

After Gard: ethically ensuring access to experimental and innovative treatment

Dominic Wilkinson^{1,2}, Julian Savulescu^{1,3}

Affiliations: 1. Oxford Uehiro Centre for Practical Ethics, Faculty of Philosophy, University of Oxford, UK. 2. John Radcliffe Hospital, Oxford, UK. 3. Murdoch Children's Research Institute, Melbourne, Australia

Correspondence: Prof Dominic Wilkinson, Oxford Uehiro Centre for Practical Ethics, Suite 8, Littlegate House, St Ebbes St, Oxford, OX1 1PT, UK. Tel: +44 1865 286888, Fax: +44 1865 286886 Email: dominic.wilkinson@philosophy.ox.ac.uk

Funding: DW was supported for this work by a grant from the Wellcome trust WT106587/Z/14/Z. JS was supported by a grant from the Wellcome Trust WT 104848Z/14/Z.

The authors declare no competing interests.

ORCID ID:

DW: 0000-0003-3958-8633

JS: 0000-0003-1691-6403

This week marked the end of the long-running legal battle over treatment for UK infant Charlie Gard.¹ International medical experts, invited by the court to examine Charlie, concluded that experimental treatment could no longer offer even theoretical benefit. His parents accepted that it was time to allow Charlie to die, while bitterly lamenting that he had missed a potential window of opportunity for treatment.²

This emotionally and ethically fraught case has divided experts and the community.³⁻⁵ It is time now to seek common ground (Box).

In this commentary, we focus on the questions raised around experimental treatment. In particular, when should parents *not* be allowed to access desired innovative treatment that offers a potential benefit to their child?

1. **Parents' role in decision-making for children.** Parents should not be permitted to choose harmful treatment options for their child – but we need to clarify what level or chance of harm is sufficient to intervene.
2. **Decisions for adults versus decisions for children.** We should make decisions about life prolonging or experimental treatment on a different basis for adults compared with children. We should in general allow adults to choose treatment for themselves even if suboptimal or potentially risky.⁶
3. **Experimental treatment.** We should have a lower threshold for allowing access where patients have no other options, and allow earlier innovative treatment
4. **The role of resources.** We need to have public debate about limited resources and how to fairly incorporate this into decisions.
5. **The role of the courts.** We need a fair, expedient way of resolving disputes between families and clinicians.
6. **Ethical decisions vs clinical decisions.** We should allow patients to access treatment options if there is reasonable disagreement by professionals.
7. **Medical tourism:** We should allow families to take their child overseas if the treatment they are seeking is legal and does not risk significant harm
8. **Challenging normative and conceptual issues.** There is a need for further ethical analysis of concepts – for example the significance of dignity in end of life care, and that of a 'life worth living'.
9. **Reflective Equilibrium, Reasons and Evidence.** Debate and decision making needs transparency (ethical and scientific) and humility (recognition that we can all be wrong).

Box: Ethical lessons from the Charlie Gard case ⁷

The standard answer to that question, is that a treatment shouldn't be provided or permitted if it would impose a significant risk of serious harm.⁸ But that raises questions about what risks are 'significant' and which harms are 'serious'. We also need to balance harms against benefits – more unpleasant or risky treatment would be acceptable if the benefits are greater or more likely.

In the Gard case, the requested treatment had never been tried, either in animal models or in other patients with his rare illness. That makes it extremely hard to know just what the risks or benefits could be. Clinicians are understandably loathe to approve untested therapies in gravely ill children who cannot consent.

However, it isn't always possible or ethical to test treatments in patients with less severe forms of a disease.⁹ For patients who are dying, without other treatment options, there may be little to lose and everything to gain, especially when downsides are minimal or can be controlled. In such situations, we should potentially allow parents to access treatment even if there is some risk and little direct evidence of benefit (Figure). Expedient assessment is important to avoid patients missing out on the chance of benefit.

At the same time, it is vital to protect dying children from interventions that have no realistic prospect of helping them, and that would cause them to suffer.¹⁰ In the face of uncertainty, particularly if a child is deteriorating, one option would be to permit strictly time-limited trials of therapy, with clear termination criteria and agreement that the treatment would be ceased (and palliative care provided) if significant side effects arise, or if no substantial benefit is seen.

How should hospitals and professionals decide whether treatment offers a realistic benefit, or would cause suffering? Clinical ethics or similar committees could play a role in gathering and considering scientific evidence and expert opinion about proposed treatment.^{10,11}

However, while consensus about treatment may be desirable,¹⁰ we suggest that agreement of all involved shouldn't be required.¹² As the Gard case makes clear, there can be very different views between highly qualified medical experts about the science. More importantly, these decisions are linked to important but vexed ethical questions— how to evaluate quality of life, how to weigh up small chances of benefit against risks of harm. It would be important for experts providing opinions about treatment to clarify whether they are offering views about scientific facts (relating to the condition or treatment in general), views about whether or not treatment should be provided for a specific child. If the latter, expert views are likely to carry more weight if they have reviewed all relevant clinical material as well as assessed the child in person.¹

Where there is reasonable disagreement between experts about whether or not the requested treatment would be in a child's best interests, parents' views should be respected. Of course, that leads to another challenge – that of determining when disagreement is reasonable or unreasonable. One test of reasonability is willingness to engage in rational, logical debate and tolerate a reasonable pluralism about value.^{3,7}

Finally, even if innovative treatment would be reasonable, it may not be affordable within a public health care system.⁴ If treatment wouldn't be in a child's best interests, it should not be provided even if parents are able to pay for it. However, where the reason not to provide treatment is on the basis of limited resources, parents should be free to access the treatment if funded independently. One option would be for families to travel overseas. However, if local health professionals have the necessary skills and ability to provide it, there should also be the option of families paying for innovative treatment while continuing to receive standard medical care within the public health system. That may raise uncomfortable questions of equity and fairness, yet requiring families to travel may be harmful for a seriously ill child and imposes a substantial additional burden.

These decisions on the cutting edge of medicine and science require both good science and good ethics (Figure). We can, and doubtless will, sometimes get it wrong – either providing treatment that ends up being harmful, or refusing novel therapies that turn out with time, to be the next best thing. But that must not stop us from striving to do the best for our current patients. It is all the more reason to learn vital lessons from those who have gone before them.

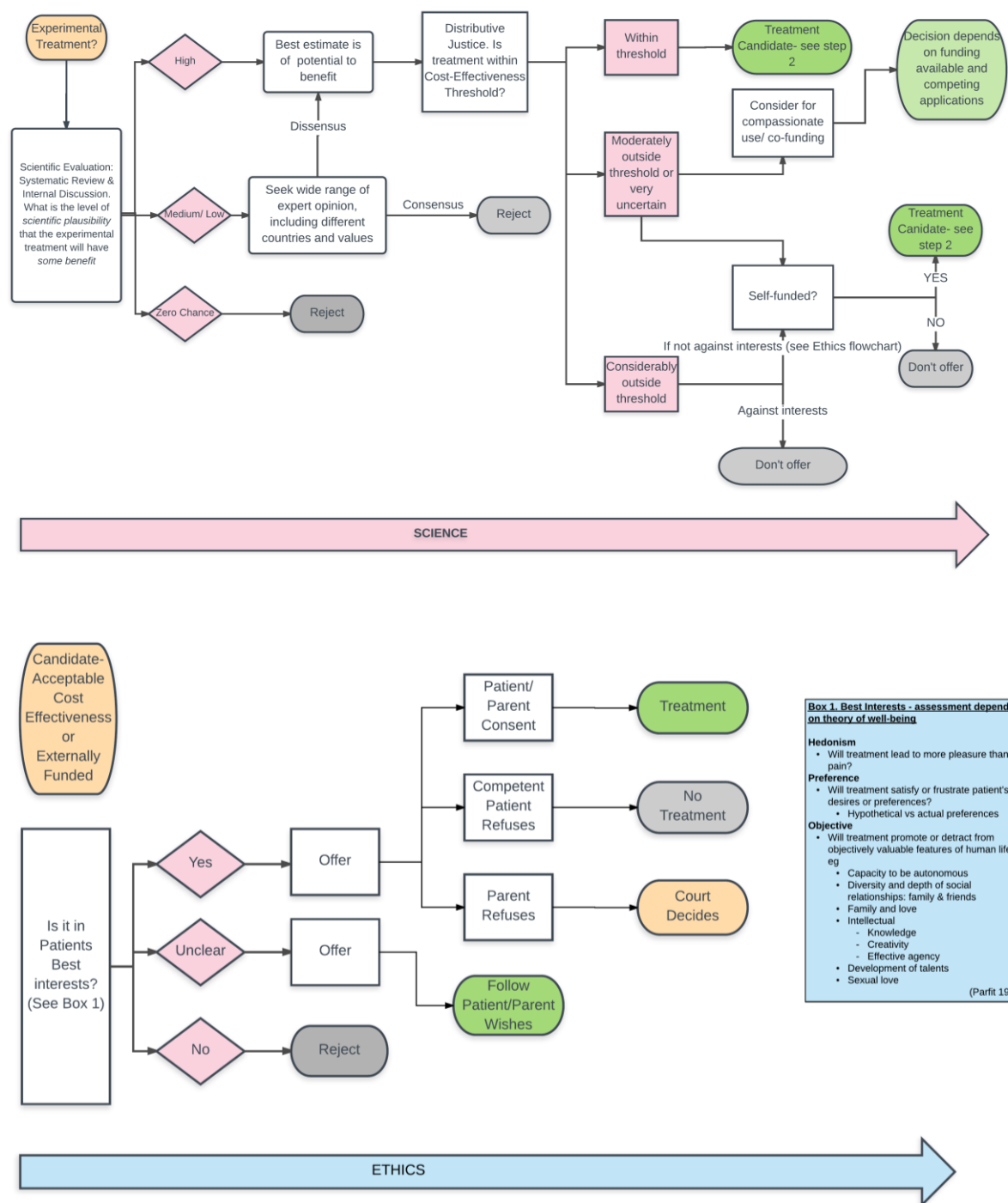


Figure: Evaluating innovative treatments A. Step 1: Is the treatment scientifically plausible? Is it affordable? B. Step 2: Is the treatment in the patient's best interests?¹³

Scientific Plausibility Experimental treatments may be at different stages in their development and testing, and be based on hypotheses that have varying degrees of confidence. The question asked is not how likely is this treatment to succeed, but what is the level of scientific plausibility. For example, a double blinded placebo controlled trial showing benefit is the highest standard. No evidence and no plausible rationale would be

Zero. Medium or low could be animal studies, or an untested treatment which nevertheless is based on a plausible scientific rationale.

Cost Effectiveness This may be extremely difficult to assess for experimental treatments whose effectiveness is unknown. However, it may be possible to assess using a range of plausible estimates of cost and benefit

Best Interests For a young child, assessment of the child's subjective experience (of pain or pleasure) may be challenging. Their own preferences and values cannot be assessed.

Objective goods should include elements that are widely agreed to be valuable in human life. They should not include values that are not shared by all in the community (for example values based on religious belief or doctrine).

1. Great Ormond Street Hospital -v- Yates and Gard – 24 July 2017. [2017] EWHC 1909 (Fam).
2. Mendick R. 'We had a chance and we were not allowed': Charlie Gard's parents blame hospital as they end legal fight to save baby's life. *The Telegraph*. 2017 24 July 2017.
3. Savulescu J. Is it in Charlie Gard's best interest to die? *Lancet* 2017; **389**(10082): 1868-9.
4. Wilkinson D. Beyond resources: denying parental requests for futile treatment. *Lancet* 2017; **389**(10082): 1866-7.
5. Truog RD. The United Kingdom Sets Limits on Experimental Treatments: The Case of Charlie Gard. *JAMA* 2017.
6. Wilkinson D, Savulescu J. Cost-equivalence and Pluralism in Publicly-funded Health-care Systems. *Health Care Anal* 2017.
7. Wilkinson D, Savulescu J. Hard lessons: learning from the Charlie Gard case. *J Med Ethics* 2017; **(forthcoming)**.
8. Gillam L. The zone of parental discretion: An ethical tool for dealing with disagreement between parents and doctors about medical treatment for a child. *Clinical Ethics* 2015; **11**(1): 1-8.
9. Savulescu J. Harm, ethics committees and the gene therapy death. *J Med Ethics* 2001; **27**(3): 148-50.
10. Brierley J, Larcher V. Compassionate and innovative treatments in children: a proposal for an ethical framework. *Arch Dis Child* 2009; **94**(9): 651-4.
11. Brierley J, Turnham H, Larcher V. Diseases desperate grown by desperate appliance are relieved, or not at all: Medical Innovation in a Children's Hospital. *Bioethics* 2017; **(forthcoming)**.
12. Wilkinson D, Truog R, Savulescu J. In Favour of Medical Dissensus: Why We Should Agree to Disagree About End-of-Life Decisions. *Bioethics* 2016; **30**(2): 109-18.
13. Parfit D. Reasons and persons. Oxford: Oxford University Press; 1984.