An Enhanced Home-Based Telemedicine Program Using Remote Examination Devices for Children with Medical Complexity: a Quality Improvement Project

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Protocol Title:	**An Enhanced Home-Based Telemedicine Program Using Remote Examination Devices for Children with Medical Complexity: a Quality Improvement Project**
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Population:	Children currently attending the UT High-Risk Children's Clinic
Number of Sites:	Single site
Study Duration:	10 months
Subject Duration:	10 months

PROJECT OVERVIEW

Optimizing the value of telemedicine is crucial to minimize exposure to infections and adverse outcomes among children with medical complexity **(CMC**) who account for~40-50% of pediatric deaths & hospital costs. Our recent Bayesian randomized quality improvement (QI) trial showed that a conventional clinic-based telemedicine program (**CTM**, video and audio) likely reduced serious illnesses and health system costs[1] as well as days of care outside the home. We now propose a randomized QI study in CMC to assess whether these outcomes are further improved by an enhanced telemedicine program (**ETM**) provided during clinic hours with mobile devices to measure temperature & oxygen saturation, auscultate the heart & lungs, and view the skin, throat, & tympanic Confirmation that the ETM program improves care and is cost effective in reducing total days of care in a medical setting will provide a strong basis to justify reimbursements and further grant funding to enable broader, sustainable adoption of ETM for CMC in other centers.

Specific Aims. We will conduct a 10-month Bayesian randomized QI study for the purpose of assessing the following study question: Will the benefits for CMC indicated above be further improved by ETM provided during clinic hours using mobile devices to measure temperature& oxygen saturation, auscultate the heart & lungs, and view the skin, throat, & tympanic

membranes in the home? We will test the hypotheses listed below[1] in a study in which 300 eligible CMC at UT Houston will be randomized at the study outset to receive either ETM (n=100) or CTM (n=200) .

- **Primary Hypothesis.** We will identify a >85% probability that ETM will reduce total days of care in a medical setting (in any clinic, ED or hospital; primary outcome) below that with CTM.
- **Secondary Hypotheses.** With the sample size assessable with the available funds, we will identify a:

  A) >67% probability that ETM will reduce serious illnesses (illnesses causing death, pediatric ICU admissions, or >7 d hospital stay) below that with CTM.

  B) >67% probability that ETM will be cost effective in reducing serious illnesses. Cost effectiveness is defined strictly in this study as reducing serious illnesses without increasing health system costs, reducing health system costs without increasing serious illnesses, or reducing both serious illnesses and health system costs. The demonstration of cost effectiveness may be particularly important to securing adequate third-party funding to enable broader, sustainable adoption of ETMfor CMC in other centers.

  C) ETM will be shown to be acceptable if not preferred to CTM by parents & caregivers as shown by a:

  1) > 67% probability that ETM increases parent ratings of care assessed using 5 questions of the Consumer Assessment of Healthcare Providers and Systems Child (**CAPHS**) 12-Month Survey preselected as most important in optimizing patient outcomes.[1]
  2) >80% probability that ETM involves less or comparable (less than 10% greater) total PCP time than that with CTM (counting time saved for clinic visits, after hours calls, and hospital consultation).
  3) >80% probability that PCPs as well as parents surveyed at the beginning and end of the study in the ETM group will express increase in satisfaction with use of ETM at trial's end.

SIGNIFICANCE

The high risk of our CMC. Overall, CMC account for 0.4% of children but ~40-50% of pediatric deaths & hospital costs.[1-4] While CMC have been variably defined,[4] our program provides a medical home for particularly high risk CMC. They must have one or more chronic illnesses, ≥ 2 hospitalizations or ≥1 pediatric ICU admission in the year before enrolling in our program, and a >50% estimated risk of hospitalization in the following year without our care; 79% of our CMC are Black or Hispanic; 88% are Medicaid insured; 90% are followed by ≥2 specialists, 25% require ongoing mechanical ventilation, and all have multiple chronic conditions.[1-3, 5, 6] Despite our multiple trials that have progressively improved their care and outcomes, [1-3, 5, 6] they remain at high risk for serious illnesses prolonged hospital stay, pediatric ICU admissions, or death. Such CMC are the kind emphasized by Schwenk to focus on the most complex and expensive patients and develop better methods to advance their care provided in medical homes. [7] Houston is now the most diverse city in the United States and is viewed as most like future cities in the U.S..[8] For this reason, it is particularly important to assess the effect of ETM on our CMC.

Telemedicine (TM) as a major gap in the literature. TM might be highly beneficial to reduce CMC exposures to COVID-19 or other potentially life-threatening infections and augment care in the home particularly for CMC whose families have financial, transportation, or language problems and face health system barriers. For these reasons, TM has been rapidly and widely implemented during the COVID-19 pandemic with a paucity of well-designed studies.[9] The four trials identified in a recent systematic review of TM for CMC [9] were all small and none identified improved medical outcomes. To our knowledge, our prior QI trial described below is the largest and first to identify clinical benefits and cost savings from CTM for CMC, and the trial we propose will be the first to both assess and compare an ETM program vs conventional TM for CMC.

BACKGROUND AND PRELIMINARY STUDIES

Experience in conducting rigorous and innovative research to improve CMC outcomes. Our prior studies using either a parallel- group or a stepped-wedge randomized design have demonstrated progressive improvements in outcomes for CMC and have been published in respected journals (JAMA, JAMA Pediatrics, J.Pediatrics, and Pediatrics). [1, 3, 6, 10] These include studies with important cost effectiveness analyses [1, 3, 6, 10] that among other benefits have helped secure support for our comprehensive care program for CMC. Our investigators also have expertise in the use of Bayesian designs and analyses in studies of

CMC [1, 3, 6, 10] and other populations[11-21] As discussed elsewhere, [10] Bayesian methods are increasingly used to clinical trials to avoid the pervasive misinterpretation of frequentist statistics [22, 23] and provide a formal method to directly estimate the probability of treatment benefit or harm.[24-26] These advantages are particularly important in studies using a limited sample size like the QI trial we propose.[27]

Success in conducting a previous randomized QI study of CTM for CMC. In this QI trial,[1] n= 422 CMC, CTM was provided with comprehensive outpatient care during regular clinic hours and compared to comprehensive care without CTM. In conservative intent-to-treat Bayesian analyses (using a neutral prior probability assuming no benefit), the (posterior) probability that the addition of CTM reduced total days of care outside the home was 99% (12.94 vs.16.94 per child-years; Bayesian rate ratio [**RR**], 0.80 (Bayesian 95% Credible Interval, 0.66-0.98). Multiple other outcomes also favored the CTM group including a 98% probability of a reduction in episodes of serious illness (0.29 vs. 0.62 per child-years; 0.68 [0.43-1.07]), and a 91% probability of a reduction in mean total health system costs (US$33,718 vs. US$41,281 per child-year; Bayesian cost ratio, 0.85 [0.67-1.08]).[8]

These results were obtained despite the original skepticism of our personnel that telemedicine would add many benefits to comprehensive care. This trial was conducted between 8/22/2018 and 3/23/2020 and stopped early when it met predefined Bayesian stopping rules shortly before COVID-19 was identified in any CMC in Houston.

Basis for the ETM intervention for high-risk CMC. Our goals in using ETM are to minimize exposure to COVID-19 and other communicable diseases in medical settings, increase convenience for the family, augment diagnosis and care for sick CMC, avoid lapses or errors in treatment, and reduce both serious illnesses and costs to the health system. As described below, ETM involves using FDA-approved, HIPAA compliant, mobile devices in the home (TytoCare™) to visualize the skin, throat, & ears, auscultate the heart & lungs, and measure temperature & oxygen saturation. This product received a 2019 Best Award from the Consumer Technology Association and a 2019 Time Magazine Best Invention Award. [28] According to the manufacturer, is now widely used in healthcare institutions, such as the Ochsner Health System. The feasibility of using these devices in the homes of CMC was demonstrated in a small randomized trial (n=24) in which connectivity was successful 96% of the time, the image and sound quality was acceptable 98% of the time, and a reduction in hospital costs was also identified.[29] In our prior QI study of TM, only two CMC (out of the 209 assigned to telemedicine) were unable to use telemedicine because of lack of Internet access or a smartphone.[1]

To verify that the feasibility, connectivity, and image and sound quality documented in the above study could be achieved in our patients, we piloted the TytoCare device in 10 typical CMC in our program. Both caregivers and clinicians reported that the devices are easy to use. The auscultation component filters out background noise providing high-quality sound, the tympanic membranes are well-visualized, and the oral examination device has a built-in tongue blade, allowing the caregiver to more easily perform an examination on childdren who may not be able to follow directions to open their mouth. We found no difficulties using these.

METHODS AND ANALYSIS PLAN

Eligibility criteria CMC must be <18 years old and have a chronic illness, ≥ 2 hospitalizations or ≥1 ICU admission in the year before joining our clinic, & a >50% estimated risk of hospitalization without our care.[4]

Randomization. As allowed under federal regulations[14, 15] and approved for our prior CTM study, we expect our IRB to approve waiver of consent for this minimal risk quality improvement study without adequate funding to provide ETM to all eligible CMC. We can then randomize our CMC at the study outset to either ETM or CTM using a computer-generated algorithm and variable block sizes in REDCap. With the funds provided, we can assign up to 100 patients to the ETM group. With 300 CMC in our program, we can then assign 200 to the CTM group. While most trials use a 1:1 randomization ratio, a 1: 2 ratio can afford greater statistical power and a more precise estimate of the treatment effect at a fixed study budget when the intervention (ETM in our study) costs considerably more per patient than the control treatment (CTM). (That is, we will have greater power in randomizing 100 patients to ETM and 200 to CTM than if we randomized 100 to each group. With our preexisting measures for routine data collection, this can be accomplished with little extra cost and effort.) To assure comparability of treatment groups at enrolment, we will stratify all eligible CMC in our program according to age (< 2 or ≥2 years) and risk (< or ≥ the median as assessed by R. Mosquera) before randomization.

Care for all participants. Each will receive the care shown to improve CMC outcomes in our prior randomized and stepped wedge studies.[5-7] Our clinic component involves comprehensive care (**CC**) designed to promote prompt, effective care at any hour. It emphasizes evidence-based treatment and includes both specialist and primary care in the same clinic, 24/7 direct cell phone access to our PCPs at all hours, same weekday care for acute illnesses, and a high staff-to-patient-ratio. As Medical Director, Dr. Mosquera, attends multiple clinics per week, backs up

the PCPs, and leads weekly staff meetings to critically review the care given by our team to any child with an ED visit or hospitalization in the prior week. Our randomized trial of CC (JAMA, 2014) showed it reduced serious illnesses, ED visits, hospitalizations, and PICU admissions by 47-69% and health system costs by $10,200 per child-year below that with usual care given by private pediatricians or faculty-supervised residents.[5] The benefits of CC following the marked expansion of our program were shown in a stepped-wedge analysis to be maintained or increased (J Pediatrics, 2019).[6] Our hospital component is a consultation service provided by our PCPs to help optimize treatment, assure ED physicians and hospitalists are well informed, and coordinate discharge planning. Our Bayesian RCT identified a 98% probability of reducing hospitalizations, a 91% probability of reducing hospital days, and a 94% probability of reducing mean health system costs.[7] Our current home component is CTM described below. The positive results of our CTM trial[8] are described above in the Background section.

The success of these components is based partly on the input of our original Parent Advisory Council (**PAC**). To maximize both its effectiveness and feasibility, the PAC will meet every at months 3, 6, and 9 with Zoom meetings as needed until the Delta variant surge subsides in Houston.

Use of CTM. Our PCPs will provide CTM during regular clinic hours as in most centers to respond to calls from parents seeking medical advice, to evaluate and recommend treatment for minor illnesses, to schedule a clinic visit if an in-person assessment is needed and to conduct appropriate follow-up visits. Unless a better platform becomes available, we plan to continue using Zoom for Healthcarewhich is HIPAA compliant and we used quite successfully in our CTM trial. The CMC enrolled in our program have already downloaded a free Zoom application to any Android or iPhone, which are owned by almost all of our patients.

Use of ETM. The ETM program will involve using FDA-approved, HIPAA-compliant, mobile devices in the home (TytoCare™) to visualize the skin, throat, & ears, auscultate the heart & lungs, and measure temperature & oxygen saturation. (*We have no financial conflict of interest or relationship with this company*.) The awards received, the wide use of these devices, the documented feasibility of using these devices in CMC homes, and the reported reduction in hospital costs are noted above.

With prior parental agreement, we will use ETM to better manage 1) acute illnesses during clinic hours whenever PCPs feel it would be helpful (for example, in judging whether a clinic or ED visit is needed); 2) chronic illnesses managed proactively with a detailed patient evaluation at least every 6 mo. in the clinic or by “virtual patient rounds” in the home by ETM. These visits

would involve the parent(s), the PCP, and if needed any of 10 specialists who attend our clinic, particularly pulmonology, gastroenterology, neurology, and physical medicine and rehabilitation. Our program social worker, nutritionist, or psychologist will be involved as needed. Each PCP will perform 2-3 virtual patient rounds per week to proactively identify medical problems, suboptimal adherence to treatment, dosing errors, or other problems and intervene before CMC develop a serious illness or require avoidable clinic visits, ED visits, or hospitalizations. These calls are expected to last 30 minutes on average.

Engagement of Underserved Populations with Families as Co-investigators. Our strong engagement with underserved populations is evident from the large number we treat, the high proportion of under-represented minorities among our CMC (88% qualify for Medicaid and 79% are African-American or Hispanic) the diversity of our team of caregivers, the high satisfaction that our patients report,[3, 10] and the progressive improvements in their outcome as noted above. This success is based in part on the input of our original Parent Advisory Council **(PAC)** in defining ways to best meet the needs and wants of CMC and their families at the outset of our program. We are now renewing the PAC as an essential feature of a strong CMC program and will provide modest reimbursement to parents for their participation. At least 3 families (either or both parents), with experience in caring for their medically complex children at home, will participate in this program giving feedback about the implementation, use and evaluation of enhanced telemedicine in our program. We are pleased to have an exceptionally qualified leader (M. Ottosen) experienced in leading parent groups. The PAC will meet every 4 mo. using Zoom while needed during the ongoing pandemic. More broadly, all families will function as coinvestigators in our study in helping us to optimize the feasibility, acceptability, efficiency, and effectiveness of providing CTM and ETM in the day-to-day effort to achieve the best possible outcomes for CMC in each treatment group.

Outcomes. Our two primary outcomes are days of care provided in a medical setting and total episodes of serious illnesses (causing death, pediatric ICU admission, and hospital stay > 7d). Secondary outcomes include cost effectiveness of ETM (defined strictly as a reduction in serious illnesses without an increase in health system costs, a decrease in health system costs without an increase in serious illnesses, or a reduction in both). Other secondary outcomes include all cause infections on admission to the hospital; total numbers of clinic visits, ED visits, hospital days, PICU days, and deaths; acceptability of ETM to parents and PCPs, and parent ratings of care assessed using the Consumer Assessment of Healthcare Providers and

Systems Survey.[1] All outcomes have obvious importance to parents, physicians, and health policy analysts.

In addition, we will collect surveys on telemedicine satisfaction, feasibility and usability from both parents and PCPs. These surveys are being developed by Dr. Ottosen and will include input from the clinical team and the PAC.

Blinding. While it is not possible for providers and parents, the statistician (Pedroza) and healthcare economist (Avritscher) will be blinded to treatment group during the trial.

Data sources and data collection. As in our prior trials, the research nurse will assess hospital logs each weekday to identify all ED visits and hospitalizations at Children's Memorial Hermann Hospital (**CMHH**) and use the electronic medical record (**EMR**) to identify all ED visits and hospitalizations of our CMC at the other 14 Memorial Hermann System hospitals in Houston. To help avoid incomplete data, our staff will continue to ask parents at each visit to identify any medical care since the prior clinic or TM visit. Parental ratings of care will be collected in the last 2 months of the 10-month trial period by the program's research nurse (M. Poe), who is not involved in patient care. Acceptability of ETM to parents and PCPs will also be collected by Dr. Poe in the 1st and last 2 months of the trial.

Total hospital-specific costs will be obtained from their cost-accounting system for each ED visit and hospitalization at any of the Memorial Hermann hospitals as our healthcare economist has done in our prior studies.[2, 3, 5, 6] Costs will be assessed from the health system perspective. Costs for physician inpatient services will be estimated using claims data and Relative Value Units (RVUs) from the Medicare Fee Schedule. Clinic costs for CC will be estimated using the total expenditures of our clinic. The mean personnel time spent providing either an ETM visit or a CTM visit will be assessed based on the start time and end time for each of these encounters as documented by the PCPs for billing purposes in the EMR. The mean personnel time spent providing an in-person office visit to each of the study patients will be tracked by the PCPs and reported to the research nurse weekly. The time spent conducting inpatient consultations will be based on the number of communications between PCPs and either the inpatient team and/or clinic subspecialists regarding hospitalized study patients and also on the number of in-person hospital consultations provided by the PCPs at CMHH. These numbers will be tracked by the PCPs and reported weekly to the research nurse. The average length of these communications and in-person hospital consultations will be estimated by the PCPs at trial's end. The total personnel time costs will be computed by multiplying the PCP time spent on each individual

service by the observed number of such services and by the time unit costs (based on personnel salaries, fringes, and overhead costs). CTM costs will include the costs of the telemedicine software (Zoom for Healthcare). ETM costs will include the costs for Zoom for Healthcare, the costs for the TytoCare kits, and the personnel time costs to assist families in installing the TytoCare application, creating an account, and learning to use the devices and software and to conduct the multidisciplinary rounds. To capture the full costs of providing CC, the above tabulated costs will be subtracted from the total clinic expenditures and the otherwise unaccounted for CC costs will be allocated to patients based on their length of follow-up during the trial. Costs for outpatient services in our center outside our clinic will be calculated using RVUs. All costs will be inflated to the year of analysis based on the Consumer Price Index for medical services.

Sample Size, Power, and Analysis Plan. Assuming a sample size of ~100:200 patients in the intervention and control groups (all enrolled at the outset of the study); a mean of 12 total days of care outside the home with CTM (as in our previous trial); a prior probability centered at rate ratio of 1.0 with 95% credible interval of 0.3–3.2; an actionable Bayesian posterior probability threshold of ≥85% to recommend a multicenter study (as discussed above), there will be 84% power at 10 mo. to detect the hypothesized difference of 4 days between the two group rates (9.6 vs 12.0; 20% reduction). If our analyses at 10mo indicate a probability of >95% of ETM reducing total days of care outside the home compared to CTM; >80% probability that ETM involves less or comparable (less than 10% greater) total PCP time than that with CTM (counting time saved for clinic visits, after hours calls, and hospital consultation); and >80% probability that PCPs as well as parents surveyed at the beginning and end of the study in the ETM group will express increase in satisfaction with use of ETM at trial's end, then recruitment will stop and final analyses will be conducted and reported. However, if our analyses at 10 mo does not meet the stopping rules but shows promising data, we will conduct a second analysis at 17 mo. If the stopping rules are not met, the study will conclude at 24 mo.

The analyses for all our hypotheses will be intent-to-treat Bayesian analyses conducted by a Bayesian statistician (Pedroza) and health economist (Avritscher) who have collaborated in multiple studies. Negative binomial multilevel models will be used to assess the total number of counts for each outcome. Differences in costs between the two treatment groups over both periods, will be assessed using a generalized linear mixed models (GLMM) with log-link and gamma distribution. All models will include age and baseline risk (stratifying variables), length of follow up (as an offset), and a random intercept to account for within-subject correlation. All

models will use a prior centered at RR of 1.0 (95% CrI, 0.3-3.2) for the treatment coefficient. Other terms in the model will use neutral priors. We will report posterior means, 95% CrIs, and posterior probabilities of benefit. All analyses will be conducted in R software using ‘rstanarm’ or ‘brms’ packages.

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