

RECENT ADVANCES IN ETHICAL CONSIDERATIONS AND INFORMED CONSENT
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I. INTRODUCTION

In recent years, significant advances in ethical considerations and informed consent practices in clinical trial have emerged to safeguard the rights and well-being of study participants. Improved informed consent processes now offer clear and understandable information to participants using multimedia tools and simplified language. Digital informed consent through electronic platforms streamlines the process and captures electronic signatures. Researchers adopt participant-centric approaches, incorporating their perspectives and preferences in trial design and consent documents. Special focus on ethical considerations for vulnerable populations ensures additional safeguards for their protection. Data privacy and security measures address concerns about personal information. The risk of real-world evidence and practical trials promotes research relevance while maintaining ethical standards. Continuous ethics oversight and global collaboration aim to harmonize ethical guidelines and temporary responsible and ethical clinical research. These advancements collectively reinforce the commitment to uphold ethical standards and prioritize participant welfare throughout the clinical trial process.

A. Importance of ethical considerations in clinical trials:

Clinical trials play a pivotal role in advancing medical knowledge, improving patient care, and developing new treatments. However, the ethical implications of conducting these trials cannot be overstated. Ethical considerations are essential to ensuring the well-being of participants, maintaining scientific integrity, and upholding public trust in the medical and research communities.

Foremost among the ethical considerations in clinical trials is the protection of participants' welfare. Trials must adhere to the principle of non-maleficence,

meaning that participants should not be exposed to unnecessary risks or harm. Rigorous informed consent processes ensure that participants fully understand the nature of the trial, potential risks, and benefits before giving their consent. Ethical review boards play a crucial role in evaluating trial protocols to ensure participant safety and to prevent undue influence or coercion.

Codes of ethics

A code of ethics serves as a foundational pillar in ensuring the ethical conduct of clinical trials, safeguarding the rights, Safety and Well-being of participants.



- **The Belmont report:** A seminal document in research ethics, outlines key principles—respect for persons, beneficence, and justice—crucial for ethical human subject's research. Published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, it remains a cornerstone of ethical research, emphasizing participant autonomy, minimizing harm, and ensuring equitable treatment. The report's enduring influence underscores its significance in guiding ethical practices and shaping research regulations, reinforcing its indispensable role in upholding the rights and welfare of research participants.
- **The declaration of helsinki:** A foundational document in medical research ethics, outlines ethical principles for conducting human research. First adopted in 1964 and revised multiple times, it emphasizes participant welfare, informed consent, and scientific rigor. Its enduring impact underscores its essential role in guiding ethical conduct in global medical research.
- **The Nuremberg code:** Formulated after World War II, lays down ethical principles for human experimentation. Its emphasis on voluntary consent, avoiding unnecessary harm, and scientific justification remains a vital influence on research ethics. This code's historical significance underscores its enduring importance in safeguarding human rights in research.
- **The U.S. common rule:** Governing human subjects research, balances ethical considerations and scientific advancement. It standardizes regulations for participant protection, informed consent, and Institutional Review Board oversight, fostering responsible and accountable research practices.

Core principles

In addition to these ethical codes, some core principles guide the work of clinical researchers. Examples include the following:



Protecting participant rights:

A well-defined code of ethics establishes a comprehensive framework for respecting participant autonomy, informed consent, and confidentiality. It emphasizes the principle of beneficence, underscoring the need to prioritize participants' well-being and ensure that their rights are upheld throughout the trial process.

Ensuring rigorous scientific integrity:

The code of ethics reinforces the imperative of scientific rigor in clinical trials. It outlines guidelines for proper trial design, unbiased data collection, transparent reporting, and unbiased interpretation of results. By adhering to these principles, the code ensures that the pursuit of knowledge and medical advancement is conducted with the utmost integrity.

Promoting Accountability and Transparency:

A robust code of ethics holds researchers, sponsors, and stakeholders accountable for their actions. It requires transparent disclosure of conflicts of interest, financial relationships, and potential biases that could influence trial outcomes. This transparency fosters public trust and ensures that decisions are made in the best interests of both participants and the broader scientific community.

Ethical Review and Oversight:

A code of ethics mandates the establishment of ethical review boards or institutional review boards (IRBs) to evaluate trial protocols and monitor ongoing studies. This oversight ensures that trials are ethically sound, minimize risks, and adhere to established ethical guidelines. IRBs play a critical role in preventing ethical violations and upholding the highest standards of participant protection.

B. Evolution of ethical principles in human experimentation:

Respecting individuals' autonomy: Autonomy involves acknowledging a patient's right to self-direction, decision-making in care, and the ability to accept or decline treatment. This concept emphasizes a patient's authority in selecting desired procedures. Upholding informed consent is crucial, encompassing comprehensive details about expectations, associated risks, and alternative choices.

Promoting beneficence: The principle of beneficence compels practitioners to act in the patient's ultimate welfare. Thoroughly assessing the procedure's potential advantages and drawbacks is essential, with the aim of

maximizing benefits and minimizing harm. Evaluating the patient's motivations and the procedure's impact on their quality of life is pivotal. The practitioner's specialization and capability to manage potential risks and side effects are paramount.

Ensuring justice: Justice underscores equitable treatment. Practitioners must honor patient preferences, comprehend the issue's depth, and educate patients on procedure expectations. Equitable distribution of research advantages and disadvantages is imperative.

Doing No Harm (Nonmaleficence): Nonmaleficence dictates preventing harm to patients. Discussing potential side effects and complications of trial procedures before enrolling participants is obligatory.

Safeguarding confidentiality: Preserving participant privacy is a cornerstone of ethical clinical research. Researchers are responsible for upholding the confidentiality and privacy of participants' personal information.

Fostering honesty: Maintaining honesty with study participants regarding trial protocols, risk-benefit evaluations, and with fellow investigators, sponsors, ethics committees, and regulatory bodies about protocol adherence and outcomes is paramount.

C. Significance of informed consent in protecting participant's rights:

The informed consent form needs to include an explanation of participant's rights and how participants will be protected. In all human-subjects research, participants should have the refuse participation or to stop their participation at any time without consequence.

II. Ethical considerations in clinical trial design:

A. Risk-benefit Assessment and Minimizing harm to participants: -

Benefit: It refers to the positive outcomes that may be achieved through a particular action or decision.

Risk: It refers to the potential negative outcomes that may be associated with a particular action or decision.

Conducting Risk-Benefit assessments:

Risk-benefit assessment is a crucial step in the ethical conduct of research, ensuring the welfare of participants while advancing scientific knowledge. Informed by principles laid out in international ethical guidelines, risk-benefit assessment evaluates the potential risks participants may encounter against the benefits that may accrue from the research. This process is fundamental to research ethics, guiding researchers, ethics committees, and institutional review boards (IRBs) in making well-informed decisions.

Role of the investigator: Investigators play a pivotal role in risk-benefit assessment, safeguarding ethical research. They identify and analyze potential risks, quantify benefits, and ensure a balanced approach. By integrating scientific expertise and ethical awareness, investigators uphold participant welfare while advancing knowledge responsibly.

Role of the IRB: IRBs (Institutional Review Boards) are pivotal in risk-benefit assessment, overseeing ethical research. They critically evaluate study protocols, assess risks and benefits, and ensure participant protection. By applying regulatory standards and ethical principles, IRBs uphold research integrity, fostering responsible advancement of knowledge.

Step 1- Recognize and differentiate hazards linked to:

- Activities carried out exclusively for the purpose of research.
- Interventions or treatments that participants would undergo even in the absence of research.
- Procedures characterized as exploratory or investigational in nature.

Step 2- Contextualize the Implementation of Research Procedures:

- Do research procedures supplement regular, standard care activities?
- Examples: Instances include supplementary blood extractions during routine draws, extended periods spent in a CT scanner for research-related imaging, the incorporation of extra biopsies, or prolonged administration of anesthesia to assess oxygen saturation levels.

Step 3- Deliberate on the Participant Cohort:

- What is the age distribution and prevailing health condition of the participants?
- Could they potentially exhibit heightened sensitivity or increased susceptibility to the risks inherent in the research?
- How is the process of pinpointing and enlisting them undertaken?

Step 4- Assessing Risk Magnitude

- Do the potential hazards associated with the research protocols align with the federal criteria for classifying as "minimal risk"?
- Should this be the case, do the procedures fall within a category that qualifies for an accelerated or exempted assessment by the Institutional Review Board (IRB)?

Step 5- Establishing IRB Evaluation Level Through Risk Evaluation:

- Granting exempting validation for studies characterized by almost negligible risk, which fit into any of the 8 specified federal classifications.
- Conducting an expedited assessment for studies with "minimal risk", aligning with any of the 9 specified federal classifications.
- Undertaking a comprehensive committee review for studies involving risks surpassing the minimal threshold.

Ways to minimize risk

Minimizing risk in research is paramount for ethical and credible outcomes. Researchers employ several strategies to achieve this. Rigorous study design and methodology, including pilot studies, ensure potential issues are identified and addressed early. Informed consent processes facilitate participant understanding and autonomy, reducing unexpected concerns. Continuous monitoring and data validation allow swift response to emerging risks. Ethical considerations guide participant selection and vulnerability assessment. Collaboration with ethics committees and stakeholders ensures diverse perspectives and comprehensive risk assessment. Incorporating safety protocols and adhering to regulatory guidelines safeguards participants. By prioritizing these measures, researchers uphold the integrity of their work, enhance participant well-being, and contribute to reliable and responsible research outcomes.

B. Ensuring scientific Validity and Rigor:

Scientific validity and rigor are essential aspects of any research study, including clinical research. They refer to the degree to which a study's design, methods, and analysis ensure that the results are accurate, reliable, and generalizable. These concepts are crucial in producing trustworthy and credible scientific findings.

Scientific validity: Scientific validity refers to the extent to which a study accurately measures or assesses the research question it aims to investigate. In other words, it evaluates whether the study design and methods are appropriate for addressing the research hypothesis or objective. A valid study should have a clear research question, well-defined study population, appropriate data collection methods, and valid outcome measures. Validity ensures that the study's conclusions are based on solid evidence and are not distorted by biases or confounding factors.

1. Scientific rigor: Scientific rigor pertains to the precision and thoroughness with which the research study is conducted. Rigorous research involves careful planning, adherence to established protocols and standards, attention to detail in data collection and analysis, and rigorous peer review. Rigorous studies are characterized by robust methodologies that can withstand scrutiny and replication, leading to more reliable and credible results.

Rigorous study design: A well-designed clinical study begins with a clear research question and hypothesis. The study design should be carefully planned to address the specific objectives, and potential biases should be minimized. Common study designs include randomized controlled trials (RCTs), cohort studies, case-control studies, and cross-sectional studies, each tailored to the research question.

Sample size calculation: Determining an appropriate sample size is essential to achieve sufficient statistical power to detect meaningful differences or associations.

Researchers should conduct a power analysis before starting the study to estimate the required number of participants for reliable results.

Randomization: Random allocation of participants into treatment or control groups helps minimize selection bias and ensures that each group has a similar baseline characteristic. Randomization enhances the validity of the study and allows for a more accurate assessment of the intervention's effect.

Blinding: Blinding, or masking, helps reduce bias during data collection and analysis. In a single-blind study, participants are unaware of their assigned treatment group, while in a double-blind study, both participants and researchers are unaware. This prevents conscious or subconscious influences on the study's outcome.

Peer review: Before publication, research findings undergo peer review, where experts in the field critically evaluate the study's methodology, results, and conclusions. This process helps identify flaws and ensures that the research meets the necessary scientific standards.

Replication of results: Replicating research findings by independent researchers is crucial to validate the initial results. Replication helps confirm the robustness of the findings and reduces the likelihood of spurious results.

Data analysis: Appropriate statistical methods should be employed to analyze the data, ensuring that the results are accurately interpreted and reported. Transparent and unbiased data analysis is essential for drawing valid conclusions.

Transparent Reporting: Researchers should provide detailed and transparent reporting of their study methods, results, and limitations. This enables other researchers to replicate the study and better assess the research's validity and applicability.

Continuous monitoring: Throughout the research process, continuous monitoring and data quality checks help ensure that the study remains on track and maintains its scientific rigor.

C. Equitable participant Selection and Avoiding exploitation:

Selecting participants fairly and avoiding exploitation is important to ensure that clinical trials are conducted ethically. Participants must be recruited in a way that is fair and unbiased, and researchers must ensure that participants are fully informed about the study. This includes providing information about the risks and benefits of participating, as well as any potential side effects or adverse events that may occur.

Researchers must also ensure that participants are not coerced into participating and that they are free to withdraw from the study at any time. Additionally,

researchers must ensure that participants are not exposed to any unnecessary risks and that they are compensated fairly for their participation.

To ensure that participants are selected fairly, researchers must use appropriate recruitment methods and ensure that the study population is representative of the population that the study is intended to benefit. This means that the study population should be diverse and inclusive, and that participants should be selected based on objective criteria.

Overall, ensuring equitable participant selection and avoiding exploitation is essential to conducting clinical trials that are ethical and scientifically valid.

D. Addressing vulnerable population's concerns:

Involves implementing targeted support, accessibility measures, and policies to ensure their well-being and inclusion. It's essential to understand their specific needs and challenges to create effective solutions that promote equality and social justice. Regularly engaging with these populations and collaborating with relevant organizations can also lead to better outcomes.

E. Placebo Use and Control group considerations:

Placebo:

A placebo is a substance or intervention with no therapeutic effect. It is often an inert substance, such as a sugar pill, saline solution, or sham procedure. Placebos are used in clinical trials to create a comparison group that receives no active treatment. The use of placebos is critical in evaluating the true efficacy of a new treatment, as it helps distinguish the specific effects of the active treatment from any potential placebo effects or natural improvements that can occur in the absence of treatment.

Placebo effect:

The placebo effect is a phenomenon where patients experience improvements in their symptoms or conditions simply because they believe they are receiving an effective treatment, even though the treatment itself is inactive. This response is driven by the patient's psychological and physiological responses to the belief in the treatment's effectiveness. It highlights the power of the mind-body connection and the importance of considering patient expectations and beliefs during clinical trials.

Control group:

A control group is a group of participants in a clinical trial who do not receive the active treatment being tested. Instead, they are given a placebo or no treatment at all. The control group serves as a baseline for comparison, allowing researchers to assess whether the active treatment has a specific effect beyond what would happen naturally or with a placebo.

Types of control groups:

There are different types of control groups used in clinical trials:

- a. **Placebo Control Group:** Participants receive a placebo, which mimics the appearance and administration of the active treatment, but lacks the active ingredient or intervention.
- b. **No-Treatment Control Group:** Participants in this group do not receive any treatment, including a placebo. This type of control group is appropriate when there is no existing standard treatment or when it is essential to assess the natural progression of a condition.
- c. **Active Comparator Control Group:** Participants in this group receive an established treatment that is already known to be effective. The active treatment is compared against the new treatment being tested to determine its superiority, non-inferiority, or equivalence.

Double-Blind Trials: In a double-blind trial, neither the participants nor the researchers know who is receiving the active treatment and who is in the control group (placebo or no treatment). This blinding helps eliminate bias and ensures that the results are not influenced by participants' or researchers' expectations or beliefs

Placebo use and control group considerations are fundamental components of rigorous clinical research. They help determine the true efficacy of treatments, minimize bias, and ensure that research results are valid, reliable, and applicable to real-world medical practices. Ethical decision-making is crucial to strike a balance between scientific integrity and participant welfare.

III. Informed Consent Process and Improvements:

A. Elements of informed Consent and Its historical development: -

In the realm of informed consent, its foundation rests upon three pivotal and indispensable components: voluntariness, the divulgence of information, and the presence of decision-making competence.

Voluntarism-

The participation in a research study must be voluntary and not coerced. Voluntarism emphasizes that individuals have the right to make their own choices about whether or not to participate in a study without any external pressure or influence. When obtaining informed consent from potential participants, researchers should ensure that the decision to participate is made freely, without any undue inducements or threats. Participants should not face negative consequences or be forced to participate against their will. Voluntarism is crucial in maintaining ethical standards in research and upholding the principles of autonomy and respect for individuals' rights. It ensures that participants are not exploited for research purposes and that their well-being and interests are given top priority throughout the study. Researchers must fully disclose all relevant information about the study, including potential risks and benefits, so that participants can make informed decisions based on their own judgment and values."

Information disclosure-

Information disclosure involves furnishing pertinent details required for a patient to arrive at an educated choice, forming a fundamental aspect of a valid informed consent process. The goal is to ensure that participants have a thorough understanding of what they are agreeing to before making an informed decision about their participation.

Decision making capacity-

Described as "the capacity to comprehend, acknowledge the implications of health choices, and create and convey decisions regarding healthcare," decision-making capacity encompasses four facets: (a) grasping the information, (b) recognizing the scenario's significance, (c) logically processing the information, and (d) articulating or demonstrating a decision.

Historical development of informed consent: -

The historical development of informed consent in clinical research can be traced back to significant events that have shaped its evolution. It began with the establishment of ethical guidelines to protect research participants and ensure their autonomy. Some key milestones include:

Nuremberg Code (1947): In response to unethical medical experiments during World War II, the Nuremberg Code emphasized voluntary informed consent as a fundamental principle for human experimentation.

Declaration of Helsinki (1964): This international ethical guideline provided further clarity on informed consent, emphasizing that participants must be fully informed about the research and give their voluntary, informed consent before participating.

Belmont Report (1979): From the United States, the Belmont Report outlined ethical principles for research involving human subjects, including respect for persons, beneficence, and justice, which underlined the importance of informed consent.

Common Rule (1991): In 1991, the U.S. Department of Health and Human Services (HHS) introduced the Common Rule, a nationwide guideline mandating informed consent for any research involving human subjects that receives federal funding.

Good Clinical Practice (GCP) Guidelines: This Guidelines, crafted by the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), underscored the significance of securing informed consent within clinical trials.

Over time, informed consent has evolved to become more patient-centered, culturally sensitive, and adapted to diverse populations. It remains a crucial aspect of

clinical research to protect the rights and welfare of research participants.

B. Challenges in obtaining informed consent in complex trial designs:**Language barriers-**

Misunderstandings may occur because of incorrect language translations. Most of the individuals sign the consent form without knowing what they are signing, which results in withdrawal of subject.

Religious influence-

Religious influence in clinical trial design can be an important consideration, particularly when working with populations that may have specific religious beliefs or practices.

False expectations-

Misunderstanding can still occur due to participant's false expectations of the experiment outcome.

Children-

Children under the age of 18 consent has to be taken from parent. Difficulty arises when parents give their consent when child refuses to assent.

Vulnerable People and Groups-

The person who is absolutely incapable of protecting their interests. Obtaining informed consent can be difficult and special care should be taken.

C. Innovations in presenting information to participation:

Interactive multimedia: Implementing interactive multimedia platforms, such as web-based portals or mobile applications, to provide engaging and easily accessible information to participants. These platforms often include videos, animations, and infographics to present complex medical concepts in a user-friendly manner.

Virtual Reality (VR) and Augmented Reality (AR):

Utilizing VR and AR technologies to create immersive experiences that allow participants to better understand the trial process, procedures, and potential outcomes.

Patient-Centric approaches: Tailoring information to meet the specific needs and preferences of individual participants. This could include providing information in multiple languages, at appropriate reading levels, or in various formats (e.g., text, audio, video).

Wearable Devices and Remote monitoring:

Introducing wearable devices and remote monitoring technologies to collect real-time data from participants, keeping them informed about their progress in the trial and enhancing their sense of involvement.

Social Media and Online communities: Utilizing social media platforms and online communities to create a

space for participants to interact, share experiences, and access relevant trial-related information.

D. Digital and Multimedia approaches to enhance informed consent comprehension:

Digital and multimedia approaches can help to simplify the informed consent process and increase participant comprehension. For example, videos can be used to explain complex procedures and concepts in a way that is easy to understand. Animations can also be used to help participants visualize what will happen during the study. Web-based tools can provide a more interactive experience, allowing participants to explore the study procedures and potential risks and benefits in a way that is tailored to their needs. Digital approaches can also be more accessible to participants who may have limited health literacy or who may not speak the language in which the consent form is written. Overall, digital and multimedia approaches can be an effective way to enhance informed consent comprehension in clinical trials, and they can help ensure that participants fully understand what is involved in the study.

E. Use of plain language and visual aids to improve participant understanding:

- ✓ Logical organization and flow of content
- ✓ Present only the most necessary information
- ✓ Use common, everyday words
- ✓ Use simplified terms and definitions
- ✓ Use the Active voice

Visual aids include black and white or color pictograms, pictures, drawings, graphics, photographs, videos, and multimedia presentations.

IV. Ethical Oversight and Institutional Review Boards (IRBs)

Ethical oversight in human research is essential to protect participants' rights and safety. Institutional Review Boards (IRBs) are independent committees that review and approve research protocols involving humans before they begin. Their primary goal is to ensure that the research meets ethical and regulatory standards. In the domain of human research, Institutional Review Boards (IRBs) play an essential role by shouldering the primary obligations of protecting the rights, security, and welfare of individuals participating in research endeavors. Their duties encompass a range of critical tasks to ensure that research adheres to ethical and regulatory standards.

First and foremost, IRBs conduct thorough protocol reviews, meticulously assessing the scientific validity and ethical considerations of proposed studies. They scrutinize research design, data collection procedures, and potential risks and benefits to participants. Equally crucial is the review of informed consent processes. IRBs assess whether potential participants receive adequate information about the study, comprehend the associated risks and benefits, and provide voluntary consent. Consent forms are also evaluated to ensure clarity and

comprehension. Moreover, IRBs perform a rigorous risk-benefit analysis, weighing potential study benefits against the risks to participants. They strive to minimize potential harm while maximizing potential benefits. Additionally, IRBs are dedicated to protecting vulnerable populations, such as children, pregnant women, prisoners, and individuals with cognitive impairments, ensuring their inclusion in research and safeguarding against exploitation.

The responsibilities of IRBs extend beyond initial approval. Ongoing oversight of approved studies is a critical aspect of their role, including periodic reviews and site visits to monitor compliance and participant safety. Data privacy and confidentiality are paramount concerns for IRBs, who assess how participant data is handled, stored, and shared, ensuring the protection of privacy rights. Addressing potential conflicts of interest is another essential task for IRBs. They examine researchers' affiliations and financial interests to ensure the integrity of the research. Furthermore, IRBs provide valuable ethical education and guidance to researchers, helping them navigate complex ethical principles, regulatory requirements, and best practices in human research. Once the study concludes, IRBs may review the study's results and support the responsible dissemination of findings. It is crucial for researchers and institutions to respect the decisions of the IRB, maintain ongoing communication, and promptly report any adverse events or concerns during the study.

In essence, IRBs play a pivotal role in upholding ethical standards in human research, prioritizing participant welfare, and ensuring that scientific advancements are achieved with integrity and utmost respect for human rights.

A. Role of IRBs in safeguarding participants' Rights and Welfare

IRBs play a vital role in safeguarding participants' rights and welfare in human research. They ensure research adheres to ethical principles and regulations, prioritizing participant well-being. In human research, Institutional Review Boards (IRBs) hold a pivotal role in safeguarding participants' rights and welfare by ensuring adherence to ethical principles and regulatory guidelines. Through comprehensive reviews, IRBs assess research protocols, evaluating study design, potential risks, and benefits to participants. They prioritize informed consent, verifying that participants fully understand the study's purpose, procedures, and potential risks before providing voluntary consent.

A critical aspect of IRBs' responsibility lies in assessing the balance between potential risks and benefits, ensuring that the research justifies any participant discomfort. Additionally, IRBs provide special protections for vulnerable populations, including children, pregnant women, prisoners, and individuals with cognitive impairments, to uphold their rights and welfare. Ongoing oversight remains a core function of

IRBs, as they monitor approved research throughout its duration, conducting periodic reviews to assess compliance and participant safety. Upholding confidentiality and data privacy is paramount, with IRBs evaluating data handling to safeguard participants' information securely.

Mitigating research risks, addressing ethical concerns promptly, and suspending or terminating studies, when necessary, exemplify IRBs' commitment to participants' welfare. Moreover, they offer guidance and education to researchers, promoting ethical research practices and cultivating a culture of integrity. Community engagement initiatives, involving representatives, foster trust between researchers and participants, aligning research with community values and needs. Overall, IRBs play a vital role as a safeguard for participants, ensuring ethical standards are upheld, and participants' rights and welfare are at the forefront of the research journey.

B. Recent developments in IRB Processes and Efficiency

IRB developments include technology integration, centralized IRBs, risk-based approaches, and enhanced training, improving efficiency and ethical standards in human research. In recent years, several developments have enhanced Institutional Review Board (IRB) processes in human research. Embracing technology, institutions have adopted electronic submission systems and digital consent forms, reducing paperwork and administrative burden. Centralized IRBs have emerged, expediting reviews for multi-site studies by conducting a single review across participating institutions. Expedited review pathways for low-risk protocols save resources, while reliance agreements enable one IRB to rely on another's review for collaborative research. Quality improvement initiatives and pre-review consultations optimize efficiency and feedback. Risk-based reviews allocate scrutiny based on potential risks, and flexible exemptions and waivers streamline the process. Emphasizing training and education empowers researchers with ethical knowledge, leading to more efficient reviews. Staying informed about current guidelines ensures adherence to ethical standards and promotes streamlined IRB processes.

C. Ensuring Transparency and Accountability in IRB decision-making

Maintaining transparency and accountability in IRB decision-making is essential for fostering trust among researchers, participants, and the community. These practices uphold ethical principles and promote responsible scientific investigations in human research. To achieve transparency and accountability in IRB decision-making, key strategies include establishing clear policies and procedures, making information public whenever possible, maintaining open communication with researchers, and conducting regular external reviews and audits. Robust conflict of interest policies,

ongoing training for IRB members, and feedback mechanisms also contribute to transparency. Continuous quality improvement efforts, transparent review criteria, and an appeals process ensure fairness and adherence to ethical principles. Additionally, IRBs should require researchers to promptly report adverse events and unanticipated problems during the study. Implementing these measures enhances the integrity of human research and safeguards participants' rights and welfare.

D. Global harmonization of ethical review processes

Global harmonization of ethical review processes in human research aims to ensure consistency, efficiency, and adherence to ethical standards worldwide. Though progress has been made, achieving full harmonization remains complex and challenging. Global harmonization of ethical review processes in human research aims to promote consistency, efficiency, and adherence to ethical standards across countries. Key initiatives include international guidelines, collaborations, standardization, capacity building, and sharing best practices. Challenges like regulatory differences and cultural considerations persist, but ongoing dialogue and collaboration are crucial for achieving harmonization while respecting each country's unique context.

V. Inclusion of underrepresented populations in clinical trials

Inclusion of underrepresented populations in clinical trials is vital for equitable access to healthcare advancements and generalizable research findings. Historical underrepresentation has led to health disparities and limited understanding of interventions' effects on diverse groups. Ensuring the inclusion of underrepresented populations in clinical trials is essential for equitable healthcare advancements and generalizable research findings. Researchers should proactively consider diversity in study design, employ culturally appropriate recruitment, and provide language accessibility. Addressing barriers to participation, fostering representation in research teams, and adopting culturally sensitive approaches are crucial. Community engagement, partnering with diverse institutions, and flexible study protocols promote inclusivity. Reporting demographic data and subgroup analyses, establishing ethics and inclusion guidelines, and raising awareness further enhance inclusiveness in clinical trials, benefiting healthcare outcomes for all.

A. Addressing disparities in clinical trial participation

Addressing disparities in clinical trial participation is essential for equitable healthcare advancements and generalizable research findings. Inclusion of historically underrepresented populations ensures medical advances benefit all and reduces healthcare inequities. Addressing disparities in clinical trial participation is crucial to ensure equitable healthcare advancements and generalizable research findings. Key approaches include increasing awareness and education about clinical trials,

conducting culturally competent outreach, collaborating with community leaders and healthcare providers, and providing language accessibility. Removing financial barriers, offering flexible study designs, and prioritizing inclusion in protocols are also important steps. Community-based research, addressing health disparities, and promoting data transparency contribute to greater diversity. Policy changes, supporting patient advocacy, and fostering collaboration across stakeholders strengthen efforts to promote inclusivity in clinical research, benefiting healthcare outcomes for all.

B. Ethical implications of underrepresentation in research

The underrepresentation of certain populations in research has ethical implications that affect both participants and society. It can lead to unfair distribution of benefits and risks, limited generalizability of results, compromised informed consent, and neglect of vulnerable populations' health needs. Additionally, underrepresentation may result in insufficient safety information and resource allocation, exacerbating disparities. Addressing these ethical concerns requires promoting diversity and inclusivity in research to advance equitable healthcare and scientific knowledge for all.

C. Strategies for improving Diversity and Inclusivity in clinical trials

Improving diversity and inclusivity in clinical trials is crucial for representative research findings and equitable healthcare advancements. Strategies include community engagement, culturally tailored outreach, language accessibility, and inclusive study design. Addressing financial barriers, partnering with diverse institutions, and promoting cultural sensitivity are important steps. Education, transparent reporting, inclusive policies, and researcher training further enhance diversity. Collaboration, data sharing, and public-private partnerships foster inclusivity in clinical trials, benefiting all individuals equally.

D. Ensuring culturally sensitive informed consent procedures

Culturally sensitive informed consent procedures are crucial to respecting the autonomy and rights of diverse research participants. Strategies include using plain language, providing translations, and involving community members in document development. Respect cultural beliefs, offer tailored information, and be flexible in the consent process. Allow ample time, use visual aids, and seek continuous feedback for improvement. By implementing these approaches, researchers can ensure ethical engagement and build trust with participants from diverse cultural backgrounds, fostering inclusive and meaningful research collaborations.

VI. Ethical Considerations in Precision Medicine and Personalized trials

Precision medicine and personalized trials present unique ethical challenges due to their focus on tailoring medical interventions to individual patients based on genetic, environmental, and lifestyle factors. Key ethical considerations include obtaining informed consent for extensive genetic testing and data usage, ensuring privacy and data protection, providing equitable access to treatments, and balancing potential benefits with possible harm. Representing diverse populations in research, handling genetic results responsibly, and promoting transparency and public engagement are crucial. Proper stewardship of genetic information, consent for data sharing, and post-trial access are also important for responsible advancement in precision medicine, ultimately benefiting patients and public health as a whole.

A. Challenges in obtaining informed consent for genomic research

Obtaining informed consent for genomic research is complex due to the sensitivity and intricacy of genetic information. Challenges include communicating the purpose and risks of genomic research in a clear manner, addressing uncertainties in research outcomes, ensuring data privacy and security, and managing familial implications of genetic findings. Participants should be informed about data sharing, future use of data, and have culturally sensitive processes for vulnerable populations. Researchers must balance comprehensive information with participants' time constraints and consent fatigue. Long-term follow-up and ongoing support are essential to uphold ethical standards and foster trust between researchers and participants in genomic research.

B. Privacy and Confidentiality concerns with personalized data

Privacy and confidentiality concerns surrounding personalized data are significant due to the sensitive nature of the information involved, such as genetic, health, and lifestyle data. Risks include re-identification, data breaches, genetic privacy implications for family members, and third-party sharing. Informed consent is crucial, covering privacy risks and data use options. Discrimination, lack of control, and cross-border data transfer are also concerns. Aggregating data can increase re-identification risk, and long-term data storage policies raise ethical considerations. Addressing these concerns necessitates robust data protection measures, transparency, and adherence to ethical principles to protect the privacy rights of research participants and ensure responsible handling of personalized data throughout its lifecycle.

C. Balancing individual Benefit and Societal implications

Balancing individual benefit and societal implications is a crucial ethical consideration across various aspects of healthcare, medical research, and public policy. This

involves weighing the advantages and risks of decisions made at the individual level against their broader impact on society. In personalized medicine and clinical trials, it means providing effective treatments while considering equitable access and scientific rigor. Healthcare resource allocation necessitates maximizing health outcomes for the entire population, taking into account individual needs. Public health interventions aim to protect individuals and communities, balancing individual rights with the common good. Ethical dilemmas in treatment decisions require considering both patient interests and fair resource distribution. Informed consent in research seeks individual benefits and contributes to public health knowledge. Biomedical research and health policy decisions aim to benefit individuals while addressing ethical concerns and promoting health equity. Achieving this balance requires careful consideration of ethical principles, scientific evidence, and societal values, involving stakeholders and transparent decision-making processes to uphold the common good while respecting individual well-being.

D. Ethical issues in returning genomic findings to participants

Returning genomic findings to research participants raises significant ethical issues that demand careful consideration. Such findings can unveil health risks and potential implications for participants and their families. Ethical concerns encompass the relevance and validity of the findings, incidental and secondary discoveries, participant preferences, and informed consent. Psychological impact, privacy, and communication of complex information also need attention. Family implications, resource allocation, and the risk of overmedicalization are additional ethical considerations. Researchers, IRBs, and stakeholders should engage in transparent discussions and establish clear policies to address these concerns responsibly, respecting participant autonomy and well-being throughout the process.

Data Sharing and Secondary use of clinical trial data

Data sharing and the secondary use of clinical trial data have become topics of increasing interest in the medical and scientific community. The potential benefits of making clinical trial data widely available are vast, including advancing scientific knowledge, promoting transparency, accelerating research, and reducing duplication of efforts. However, data sharing also presents challenges related to patient privacy, data governance, and potential misuse of the data. This review article aims to explore the advantages, challenges, and ethical considerations surrounding data sharing and secondary use of clinical trial data.

Ethical considerations in sharing clinical trial data:

- 1. Transparent data sharing policies:** Institutions and funding bodies should establish clear and comprehensive data sharing policies to address ethical concerns and ensure responsible data use.

- 2. Anonymization and De-Identification:** Stripping personal identifiers and using robust anonymization techniques can protect patient privacy while enabling data sharing.
- 3. Respect for participant autonomy:** Researchers should prioritize obtaining informed consent that explicitly addresses data sharing and potential uses, allowing participants to make informed decisions.
- 4. Collaboration and Attribution:** Researchers who share their data should receive appropriate credit, fostering a culture of collaboration and incentivizing data sharing.

Advantages of data sharing:

- 1. Accelerating research:** Data sharing allows researchers to access a broader pool of data, leading to a more comprehensive analysis and faster scientific progress.
- 2. Reproducibility and Verification:** Transparent access to raw clinical trial data enables other researchers to verify study findings and reproduce results, increasing the reliability of scientific research.
- 3. Facilitating Meta-Analyses:** Pooled data from multiple clinical trials can lead to more robust meta-analyses, yielding deeper insights and more accurate conclusions.
- 4. Cost Savings:** Data sharing reduces the need for redundant trials, saving both time and resources.

Challenges in data sharing:

- 1. Patient Privacy and Informed consent:** Protecting patient privacy is paramount, as sensitive health information can be vulnerable to potential data breaches. Obtaining informed consent from trial participants for data sharing poses a challenge, as the initial consent might not have covered broad sharing purposes.
- 2. Data standardization:** Harmonizing data from various sources is essential to ensure compatibility and interpretability, but it can be difficult due to differences in data collection methods and formats.
- 3. Intellectual property concerns:** There might be conflicts between researchers' interests in gaining recognition for their efforts and the broader scientific community's interest in sharing data openly.
- 4. Data misuse:** There is a risk that shared data could be used for unintended purposes, such as targeting vulnerable populations or compromising patient safety.

Ensuring participant privacy and data security in data sharing initiatives:

Data sharing initiatives have emerged as powerful tools for advancing scientific research. However, the growing concern over participant privacy and data security poses significant ethical challenges. To maintain public trust and protect participant rights, robust privacy measures and data security protocols must be implemented.

Researchers and organizations must adhere to stringent guidelines to anonymize data, control access, and encrypt sensitive information. Collaborative efforts between stakeholders and regulatory bodies are essential to strike a balance between data sharing and participant privacy, fostering responsible and ethical data sharing practices.

Post-Trial access to investigational products:

Post-trial access to investigational products (PTAIP) is a critical issue in clinical research that involves providing access to experimental therapies to trial participants after the completion of a clinical trial. While it is an ethical imperative to offer PTAIP, striking a balance between access, safety, and efficacy is essential. This review article explores the ethical considerations surrounding PTAIP, the challenges of balancing access with safety and efficacy, and the regulatory perspectives on implementing PTAIP.

Ethical obligations to provide access to study interventions after the trial:

The ethical imperative for PTAIP is rooted in the principles of respect for persons, beneficence, and justice. Respect for persons involves treating trial participants with dignity and ensuring their autonomy in deciding whether to participate in PTAIP. Beneficence dictates that researchers must prioritize participants' well-being, providing them with potentially life-saving or life-improving treatments. Justice demands fair and equitable access to the benefits of research, including access to investigational products for participants who contributed to the advancement of medical knowledge.

Balancing access with considerations of safety and efficacy:

While PTAIP is ethically compelling, it also raises concerns about the safety and efficacy of investigational products. During clinical trials, these products are rigorously tested to determine their safety and effectiveness. Granting access to experimental therapies before regulatory approval or without complete data on their risks and benefits could pose potential harm to patients. Balancing access with safety and efficacy requires careful consideration of several factors, including:

- 1. Data sufficiency:** Researchers must ensure that there is enough data from the clinical trial to support the potential benefits and risks of the investigational product before offering PTAIP.
- 2. Benefit-Risk assessment:** An individualized benefit-risk assessment should be conducted for each participant seeking PTAIP, taking into account the severity of their condition and available treatment options.
- 3. Informed consent:** Participants should be fully informed about the uncertainties surrounding the investigational product and the potential risks and benefits, allowing them to make an autonomous decision about PTAIP.

Regulatory Perspectives on Post-Trial Access:

Regulatory agencies play a crucial role in determining the conditions under which PTAIP can be granted. While some agencies recognize the ethical obligation to offer PTAIP, they also emphasize the need for robust evidence of safety and efficacy. This often involves a careful evaluation of the available data, the potential risks, and the level of unmet medical need for the patient population. Moreover, regulatory perspectives on PTAIP may differ among countries, creating challenges for multinational trials and global access to investigational products.

Ethical challenges in global clinical trials:

Global clinical trials have become essential for the development of new medical treatments and interventions. Conducting trials across different countries and cultures presents various ethical challenges that demand careful consideration. This review article explores the ethical complexities involved in global clinical trials, with a particular focus on addressing cultural and social differences, ensuring compliance, and reducing disparities to promote ethical research practices.

Cultural and Social differences affecting ethical considerations:

Conducting clinical trials in diverse cultural settings necessitates sensitivity to local norms, beliefs, and practices. Ethical challenges arise when informed consent is obtained, as cultural variations may influence participants' understanding and decision-making processes. Researchers must engage in culturally competent communication to bridge these gaps and ensure meaningful informed consent. Additionally, cultural disparities may lead to variations in disease prevalence and treatment outcomes, which should be acknowledged and accounted for in the trial design and data analysis.

Ensuring compliance with international ethical guidelines:

Maintaining ethical standards in global clinical trials requires adherence to international guidelines, such as the principles outlined in the Declaration of Helsinki and the guidelines established by the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-GCP). However, ensuring compliance with these standards across diverse jurisdictions with different regulatory systems can be challenging. Collaborating with local experts and regulatory bodies is crucial to navigating the complex regulatory landscape and ensuring adherence to ethical principles.

Addressing disparities in resource-limited settings:

Global clinical trials may inadvertently exacerbate existing health disparities between high-income and low-income countries. The availability of cutting-edge treatments and interventions in well-resourced countries while withholding them from resource-poor regions

raises ethical concerns. To address this, researchers must strive for equitable access to healthcare interventions and ensure that the benefits of research are fairly distributed. Implementing tiered pricing and access programs can be practical approaches to reduce disparities and make novel treatments more accessible to vulnerable populations.

CONCLUSION

Over the past few years, there has been noteworthy progress in addressing ethical aspects and refining informed consent within clinical trials. This progression emphasizes the importance of safeguarding participant well-being, ensuring transparency, and promoting inclusivity. This transformation is reflected in the increased vigilance of ethics committees, the introduction of inventive technology-driven consent approaches, and a renewed emphasis on diverse participant inclusion. These advancements collectively foster a research environment that centers on participants, aligns with ethical principles, and preserves the integrity of scientific inquiry while respecting individual rights.

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