



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

John Chaplin

Sahlgrenska Academy at the University of
Gothenburg, Sweden



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 evidence for the effectiveness and safety 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**

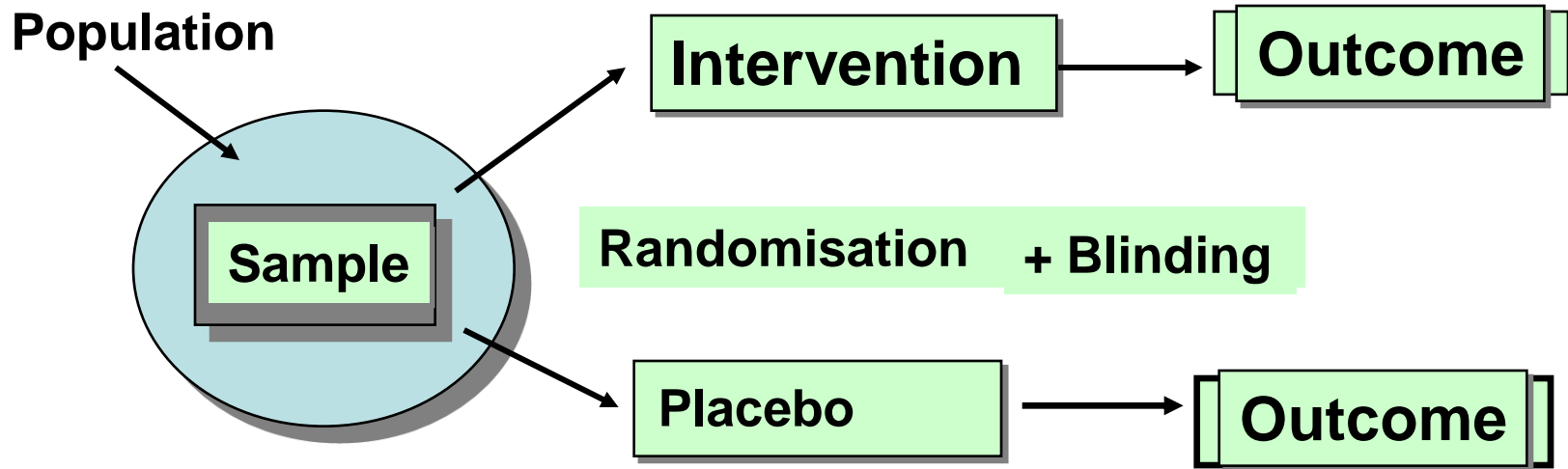


Summary of Phases I-IV

| | # Subs. | Length | Purpose | <u>Yr</u> <u>2010</u> |
|------------------|------------------------------------------------|---------------------------------------|------------------------------------------------------------------------------------------------------|--------------------------|
| 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!

