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Responding to vulnerability in research

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Defining vulnerability in research

- Vulnerable: those who are relatively incapable of protecting their own interests (CIOMS)
- Vulnerable: those who have an increased likelihood of being wronged or of incurring additional harm (DoH)
- CIOMS and DoH: not a feature of a group, although groups may be vulnerable (eg children)
- CIOMS: Variety of factors (layers) can make individuals vulnerable
  - Participating in research may be such a layer
  - Being incompetent certainly is

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Responding to vulnerability in research ethics guidelines

- CIOMS (2016) gln 15-19
  - Different glns for different groups

- Declaration of Helsinki (2013) gln 19, 20, 28
  - Different guidelines for different aspects but applicable for all vulnerable groups

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Declaration of Helsinki 19 &20

19 “Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm. All vulnerable groups and individuals should receive specifically considered protection.”

20 “Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.”

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Closer look at DoH 20: subsidiarity

- Declaration of Helsinki (2013) gln 20:
  - Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

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Closer look to DoH 20: group-specificity

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  - Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

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DoH 28 on research with incompetent persons

"These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden."

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Closer look at DoH 28: risks

- In case of therapeutic research the general provisions on risk apply (16):

  "Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects."

- In case of non-therapeutic research only minimal risk and minimal burdens are accepted

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CIOMS 17 Research involving children and adolescents (1)

Children and adolescents must be included in health-related research unless a good scientific reason justifies their exclusion. As children and adolescents have distinctive physiologies and health needs, they merit special consideration by researchers and research ethics committees. However, their distinctive physiologies and emotional development may also place children and adolescents at increased risk of being harmed in the conduct of research. Moreover, without appropriate support, they may not be able to protect their own interests due to their evolving capacity to give informed consent. Specific protections to safeguard children's rights and welfare in the research are therefore necessary.

CIOMS 17 Research involving children and adolescents (2)

Before undertaking research involving children and adolescents, the researcher and the research ethics committee must ensure that:

- a parent or a legally authorized representative of the child or adolescent has given permission; and
- the agreement (assent) of the child or adolescent has been obtained in keeping with the child's or adolescent's capacity, after having been provided with adequate information about the research tailored to the child's or adolescent's level of maturity.

If children reach the legal age of maturity during the research, their consent to continued participation should be obtained.

In general, the refusal of a child or adolescent to participate or continue in the research must be respected, unless, in exceptional circumstances, research participation is considered the best medical option for a child or adolescent.

CIOMS 17 Research involving children and adolescents (3)

For research interventions or procedures that have the potential to benefit children or adolescents, the risks must be minimized and outweighed by the prospect of potential individual benefit.

For research interventions or procedures that have no potential individual benefits for participants, two conditions apply:

- the interventions and procedures should be studied in adults first, when these interventions and procedures target conditions that affect adults as well as children and adolescents, unless the necessary data cannot be obtained without participation of children or adolescents; and
- the risks must be minimized and no more than minimal.

When the social value of the studies with such research interventions and procedures is compelling, and these studies cannot be conducted in adults, a research ethics committee may permit a minor increase above minimal risk.

Closer look at CIOMS 17: subsidiarity?

- General provision:

"Children and adolescents must be included in health-related research unless a good scientific reason justifies their exclusion."

- The reverse of DoH!

- For non-therapeutic research:

"the interventions and procedures should be studied in adults first, when these interventions and procedures target conditions that affect adults as well as children and adolescents, unless the necessary data cannot be obtained without participation of children or adolescents"

- Here subsidiarity is used, but limited

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Closer look at CIOMS 17: group-specificity?

"For research interventions or procedures that have the potential to benefit children or adolescents, the risks must be minimized and outweighed by the prospect of potential individual benefit.

For research interventions or procedures that have no potential individual benefits for participants, two conditions apply:

- the interventions and procedures should be studied in adults first, when these interventions and procedures target conditions that affect adults as well as children and adolescents, unless the necessary data cannot be obtained without participation of children or adolescents; and
- the risks must be minimized and no more than minimal."

So no group specificity, but social value as general condition

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Closer look at CIOMS 17: risks?

For research interventions or procedures that have the potential to benefit children or adolescents

- risks must be minimized and
- outweighed by the prospect of potential individual benefit.

For research interventions or procedures that have no potential individual benefits for participants, two conditions apply:

- the interventions and procedures should be studied in adults first if possible (…), and
- the risks must be minimized and no more than minimal.
- When the social value of the studies is compelling, and these studies cannot be conducted in adults, a research ethics committee may permit a minor increase above minimal risk

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The vulnerability toolkit: mechanisms to protect #1

- Group specificity
- Special conditions on post trial access
- Special conditions on risk
  - Minimal
  - Minor increase over minimal
- Subsidiarity principle: could not have been done with other non-vulnerable group

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The vulnerability toolkit #2

Consent-related options:

- Informed consent by (a limited list of) proxies
- Assent (more than absence of dissent)
- Independent advocates
- Community involvement

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Questioning the toolkit general issues#1

- Should all vulnerable persons be equally protected? Or are there morally relevant differences? CIOMS thinks there are.
- If vulnerability is not a group characteristic, should the protections be? Should RECs chose the proportionate protection mechanism, instead of guidelines with one-size-fits-all appoaches? Or researchers?

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Questioning the toolkit general issues #2

- How to balance protection and access?
- Should it make a difference whether the participants can benefit from the research or not?
- DoH seems to also protect vulnerable groups who participate in therapeutic research. Overly protective?

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Questioning the toolkit specific issues #1

- Group specificity
  - This condition creates (very) local social value.
  - Why does that help? The interests of the vulnerable may still be subsumed to those of others (albeit from the same group)
  - Why should vulnerable groups be prevented from helping other (vulnerable) groups?

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Questioning the toolkit specific issues #2

- Special conditions on post trial benefits (other than access to intervention drug)
  - Only for vulnerable (DoH)? Or depending on setting (CIOMS)?
- Special conditions on risk
  - May hamper development of interventions
- Subsidiarity principle
  - (non-)generalizability is a normative claim

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Conclusion

- Variety of responses to vulnerability available
- At the moment no coherent response: we need to be clearer about when to use which protection and why
- CIOMS tries to provide a reasonable answer

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