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Early-phase clinical trials of bio-artificial organ technology: a systematic review of ethical issues

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VANGUARD

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INTRODUCTION

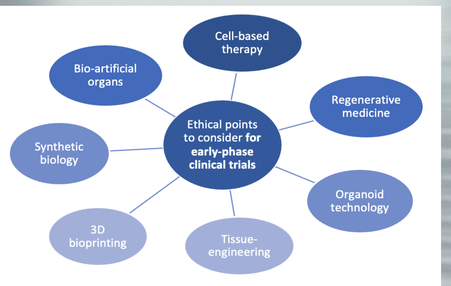
- In preclinical research settings **bio-artificial organs** are being developed
- **First-in-human transplantation trials** will eventually be launched
- Research participants could be exposed to **serious risks** (e.g. toxicity and tumorigenesis)[1]
- **No ethical guidance** for the conduct of early-phase transplantation trials of bio-artificial organs
- It could be difficult for **research ethics review committees (RECs)** to evaluate the ethical acceptability of early-phase clinical trials

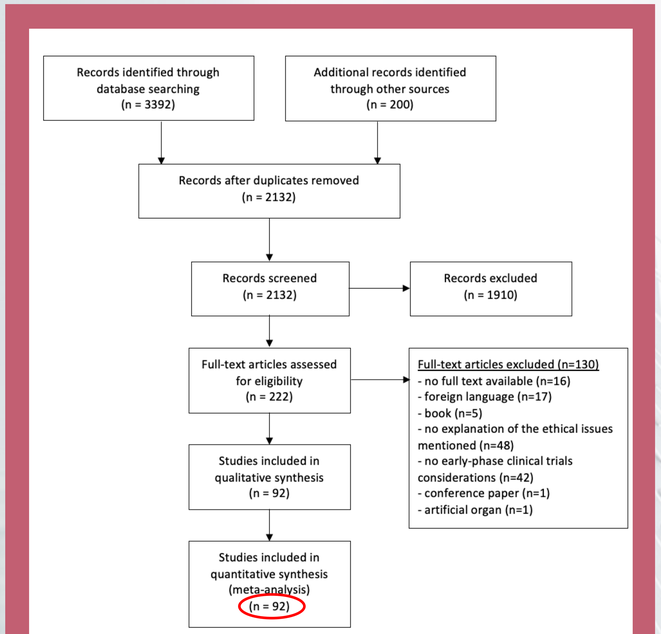
AIM

To **systematically examine** the published literature on **early-phase clinical trials** in the **adjacent fields** of regenerative medicine, and to undertake **a thematic analysis** of relevant ethical points to consider **for early-phase clinical trials of transplantable bio-artificial organs**

METHOD

- **Systematic** review
- All titles and abstracts were screened until **September 2021**
- **No restriction** for date of publication
- **Qualitative content analysis**





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1. Kimmelman J. Ethics, ambiguity aversion, and the review of complex translational clinical trials. Bioethics (2012) 26:242–50. 10.1111/j.1467-8519.2010.01856.x

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https://vanguard-project.eu

RESULTS

- **92 articles** were included
- 2003 - 2021
- 7 adjacent research fields
- Most articles published in cell-based therapy
- **6 empirical studies**
  - 3 patient perspectives
  - 3 professional perspectives
- **Six themes** were identified: cell sources, risk-benefit assessment, patient selection, trial design, informed consent, and oversight and accountability

CONCLUSIONS

- Ethical considerations from **adjacent research** fields maybe useful
- Insight in **patients' perspectives** on bio-artificial organ technologies will be essential to realize **the social value** and to determine **the conditions** for ethically responsible and acceptable **clinical translation**
- The 6 themes may play out differently in **specific bio-artificial organ** technologies, and may vary with organ type; hearts vs. kidneys
- This review is valuable for researchers, research ethics review boards, policy makers and clinicians with an interest in regenerative medicine and **involved in the translation of bio-artificial organs for clinical transplantation**

1. Cell sources

Several types of cell sources could be used to generate a bio-artificial organ, each with their own sets of ethical considerations

Xenogeneic *Allogeneic donor* *Autologous* *Modified/manipulated*

2. Risk-benefit assessment

A favorable risk-benefit ratio means that the risks and burdens of trial participation must be outweighed by the expected scientific or social value, and the potential benefits for individual participants

3. Patient selection

In patient selection, researchers should consider the availability of effective alternative treatment options, the probability of (high) risks and the potential benefits for individual patients

4. Trial design

For transplantable bio-artificial organ technologies, new trial designs are required to test safety and efficacy.

Involve surgeons early on *Combine safety and efficacy outcomes* *Include patient reported outcomes*

5. Informed consent

A valid informed consent requires that participants are adequately informed about relevant aspects of research participation

Communicate risks and benefits *Avoid overestimating benefits* *Protect right to withdraw*

6. Oversight and accountability

Researchers should be transparent and careful with their communication with patients and the general public to maintain trust in bio-artificial organ technologies

Pre-register clinical trials *Be open to international collaboration* *Organize interdisciplinary dialogues*