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Ethical Principles for Medical Research Involving Human Participants

The Declaration of Helsinki[1], a set of international ethical principles for medical research, published its latest version in October 2024. A new version is produced every decade, the previous iteration in October 2013. The Declaration, which was first adopted in 1964, contains 37 ethical principles for research involving human beings. It grew out of past major ethics research failures. During its 60-year existence it has been the most influential code in the guidance of medical research ethics. While the basic principles have stood the rest of time, new versions are required from time-to-time to keep pace with contemporary issues that arise in the conduct of research[2]. A case in point is the rapid growth in artificial intelligence (AI) and its threat to patient confidentiality. AI is now used in clinical drug development, and patient selection to accelerate clinical trials. This latest version is the product of a 30-month long review process. A working group was created across 19 countries. There were 8 regional meetings around the globe, and two public consultations[3].

Words are important. Throughout the latest version, the term subjects has been replaced by the term participants. This is a more respectful term and it recognises that the individual volunteer is a partner in the research project. It is pointed out that the code of ethical practice applies both to patients and to healthy volunteers. Item 4 states that it is the duty of the physician and the research team to safeguard the wellbeing and rights of those participating in the research. There must be an emphasis on safety, effectiveness, efficiency, accessibility, and quality. Item 7 points out that the purpose of undertaking research on humans is to understand the causes, development, and effect of diseases: and to improve therapeutic interventions.

Item 12 states that medical research must be only undertaken and led by individuals with the appropriate training, education, and experience. The importance of good supervision is emphasised, and scientific integrity is essential. Researchers must never engage in research misconduct. Item 14 addresses the matter of conflicts of interest. Physicians who combine medical research with medical care should only involve their patients in research to the extent that is safe, justified, and has the potential to be beneficial. There is a section devoted to risks, burdens, and benefits. Item 16 states that research involving human participants can only be undertaken when its importance outweighs the potential risks and burdens. Measures to minimise complications must be implemented. If it emerges that the risks outweigh the benefits, the research must be discontinued.

The document identifies that some individuals or groups are more vulnerable as research participants and may be more likely to have an adverse event. These groups include children,

the elderly, pregnant women, and patients with disabilities. It is now better appreciated that their exclusion from research studies can perpetuate their disadvantage in benefiting from advances in medical care. The harms of inclusion have to be weighed against the harms of exclusion. This concept of moving away from exclusion towards inclusion in a responsible way is also being advocated by the FDA. Item 21 underlines the importance of rigorous design. The methodology must be scientifically sound in order to avoid subsequent research waste. The research protocol must include information on the aims, methods, anticipated benefits, and potential risks and burdens. White and Barnett have welcomed this point[4]. They quote Doug Altman, a statistician who 30 years ago urged that there should be less research, better research, and research done for the right reasons. Item 36 makes the related point that researchers have an obligation to publish and disseminate their findings. Negative findings are important in the prevention of a piece of research being needlessly repeated by other groups. The input of a statistician at an early stage in the protocol design can help eliminate poor methodology and enhances the likelihood of subsequent publication.

There is a section on research ethics committees (REC). The proposed research protocol must be submitted to the REC for approval. The REC must be transparent in its functioning and have independence in its decision making. It must be able to resist undue influence from the researchers, sponsors, and other outside institutions. It must have sufficient resources to ensure its independence. The committee must have at least one member of the general public. The REC must have the right to monitor, recommend changes, or to suspend an ongoing research study. No amendment to a research study can be made by the researchers without the approval of the REC.

Item 25 emphasises that there must be free and fully informed consent. The details of the research must be explained in plain language, and it must be clear to the participant what is being asked of them. Any risks or possible complications must be explained. The participant must be informed that they are under no obligation to participate in the research and that they free at any stage to withdraw from the it. The participant's freely given signed consent must be obtained and recorded.

Item 32 has been rewritten to address informed consent requirements for collection, storage, and secondary use of data and biological material[5]. In situations where consent for secondary research is not possible, the researchers must apply and obtain approval from an ethics committee. Ethical principles must be upheld even during a public health emergency. The Covid-19 pandemic highlighted the difficulty of balancing of rapid scientific advances with ethics and integrity. Unproven interventions to alleviate pain and suffering must not bypass ethical safety measures or evade evaluation by controlled clinical trials.

Finally, Item 33 considers the use of placebos in trials. It is a matter that raised considerable debate. A placebo is acceptable if no proven intervention exists or where the withholding of a recognised treatment poses negligible risks to the participant. However, extreme caution needs to be taken when using the latter indication. In addition, there is the consideration of post-trial access for participants who still need the intervention[6].

This Declaration is an important document and its guiding principles must be adhered to by all undertaking research on human participants.

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Editor

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