Commentary

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Not Just Small Adults: Has the Time Come for Pediatric Clinical Research to have its Own Methodology?

Lois W Sayrs[1,3]* and David M Notrica[2,3]

[1]*Children's Hospital of Orange Country Research Institute, USA*

[2]*Phoenix Children's Hospital, USA*

[3]*University of Arizona College of Medicine-Phoenix, USA*

***Corresponding author:** Lois W Sayrs, Children's Hospital of Orange Country Research Institute, University of Arizona College of Medicine-Phoenix, USA

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ABSTRACT

Conducting pediatric research presents unique methodological challenges that necessitate the establishment of a separate pediatric research methodology. This paper argues for the widespread recognition and implementation of a specialized research methodology, one that is best suited to optimize the effectiveness of pediatric clinical decisions, tailored to address challenges specific to pediatric research and therefore, optimizes outcomes for pediatric patients.

Abbreviations: RCT: Randomized Controlled Trials; PRCT: Pragmatic Randomized Control Trial Designs; PNRT: Pragmatic Non-Randomized Research Trial Designs; AYA: Adolescence and Young Adulthood; MCT: Multicenter Trial

Introduction

Conducting pediatric research presents unique methodological challenges that necessitate the establishment of a separate pediatric research methodology. Limitations inherent in conducting pediatric clinical research, especially randomized controlled trials (RCTs) are well-described [1]; and recently, the implications of these limitations on publication rates for non-RCT pediatric research in high impact peer-reviewed journals has been noted [2]. While there is general acceptance of the value of real-world evidence to pediatric research the benefits for relying more heavily on pragmatic designs in pediatric clinical research has not, as yet, been fully explored [3]. A pragmatic research design is a novel trial innovation that utilizes real-world naturalistic experiments and minimizes bias via post-hoc management of methodological issues arising from a lack of random assignment. Pragmatic randomized control trial designs (pRCTs) and other pragmatic non-randomized research trial designs (pNRTs) afford greater flexibility and better mimic real-world clinical decision-making [4]. As such, their value to pediatric research cannot be overstated. This paper argues for the widespread recognition and implementation of a specialized research methodology, one that is best suited to optimize the effectiveness of pediatric clinical decisions, tailored to address challenges specific to pediatric research and therefore, optimizes outcomes for pediatric patients. By describing key features of this new methodology, clinical investigators can gain greater comfort and familiarity with methods to advance pediatric research more quickly and effectively.

A separate pediatric methods could incorporate, rather than ignore developmental stages- Children undergo physical, cognitive, and emotional development, oftentimes rapidly. When pediatric research ignores these changes, results do not account for the effects of developmental stages that may change patient outcomes. Age-specific diagnostic tools should be the standard for measurement and more

pediatric research should focus on developing these age-specific measures. Pediatric research should also acknowledge age-appropriate study designs and outcome measures that include long-term follow-up-throughout childhood, adolescence and young adulthood (AYA). Specific recruitment strategies for long-term tracking should be the norm in pediatric research designs to capture proximate and distal effects of treatments and interventions. Identifying developmental milestones, using age-specific assessments, and capturing outcomes in longitudinal designs can easily be integrated into pediatric pRCTs; and results reported periodically as treatment regimes shift and children age to assess response to interventions.

Pediatric research could study patients de novo rather than replicate adult studies- Pediatric research must gain autonomy of research rather than assume pediatric questions parallel adult questions. While there are similarities, the differences far outweigh the benefits from replication. A separate methodology would provide a strong foundation for that autonomy. When pediatric research replicates adult research hypotheses, it is easy to omit unique etiologies and developmental issues of the disease or condition that differentiate adults and children. Replication of adult studies also promulgates bias and undermines the validity and reliability of pediatric research by ignoring relevant pediatric characteristics not studied in an adult context. In pediatric research, there are many instances where etiologies are unknown, observational research is limited, mechanisms and their interaction with other systems are not well-understood, or complex comorbidities confound the value of the experimental design. By assuming these characteristics follow adult patterns, pediatric research may be wasting precious research resources investigating irrelevant aspects of a condition. When pediatric research follows the clinician's observations as well as the family's and child's experience, research questions generated would not likely replicate the adult research literature. Rather the questions would reflect meaningful clinical and patient experience.

Pediatric research could lean into heterogeneity to the benefit of the patient-Children in pediatric research often demonstrate wide variability in their demographics and clinical characteristics. Since traditional experimental studies often have strict exclusion rules, pediatric studies have had to choose between very small samples or permit heterogeneity, both of which limit the applicability of the RCT to pediatric clinical practice. In the last decade, however, increasing reliance on collaboration among children's hospitals (e.g. Children's Oncology Group) has supported more opportunities for the multicenter trial (MCT), a recognition that heterogeneity may bring benefits as well as costs. A distinct pediatric research methodology would recognize the value of pragmatic designs such as cross-over within-group designs, N-of-1 repeated measures designs, and wedge cluster designs that can be used to test hypotheses of interest. In combination with innovative collaboration strategies, specialized pediatric research networks, these research collaboratives can promote the utilization of pRCTs and build clinically meaningful registries targeting specific diseases, conditions and diagnoses. Wider use of pRCTs will also promote the value of heterogeneity to clinical research, demonstrating who benefits from new treatments much faster than with traditional RCTs. Combination MCT/pRCTs will afford the greatest opportunity in pediatric clinical research to test important hypotheses with sample sizes powered for even the rarest events. By incorporating methods that easily manage heterogeneity, study results will have more immediate utility to clinical decision-making.

Pediatric research could explore innovative data collection strategies to facilitate research- A separate pediatric methodology is also better able to address unique trial challenges around patient/family engagement, trial recruitment and informed consent. For example, a pediatric methodology could easily test the effect of family consent rooms, use surrogate decision-makers in simulations and create child-friendly assent processes to obtain informed consent in accordance with children's and their families' needs and capacities. Challenges of data collection could also be more functionally explored, including the added value of parental reports, clinician assessments, child/AYA narratives, parent videos and self-reports. A dedicated methodology would be able to focus on refining data collection techniques and validating measurement tools to enhance the accuracy and reliability of pediatric research outcomes. Natural interdisciplinary collaborations in pediatrics across medical specialties to optimize clinical outcomes could also be leveraged for research to collect wide ranging data of most use to diagnosis and treatment. Exploiting these natural patient-centered collaborations would not only bring together expertise from various fields but also promote integrative child-centered care.

Conclusion

A unique pediatric research methodology would incorporate designs that allow for significant differences between children and adults, account for developmental stages, more effectively utilize patient, treatment and outcome heterogeneity, ensure the inclusion of appropriate safeguards, optimize participant recruitment and engagement, promote a child-centered development of evidence-based treatments and interventions, and ultimately improve the health and well-being of children. By recognizing the heterogeneity of pediatric populations, the heterogeneity of treatments and outcomes, a separate pediatric research methodology can strengthen the quality and applicability of pediatric research, thus benefiting the patients we treat.

References

1. Duffett M, Choong K, Hartling L, Menon K, Thabane L, et al. (2013) Randomized controlled trials in pediatric critical care: a scoping review. Critical care 17: 1-9.
2. Sanger T (2023) Neurological research in children: challenges and misconceptions. The Lancet Neurology 22(6): 474-475.

3. Horton DB, Blum MD, Burcu M (2021) Real-world evidence for assessing treatment effectiveness and safety in pediatric populations. The Journal of Pediatrics 238: 312-316.

4. Sox HC, Lewis RJ (2016) Pragmatic Trials: Practical Answers to "Real World" Questions. JAMA 316(11): 1205-1206.

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Lois W Sayrs. Biomed J Sci & Tech Res

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