2nd Congress on Paediatric Palliative Care
'A Global Gathering'

Too precious to study, or too important not to ?

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FONDAZIONE
MARUZZA
LEFEBVRE
D'OVIDIO
ONLUS
Gold Medal
of Merit for services
to Public Health
2013
CHARTER OF THE THE RIGHTS
OF THE DYING CHILD
THE TRIESTE CHARTER

Too precious to study, or too important not to ?

- Introduction
- The origins of duty
- Compassion:
  - a duty to protect
  - a duty to study
  - a duty to be studied
- What makes research ethical ?
- Conclusion

Introduction

Rules:

“It’s your job to care”

Outcome:

“Caring makes things better for everybody”

A duty of care

Rules:

“It’s your job to care”

Outcome:

“Caring makes things better for everybody”

A duty of care

Compassion:

“If you care about someone,
It is natural to behave in a certain way towards them”

Duty as compassion…

Compassion as duty…

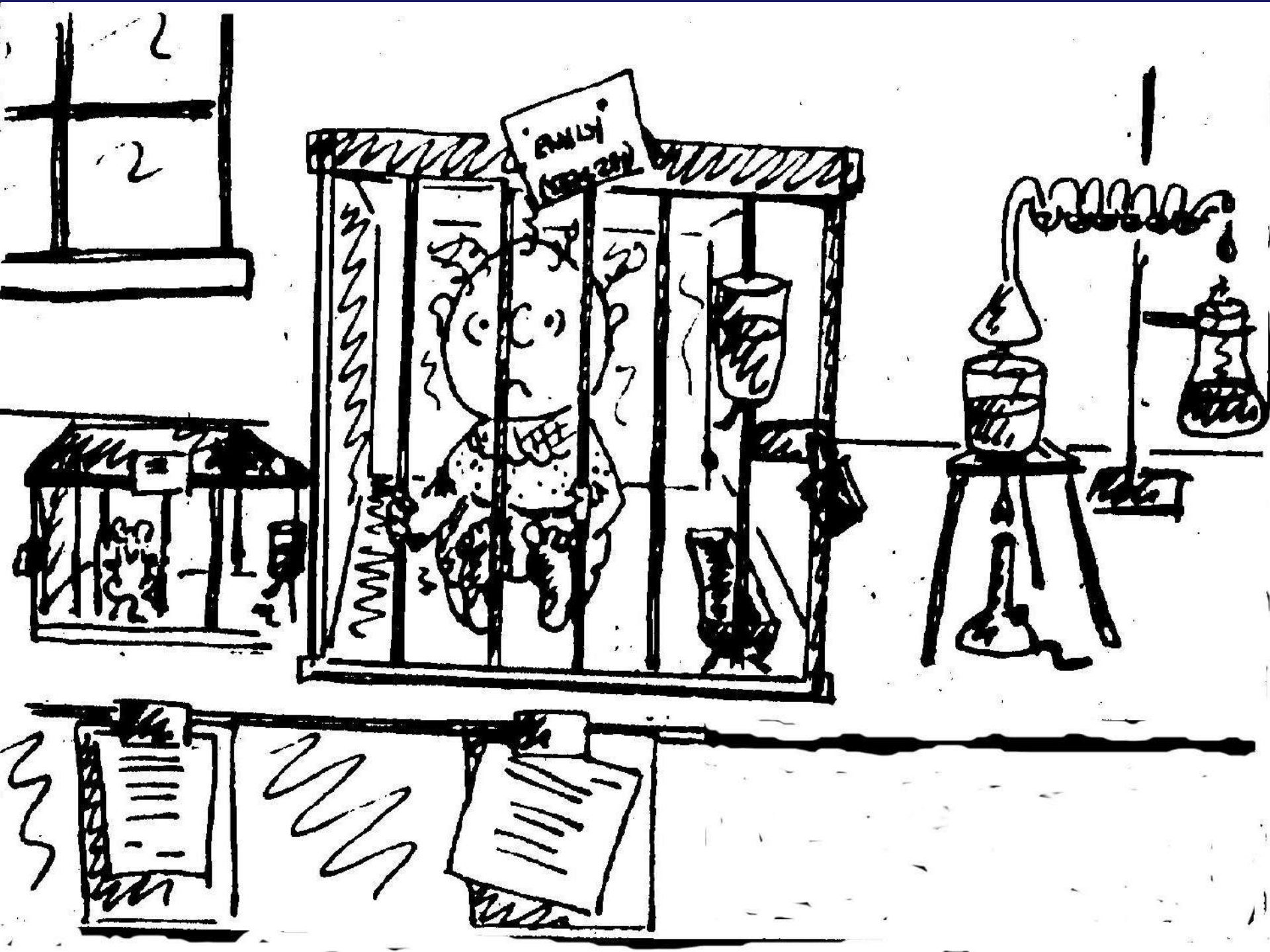
- To protect the child from research

Compassion as duty…

- To protect the child from research

"… to experiment on children in ways that are not related to them as patients is already a sanitised form of barbarism [that] pays no attention to the faithfulness-claims which a child, simply by being a normal or a sick or a dying child, places upon us and medical care. We should expect no significant exceptions to this canon of faithfulness to the child"

Paul Ramsey *The Patient as Person* (New Haven, Connecticut: Yale University Press, 1970).



Compassion as duty…

- To protect the child from research
- To protect the child from unresearched interventions

Survey of unlicensed and off label drug use in paediatric wards in European countries

Sharon Conroy, Imti Choonara, Piero Impicciatore, Angelika Mohn, Henrik Arnell, Anders Rane, Carmen Knoeppel, Hannsjoerg Seyberth, Chiara Pandolfini, Maria Pia Raffaelli, Francesca Rocchi, Maurizio Bonati, Geert 't Jong, Matthijs de Hoog, John van den Anker on behalf of the European Network for Drug Investigation in Children

Abstract

Objective To determine the extent of use of unlicensed and off label drugs in children in hospital in five European countries.

Design Prospective study of drugs administered to children in general paediatric medical wards over four weeks.

Setting Children's wards in five hospitals (one each in the United Kingdom, Sweden, Germany, Italy, and the Netherlands).

Subjects Children aged 4 days to 16 years admitted to general paediatric [illegible]

Main outcome measure Proportion of drugs that were used in an unlicensed or off label manner.

Results 2262 drug prescriptions were administered to 624 children in the five hospitals. Almost half of all drug prescriptions (1036; 46%) were either unlicensed or off label. Of these 1036, 872 were off label and 164 were unlicensed. Overall, [illegible] patients (421; 67%) received an unlicensed or off label drug prescription.

Conclusions Use of off label or unlicensed drugs to treat children is widespread. This

medical and surgical wards,[3] and a neonatal intensive care unit.[7] We wished to determine the extent of unlicensed and off label drug use in several countries within the European Union. This is important in view of the new European guidance on the clinical investigation of medicinal products in children.[8]

Methods

We studied a paediatric medical ward in each of the participating centres (Derby, United Kingdom; Uppsala, Sweden; Marburg, Germany; Bergamo, Italy; Rotterdam, Netherlands) prospectively for four consecutive weeks during 1998. The wards in Derby and Bergamo admitted mainly general paediatric patients, with Derby including children who had had surgery. The wards in Marburg and Uppsala had a mixture of general paediatric and respiratory cases (including cystic fibrosis). The ward in Rotterdam had the fewest general paediatric cases, containing children with cardiac, oncological, renal and

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University

Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees

Neena Modi,[1] Jyotsna Vohra,[1] Jennifer Preston,[2] Catherine Elliott,[3] William Van't Hoff,[2] Jane Coad,[4] Faith Gibson,[4] Linda Partridge,[5] Joe Brierley,[1] Vic Larcher,[1] Anne Greenough,[1,6] for a Working Party of the Royal College of Paediatrics and Child Health

BACKGROUND

The British Paediatric Association, the forerunner of the Royal College of Paediatrics and Child Health (RCPCH), first published guidance in relation to research involving children in 1980.[1] Prior to this time, little clinical research involved children. The 1980 guidance initiated a sea change, stating 'research involving children is important', 'should be supported and encouraged' and 'research which involves a child and is of no benefit to that child (non-therapeutic necessarily either uneth-

and governance of research, with the involvement of a number of agencies, most recently the Health Research Authority.[5] There is a greater focus on involving children and their parents more actively in the design, review and conduct of studies. The ways in which society views clinical research have also continued to evolve. The Declaration of Helsinki that sets out the ethical principles that underpin medical research involving *all* human subjects has had two notes of clarification and seven amendments, the most recent in 2013.[6]

In recognition of these changes, a led by the RCPCH was estab-

responses to treatments differ in children and adults, hence, conclusions extrapolated from studies in adults often have limited relevance and may be harmful. Innovative or experimental treatments are not necessarily better than existing treatments[8] and without information from research there will be continuing uncertainties in the care that children receive. The RCPCH recognises the need to increase and strengthen children's research.[9] The RCPCH supports the conduct of research in children that has the objectives of understanding, preventing and treating disease and preserving health. All clinical research must be reviewed and approved by a research ethics committee.

RESEARCH RISK

Every research study must be preceded by a careful assessment of predictable risks in comparison with possible benefits to the individual and the population affected by the condition. Measures to minimise risk include appropriate research design, delivery by personnel trained in the procedures to be used and experienced in caring fo children, and methods to reduce th volumes of blood or tissue required Blood sampling is often regarded as concern in relation to the pain, and ri of research participation. However, effe

"Children require protection, but this should not preclude the claim of other rights, including the right to the highest standard of healthcare, to be informed, express their views, and influence decisions made about them…and have their care *assured by research* "

Modi, N. et al *Arch. Dis. Ch.* Vol 99 (10) 2014

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Compassion appears to require us

both to do research in children …

and to avoid it !

Compassion as duty…

- To protect the child from research
- To protect the child from unresearched interventions

Compassion as duty…

- To protect the child from research
- To protect the child from unresearched interventions
- To participate in research that will help others

Compassion as duty…

- To protect the child from research

"… it is possible for children between the ages of five and fourteen years to benefit morally from involvement in clinical research. If that is the case, it is possible for them to be involved as more than mere means."

Richard McCormick
Experimentation in Children: Sharing Sociality
(Hastings Center Report Dec 1976 pp 41 - 46).

Compassion as duty…

We are doing children a disservice if we:

- assume that they cannot want to help others
- decree arbitrarily that they should not be allowed to do so by participating in research

Compassion as duty…

We are doing children a disservice if we:

- assume that they cannot want to help others.
- decree arbitrarily that they should not be allowed to do so by participating in research that is ethical.

What makes research ethical ?

Any harms must be justified by benefits.

Therefore:

1. Project must ask an important question.
2. It must be able to answer that question.
3. The answer should not be knowable by other [less harmful] means.

What makes resea ical

its.

Efficacy of oxycodone in neuropathic pain

A randomized trial in postherpetic neuralgia

C. Peter N. Watson, MD, FRCP(C); and Najib Babul, PharmD

Article abstract—*Objective:* Although opioid analgesics are used in the management of neuropathic pain syndromes, evidence of their efficacy remains to be established. We evaluated the clinical efficacy and safety of oxycodone in neuropathic pain using postherpetic neuralgia as a model. *Methods:* Patients with postherpetic neuralgia of at least moderate intensity were randomized to controlled-release oxycodone 10 mg or placebo every 12 hours, each for 4 weeks, using a double-blind, crossover design. The dose was increased weekly up to a possible maximum of 30 mg every 12 hours. Pain intensity and pain relief were recorded at weekly visits. Clinical effectiveness, disability, and treatment preference were also assessed. *Results:* Fifty patients were enrolled and 38 completed the study (16 men, 22 women, age 70 ± 11 years, onset of postherpetic neuralgia 31 ± 29 months, duration of pain 18 ± 5 hours per day). The oxycodone dose during the final week was 45 ± 17 mg per day. Compared with placebo, oxycodone resulted in pain relief (2.9 ± 1.2 versus 1.8 ± 1.1, $p = 0.0001$) and reductions in steady pain (34 ± 26 versus 55 ± 27 mm, $p = 0.0001$), allodynia (32 ± 26 versus 50 ± 30 mm, $p = 0.0004$), and paroxysmal spontaneous pain (22 ± 24 versus 42 ± 32 mm, $p = 0.0001$). Global effectiveness, disability, and patient preference all showed superior scores with oxycodone relative to placebo (1.8 ± 1.1 versus 0.7 ± 1.0, $p = 0.041$; 67% versus 11%, $p = 0.001$, respectively). *Conclusions:* Controlled-release ± 0.8 versus 0.7 ± 1.0, $p = 0.041$; 67% versus 11%, $p = 0.001$, respectively). *Conclusions:* Controlled-release effective analgesic for the management of steady pain, paroxysmal spontaneous pain, and allodynia, ge postherpetic neuralgia.

diagnostic grouping of patients with neuropathic . However, no information is available on algesic response can be sustained with ut the development of unac- ential effects of opioid l spontaneous ociated

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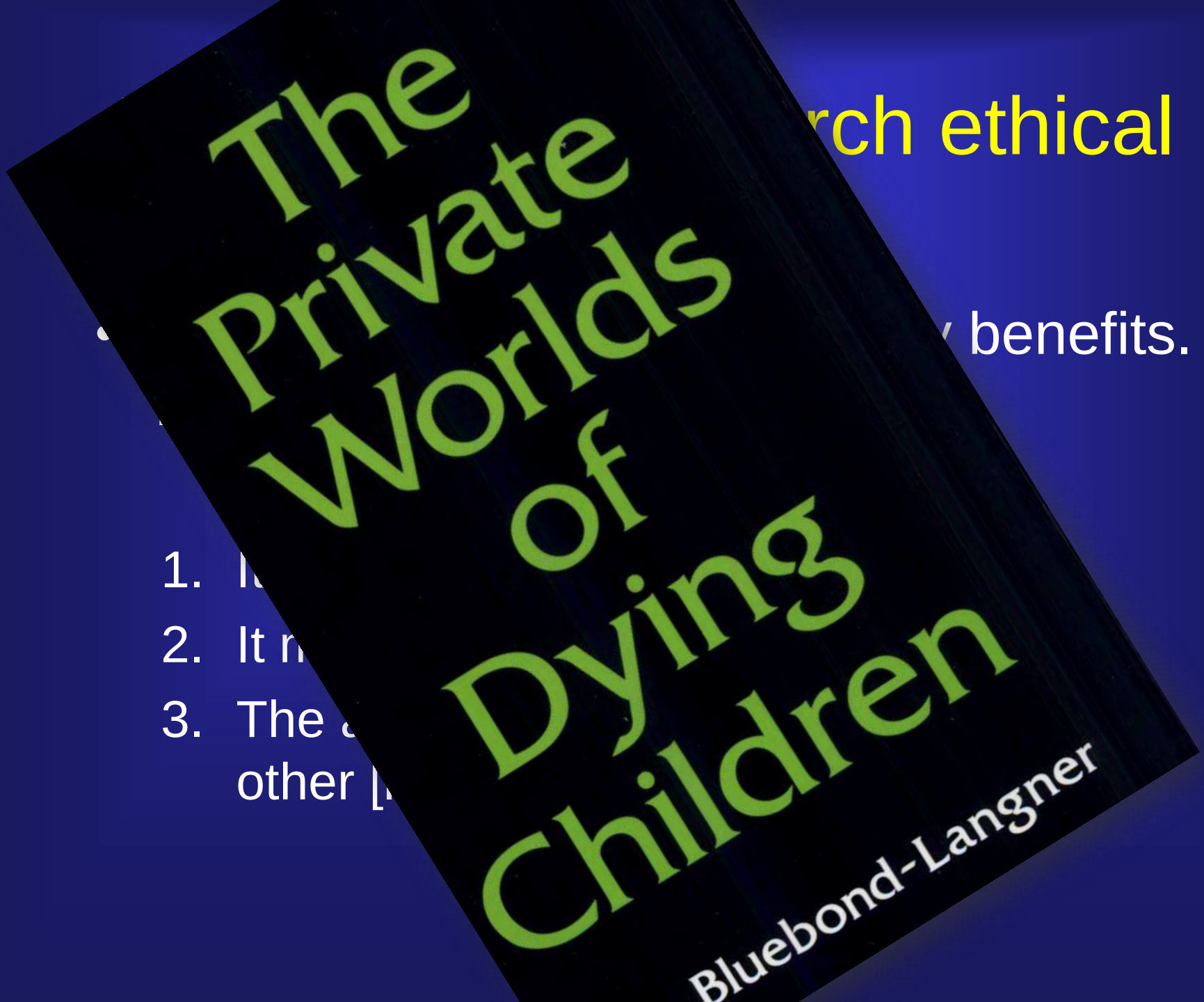

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- A duty of care must be rooted in compassion – care (not duty) is motive.
- Preventing children from participating in ethically sound research is not the only compassionate response.
- Ethically sound research must ask an important question and be able to provide an answer that is not already knowable by other means.