Transparency and Accountability of Pediatric Trials: Should Consent Rate Reporting Be Mandatory?

The study of Lonhart et al in this volume of *The Journal* sends a warning about reporting consent rates in pediatric trials.[1] They analyzed 696 articles from MEDLINE presenting pediatric randomized controlled trials and showed that 60% (n = 418) of them did not report rates of consent for trial participants, or the consent rate was unclear. Among 278 trials that did report the number of consenting subjects, the average consent rate was high (83%), but for 26% of these trials, the average consent rate was less than 70%, which may introduce a bias related to the representativeness of the target population. Overall, the consent rates were greater for trials of vaccination interventions (90%) in comparison with behavioral interventions (79%), and for industry-funded trials (86%) in comparison with government-funded trials (79%). This study raises important questions related to the ethics of pediatric trials and to the quality and validity of evidence from pediatric trials.

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From the ethical point of view, consent for a clinical trial is a prerequisite for a complex process with active involvement of a participant, in which the participant must receive sufficient information about the trial to understand what the trial is about and to have sufficient time to ask questions and discuss with close persons whether to participate in the study. In pediatric trials, the age of consent for participants is important, as well as the age when assent from the child should be obtained in addition to the consent from the parents/guardians. A recent survey by the Pediatric Assent Initiative in the US and internationally[2] collected experiences of children, parents, and professionals with assent in pediatric research and called for more standardized and age-appropriate practices for obtaining assent so that pediatric patients can make fully informed decisions.

The study from Lonhart et al did not differentiate between consent and assent, but we expect that there is variability in how different regulatory systems define these ages.[1] For example, the document on the ages for consent and assent for clinical trials compiled by the European Network of Pediatric Research at the European Medicines Agency shows quite a variety of ages for assent, including Finland, which defines assent as early as a child is literate.[3] The study by Gates et al looked at reporting of consent in a random sample of 300 published studies involving children from the Cochrane Central Register of Controlled Trials.[4] They found that the fact that consent was obtained was reported by almost all studies (92%), but only 13% reported who obtained the consent. For trials with school children, 68% reported that assent was obtained. Consent/assent rates were not reported.

Lonhart et al argue for greater transparency surrounding consent to improve future clinical trials, especially with regard to their feasibility and implementation, as well as development and budgeting.[1] To achieve this, the current standards of registering and reporting consent rates should also be improved. Details about consent during the randomization process should be a part of the trial registration. After the trial, registration of the results and trial data should include basic information about the characteristics of nonrespondents and the reasons for not giving consent, because they often differ in personal characteristics.[5] Consolidated Standards of Reporting Trials, or CONSORT, the standard for reporting randomized controlled trials, does not address reporting consent methodology or consent rates, although it mentions that obtaining informed consent is an integral part of implementing the randomization process.[6] Some researchers proposed an extension of CONSORT for pediatric trials, which includes the following item: "Was information about research provided to children and assent taken (appropriate for age)?" under ethical considerations in the Methods section,[7] but reporting of consent rates is again not mentioned.

We know that reporting guidelines work,[8] so the logical next step would be to address the issues surrounding consent in the next revision of CONSORT in general and for pediatric trials specifically. It is up to all involved in pediatric trials—researchers, both those directly involved in trials and those producing evidence synthesis, regulatory and ethics bodies, granting organizations, patients, and journal editors—to resolve the issue of full transparency of the consenting process, to increase the accountability and quality of pediatric trials. ■

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Automated Office Blood Pressure Measurement for the Diagnosis of Hypertension

Accurate blood pressure (BP) measurements are important for the diagnosis and treatment of hypertension in children and adolescents. Hypertension is a significant risk factor for a number of chronic conditions in children and adults, including cerebrovascular disease, coronary artery disease, congestive heart failure, renal failure, and stroke. Unfortunately, the prevalence of pediatric hypertension has significantly increased as a result of childhood obesity.[1] Hypertension is routinely diagnosed using office BP measurements, which should be interpreted using the Task Force Office Blood Pressure reference thresholds guidelines.[2-4] This process requires knowledge of the patient's height percentile.

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There are a number of methods for BP measurements, and we are about to learn that there now is another one which may serve as an attractive alternative. The 4 most widely used methods are conventional manual BP measurement through the use of a sphygmomanometer (now rarely used due to mercury concerns); an aneroid or oscillometric device (often also named a digital device) in the clinic setting and herein referred to as office BP; conventional BP measurement, through the use of an aneroid or oscillometric device outside of the clinic setting; arterial BP measurement, an invasive method usually done in a hospital setting; and ambulatory 24-hour BP monitoring (ABPM) using an oscillometric device.

Office BP is used most often in the clinical setting. However, one-third of children with office BP-based hypertension also have white-coat hypertension, which does not require treatment.[5,6] Furthermore, office BP measurements are insensitive to masked and nighttime hypertension, which can independently influence end-organ damage.[6,7]

ABPM is used in clinical practice to better characterize hypertension and to guide therapeutic decisions.[5-7] This method can diagnose white-coat, masked, and nighttime hypertension. The American Academic of Pediatrics and the European Society of Hypertension published guidelines for the use of ABPM.[2-4] There is also a version for Canada.[8] Abnormal ABPM readings and confirmation of end-organ damage serve as the gold standard for the diagnosis of hypertension. Although there are some differences when applying either the American or European guidelines,[9] all of them call for the use of ABPM for the confirmation of hypertension. Furthermore, routine ABPM is strongly recommended to regularly assess severity and determine circadian BP patterns. However, ABPM is not widely available because it involves specialized instrumentation, trained staff, and other costs that are nonreimbursable in many regions of the world. In fact, reimbursement for ABPM varies widely among the different states in the US and in Canada. Another limitation is the frequent need for shipment of the ABPM monitor at cost for the hospitals, which is not reimbursed. Moreover, wearing the ABPM monitor for 24 hours is not convenient for small patients and may explain the significant intrapatient variability of ABPM in the pediatric setting.[10] As such, an abbreviated version of automated BP monitoring would be desirable.

In this volume of *The Journal*, Coral Hanevold et al describes a novel study that determined the level of agreement between automated office BP (AOBP), auscultated (manual) office BP, and ABPM to correctly identify hypertension in patients less than 18 years of age.[11] Hanevold et al introduced us to a fifth method, and it is essentially the measurement of BP

ABPM	Ambulatory 24-hour blood pressure monitoring
AOBP	Automated office blood pressure
BP	Blood pressure

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