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Intervention Research to Improve Care and Outcomes for Children with Medical Complexity and their Families

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Abstract

Healthcare and outcomes for children with medical complexity (CMC) and their families can be improved by conducting well-conceived, designed, implemented, and analyzed research studies of clinical interventions. This article presents a framework for how to approach the study of clinical interventions for CMC, including 7 key questions and example answers to each: (1) What intervention questions should be our focus? (2) What barriers to intervention research exist? (3) How do we design and optimize interventions? (4) How do we characterize and select patients to enroll? (5) How can we enhance data collection and integration? (6) How can we improve enrollment and participation? And (7) which intervention experimental designs should we choose? By exploring each of these key aspects of intervention-based research, we hope to expand thinking about and spark ideas for specific research projects focused on clinical interventions for CMC.

INTRODUCTION

We believe that the healthcare and outcomes for children with medical complexity (CMC) and their families can be improved by conducting well-conceived, designed, implemented, and analyzed research studies of clinical interventions.

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Declaration of Competing Interest

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We are certainly not alone in our belief, although our emphasis on *interventions* may not yet be commonly held. PubMed currently lists more than 2,000 studies for "children with medical complexity." These mostly epidemiological, health services, and qualitative studies have commonly focused on the identification and characterization of children with CMC, analyses of their patterns of healthcare utilization including their frequent hospitalizations, studies of associated costs/charges of care, and initial evaluations of complex care programs and care coordination strategies.[1–8] This significant body of research has illuminated the myriad challenges and opportunities for advancing the care of CMC. But far less often have studies rigorously evaluated clinical interventions and program models using experimental study designs.

We encourage the field of complex care to mindfully shift focus to the study of clinical interventions. While all forms of research questions and modes of study are valuable (and we have and will continue to engage in them), our field unquestioningly needs more rigorous intervention studies. In what follows, we pose 7 questions and offer our current best answers to each:

1. What intervention questions should be our focus?
2. What barriers to intervention research exist?
3. How do we design and optimize interventions?
4. How do we characterize and select patients to enroll?
5. How can we enhance data collection and integration?
6. How can we improve enrollment and participation?
7. Which intervention experimental designs should we choose?

WHAT INTERVENTION QUESTIONS SHOULD BE OUR FOCUS?

The most impactful research questions to answer are not prescribed by others, no matter how well informed, but instead discovered or derived by inquisitive individuals and teams. Certainly, stakeholder-driven prioritization of research topics regarding CMC have their place, including social determinants of health (SDH), caregiving, clinical-model refinement, value, and youth-to-adult transitions, care coordination activities, and health and symptom management[10]. We encourage the diversity of ideas and questions, and also the fusion of creative insight and rigorous thought needed to transform these topics into answerable research questions.

What we offer, then, is a general framework of research questions (Table 1) meant to expand our thinking and spark ideas for specific research projects. Foundational questions clarify the problem that the intervention is intended to address and inform the intervention design. Intervention design questions seek to improve the intervention's efficacy. Intervention effectiveness questions address whether the intervention works and to what degree. Value questions evaluate the costs involved and merge that information into the evaluation. Implementation questions probe how to enact the intervention in the real world for best and lasting benefit. Under these broad headings are more specific questions. To illustrate

how these can be used, we have presented several specific examples regarding understudied therapies and interventions (Table 2).

WHAT BARRIERS TO INTERVENTION RESEARCH EXIST?

Conducting experiments to study specific interventions can be difficult. Significant barriers have impeded intervention-based research in CMC, like those experienced in the field of rare disease research.[11] Several are worth mentioning. First, there is a tendency to implement and evaluate broad clinical interventions delivered to a heterogenous patient population (e.g., exposure of a CMC to an outpatient complex care clinical program)—even when the care provided lacks specificity and a variety of outcomes are measured—because the clinical need is high. Second, the heterogeneity of the underlying chronic conditions can present difficulties in the identification and recruitment of appropriate study populations. Third, existing data sources (e.g., administrative claims data) containing the necessary analytic variables (for example, clinical data, patient-reported outcomes, etc.) may not be readily available or easily linked. Fourth, a great deal of focus has been placed on hospital-based care; much less attention has been devoted to outpatient, school, and homecare settings, where many CMC spend the bulk of their time. Creative solutions are needed to overcome each of these barriers, and below we will consider different ways that researchers may address these obstacles.

HOW DO WE DESIGN AND OPTIMIZE INTERVENTIONS?

Before designing an experiment, thorough characterization of the intervention is essential. Conceptually, an intervention must move the lever on some target that is a key driver of the main outcome of interest for (ideally) all applicable CMC. Proper targeting of the intervention is important both in intervention design and then in the study, which should only include patients who have the target. Consider a study that exposes all CMC to an intervention (e.g., case manager / care plan) that not all of them clearly need. Because the intervention wasn't specifically targeted to a relevant group who might benefit from the intervention, a negative study occurs, for which the study team concludes that the intervention was not clinically effective. In contrast, had the intervention focused on a subset of CMC with the target, then the study would have been better calibrated to assess effectiveness.

Next, the components of an intervention must be specified, as well as the doses of each component. For simple interventions, such as a study of a medication to treat a symptom, describing the intervention is straightforward. However, at a clinical program or pathway level, the intervention might consist of a collection of activities to improve clinical outcomes and reduce acute healthcare utilization. For example, consider a clinical intervention for CMC undergoing spinal fusion for neuromuscular scoliosis consisting of a bundle of health services to optimize health before surgery to reduce post-operative morbidity and mortality (Table 2). These more complex multi-component interventions may have inconsistent or vague definitions and/or implementation protocols.[12] Clarifying the components is particularly important for program-level interventions, so that feasibility,

generalizability, and scalability of the intervention can be assessed for dissemination and implementation across different healthcare systems and settings.

Finally, research methodologists have argued that healthcare researchers often move too quickly from piloting interventions directly to conducting randomized clinical trials (RCT) without first optimizing the intervention, which ultimately may impede efficient evaluations of effectiveness.[13, 14] Using the example of CMC undergoing spinal fusion for neuromuscular scoliosis, pilot work may indicate that, among other things, important components may include (A) nutrition management, (B) respiratory optimization, and (C) development of a post-operative pain management plan. A common strategy is to move directly to evaluation of these bundled services on patient outcomes. Design optimization allows the investigator to efficiently determine what combination(s), timing, personnel, setting, etc., of implementation for A, B, and C are most effective.[14, 15] The Multiphase Optimization Strategy (MOST) is a framework that is increasingly being applied to multicomponent behavioral and biobehavioral medical interventions.[14, 16] MOST involves optimization of the components through factorial experiments to identify the intervention that is expected to be optimally effective.[14, 16] Other variations of factorial trials exist that offer investigators the ability to define, for example, the optimal sequencing of components of an intervention.[17]

HOW DO WE CHARACTERIZE AND SELECT PATIENTS TO ENROLL?

Heterogeneity among CMC presents a significant research challenge, both at the individual and program levels. To date, a relatively small set of markers of clinical severity are routinely utilized in health services research, including variables like number (“dose”) of complex chronic conditions, the presence of technology, and prior healthcare utilization (outpatient, emergency, and inpatient stays). Health services research and quasi-experimental studies will benefit from powerful adjustment capabilities, as will even RCTs, either for block randomization or post-RCT analysis of results.

Markers of Clinical Severity

More robust standardized markers of clinical severity are needed, and these may vary depending on the study population or the outcome of interest. At the population level, the type or number of chronic conditions may be sufficient to identify and adjust for severity of illness. However, diagnosis and procedure code-based adjustments may be less useful in identifying CMC with functional limitations who might benefit from specific clinical interventions, such as home nursing services or outpatient therapies. Additional categories of administrative data that may help distinguish CMC include: specialty care, medications, medical equipment, nursing, diagnostic testing, diet/nutrition, therapies, care coordination, and education.[2] Standardized code sets that capture these domains, such as administrative codes to identify respiratory medical equipment and supplies, could serve as add-on modules for current classification schemes.[18] Similarly, commonly employed administrative definitions of chronic medication use or polypharmacy may serve as markers of patient acuity or severity.[19, 20] Because functional impairments may be associated with

receipt and intensity of Early Intervention outpatient therapies, therapy claims may provide an opportunity to assess clinical severity.[21]

Beyond administrative data, there are opportunities to leverage more detailed clinical information about CMC to improve classification of severity. A variety of clinical severity scores exist in the adult and geriatric literature, but fewer tools have been trialed in the pediatric realm. As an example, the Clinical Frailty Scale is a tool used for geriatric patients to generate a composite frailty score from domains like medical comorbidity, function, and cognition.[22] Pediatric cardiologists have adapted the Clinical Frailty Score to define functional phenotypes among children and adolescents with cardiac disease and found that the developmentally adapted domains differentiated severity between children with cardiac disease and controls.[23] Similarly, among children with chronic liver disease, the Clinical Frailty Score identified the sickest children not captured by standard laboratory measures alone.[24] Other adult measures have shown promise in assessing the physical status of children, including those with chronic conditions, such as the American Society of Anesthesiologists Physical Status classification system to capture pre-operative anesthesia risk measurements.[25]

Additional Patient Complexity Factors

Social determinants of health (SDH) clearly influence individuals' health status, but are not robustly accounted for in CMC research.[26–28] The Centers for Disease Control defines social determinants of health as "life-enhancing resources, such as food supply, housing, economic and social relationships, transportation, education, and health care, whose distribution across populations effectively determines length and quality of life." Investigators used the 2017 National Survey of Children's Health to examine associations between a child's level of medical complexity and SDH variables (e.g., poverty, poor parent mental health, parent incarceration, etc.).[26] They observed a high prevalence of SDH challenges, especially among CMC, concluding that longitudinal data are needed to determine the temporal influences and directionality of the relationship between SDH and CMC. To do so, enhanced SDH data are needed. Some complex care programs administer psychosocial screener questionnaires at every patient visit, which capture information about issues like food insecurity or housing issues.[29]

Mental health conditions among CMC impact healthcare utilization and spending.[30] Children with chronic physical conditions and complex chronic conditions who also have mental health diagnoses have been shown to be disproportionally represented among the highest-spending Medicaid populations.[30, 31] In a study of hospital readmissions of adolescents and young adults with complex chronic diseases such as type 1 diabetes, sickle cell disease, or cystic fibrosis, mental health diagnoses such as anxiety, depression, and chronic pain were among the most common coexisting chronic conditions.[32]

Parent/Caregiver Characteristics

Given the significant role of parents and caregivers in caring for CMC, assessing parental characteristics is integral to implementing interventions and understanding healthcare outcomes.[33, 34] Factors as simple as who reports a child's health needs and developmental

concerns can result in significantly different assessments; in two parent households, fathers were less likely than mothers to identify special healthcare needs or unmet healthcare needs.[35] Parents' own physical and mental health may be associated with the care they provide to their CMC.[36] Parent caregivers commonly report higher levels of stress, poor sleep, depression and anxiety, without consistent access to respite needs[37–39]; interventions for CMC should improve rather than worsen caregiver burden and routine measures of parenting stress should be employed. Validated measures of caregiver burden, such as the Revised Burden Measure, may allow inclusion of parent characteristics in studies.[40]

HOW CAN WE ENHANCE DATA COLLECTION AND INTEGRATION?

To make sophisticated adjustments and to study patient-centered outcome measures, data elements are required beyond what have typically been available in administrative databases (Table 2). Once collected, this data needs to be integrated to be analyzed.

Clinical Data

Many studies would benefit from the addition of clinical data both from inpatient and outpatient settings. Using the example of the spinal fusion example (Table 2), the inclusion of pre- and post-surgical weights, pain scores, basic lab and radiology results would provide far greater insights than administrative diagnosis and utilization data alone. A different type of research question, such as determining whether bisphosphonates are effective treating osteopenia in children with neurological impairment (Table 2), might require detailed medication data (ingredient, dose, dose frequency, and dosage form), DEXA scan results, and bone health laboratory values. Traditionally, these types of data have been unavailable or difficult to routinely acquire, but institutional data warehouses populated from electronic health record data are increasingly able to facilitate these studies. Clinical research networks, such as PEDSnet, with common data models that can link these data between institutions can enhance sample sizes, especially for CMC with rarer conditions.[41] Additionally, patient registries and clinical databases already exist for certain rare disease populations and could potentially provide curated clinical data.[42]

Patient- (and Parent-) Reported Information and Outcomes

Patient-reported outcomes (PROs) have been used extensively in adult and geriatric research and can provide rich and measurable patient-relevant study data. Because the caregivers of CMC often provide in-home bedside care to their children, their assessments of symptoms over time are particularly valuable. Psychosocial screeners, depression screens, information about current symptoms, and medication reconciliation data are commonly collected during clinical care or even between episodes of care via mobile technology and can provide powerful insights about patient-centered outcomes. Using the example of sleep pharmacotherapy (Table 2), administrative data may allow researchers to assess fills and discontinuations of sleep medications, but these are only proxies for outcomes; parent and patient-reported symptom data are essential to assessing effectiveness of sleep pharmacotherapy. Standardized symptom tools are available, providing tested pediatric outcome tools to measure variety of symptoms[43], but care needs to be taken that these tools will work for CMC. Clinicians and researchers within the field of pediatric palliative care

have employed a pediatric version of the Memorial Symptom Assessment Scale (MSAS), which measures the frequency, severity, and bother of multiple symptoms, to longitudinally track children's symptom burdens. Such data have proven useful to direct medication use, therapies, and other interventions.[44, 45]

HOW CAN WE IMPROVE ENROLLMENT AND PARTICIPATION?

Prospective intervention-based research will require investigators to recruit and enroll patients who meet study criteria, and then to enable them to fully participate, potentially over extended periods of time.

Efficient Patient Identification

Diagnosis-based identification of patients has enabled the conduct of health services research at the population level. However, the use of ICD-based definitions alone to identify CMC for certain clinical interventions or to enroll into clinical trials poses potential problems due to their test characteristics, namely their high sensitivity and low specificity. With broader, more heterogenous collections of codes, data-driven re-evaluations of code schemes may be useful.

For example, in 2012, the original set of neurological impairment codes were published, and were shown to be sensitive for a broad range of severities.[7] In 2019, these codes were revised with a focus on those with the highest healthcare utilization to improve identification of children with the most severe neurological impairments.[46]

Still, as discussed earlier, functional limitations are not easily captured by diagnosis and procedure codes alone, which may increase the risk of misclassification bias and limits their clinical utility for identification of CMC. To address these issues, investigators proposed a stepwise approach for identifying children with medical complexity that has proven useful to enroll CMC in clinical research studies.[2, 44] Following the suggested scheme, an investigator would first use diagnosis and procedure schemes to identify an initial population of children. Next, to address variation in functional limitations, the investigator would apply additional claims-based criteria such as the use of certain medications or medical devices, to further restrict the sample of potential study participants. Finally, a more focused clinical screener or questionnaire could be used to identify and target children meeting additional clinical criteria for functional impairments, unmet needs, etc.[2]

With richer clinical data sources, like the electronic health record, data scientists have started to create computable phenotypes. Akin to the first 2 steps of the aforementioned approach, this strategy involves the use of clinical data elements (beyond just diagnoses and procedure codes) and logical expressions to identify reliable, reproducible phenotypes of patients across different data sources.[47] For research networks (like PEDSnet) or clinical rare disease registries that contain the necessary data, this approach has proven efficient to identify research participants.[48, 49]

Enabling Participation from Home

The 2020 COVID-19 pandemic accelerated the use of electronic modes of research, including the use of digital platforms to manage study enrollments, consents and assents, and even the conduct of studies.[50] A variety of tools are available to CMC researchers; REDCap alone includes capabilities to support online consenting, signature capture, document management, online and text-based survey tools; and data management and reporting.[51, 52] With the widespread uptake of secure HIPAA-compliant videoconferencing software, video-based research solutions are possible. Broadly, two types of models exist for online research: the "parent-report" model, where information is collected exclusively through the parent/guardian, and the "direct data-collection" model where information is also collected from children through on-screen interactions or digital sensor sources like home monitoring devices.[50] A non-exhaustive list of potential benefits of using online platforms for research includes: reducing barriers to participation by eliminating travel for in-person visits that can be difficult for CMC; allowing participants to complete study items on their own time; enabling more frequent, longitudinal contact; and increasing the potential universe from which to enroll CMC with rarer diseases.[53]

WHICH INTERVENTION EXPERIMENTAL DESIGN SHOULD WE CHOOSE?

A range of rigorous study designs exists that may be applicable to intervention research among CMC, including experimental trials (where investigators assign study participants to intervention groups) to quasi-experimental designs (where investigators do not assign study participants to intervention groups). Within these groupings, many types of specific study designs exist. We will present just a few examples of relevant study designs and discuss the strengths and limitations of each study design as it pertains to individual- or program-level intervention studies in CMC.

Randomized Controlled Trials

Although randomized controlled trials (RCTs) remain the gold standard for evaluation of interventions and therapies, RCTs are infrequently utilized in the population of CMC due to challenges specific to CMC. When appropriate, RCTs should be considered to evaluate interventions, medications, and therapies, for example, to assess the effect of a pre-surgical pathway on reducing length of stay or to assess the effect of trazodone on sleep in CMC (Table 2).[54] The most important benefit of an RCT is that the effectiveness of an intervention can be isolated and measured, controlling for other patient characteristics and unmeasured confounding variables. Different types of randomizations can be employed to address practical aspects of an RCT and reduce confounding. In stratified randomization, strata are constructed based on important prognostic variables (for example, by major complex chronic condition organ system category) and then the sample is constructed from simple random sampling from the strata. This can be useful when the study population is heterogeneous and an investigator wishes to understand how the intervention differs between strata. Cluster randomization involves administering an intervention to clusters of subjects (for example, at a clinic or hospital level) by simple randomization. This type of randomization is useful when interventions cannot be directed toward individuals, such as when a hospital- or clinic-wide intervention is implemented (Table 2).

RCTs are not without challenges.[11] One major challenge to conducting RCTs is that equipoise must be present, such that no preference exists between 2 or more available treatments, and this is often a limiting factor. Among CMC, clinicians may favor intervention despite uncertainty given the severity of underlying conditions and symptoms, the lack of alternatives, and the lack of data about adverse consequences. In this case, the use of placebo controls or "no-treatment" controls may be unethical, and an active treatment control group who receive the current standard of care treatment is preferable. Furthermore, the heterogeneity of the underlying diagnoses and symptoms among CMC may increase between subjects' variation and may require unrealistic sample sizes to ensure generalizability within the population. RCTs to evaluate orphan drugs frequently have total sample sizes <50.[55] Traditional parallel group trials, where the intervention group is compared concurrently to the control group, may thus be inefficient. Finally, small-sample trials are particularly vulnerable to improper randomization and blinding, and these trials may suffer statistical consequences from participant withdrawal or loss to follow up.

Crossover Trials—Cross-over designs, where each subject is randomized receive both the treatment and control in a different order, reduce the required sample size and avoid the ethical concerns related to placebo arms. In this situation, subjects serve as their own controls which allows researchers to control for within-subjects differences and can help mitigate the issues related to heterogeneity among CMC. Repeated measures studies are thus more efficient than between-subjects designs, meaning that fewer patients are needed to recruit the necessary number of participants. This is particularly relevant for prospective studies of interventions in CMC, where recruitment may be difficult and slow. Downsides are that repeated measures studies are susceptible to time-related effects, including external events, aging of participants during the study period, and participant drop-outs that may introduce bias. Additionally, carryover effects from earlier interventions may impact the measured outcomes of the studied intervention, so crossover designs require a longer study duration with a washout period between interventions, but this is well-suited to CMC, who by definition have chronic medical conditions.

Stepped Wedge Trials—Recruitment and randomization cannot always occur at the level of the patient. For interventions delivered at a provider- or program-level, the stepped wedge cluster randomized trial design improves the ability to evaluate and measure service delivery interventions.[56] Consider the example whether the presence of a clinic-based health navigator to address SDH concerns improves health outcomes (Table 2); it may not be practical, feasible, or ethical to randomize individual patients to this intervention. A stepped wedge study design is a pragmatic trial that involves the random, sequential crossover of patient clusters (perhaps clustered at the level of a hospital or a complex care program) from the control state to the intervention phase until all patient clusters have completed the intervention.[57]

Quasi-Experimental Designs

Several quasi-experimental designs, where the intervention is not randomly assigned, may be appropriate for studies within the population of CMC. Study subjects are still allocated to an intervention or control group, but this assignment occurs due to a naturally

occurring assignment mechanism.[58] For example, complex care clinics at 2 or more different institutions may treat neurologically impaired patients differentially with respect to bisphosphonates to promote bone health (Table 2), allowing for a natural experiment to evaluate the effectiveness of the medication. Just like with randomized controlled trials, many designs exist with varying degrees of design quality.[58–60] The strongest quasi-experimental designs utilize pre-intervention and post-intervention measurements for the intervention group and involves an untreated control group. Several methods can adjust for confounding and bias, including matching, stratification, multivariate adjustment, propensity scores, and instrumental variables.[61]

Interrupted Time Series Analysis—When an intervention is implemented across a population and a suitable control group is not available, an interrupted time series analysis design may be useful. Consider the example where there is statewide adoption of a stepwise seizure action plan to be used by parents and schools (Table 2). Interrupted time series analysis allows investigators to assess program-level interventions by leveraging repeated measures over time before and after the intervention.[62] As opposed to simple pre-post analyses, where outcome means are compared once before and once after an intervention, the interrupted time series design accounts for important pre-intervention trends.[63]

CONCLUSION

Within the field of complex care, a strong foundation of epidemiolocal and health services research has resulted in vast and compelling evidence that CMC are a population of children who require continued special attention and on-going research investigation. With an increasing focus on how to provide effective, comprehensive care to CMC, there exists an urgent need for CMC researchers to study interventions at both the patient and program levels. Rather than relying on extrapolated evidence or descriptive reports, clinicians who care for CMC can instead implement rigorously studied interventions with favorable patient-centered outcomes.

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Abbreviations;

CCC	complex chronic condition
CMC	children with medical complexity
MOST	Multiphase Optimization Strategy
PRO	patient reported outcome

RCT	randomized controlled trial
SDH	social determinants of health

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Table 1.

Framework of intervention research domains and general clinical questions.

Clinical Question
Formative Research on the Intervention
Why does [health problem] occur in CMC?
What is the pathogenesis of [health problem]?
What is the prevalence of [health problem]?
What are the risk factors for [health problem]?
How does the severity of [health problem] change over time?
Design of the Intervention
What can be done to prevent/mitigate [health problem]?
What is the best user-centered design for [intervention] to address [problem]?
How patient/family centered is [intervention]?
How feasible is [intervention]?
Clinical Effectiveness of the Intervention
How clinically effective is [intervention] for [problem]?
How much does [intervention] improve health / functioning / quality of life?
How well does [intervention] prevent [disease/outcome]?
Is [intervention A] more clinically effective than [intervention B]?
How safe, equitable, and timely is [intervention]?
Value of the Intervention
How cost effective is [intervention]?
Is [intervention A] more cost effective than [intervention B]?
Implementation, Scale, and Spread of the Intervention
What are the barriers and facilitators of implementing [intervention]?
How much variation in [intervention] exists in clinical practice?
What’s the best way to implement [intervention]?
What’s the best way to decide whether to use/undergo [intervention]?
What’s the best way to sustain use of [intervention]?
What’s the best way to pay for [intervention]?
What policies best enable use of [intervention]?

Table 2.

Examples of study designs and data elements well-suited to answer selected research questions.

Example Research Questions	Example Interventions	Patient-Centered Outcomes	Types of Data Required	Possible Study Designs
Is trazodone an effective medication for sleep problems in children with NI?	Trazodone therapy	• Sleep quality • Participation in school/therapies • Caregiver mental health	• Patient/parent-reported outcomes • Caregiver data • Pharmacy data	Randomized-controlled trial, either placebo controlled or with active control (melatonin)
How do we best prepare children with medical complexity for major, high-risk surgeries? Are their post-operative outcomes better if we prepare them before surgery?	Pre-surgical optimization of nutrition, respiratory condition, and pain management	• Length of stay • ICU utilization • Adequate pain control • Return to baseline health and functioning • Improvement of symptoms • Return to school/ outpatient therapies	• Administrative/ billing • Patient/parent-reported outcomes • Clinical and lab data	Randomized-controlled trial, cluster randomized at hospital level
Does access to family navigator services to address needs related to social determinants of health improve health outcomes?	Routine provision of family navigation services within complex care programs	• Connected to services • Caregiver mental health • Fewer emergency visits and hospitalizations	• Administrative/ billing • Patient/parent-reported outcomes • Caregiver data	Stepped-wedge cluster-randomized trial
Are bisphosphonates effective for treating osteopenia in children with severe NI?	Bisphosphonate therapy	• Improvement in bone mineral density • Reduction in fractures	• Administrative/ billing • Clinical and lab data • Pharmacy data	Comparison of pre-intervention and post-intervention measurements for the intervention group to an untreated control group
Would a seizure action plan that goes beyond just giving rectal diazepam make a difference in epilepsy hospitalizations?	Statewide implementation of a stepwise seizure action plan	• Reduction in epilepsy-related emergency visits and hospitalizations	• Administrative/ billing • Pharmacy data	Interrupted time series analysis