SUMMARY

Introduction:

Clinical trials require an enormous amount of money and time, but only a small percentage of tested therapies are eventually approved for human use. This may be significantly influenced by the quality of the research itself, which in turn is negatively affected by errors accumulating at all stages of clinical and preclinical trials. These errors are collectively known as research waste. One of the basic requirements for clinical trials is that they have the potential to generate high-quality data. They will then have so-called social value – the potential to bring direct benefit to the patient/participant or, indirectly, to the population to which they belong. Accumulation of research waste reduces this potential, and therefore has a very negative impact on the social value of research. Some populations of research participants require special treatment and protection, for example because of their inability to give informed consent. One of these populations are children. So far, there are no sufficient criteria that would allow the assessment of social value at various stages of research. It is not clear how to make this assessment prospectively, especially in early-phase studies involving pediatric population and in medical fields such as oncology, where it is difficult to develop effective and safe therapies.

Aim:

The aim of this dissertation is to assess the social value of early-phase oncology trials involving pediatric population, and to evaluate aspects of research waste in selected clinical trials, done in pediatric population. Another aim is to develop criteria which will help in the prospective assessment of social value provided by selected types of clinical trials.

Methods:

The following dissertation consists of meta-research and theoretical analysis articles. The former are based on the systematic review methodology, and provide data on social value and research waste in clinical trials. The meta-study of social value looked at pediatric phase 1 studies. The cross-sectional analysis assessed an aspect of research waste, i.e. insufficient publication of results. This study looked at trials registered on the ClinicalTrials.gov platform, associated with at least one Polish academic medical center. The latter group of articles in the following dissertation are

theoretical analyzes. They aim to summarize data from meta-research, and develop criteria helpful in the prospective assessment of social value of selected clinical trials.

Results:

The analysis of social value shows, that the treatments tested in 5% of analyzed studies are eventually approved by a regulatory agency for use in the tested indication. Our analysis also shows that more than 1/3 of the treatments tested in phase 1 move on to further phases of clinical trials. These studies therefore influence further development of the tested interventions, even if they do not contribute to the marketing approval. The studies included in the analysis, were also widely cited by a variety of primary research articles from other fields of biomedical science. The cross-sectional analysis of clinical trials with pediatric population, conducted in Polish academic medical centers, showed that the percentage of trials that publish results is relatively high. However, the results of only half of the published studies were made available online or in the form of a publication within 2 years of the study end, i.e. in line with the current requirements. This reduces the social value of these trials – if they are not published quickly enough, they have no chance of contributing to the advancement of science. In the theoretical articles included in this dissertation I propose solutions to strengthen the system of prospective evaluation of newly proposed clinical trials. These solutions could replace the current standards, contribute to the elimination of research waste and thus increase the social value of research done in pediatrics. I also outline that even if various pediatric studies show little direct benefit (clinical value) to the participant, without them it would be impossible to develop many fields of biomedical science and raise public awareness of many diseases.

Conclusion:

The accumulation of research waste in clinical trials can have serious financial and ethical consequences. Waste reduces the scientific and social value of a study by lowering the quality of obtained evidence. In addition to its immediate clinical value, the social value of a trial provides important justification for exposing participants to various forms of risk. There is a need for continuous evaluation of clinical trials, from the planning stage, through monitoring, up to their completion. It is necessary to implement before the start of research procedures, solutions that will make sure that the research is based on high-quality data, has a strong research hypothesis, and a good chance of publishing the results after its completion.