Overview of the RESPECT project and the paediatric clinical trials landscape.

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The Paediatric Regulation (2007)

- To improve the health of children in Europe by:
  - *facilitating the development and availability of medicines for children aged 0 to 17 years,*
  - *ensuring that medicines for use in children are of high quality, ethically researched, and authorised appropriately,*
  - *improving the availability of information on the use of medicines for children,*
- without:
  - *subjecting children to unnecessary trials, or delaying the authorisation of medicines for use in adults.*

Health care built on clinical evidence.

Health care should be built on the results from clinical studies so that we have <u>evidence for the effectiveness and safety</u> of treatments being offered to children.

Over 50% of the medical products used in child health care are not tested or authorised for use in this age group.

Health care professionals have no alternative but to use medicines "off-label", judging the suitability and the correct dose of these medicines themselves in the absence of paediatric labelling information.

This poses significant risks of inefficacy and/or adverse reactions for children.

Clinical evidence from Clinical Trials:

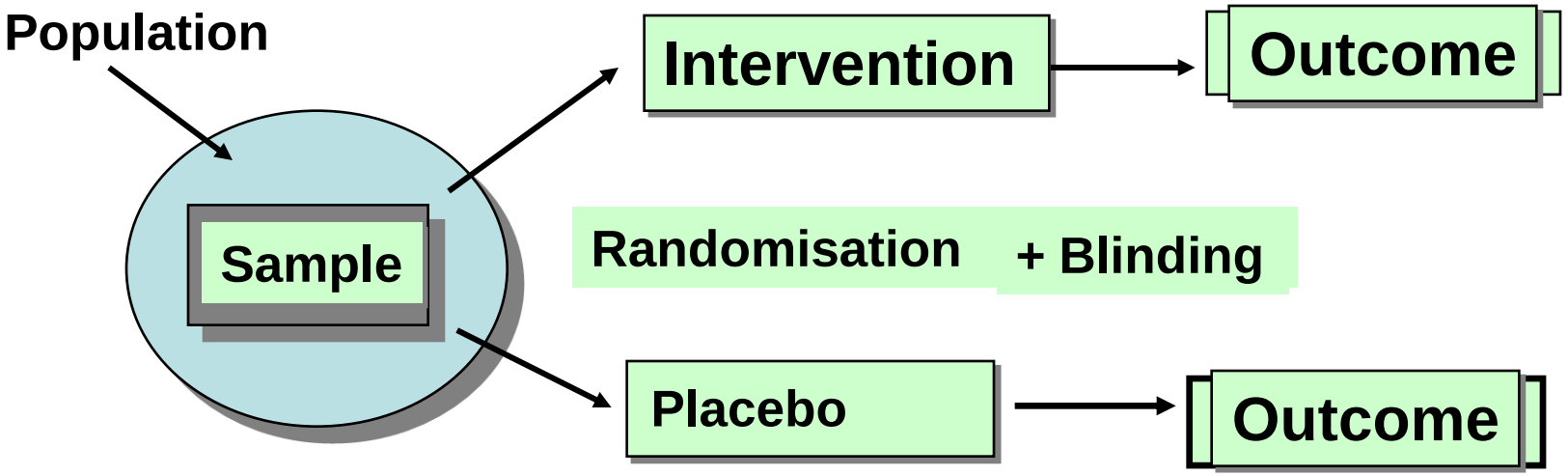
A clinical trial is a study that examines the actions of a drug or intervention on human subjects.

- **Involve human subjects**
- **Focus on unknowns: safety and effectiveness**
- **Proceeds clinical use**
- **Specific inclusion/exclusion criteria**
- **Sample size based on statistical power calculations**

Summary of Phases I-IV

	# Subs.	Length	Purpose	Yr 2010
Phase I	**20 – 100 healthy**	**Several months**	**Mainly Safety**	**1383**
Phase II	**20 – 300 healthy & patients**	**Several months-2 yrs.**	**Short term safety; mainly effectiveness**	**1185**
Phase III	**300 – 3000 patients**	**1-4 yrs.**	**Safety, dosage & effectiveness compared to the standard treatment (equipoise)**	**918**
Phase IV	**Post marketing patients**		**Safety surveillance and efficacy from long term use.**	**707**

Basic phase III trial design



- Why do a randomized blinded trial
  - minimize confounding
  - minimize co-interventions
  - minimize biased outcome ascertainment

Why perform clinical trials in children?

- Children are a unique population with distinct developmental and physiological differences from adults.

- Clinical trials in children are essential in order to develop age-specific, empirically-verified therapies and interventions.

- If children don't participate then paediatric medical development is severely limited.

Why are there problems recruiting children into clinical trials?

- From the protocol
  - **Inclusion criteria is very strict.**

- From the clinic
  - **Concerns about children's safety.**
  - **Clinic staff unwilling to jeopardize treatment status.**
  - **Belief that children can't make the judgment to participate.**
  - **Time & effort of the clinical staff.**

Why are there problems recruiting children into clinical trials?

- From the patient approached by their physician
  - **Sense of being overwhelmed.**
  - **Difficulty in judging risk.**
  - **Satisfaction with status quo.**
  - **Increased burden of participation.**
  - **Possibility of missing out on treatments because locked into the trial.**
  - **Children refuse.**

- From the patient not approached by their physician
  - **Lack of information about what trials are taking place.**
  - **Afraid or suspicious of medical research.**

EC Cooperation Work Programme HEALTH-2007-4.1-4: Identifying patients' needs in the clinical trials context.

- How can patients get the clinical outcomes that really matter to them?
- How can the patients needs be integrated into clinical trials?
- How can patients be better mobilised and empowered?

Micro needs

- Satisfying additional health care needs
- Respect for the individual
  - Realistic information (not false hope)
- Control
  - over the decision to participate.
    - Decision tools
    - Access to support (second opinion)
    - Access to as much information as possible (concerning: side-effects, insurance, …)
    - What is the importance of the trial
  - over how to contribute.
    - Appointment times
    - Time in the clinic
- Being valued
  - Receiving the results (including negative results)

Macro needs

- Knowledge about clinical trials
- Inclusiveness - the patient group defines unmet needs etc.
- Transparency of the process so that all possible participants could be included.

Modifiers

- The child's medical condition
  - Seriousness of the child's illness
  - Age of the child
  - Perceived need for health care / to be involved
- Interpretation of the trial
  - Level of risk involved and interpretation of risk
  - Trust
  - Experience (of trials or health care) (experience of staff attitudes)
- Practical issues (time, distance, supervision of siblings…)
- Knowledge and Health Beliefs of the parent and child
  - Family/child beliefs about research

Conclusions

- Health care must be knowledge-based. Clinical trials provide the evidence upon which health care should be based.

- Empowered families and their organisations can take an active role in the CT process having more input into what trials are carried out and how they are carried out.

- Closer cooperation between all clinicians, patients, patient organisations, pharma and regulators will lead to an enrichment of both the patient's and the professionals' understanding of the medical condition.

- Greater knowledge, openness integration and increased trust in health care research will empower patients and lead to patients getting the clinical outcomes that really matter to them.

- Together we can be co-producers of improved health care

All stakeholders can work together!