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His presentation: 'The Ethics of Placebo Controlled Studies'

Will argue that:

- Our approach to the use of placebo ought to be precautionary (essentially an endorsement of the Helsinki position 2013.33)

But

- Ethical care/ treatment needs to be premised upon the best science
- Research creates vulnerabilities for research subjects which ought to be acknowledged
- Researchers have a duty of care to do no wrong ('Do least possible harm but do no wrong'!) – it is not wrong to cause or risk harms when certain strict conditions are met:
    - a risk of some harm may be permissible when, the harms are minimised
    - the harms risked are proportionate (risk/ benefit ratio)
    - the harms, if realised, are likely to leave the participant no worse off
    - the potential extent/ severity of harms may be uncertain/unknown

1) There are strong moral reasons for conducting scientifically robust research into new therapies and there are equally strong reasons 2) to protect the rights, interests and wellbeing of patients – such reasons are the basis of moral duties. Sometimes these moral duties are in conflict.

We must be convinced that it is morally justified to ask appropriate participants (be they healthy volunteers or patients) to run the risk of suffering the known and unknown harms by participating in research. But this does not amount to an *obligation* to participate only a reasonable expectation that some will say yes.

For those planning and designing (and sanctioning) clinical research broadly, researchers, they must be convinced that the research design satisfies 1) with an eye to the interests of no particular patient but all relevant patients, and secondly the wider interests of society.

For those primarily concerned with the responsibility for the management of everyday care of patients, clinicians, then they must be persuaded that 1) does not conflict with their view of 2) or they must be permitted the appropriate discretion to form a different judgement e.g. that it would not be in the interests of *this particular patient* to enter a placebo controlled trial – this seems consistent with clinical equipoise (Freedman B. NEJM; 317:141-5, 1987, Miller PB, Weijer C. Kennedy Institute of Ethics Journal 13:93-118, 2003)

Patients must have the best advice available to them, and alongside the guidance of a trusted physician, they must also have access to the reasoning of those who have planned (an ethically approved) research project.

They must be allowed the freedom to make their own decision without constraint

In order to determine what is the reasonable and morally prudent position for NMO patients then a number of questions need to be addressed:

1. Is there a standard of care?

- How has the standard been established – against placebo/ no treatment?
- Are there common examples of 'on treatment' relapses?
- Are there common examples of 'off treatment' remissions?

2. Research design

- Is a placebo necessary?
- Is it necessary to withdraw or withhold standard treatment/s
- Will there be the smallest possible placebo group?
- Will the study involve a cross-over or an open label extension?
- Will 'on placebo' relapses result in immediate withdrawal and administration of rescue therapy

3. Rights and duties of patients

- Reasonable expectation that research will happen (right to research)
- Reasonable expectation that they will make a contribution to the research effort (duty to consider participation)
- Reasonable expectation that they will have a voice at the research table (upstream consultation)
- As a member of a patient forum said recently 'Why wouldn't we be at the table?'

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