinics with the intervention will have higher rates of short course antibiotics for SSTI versus control clinics. In addition, those randomized to the study intervention sites will receive the following behavioral economic strategies: (1) Epic order panel for cellulitis, impetigo, and abscess with prepopulated duration fields regarding prescriptions; (2) accountable justifications to document reasoning (in a free text field) when the default duration is overridden; and (3) visual reminders placed in intervention clinics about the available Epic order panel. Encounter data for specific diagnosis codes with skin and soft tissue infections will then be collected and analyzed to include clinic location, patient demographics and presenting clinical characteristics, diagnoses, antibiotic treatment (name, dose, duration), and clinician prescriber names. Prescriptions for systemic antibiotics for the selected diagnoses will be reviewed and analyzed for rates of long and short course antibiotics. Rates of short and long antibiotics will be compared between the intervention and control groups.

An education session (virtual via department meeting) will be provided at start of study to all clinics. The education session will include a succinct overview of current local and national treatment guidelines for SSTI. These guidelines include the 5-day and 7-day recommended durations mentioned in the previous paragraph. All clinics will be informed of the presence of order panel for diagnoses of interest. The information included in the order panel will vary based on whether a clinic resides in the control or intervention group. Control order panel will include only antibiotic names and doses. Intervention order panel will include default duration based on SSTI diagnosis.

For the secondary objective, patient demographic and clinical characteristics and clinician prescriber characteristics will be analyzed to determine which factors impact short versus long antibiotic treatment duration.

2.2 Clinician prescribers will provide prescriptions to patients for SSTI based on previously published national and local guidelines as well as prescriber preference/practice. Patients in primary care clinics receiving antibiotic prescriptions for SSTI will also serve as study subjects. No additional risks are incurred by subjects (clinician prescribers and patients) by participation in this study. For clinician prescribers in clinics randomized to the intervention group, use of the Epic order panel will be optional. Patients receiving care for SSTI in the NCH primary care clinics will receive no more than minimal risks as clinician prescribers will be providing treatment for SSTI as previously done, except for the optional use of the order panel. The study involves no direct interaction with clinic patients, and implementation of the BE interventions does not increase risks associated with treatment of SSTI.

2.3 This study will utilize an existing retrospective and ongoing prospective dataset created by Quality Improvement Services for the routine activities of the NCH Antimicrobial Stewardship Program. All data is queried from Epic. Clinician prescriber and patient information for encounters with the following diagnosis codes will be obtained: A46 (cellulitis), L03 (cellulitis and acute lymphangitis), J34 or L02 (abscess, furuncle), or L01 (impetigo). Data from encounters for the aforementioned diagnoses will be collected if patients are 3 months of age (at minimum) and prescribed enteral antibiotics. The following encounters will be excluded: animal or human bite wound, immunocompromised patients, a concomitant non-SSTI diagnosis treated with an antibiotic during the same encounter, or an SSTI visit in the 7 days prior to the index encounter. Patient data collected will encompass patient demographics, clinical signs and symptoms, diagnosis codes, available culture data, antibiotic treatment (name, route, and duration), and clinician prescriber name.

Clinician prescriber characteristics and demographics will be obtained from NCH website/intranet by manual extraction by primary investigators.

2.4 Source records include the aforementioned monthly report from QIS (extracted from Epic) and manual chart review.

3.0 Data Banking

3.1 Data will be stored in a password-protected file on a secure NCH drive for at least 6 years after completion of the study and after publication of the study, and accessed only by principle investigators and co-investigators listed on the IRB.

3.2 We plan to use the data only for the study described in this protocol. We will not release any data to other individuals without prior approval from the IRB. Future research using the same data will prompt an addendum to this protocol or submission of a new IRB.

4.0 Inclusion and Exclusion Criteria

4.1 NCH Primary Care clinic patients to which enteral antibiotics are prescribed for the diagnoses below (see section 4.2) and corresponding clinician prescribers of antibiotics for SSTI (cellulitis, abscess, impetigo) in NCH PCCs will be included within the study. Clinicians who begin work in PCCs on or after August 1, 2021 until March 2023 will be included.

4.2 Encounters to be included will be those with patients age 3 months and older *AND* with diagnosis codes A46 (cellulitis), L03 (cellulitis and acute lymphangitis), J34 or L02 (abscess, furuncle), or L01 (impetigo) *AND* those who received a prescription for an enteral antibiotic. The following encounters will be excluded: animal or human bite wound, immunocompromised patients, a concomitant non-SSTI diagnosis treated with an antibiotic during the same encounter, or an SSTI visit in the 7 days prior to the index encounter.

5.0 Vulnerable Populations

5.1 Primary care clinic patients, which will include patients over the age of 3 months.

6.0 Number of Subjects (Records)

6.1 Since this study includes patient encounters throughout the NCH primary care network, all clinicians who see patients in the NCH primary care clinics will be included. Currently, there are 98 clinician prescribers who will be included within the study. New clinicians who are hired during the study will be included as well. Based on retrospective data of the previous 12 months, there were approximately 1000 encounters (including information about the patients for these encounters) with just over 600 systemic antibiotic prescriptions. Based on this data, we expect there will be a similar number of encounters and antibiotic prescriptions which would meet inclusion for this study. Assuming an encounter/prescription sample size of 600 (300 intervention, 300 control), power analysis demonstrated greater than 80% power to detect an 11.24% or greater absolute difference in the rate of short-course prescriptions between intervention and control, with a 5% type I error rate (alpha= 0.05), assuming a baseline 53% short-course prescription rate in the control group.

7.0 Recruitment Methods

7.1 Patients with diagnoses of interests and prescribed enteral antibiotics and the corresponding clinician prescribers from NCH Primary Care clinics will be included in study protocol. No active recruitment will

be performed. NCH Primary Care Pediatrics leadership- Alex Kemper, MD, Division Chief and Dane Snyder, MD, Section Chief, have been informed about this potential research project and are supportive of the proposed work.

7.2 The behavioral interventions will be implemented at the clinic level, thus all clinicians in the NCH primary care network will be included.

7.3 Patient's receipt of enteral antibiotics for diagnoses of interest (see section 4.2) will qualify a patient for inclusion in the study. Active clinic participation (providing direct clinical care and/or supervision to trainees) and prescribing will qualify clinician prescribers for inclusion in study.

7.4 No recruitment materials

7.5 No payment will be provided for study participation.

8.0 Withdrawal of Subjects

8.1 Because this study will randomize at the level of a group of clinics (regions) with minimal risk to clinician prescribers and no direct interaction with patients, we are requesting a waiver of informed consent. Thus, clinician prescribers will not be able to withdraw from the research except by ending their employment in the NCH PCCs as standard of care clinicians. The interventions in the study include education and order panels, which clinicians are not forced to use. Encounter data from each clinician will be analyzed by quadrant. Clinician prescribers who end their employment in the NCH PCCs during the study, the data for their SSTI encounters will be continue to be included.

9.0 Data Management and Confidentiality

9.1.1 Password-protected excel file of study data will be stored on a secure NCH drive.

9.1.2 Data to be stored until the publication of the research and a minimum of 6 years after the completion of the study

9.1.3 Only investigators included on IRB will have access to study data.

9.1.4 Data will not be transmitted to or from external institutions.

9.1.5 Data will not be transmitted

10.0 Provisions to Protect the Privacy Interests of Subjects

10.1 For clinician prescribers, any personal information used in the study will be that information publically available on the NCH website (e.g. details of medical training). There will be no direct interaction with patients in this study.

10.2 n/a

10.3 Information about clinician prescribers will be obtained from the NCH website, this is publicly published data. For patients, the research team will only access information available in Epic. Patient name will not be recorded. Patients will not be contacted by the research team.

11.0 Economic Burden to Subjects

11.1 There is no additional economic burden bestowed upon subjects based on inclusion in study.

11.2 Subjects will receive no compensation for study participation.

12.0 Consent Process

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

12.1.1 We believe this study meets the criteria for waiver of consent. The study involves no more than minimal risk to subjects and the BE interventions are not compulsory. Because the BE interventions will be randomized at the region (ie, group of clinics) level, it could not be practicably carried out by obtaining the informed consent of each individual clinician prescriber or each patient with the qualifying condition (SSTI diagnosis and receipt of enteral antibiotic).

13.0 Setting

13.1.1 Primary care clinic patient with SSTI diagnoses and receipt of enteral antibiotic with corresponding clinician prescribers working the NCH primary care clinics will be the subjects for this study. The study does not involve recruitment of potential subjects.

13.1.2 All study activities will occur in the NCH PCCs.

14.0 Resources Available

14.1 By default, practice within NCH PCCs will enroll clinician prescribers into this research study. There are 98 clinician prescribers active within NCH PCCs at this time and. See section 6.1 for a description of the sample size analysis. Based on preliminary data, we should be able to include the necessary number of encounters/patients (up to 1000 encounters) within 12-16 months.

14.1.1 This study, its implementation, data collection, and analysis as well as publication of results are the main scholarly project for infectious diseases fellowship of principle investigator, K. Broussard, MD. Over the next two years, ~75% of Dr.

Broussard's time will be devoted to conducting this project and formulating a manuscript of the results.

14.1.2 The study includes the 14 NCH Primary care clinics.

14.1.3 Participants may access medical and psychological resources provided to all NCH employees as outlines by NCH Health and Wellness department. No additional resources are provided to study subjects through our study protocol.

14.1.4 Individuals involved with study design, research procedures, educational sessions, and data analysis are involved in current IRB and aware of study protocol. Information has been provided verbally in research meetings and in print form by distribution of this research protocol.

15.0 Protected Health Information Recording

1.0 Indicate which subject identifiers will be recorded for this research.

☐ Name
☐ Complete Address
☐ Telephone or Fax Number
☐ Social Security Number (do not check if only used for ClinCard)
☒ Dates (treatment dates, birth date, date of death)
☐ Email address , IP address or url
☒ Medical Record Number or other account number
☐ Health Plan Beneficiary Identification Number
☐ Full face photographic images and/or any comparable images (x-rays)
☐ Account Numbers
☐ Certificate/License Numbers
☐ Vehicle Identifiers and Serial Numbers (e.g. VINs, License Plate Numbers)
☐ Device Identifiers and Serial Numbers
☐ Biometric identifiers, including finger and voice prints
☐ Other number, characteristic or code that could be used to identify an individual
☐ None (Complete De-identification Certification Form)

2.0 Check the appropriate category and attach the required form* on the Local Site Documents, #3. Other Documents, page of the application. (Choose one.)

☐ Patient Authorization will be obtained. (Include the appropriate HIPAA language (see Section 14 of consent template) in the consent form OR attach the HRP-900, HIPAA AUTHORIZATION form.)
☒ Protocol meets the criteria for waiver of authorization. (Attach the HRP-901, WAIVER OF HIPAA AUTHORIZATION REQUEST form.)

- ☐ Protocol is using de-identified information. (Attach the HRP-902, DE-IDENTIFICATION CERTIFICATION form.) (Checked "None" in 1.0 above)
- ☐ Protocol involves research on decedents. (Attach the HRP-903, RESEARCH ON DECEDENTS REQUEST form.)
- ☐ Protocol is using a limited data set and data use agreement. (Contact the Office of Technology Commercialization to initiate a Limited Data Use Agreement.

*Find the HIPAA forms in the IRB Website Library, Templates.

Attach the appropriate HIPAA form on the "Local Site Documents, #3. Other Documents", page of the application.

3.0 How long will identifying information on each participant be maintained? At least 6 years after the completion of the study

4.0 Describe any plans to code identifiable information collected about each participant. Identifiable information will be coded prior to sending data for statistical analysis.

5.0 Check each box that describes steps that will be taken to safeguard the confidentiality of information collected for this research:
Research records will be stored in a locked cabinet in a secure location
x- Research records will be stored in a password-protected computer file
The list linking the assigned code number to the individual subject will be maintained separately from the other research data
x- Only certified research personnel will be given access to identifiable subject information

6.0 Describe the provisions included in the protocol to protect the privacy interests of subjects, where "privacy interests" refer to the interest of individuals in being left alone, limiting access to them, and limiting access to their information. (This is not the same provision to maintain the confidentiality of data.) No personal information will be obtained about subjects (clinician prescribers) which is not already public domain (published on NCH website). There will be no direct interaction with patients, and only study investigators will have access to patient information.

Confidential Health Information

1.0 Please mark all categories that reflect the nature of health information to be accessed and used as part of this research.

- ☒ Demographics (age, gender, educational level)
- ☒ Diagnosis
- ☒ Laboratory reports
- ☒ Radiology reports
- ☐ Discharge summaries
- ☒ Procedures/Treatments received
- ☒ Dates related to course of treatment (admission, surgery, discharge)
- ☐ Billing information
- ☒ Names of drugs and/or devices used as part of treatment
- ☒ Location of treatment
- ☒ Name of treatment provider
- ☐ Surgical reports
- ☒ Other information related to course of treatment
- ☐ None

2.0 Please discuss why it is necessary to access and review the health information noted in your response above. Analysis of prescriptions and duration of antibiotics for study diagnosis codes are necessary for the main portion of our study. Procedure data is needed to know if abscess was drained or not (to determine if guideline-concordant antibiotic duration provided). Demographics of patients will allow us to analyze what patient factors are associated with short vs long antibiotic durations for SSTI. Provider name and location of treatment will allow analysis of antibiotic duration on the provider and clinic level respectively.

3.0 Is the health information to be accessed and reviewed the minimal necessary to achieve the goals of this research? ☒ Yes ☐ No

4.0 Will it be necessary to record information of a sensitive nature? ☐ Yes ☒ No

5.0 Do you plan to obtain a federally-issued Certificate of Confidentiality as a means of protecting the confidentiality of the information collected? ☐ Yes ☒ No