**Protocol**

**The Sunflower Pediatric Clinical Trials Research Extension**

**SPeCTRE**

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10. **Rationale and Specific Aims**

Clinical trials are the gold standard for assessing the effectiveness and safety of treatments in the medical field. Children routinely receive medical therapies that have not been studied in clinical trials involving pediatric subjects.1 Over 75% of hospitalized children may receive a medication “off-label” (i.e. in a manner not explicitly approved in children).1,2 The use of off-label medications puts children at an increased risk of adverse events not seen in adults, due to potential differences in drug metabolism, distribution, and/or efficacy.3,4 Additionally, nearly 20% of US children are affected by at least one chronic medical condition,5 but clinical trials focused on the etiology, prevention, and/or treatment of these illnesses are often limited. 6,7 Residents of rural areas in particular are more likely to report limited access to and/or awareness of available clinical trials.

Children enrolled in clinical trials report several benefits for themselves and others, including: 1) increased treatment options for their illness; 2) improved understanding of their disease; and 3) the opportunity to help other people suffering from the same illness.7 Thus, there is a critical need to increase the opportunity for children, including remote rural children, to participate in clinical trials.

The purpose of the current proposal is to form the Sunflower Pediatric Clinical Trials Research Extension (SPeCTRE) network. The purpose of this network is to provide access for underserved and rural children in the state of Kansas to participate in state-of-the-art clinical trials and transfer findings so that they may benefit the health of all children. As part of the development of this network, we seek to identify barriers and facilitators to clinical trials participation as part of longitudinal outreach and engagement efforts. Thus, we propose the following specific aim:

**Specific Aims**

**Increase the awareness of clinical trials opportunities to Kansas children through education and outreach.**

* We propose to conduct a survey in health care providers and caregivers to assess knowledge, perceptions, and barriers about clinical trials.
* We also plan to conduct focus groups with health care providers and caregivers to identify needs and barriers to clinical trial participation.
* We aim to expand the enrollment of children into Pioneers, a regional clinical trials participant registry supported by KUMC, CMKC, and other leading regional medical and academic centers.

1. **Background and Significance**

Researchers, children, and families face significant barriers to participating in pediatric clinical trials.8-11 First, financial drivers to conduct pediatric clinical trials are often absent due to the lower prevalence of most pediatric diseases, which ensures that the market for any new therapy is much smaller compared to adult diseases. This lower disease prevalence also requires researchers to enroll children at many performance sites, thus increasing the complexity and cost to attain the sample size necessary to complete a clinical trial. Additionally, fewer pediatric health care providers feel comfortable participating in clinical trials, resulting in a workforce shortage of pediatric clinical researchers.9,11 When surveyed, children and families often report that: 1) they have a limited understanding of how clinical research works;9,12,13 2) they are unaware of available clinical trials;9 and 3) they are concerned about the potential harms of clinical trials participation and uncertain of any benefits.14 These barriers are further compounded for children in rural communities, where distance from major medical centers, trained investigators, and clinical trials performance sites makes participation logistically difficult.9,11

By establishing the Sunflower Pediatric Clinical Trials Research Extension (SPeCTRE), the IDeA States Pediatric Clinical Trials Network (ISPCTN) will gain access to a robust institutional infrastructure that has successfully delivered healthcare to children in rural and underserved areas across Kansas (and bordering communities in both Oklahoma and Nebraska) for more than 30 years. This infrastructure is already used to conduct clinical trials in pediatric obesity, mental health, autism, and oncology. The formation of SPeCTRE will help expand this research infrastructure through the development and strengthening of regional collaborations that increase the number of rural health care providers participating in research, engage more patients and families in clinical trials participation, and identify and test novel approaches to surmounting geographic, cultural, and institutional barriers to clinical trials participation faced by children and their families in the rural Midwest.

**Significance of the proposed Study**

It is established that there is a need to increase the opportunity for children, including remote rural children, to participate in clinical trials.

The proposed study is significant as stated below:

* Provide awareness and education about clinical trial opportunities for children in rural and underserved areas of Kansas and neighboring IDeA states.
* Provide enhanced opportunities for children to participate in clinical trials within Kansas and neighboring IDeA states.
* Increase the capability of pediatric clinicians and researchers within Kansas to develop and conduct clinical trials.

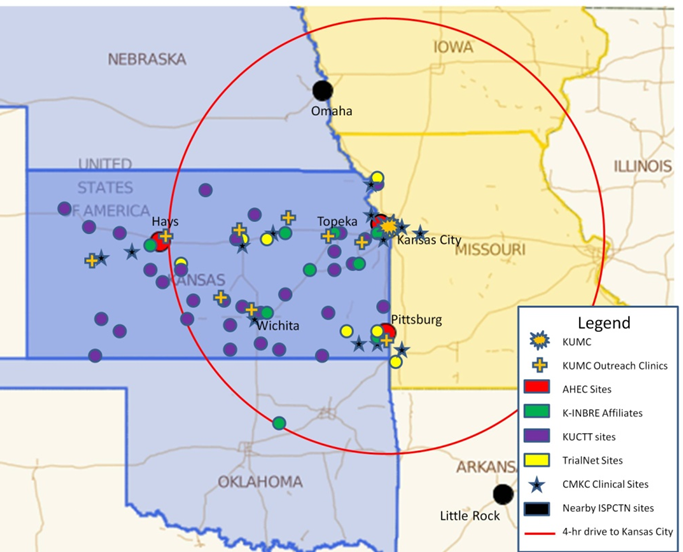
1. **Study Procedures**

**Study Design**

We plan to conduct surveys in health care providers and caregivers. We also plan to conduct focus groups with health care providers and caregivers within Kansas and Missouri as outlined in the table 2 below.

**Study Setting**

The University of Kansas Medical Center (KUMC) sponsors three Area Health Education Centers (AHECs) that provide clinical, educational and research infrastructure to rural communities across Kansas. We have secured the necessary support using the resources available at KUMC, CMKC’s, Unified Government of Wyandotte County Health Department, and Women Infants and Children (WIC) Kansas City-based facilities and outreach clinics. Additional sites include Wichita's, KS KUMC’s pediatric clinic on Carriage Parkway and Babytalk participants from Wesley Medical Center, Via Christi and HealthCore Clinic (and FQHC) (figure1). Only SPeCTRE staff or KU Wichita staff will perform study procedures. None of the Unified Government of Wyandotte County Health Department or WIC staff will be utilized to conduct the caregiver surveys.

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*Figure 1. available performance sites for SPeCTRE*

We also plan to use Pioneers, a regional clinical trials participant registry supported by KUMC, CMKC, and other leading regional medical and academic centers.

**Implementation Plan**

The four-year study will proceed in three phases. Phase I will consist of curriculum development and training. Phase 2 will be assessment and pilot testing. Phase 3 will focus on data analysis and developing interventions to increase participation of health care providers, caregivers and children to IDeA States Pediatric Clinical Trials Network (ISPCTN) clinical trials.

|  |  |  |
| --- | --- | --- |
| **Phase 1: Curriculum development and training** | Hiring and training staff, development of training manuals; development of survey instruments; development of focus group materials; creating recruitment and educational materials | Yr 1 |
| **Phase 2: Assessment and pilot testing** | Recruitment of participants; implementing and pilot testing survey instruments; conducting focus groups; outreach and awareness; collecting preliminary data | Yr 1 -Yr 2 |
| **Phase 3: Data analysis and development of interventions** | Post-pilot testing assessments; data cleaning and analysis; developing interventions tailored to the results; presentations at scientific and community conferences; manuscript and grant preparation | Yr 3- Yr 4 |

**Phase 1**

The objective of this phase is to develop survey instruments to examine knowledge, perceptions, and barriers about clinical trials within Kansas and Missouri. In this phase, we also plan to develop focus group materials. We plan to include community members input in all phases of our curriculum development.

We have identifiednursecoordinators at KUMC-sponsored AHEC clinics who will help us implement the initial pilot testing of surveys at AHEC clinics and at regional health fairs.

We have also identified a research assistant who will conduct focus groups under the supervision of Dr. Ann Davis. Dr. Davis has experience in conducting qualitative study in rural Kansas focused on pediatric obesity tailored to the needs of rural families. Dr. Davis has helped in the development of focus group moderator’s guide. Dr. Davis will provide in-service trainings to potential moderators on how to communicate with participants and how to gather good qualitative information relevant to this study.

**Phase 2**

The objective of this phase is

* outreach and public education
* to recruit participants
* pilot testing survey instruments
* conducting focus groups
* collecting preliminary data

Through our established network, we plan to do face-to-face education about clinical trials with health care providers and caregivers. We will reach out to rural community through health fairs and local meetings and conduct surveys and focus groups. Table 2 outlines the procedure for surveys and focus groups.

**Table 2: Survey and focus group procedures**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study Design** | **Participants** | **Recruitment** | **Inclusion Criteria / Exclusion Criteria** |
| Survey | Health care providers | Through AHEC clinics and word of mouth | *Inclusion Criteria:*   1. Age 18 years or older 2. Provide verbal consent   *Exclusion Criteria:*   1. Under the age of 18 years 2. Unwilling or unable to provide verbal consent 3. Not interested in completing the survey |
| Survey | Caregivers | Word of mouth and pioneers and frontier registries | *Inclusion Criteria:*   1. Age 18 years or older 2. Provide verbal consent   *Exclusion Criteria:*   1. Under the age of 18 years 2. Unwilling or unable to provide verbal consent 3. Not interested in completing the survey |
| Focus Group | Health care providers | Through AHEC clinics and word of mouth | *Inclusion Criteria:*   1. Age 18 years or older 2. Provide written consent   *Exclusion Criteria:*   1. Under the age of 18 years 2. Unwilling or unable to provide written consent |
| Focus Group | Caregivers | Word of mouth and pioneers and frontier registries | *Inclusion Criteria:*   1. Age 18 years or older 2. Provide written consent   *Exclusion Criteria:*   1. Under the age of 18 years 2. Unwilling or unable to provide written consent |

**Survey Procedure**

To examine knowledge, perceptions, and barriers about clinical trials, we plan to conduct surveys in health care providers and caregivers. The survey will measure basic demographic characteristics, perceptions, and barriers of participants to clinical trials. The survey will mostly consist of closed-ended questions measured on 5-point Likert scale. The survey will be anonymous and will not include participant’s identifiable information. We plan to survey approximately 100 participants. The survey will take approximately 10 minutes to complete. Participants will be given an option either of self-administration or interviewer administration.

**Focus Group Procedure**

We also plan to conduct focus groups with health care providers and caregivers to learn about their needs and barriers to clinical trials. We will begin with 2 focus groups in each category and will increase the number later if the data are not saturated. Each focus group will consist of approximately five to seven individuals and will last for approximately 1- 2 hours. Focus groups will be recorded on an audio-tape and transcribed verbatim. Participants will provide a written consent prior to start of a focus group. Participants who do not provide a written consent will not be eligible to participate in the focus group. Focus group moderators will be trained on how to conduct a focus group. Participants will be offered a light meal and refreshments.

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| --- | --- |
| Sampling Frame for focus groups | |
| Health care providers | 2 |
| Caregivers | 2 |
| **Total** | 4 (N=28) |

**Focus group moderator’s guide**

We will initially develop our focus group moderator’s guide based on the responses from the baseline survey. The topics that we will discuss in focus groups include the following:

* Lack of knowledge
* Risk and benefit
* Language barrier
* Distance barrier
* Healthcare barrier
* Health insurance barrier
* Trust issues and race / ethnicity barrier
* Social and cultural barrier
* Financial barrier

Focus groups questions for caregiver:

*Lack of knowledge:*

* Have you ever heard about the term, “Clinical Trial”?
* What do you understand and know about clinical trials?
* Have you ever been invited to participate in a clinical trial?
* Do you know anybody (family members or friends) who have ever participated in a clinical trial?

*Attitudes:*

* How do you feel about people participating in a clinical trial?
* What would make you more willing to participate in a clinical trial?
* What are some of the reasons that would make you take part in a clinical trial?
* How important do you think clinical trials are to you and your family? Why?
* What type of research do you think is needed in your area?
* What are the top health issues which need to be addressed in your area?
* What type of resources would you like to see about clinical trials?
* Do you feel discrimination and bias when you go to your provider?
* What are your perceptions about clinical trials?

*Top Barriers:*

* According to you what are the top barriers that you experience in a clinical trial research study?
* Fear
* Trust
* Health insurance coverage and cost issues
* Lack of awareness
* Lack of time
* Transportation
* Health care provider
* Quality of life issues (side effects, etc)
* Language barrier
* Immigration

Focus groups questions for health care provider:

*Lack of knowledge*:

* What do you understand and know about clinical trials?
* How much knowledge do you have about clinical trials?
* Are you aware of what type of clinical trials are available in your area?

*Attitudes:*

* Do you feel overwhelmed when you hear the term, “research”?
* Do you think it is important to study new interventions / treatments before they are implemented?
* Do you or your practice have any negative perceptions about research?

*Lack of Participation:*

* Has your practice ever enrolled participants into clinical trials?
* How comfortable are you enrolling participants into clinical trials?
* How much interest do you have in engaging your community into clinical trials?
* How conducive is to conduct research at your practice?
* Do you feel you are under staffed and not trained to conduct research at your practice?

*Support Research:*

* Would you like to learn more about clinical trials?
* How would you like to learn about clinical trials?
* What would you like to learn about clinical trials?

*Top Barriers:*

* According to you what are the top barriers that you experience in a clinical trial research?
* protocol concerns
* Informed consent concerns
* rigid inclusion or exclusion criteria
* no trials available for advance diseases
* unavailability of appropriate clinical trial
* health insurance coverage and cost issues
* lack of time
* transportation
* quality of life issues (side effects, etc)
* language barrier
* Non - compliant patients

**Phase 3**

**Data analysis and Data management**

Our data collection will include both quantitative and qualitative techniques. We will use descriptive analysis for quantitative data and text analysis for qualitative data. Qualitative analyses will follow grounded theory approach. The focus groups will be transcribed and analyzed using the accepted qualitative analysis techniques of Morgan and Krueger.47,48 Any discrepancies on themes will be resolved prior to dissemination. The Co-I Davis has the necessary training/experience to conduct focus group studies, and she has been published in this area.19,49,50

1. **Risks and Benefits of Research**

**Potential Risks and Protection against Risks**

Risks to Surveys:

There are no potential risks to participate in surveys. Surveys will be either self-administered or administered by a trained research staff in-person or over the phone. To protect the privacy and confidentiality of participants in survey questionnaire, individuals will not be identified to their responses.

Risks to Focus Groups:

Risks to participate in focus groups are very minimal. The possible risks include psychological damage while discussing clinical trials. However, the group responses will be de-identified and unlikely to be harmful. Participants will be given an opportunity to ask questions about the topics to be discussed in focus groups. Participants who feel uncomfortable about the discussion will be given an opportunity to drop out at any time without any penalty.

**Potential Benefits**

There is no monetary or gift card compensation to participants for completing the surveys and for participating in focus groups. However, food/refreshments will be provided to participants during focus groups for their contribution.

We believe that the responses from the survey questionnaires and focus groups will help us identify barriers to clinical trials to develop interventions to increase recruitment and enrollment of pediatric population into clinical trials in the rural Kansas.

1. **Plan for Monitoring and Reporting**

The PI is responsible for monitoring and reporting all unanticipated problems.

1. **Data Collection and Protection**

Participants will be de-identified from survey questionnaire. Focus group transcripts will be de-identified. No individual will be identified to themes or subthemes. All data will be presented in an aggregate form, with no identification to individuals.

1. **Study Withdrawal Procedure**

Participants who wish not to continue participating may withdraw any time from the study without any penalty.

1. **Record Retention**

All focus group audiotapes, transcripts, and surveys will be kept locked at KUMC in a secured location. The records will be accessed only by the designated research staff. Study records will be retained and destroyed per KUMC IRB guidelines

1. **References**

1. Roldan T, Villamanan E, Ruano M, Larrubia Y, Gomez-Salcedo P, Herrero A. Analysis of clinical trials and off-label drug use in hospitalized pediatric patients. Arch Argent Pediatr. 2014;112(3):249-53. doi: 10.1590/S0325-00752014000300009. PubMed PMID: 24862807.

2. Shah SS, Hall M, Goodman DM, Feuer P, Sharma V, Fargason C, Jr., Hyman D, Jenkins K, White ML, Levy FH, Levin JE, Bertoch D, Slonim AD. Off-label drug use in hospitalized children. Arch Pediatr Adolesc Med. 2007;161(3):282-90. doi: 10.1001/archpedi.161.3.282. PubMed PMID: 17339510.

3. Saiyed MM, Lalwani T, Rana D. Is off-label use a risk factor for adverse drug reactions in pediatric patients? A prospective study in an Indian tertiary care hospital. Int J Risk Saf Med. 2015;27(1):45-53. doi: 10.3233/JRS-150642. PubMed PMID: 25766066.

4. Bellis JR, Kirkham JJ, Thiesen S, Conroy EJ, Bracken LE, Mannix HL, Bird KA, Duncan JC, Peak M, Turner MA, Smyth RL, Nunn AJ, Pirmohamed M. Adverse drug reactions and off-label and unlicensed medicines in children: a nested case-control study of inpatients in a pediatric hospital. BMC Med. 2013;11:238. doi: 10.1186/1741-7015-11-238. PubMed PMID: 24229060; PMCID: PMC4231613.

5. Kitsantas P, Kornides ML, Cantiello J, Wu H. Chronic physical health conditions among children of different racial/ethnic backgrounds. Public Health. 2013;127(6):546-53. doi: 10.1016/j.puhe.2013.02.006. PubMed PMID: 23583033; PMCID: PMC4086459.

6. Cohen E, Patel H. Responding to the rising number of children living with complex chronic conditions. CMAJ. 2014;186(16):1199-200. doi: 10.1503/cmaj.141036. PubMed PMID: 25316900; PMCID: PMC4216247.

7. Luchtenberg M, Maeckelberghe E, Locock L, Powell L, Verhagen AA. Young People's Experiences of Participation in Clinical Trials: Reasons for Taking Part. Am J Bioeth. 2015;15(11):3-13. doi: 10.1080/15265161.2015.1088974. PubMed PMID: 26575802.

8. Hamm MP, Scott SD, Klassen TP, Moher D, Hartling L. Do health care institutions value research? A mixed methods study of barriers and facilitators to methodological rigor in pediatric randomized trials. BMC Med Res Methodol. 2012;12:158. doi: 10.1186/1471-2288-12-158. PubMed PMID: 23078589; PMCID: PMC3503580.

9. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron CD. Barriers to clinical trial participation: a comparison of rural and urban communities in South Carolina. J Community Health. 2014;39(3):562-71. doi: 10.1007/s10900-013-9798-2. PubMed PMID: 24310703.

10. Connor EM, Smoyer WE, Davis JM, Zajicek A, Ulrich L, Purucker M, Hirschfeld S. Meeting the demand for pediatric clinical trials. Sci Transl Med. 2014;6(227):227fs11. doi: 10.1126/scitranslmed.3008043. PubMed PMID: 24622511; PMCID: PMC4104358.

11. Tanner A, Kim SH, Friedman DB, Foster C, Bergeron CD. Barriers to medical research participation as perceived by clinical trial investigators: communicating with rural and african american communities. J Health Commun. 2015;20(1):88-96. doi: 10.1080/10810730.2014.908985. PubMed PMID: 25204763.

12. Patterson CA, Chavez V, Mondestin V, Deatrick J, Li Y, Barakat LP. Clinical Trial Decision Making in Pediatric Sickle Cell Disease: A Qualitative Study of Perceived Benefits and Barriers to Participation. J Pediatr Hematol Oncol. 2015;37(6):415-22. doi: 10.1097/MPH.0000000000000216. PubMed PMID: 25072368.

13. Barakat LP, Schwartz LA, Reilly A, Deatrick JA, Balis F. A Qualitative Study of Phase III Cancer Clinical Trial Enrollment Decision-Making: Perspectives from Adolescents, Young Adults, Caregivers, and Providers. J Adolesc Young Adult Oncol. 2014;3(1):3-11. doi: 10.1089/jayao.2013.0011. PubMed PMID: 24669354; PMCID: PMC3955960.

14. Barakat LP, Patterson CA, Mondestin V, Chavez V, Austin T, Robinson MR, Li Y, Smith-Whitley K, Cohen R. Initial development of a questionnaire evaluating perceived benefits and barriers to pediatric clinical trials participation. Contemp Clin Trials. 2013;34(2):218-26. doi: 10.1016/j.cct.2012.11.001. PubMed PMID: 23149214.

15. Sweet SN, Ginis KA, Estabrooks PA, Latimer-Cheung AE. Operationalizing the RE-AIM framework to evaluate the impact of multi-sector partnerships. Implement Sci. 2014;9:74. doi: 10.1186/1748-5908-9-74. PubMed PMID: 24923331; PMCID: PMC4072487.

16. McCulloh R, Koster M, Ralston S, Johnson M, Hill V, Koehn K, Weddle G, Alverson B. Use of Intermittent vs Continuous Pulse Oximetry for Nonhypoxemic Infants and Young Children Hospitalized for Bronchiolitis: A Randomized Clinical Trial. JAMA Pediatr. 2015;169(10):898-904. doi: 10.1001/jamapediatrics.2015.1746. PubMed PMID: 26322819.

17. DeVincenzo JP, Whitley RJ, Mackman RL, Scaglioni-Weinlich C, Harrison L, Farrell E, McBride S, Lambkin-Williams R, Jordan R, Xin Y, Ramanathan S, O'Riordan T, Lewis SA, Li X, Toback SL, Lin SL, Chien JW. Oral GS-5806 activity in a respiratory syncytial virus challenge study. N Engl J Med. 2014;371(8):711-22. doi: 10.1056/NEJMoa1401184. PubMed PMID: 25140957.

18. Davis AM, James RL, Boles RE, Goetz JR, Belmont J, Malone B. The use of TeleMedicine in the treatment of paediatric obesity: feasibility and acceptability. Matern Child Nutr. 2011;7(1):71-9. doi: 10.1111/j.1740-8709.2010.00248.x. PubMed PMID: 21108739; PMCID: PMC3071528.

19. Davis AM, James RL, Curtis MR, Felts SM, Daley CM. Pediatric obesity attitudes, services, and information among rural parents: a qualitative study. Obesity (Silver Spring). 2008;16(9):2133-40. doi: 10.1038/oby.2008.312. PubMed PMID: 18551114; PMCID: PMC2701507.

20. Gallagher KS, Davis AM, Malone B, Landrum Y, Black W. Treating rural pediatric obesity through telemedicine: baseline data from a randomized controlled trial. J Pediatr Psychol. 2011;36(6):687-95. doi: 10.1093/jpepsy/jsr011. PubMed PMID: 21372069; PMCID: PMC3131699.

21. Davis AM, Sampilo M, Gallagher KS, Landrum Y, Malone B. Treating rural pediatric obesity through telemedicine: outcomes from a small randomized controlled trial. J Pediatr Psychol. 2013;38(9):932-43. doi: 10.1093/jpepsy/jst005. PubMed PMID: 23428652; PMCID: PMC3785218.

22. Reese RM, Braun MJ, Hoffmeier S, Stickle L, Rinner L, Smith C, Ellerbeck K, Jamison R, Wendland M, Jarrett L, Hadorn M. Preliminary Evidence for the Integrated Systems Using Telemedicine. Telemed J E Health. 2015;21(7):581-7. doi: 10.1089/tmj.2014.0124. PubMed PMID: 25898157.

23. Jacobson JD, Ellerbeck KA, Kelly KA, Fleming KK, Jamison TR, Coffey CW, Smith CM, Reese RM, Sands SA. Evidence for alterations in stimulatory G proteins and oxytocin levels in children with autism. Psychoneuroendocrinology. 2014;40:159-69. doi: 10.1016/j.psyneuen.2013.11.014. PubMed PMID: 24485488; PMCID: PMC4259400.

24. Kluding PM, Denton J, Jamison TR, Brooks W, Blackwell K, Lantos JD, Waitman LR, McMahon TM, Choudhary A, Bott MJ, Greiner A, Klaus S, O'Brien-Ladner A, Aaronson LS, Burns J, Barohn R. Frontiers: Integration of a Research Participant Registry with Medical Clinic Registration and Electronic Health Records. Clin Transl Sci. 2015;8(5):405-11. doi: 10.1111/cts.12309. PubMed PMID: 26243261; PMCID: PMC4673893.

25. Sabesan S, Burgher B, Buettner P, Piliouras P, Otty Z, Varma S, Thaker D. Attitudes, knowledge and barriers to participation in cancer clinical trials among rural and remote patients. Asia Pac J Clin Oncol. 2011;7(1):27-33. doi: 10.1111/j.1743-7563.2010.01342.x. PubMed PMID: 21332648.

26. Avis NE, Smith KW, Link CL, Hortobagyi GN, Rivera E. Factors associated with participation in breast cancer treatment clinical trials. J Clin Oncol. 2006;24(12):1860-7. doi: 10.1200/JCO.2005.03.8976. PubMed PMID: 16622260.

27. Waitman LR, Aaronson LS, Nadkarni PM, Connolly DW, Campbell JR. The Greater Plains Collaborative: a PCORnet Clinical Research Data Network. J Am Med Inform Assoc. 2014;21(4):637-41. doi: 10.1136/amiajnl-2014-002756. PubMed PMID: 24778202; PMCID: PMC4078294.

28. Boom JA, Nelson CS, Kohrt AE, Kozinetz CA. Utilizing peer academic detailing to improve childhood immunization coverage levels. Health Promot Pract. 2010;11(3):377-86. doi: 10.1177/1524839908321487. PubMed PMID: 18955545.

29. Colon-Emeric CS, Lyles KW, House P, Levine DA, Schenck AP, Allison J, Gorospe J, Fermazin M, Oliver K, Curtis JR, Weissman N, Xie A, Saag KG. Randomized trial to improve fracture prevention in nursing home residents. Am J Med. 2007;120(10):886-92. doi: 10.1016/j.amjmed.2007.04.020. PubMed PMID: 17904460; PMCID: PMC2288656.

30. Price-Haywood EG, Roth KG, Shelby K, Cooper LA. Cancer risk communication with low health literacy patients: a continuing medical education program. J Gen Intern Med. 2010;25 Suppl 2:S126-9. doi: 10.1007/s11606-009-1211-6. PubMed PMID: 20352506; PMCID: PMC2847095.

31. Hewitt CE, Kumaravel B, Dumville JC, Torgerson DJ, Trial attrition study g. Assessing the impact of attrition in randomized controlled trials. J Clin Epidemiol. 2010;63(11):1264-70. doi: 10.1016/j.jclinepi.2010.01.010. PubMed PMID: 20573482.

32. Sharma NS. Patient centric approach for clinical trials: Current trend and new opportunities. Perspect Clin Res. 2015;6(3):134-8. doi: 10.4103/2229-3485.159936. PubMed PMID: 26229748; PMCID: PMC4504054.

33. Viswanath K, McCloud R, Minsky S, Puleo E, Kontos E, Bigman-Galimore C, Rudd R, Emmons KM. Internet use, browsing, and the urban poor: implications for cancer control. J Natl Cancer Inst Monogr. 2013;2013(47):199-205. doi: 10.1093/jncimonographs/lgt029. PubMed PMID: 24395992; PMCID: PMC3881997.

34. Curro FA, Robbins DA, Millenson ML, Fox CH, Naftolin F. Person-centric clinical trials: an opportunity for the good clinical practice (GCP)-practice-based research network. J Clin Pharmacol. 2013;53(10):1091-4. doi: 10.1002/jcph.138. PubMed PMID: 23868608.

35. Van Acker R, De Bourdeaudhuij I, De Cocker K, Klesges LM, Cardon G. The impact of disseminating the whole-community project '10,000 Steps': a RE-AIM analysis. BMC Public Health. 2011;11:3. doi: 10.1186/1471-2458-11-3. PubMed PMID: 21205290; PMCID: PMC3022698.

36. Jilcott S, Ammerman A, Sommers J, Glasgow RE. Applying the RE-AIM framework to assess the public health impact of policy change. Ann Behav Med. 2007;34(2):105-14. doi: 10.1080/08836610701564055. PubMed PMID: 17927550.

37. Joseph G, Dohan D. Recruiting minorities where they receive care: Institutional barriers to cancer clinical trials recruitment in a safety-net hospital. Contemp Clin Trials. 2009;30(6):552-9. doi: 10.1016/j.cct.2009.06.009. PubMed PMID: 19580887.

38. Mattioli L, Goertz K, Ardinger R, Belmont J, Cox R, Thomas C. Pediatric cardiology: auscultation from 280 miles away. Kans Med. 1992;93(12):326, 47-50. PubMed PMID: 1287282.

39. Spaulding R, Stevens D, Velasquez SE. Experience with telehealth for sleep monitoring and sleep laboratory management. J Telemed Telecare. 2011;17(7):346-9. doi: 10.1258/jtt.2011.110202. PubMed PMID: 21967997.

40. Spaulding RJ, Russo T, Cook DJ, Doolittle GC. Diffusion theory and telemedicine adoption by Kansas health-care providers: critical factors in telemedicine adoption for improved patient access. J Telemed Telecare. 2005;11 Suppl 1:107-9. doi: 10.1258/1357633054461903. PubMed PMID: 16036015.

41. Duncan AB, Velasquez SE, Nelson EL. Using videoconferencing to provide psychological services to rural children and adolescents: a review and case example. J Clin Child Adolesc Psychol. 2014;43(1):115-27. doi: 10.1080/15374416.2013.836452. PubMed PMID: 24079653.

42. Waitman LR, Warren JJ, Manos EL, Connolly DW. Expressing observations from electronic medical record flowsheets in an i2b2 based clinical data repository to support research and quality improvement. AMIA Annu Symp Proc. 2011;2011:1454-63. PubMed PMID: 22195209; PMCID: PMC3243191.

43. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010. PubMed PMID: 18929686; PMCID: PMC2700030.

44. Kotloff KL, Halasa NB, Harrison CJ, Englund JA, Walter EB, King JC, Creech CB, Healy SA, Dolor RJ, Stephens I, Edwards KM, Noah DL, Hill H, Wolff M. Clinical and immune responses to inactivated influenza A(H1N1)pdm09 vaccine in children. Pediatr Infect Dis J. 2014;33(8):865-71. doi: 10.1097/INF.0000000000000329. PubMed PMID: 25222307; PMCID: PMC4166548.

45. Kearns GL, Leeder JS, Gaedigk A. Impact of the CYP2C19\*17 allele on the pharmacokinetics of omeprazole and pantoprazole in children: evidence for a differential effect. Drug Metab Dispos. 2010;38(6):894-7. doi: 10.1124/dmd.109.030601. PubMed PMID: 20223877; PMCID: PMC2879959.

46. Cirillo I, Vaccaro N, Redman R, Black PL, Kearns GL. Pharmacokinetics of single-dose doripenem in adults with cystic fibrosis. J Clin Pharmacol. 2012;52(11):1645-53. doi: 10.1177/0091270011427564. PubMed PMID: 22174436.

47. Morgan DL. Qualitative content analysis: a guide to paths not taken. Qual Health Res. 1993;3(1):112-21. PubMed PMID: 8457790.

48. Kennedy C, Kools S, Krueger R. Methodological considerations in children's focus groups. Nurs Res. 2001;50(3):184-7. PubMed PMID: 11393641.

49. Davis AM, Boles RE, James RL, Sullivan DK, Donnelly JE, Swirczynski DL, Goetz J. Health behaviors and weight status among urban and rural children. Rural Remote Health. 2008;8(2):810. PubMed PMID: 18426334; PMCID: PMC2702202.

50. Davis AM, Canter KS, Stough CO, Gillette MD, Patton S. Measurement of mealtime behaviors in rural overweight children: an exploratory factor analysis of the Behavioral Pediatrics Feeding Assessment Scale. J Pediatr Psychol. 2014;39(3):332-9. doi: 10.1093/jpepsy/jst089. PubMed PMID: 24326908; PMCID: PMC3959263.

51. McQuillan RF, Silver SA, Harel Z, Weizman A, Thomas A, Bell C, Chertow GM, Chan CT, Nesrallah G. How to Measure and Interpret Quality Improvement Data. Clin J Am Soc Nephrol. 2016. doi: 10.2215/CJN.11511015. PubMed PMID: 27016496.

52. Perla RJ, Provost LP, Murray SK. The run chart: a simple analytical tool for learning from variation in healthcare processes. BMJ Qual Saf. 2011;20(1):46-51. doi: 10.1136/bmjqs.2009.037895. PubMed PMID: 21228075.

53. Lawal AK, Rotter T, Kinsman L, Sari N, Harrison L, Jeffery C, Kutz M, Khan MF, Flynn R. Lean management in health care: definition, concepts, methodology and effects reported (systematic review protocol). Syst Rev. 2014;3:103. doi: 10.1186/2046-4053-3-103. PubMed PMID: 25238974; PMCID: PMC4171573.

54. Nelson EC, Splaine ME, Batalden PB, Plume SK. Building measurement and data collection into medical practice. Ann Intern Med. 1998;128(6):460-6. PubMed PMID: 9499330.

55. Guinane CS, Sikes JI, Wilson RK. Using the PDSA cycle to standardize a quality assurance program in a quality improvement-driven environment. Jt Comm J Qual Improv. 1994;20(12):696-705. PubMed PMID: 7881519.