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Emerging Ethics Assessment Challenges In Paediatric Clinical Trials and Revision of Declaration Of Helsinki - What Will Change?

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ASSESSMENT CHALLENGES

- Recognition of the importance of children's participation *vs* duty for their protection - *Excessive* Ethical Paternalism;
- Children as social actors, willing and able to make decisions about (participating in) research;
- Child involvement in *designing* and/or assessing trials;
- Parents as children's representatives: (possible) interests in conflict;
  - Child/parents centrality: how *mandatory* should be the request for getting them involved in the trial design and/or defining (patient-reported) outcomes;
- Specific *new* disease´s expertise *vs common* pediatric diseases: need for adapting (adult) trial study teams for pediatric field and/or needs;

ASSESSMENT CHALLENGES

- Biological samples and biobanking: secondary (and future) use of data – need for reconsent in the adulthood (?);
- Decentralized Clinical Trials: (potential) impact on the safety of the participants (risk-benefit) as well as on the integrity of the data and the scientific validity of the results:
  - Possible dilution of responsibilities; awareness of risks (nature of the information and minors understanding); Trust; Commitment & patients follow up
- Artificial intelligence: easier CT conduction & (potential) benefits *vs* patients' safety (and underprotection);
- Public health emergencies: direct benefit *vs* duty of protection and the principle of prior evidence (on efficacy and safety) from adults;
- *New* ethical and legal framework: CT Regulation, European Health Data Space (EHDS) Regulation and Declaration of Helsinki revision.

CT REGULATION

- Considerations on minimal risk as a requirement to authorize pediatric CT: heterogeneous interpretations & vagueness *definition* of risk → uncertainties when assessing trial protocols;
- Low-intervention trials: opportunity for testing off-label uses of drugs *vs* flexibility and simplification of procedures challenge the trial assessment;
- Secondary use of data: beyond an opportunity raises ethical questioning;
- (Very)Restrictive legal framework *vs* (all) the recognized ethical pediatrics´ standards;
- Decisive role of the RMS: excessive paternalism hindering minors' inclusion & CT approval.

EHDS REGULATION

- The interoperability and a single market with a common access point for data: essential to foster research (particularly) for rare diseases *vs* privacy breaches - Enough control?
- *Risk* of re-identification of anonymised or pseudonymised health data;
- Opt-out mechanisms: patients (children & parents) preferences/rights *vs* (possible) barriers for the cross-border health research
  - Really accessible and easily understandable opt-out mechanism?
  - Opt-out overridden because of research´s important public interest!

Do HELSINKI REVISION – What will change?

- Commitment of ALL involved in medical research instead of OTHERS [than physicians], specifying:

  While the Declaration is adopted by physicians, the WMA holds that these principles shuld be upheld by ***all individuals, teams, and organizations*** *involved in medical research, as they are fundamental to respect for and protection of all research participants, whether patients or healthy volunteers* (pr.2.)

➢ Prospect of incremented protection

Do HELSINKI REVISION – What will change?

- More than respect for all human subjects and protection of their health and rights:
  - **further provisions** regarding *inequities and distribution of benefits, risks and burdens* &
  - ***meaningful engagement*** *with potential and enrolled participants and their communities should occur before, during, and following research &*
  - ***empower participants****: to share their priorities and values; and participation in study design, implementation, and other relevant activities; and engage in understanding and disseminating results;* (pr.7.)

➢ Foresees better protection (children included)

Do HELSINKI REVISION – What will change?

- The physician as researcher extended to *other qualified researchers* – Less protection and/or expertise, particularly regarding paediatrics experience?
- Further and extended considerations regarding vulnerability:

  *Some individuals, groups, and communities experience more vulnerability as research participants due to **factors that may be fixed or contextual and dynamic**, and thus are at greater risk of incurring harm. When such individuals, groups, and communities have distinctive health needs, **their exclusion from medical research can potentially perpetuate or exacerbate their vulnerability and disparities*** (…)

➢ Fosters the development of paediatric CT and/or the inclusion of younger children?

- Reinforcement of post-trial provisions – better benefits´ assurance

Do HELSINKI REVISION – What will change?

- Strengthening Informed Consent Principle (and methodologies):
- as ***an essential component of respect for individual autonomy &***
- for a potential participant (incapable) and **minor child** able to give assent, the consent of the legally authorized representative has to take into consideration ***any preferences and values expressed by the potential participant*** [minor]
- *special attention to the specific **information and communication needs** of individual potential participants.* (pr.25,26,28,29)

- Binds the *collection, storage, and foreseeable secondary use of biological material and identifiable (or re-identifiable) data* to the Declaration of Taipei – better clarification on research with data.

To Conclude

- New emerging challenges for ethical (and scientific) assessment under new ethical and legal framework with (potential) opportunities & better regulations together with (potential) inadequate children protection; and potential conflicts between several provisions, namely with DoH revision;
- Capacity building and training need to be continued & awareness of underprotection risk is required;
- New patient centricity paradigm demands special attention to children's whishes, preferences and choices, their willingness, assent or refusal & (mostly) active involvement in the design of CT.

❖ Children´s future health *depends* on the success of paediatric research.

Thank you!

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