Research in disease outbreaks

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Agenda




- Humanitarian response and research
- Beneficence & non-maleficence
- Consent – Respect for person
- Ethical review and oversight

Scientific validity and alternative trial designs

- Disasters unfold quickly and study designs need to be chosen so that studies will yield meaningful data in a rapidly evolving situation
- Without scientific validity, the research lacks social value and must not be conducted

need to be carefully balanced

- The need to generate knowledge quickly,
- Maintain public trust,

and

- Overcome practical obstacles to implementing research

- the need to ensure the scientific validity of the research

and

- uphold ethical principles in its conduct

Humanitarian response and research in the acute phase of diseases outbreaks.

- The first and foremost obligation in acute disaster situation = to respond to the needs of those affected.
- An obligation exists to conduct health-related research because
  - disasters can be difficult to prevent, and
  - the evidence base for effectively preventing or mitigating their public health impact is limited.

Humanitarian response and research in the acute phase of diseases outbreaks.

- the studies do not unduly compromise the disaster response.
- integrate the research activities with humanitarian response.
- all studies must be responsive to the health needs or priorities of the affected populations, and
- it must not be possible to conduct the research outside a disaster situation.

Informed consent

- Even though most disaster victims are under duress, it is important to obtain their informed consent for study participation and especially to emphasize the difference between research and humanitarian aid.
- The informed consent process must be designed in a way that is comprehensible and sensitive to persons who are under duress

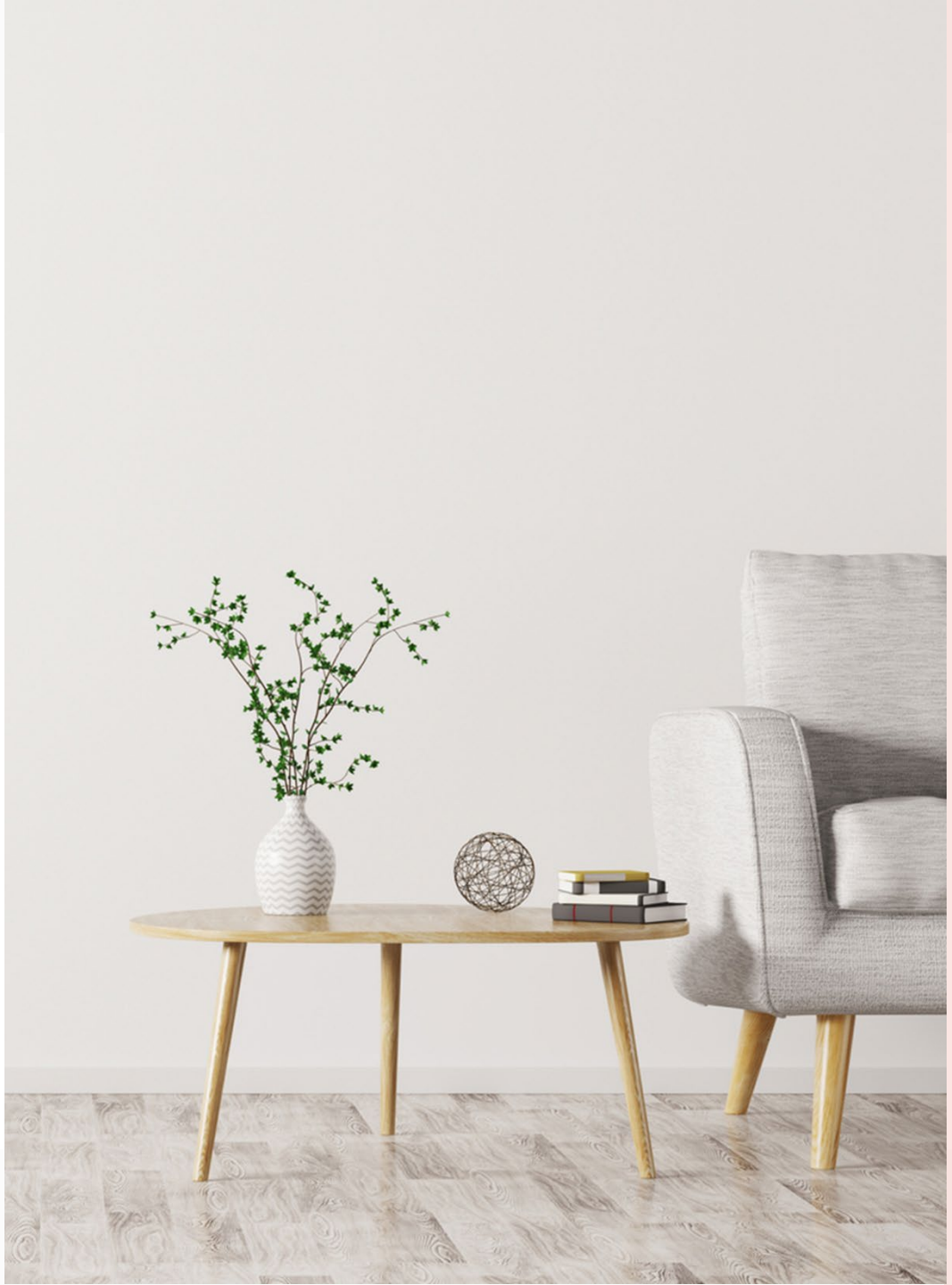
Individual informed consent may be waived for the sharing and analysis of surveillance data

- When a study is performed under a public health mandate or **by** public health **authorities**, such as disease surveillance, normally neither ethical review nor a waiver of consent is needed because the activity is **mandated by law**
- Research projects using data from one or more mandatory population-based registries should be submitted to a research ethics committee, except for data analyses involving internal institutional activity of a registry.

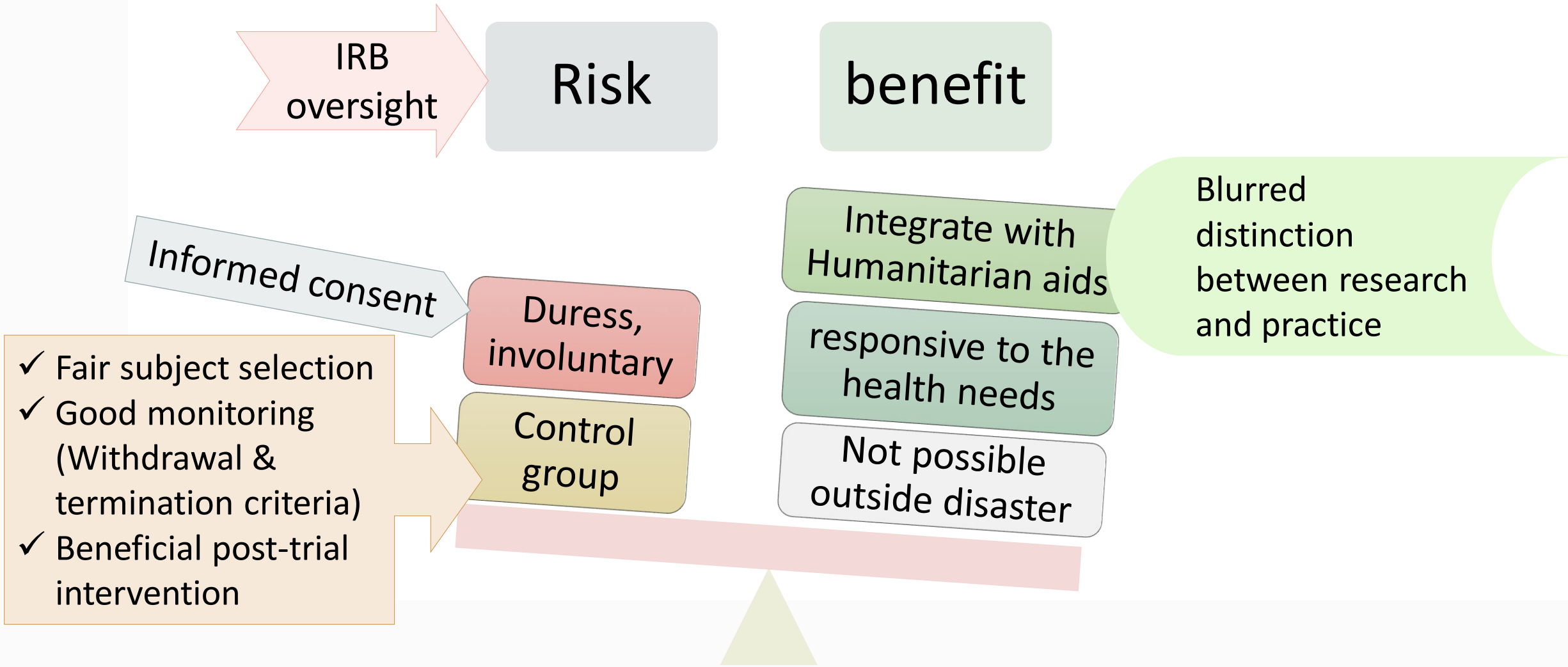
การวิจัยในมนุษย์ในกรณีเร่งด่วน
ที่ต้องรีบดำเนินการในภาวะฉุกเฉิน
มีระเบียบหลักเกณฑ์หรือข้อยกเว้น
ที่ไม่ต้องดำเนินการตามขั้นตอนปกติ
หรือไม่ อย่างไร

การเก็บสิ่งส่งตรวจทางจมูกและปากเพื่อตรวจหาเชื้อโคโรนาไวรัส ๒๐๑๙ จำนวน ๕ ครั้ง และเจาะเลือดจำนวน ๒ ครั้ง ในผู้ที่ต้องกักตัว

มีลักษณะเป็นการวิจัยในมนุษย์หรือไม่ อย่างไร



Research in disaster & disease outbreak



Potential individual benefits and risks of investigational interventions and emergency use outside clinical trials

- When facing a serious, life-threatening infection, many people are willing to assume high risks and use unproven agents within or outside of clinical trials.

realistically assess the potential individual benefits and risks of experimental interventions
communicate these clearly to potential participants

- Emergency use can compromise recruitment of research participants and therefore undermine the conclusion of trials.
- Widespread emergency use with inadequate data collection about patient outcomes must be avoided.

Equitable distribution of risks and benefits

- It may be acceptable to prioritize certain populations in study enrolment - for example, front line workers often put themselves at risk during a disaster such as an epidemic, and if experimental interventions are effective, these workers would be able to help more patients.
- The exclusion of especially vulnerable populations must be justified

General considerations for controlled clinical trials

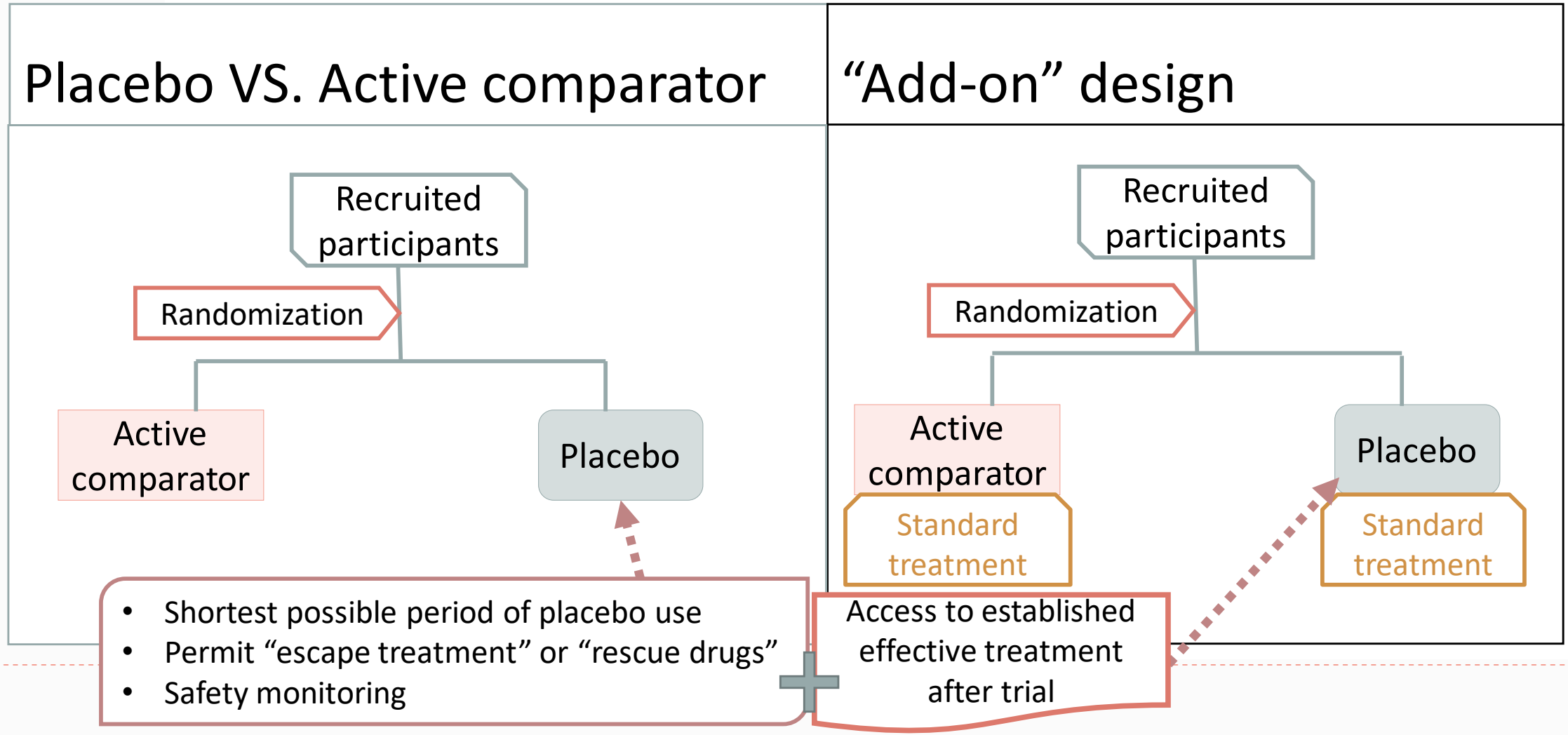
CIOMS 2016 guideline 5

- The use of placebo controls in clinical trials creates the potential for conflict between the demands of sound science and the obligation to safeguard the health and welfare of study participants.
- Randomization is the preferred method for assigning participants to the arms of controlled trials.
- "add-on designs" comparing the effects of potential new interventions against a placebo control = all participants receive the established effective intervention + randomized the investigational intervention or placebo - when an established effective intervention exists for the condition under investigation

Controlled clinical trials

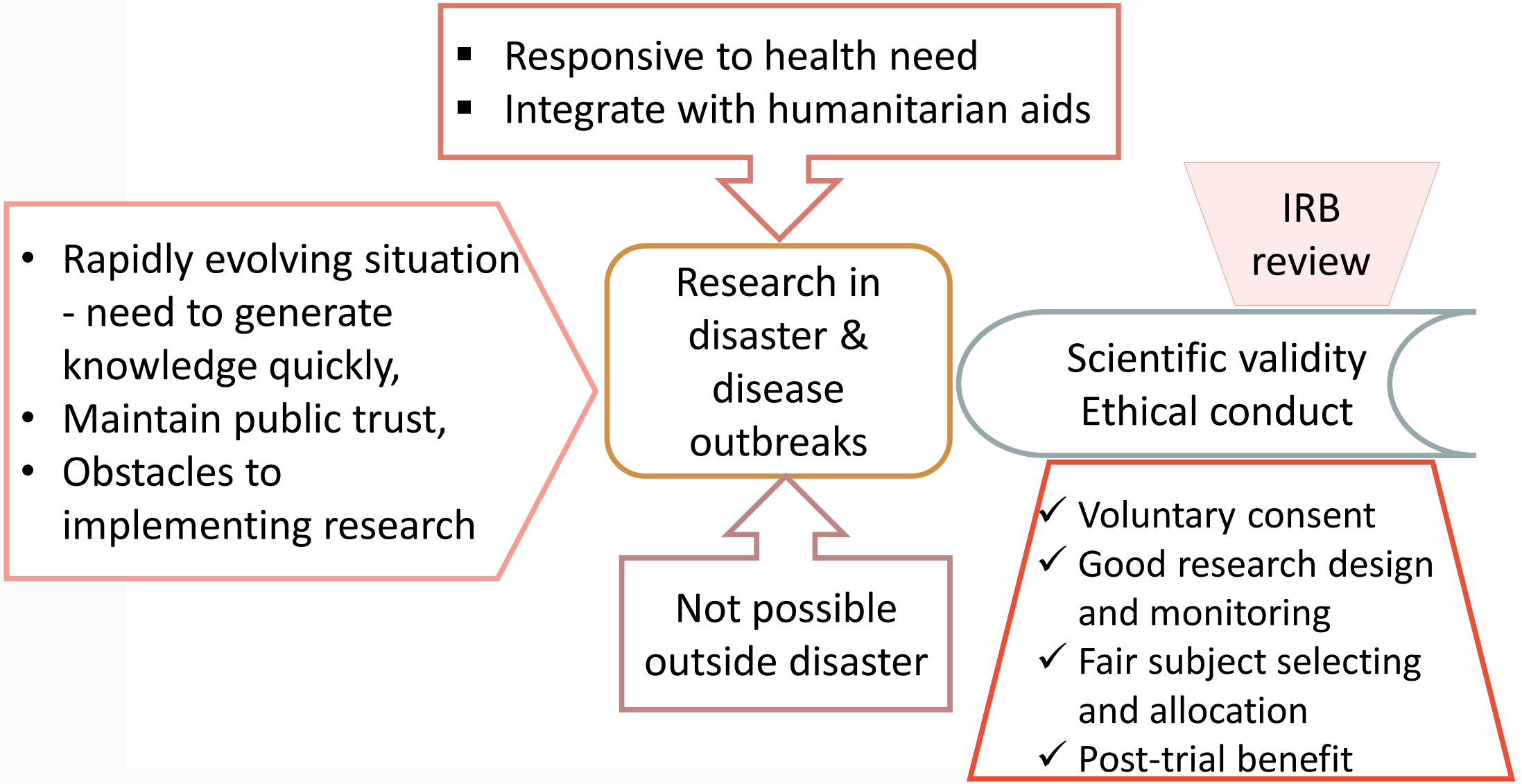
CIOMS 2016 guideline 5

Random subject allocation to study arms



Ethical review and oversight

- Procedures should be developed to facilitate and accelerate ethical review in a situation of crisis
- a specialist ethics committee (perhaps on a national or regional level) may conduct an initial accelerated review of study protocols and continue oversight if studies raise significant ethical concerns.
- Local ethics review should be carried out whenever possible.


Responsive to health need
Integrate with humanitarian aids
Rapidly evolving situation - need to generate knowledge quickly,
Maintain public trust,
Obstacles to implementing research
Research in disaster & disease outbreaks
Not possible outside disaster
IRB review
Scientific validity
Ethical conduct
✓ Voluntary consent
✓ Good research design and monitoring
✓ Fair subject selecting and allocation
✓ Post-trial benefit

Ethical consideration

- Vulnerability – informed consent process
- Conflict of interest
- Withdrawal and Termination criteria
- Data safety monitoring Board (DSMB)
- Compassionate use

Compassionate /Humanitarian Use

- In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering.

Compassionate /Humanitarian Use

- This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy.
- In all cases, new information should be recorded and, where appropriate, made publicly available.

Declaration of Helsinki

CIOMS 2016 Guideline 20
Research in disasters and disease outbreak

- it is important to obtain their informed consent for study participation and especially to emphasize the difference between research and humanitarian aid.

- Additional safeguard for high risk research
  - (participants) withdrawal criteria
  - (early) research termination criteria
  - Data Safety Monitoring Board (DSMB) - interim analysis for randomized controlled trial

Justice for Placebo (Control) group

Conflict of Interest - Definition

- other interests that conflict with the ethical conduct of research
- conflicts between the primary goal of health-related research and secondary interests

Conflicts of interest can influence
- ✓the choice of research questions and methods,
- ✓Recruitment and retention of participants,
- ✓interpretation and publication of data, and
- ✓the ethical review of research.

Conflict of interest

Reputational and Financial conflicts of interests

Academic conflicts of interest – recognition
Professional conflicts of interests – researchers' careers when applying for research funding or promotion.
Financial conflicts of interest

Researchers often serve as members of research ethics committees

Management of conflicts of interest

1. Education of researchers and research ethics committees - Raising awareness of conflicts of interest, as well as the importance of managing such conflicts
2. Disclosure of interests to research ethics committees
3. Disclosure of interests to participants – in the informed consent discussion and documents
4. Mitigation of conflicts

- No leading role in research design & consent process
- Not as a PI
- Independent monitoring

Thank You