



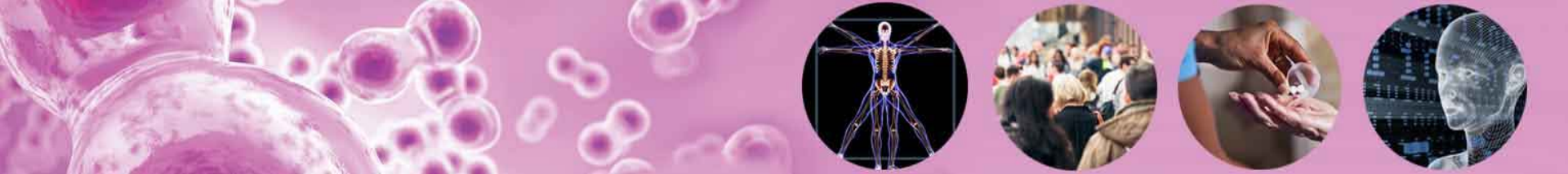
Risk, rights and responsibility in human genome editing

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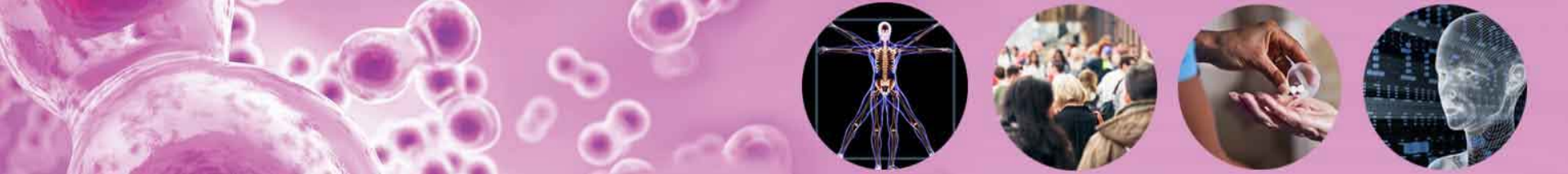
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Heritable and somatic editing should be considered in tandem

- Assessment of risks: when is it *safe enough*?
 - In light of possible benefits
 - In comparison to possible alternatives
 - Including 'do nothing'
 - And somatic editing
- Which option offers the best balance of risks and benefits, all else being equal?
- Heritable (HGE) vs somatic genome editing (SGE): risks not *necessarily* qualitatively different
- Somatic editing also affects genes of future generations
 - Both individual and population implications
- Choice to use somatic rather than heritable approach:
 - Mutations may be passed on that otherwise would not be
 - Or constrains reproductive options of next generation
- Heritable GE: 'artificial' rather than 'natural' mutations
 - But not clear that this is morally relevant



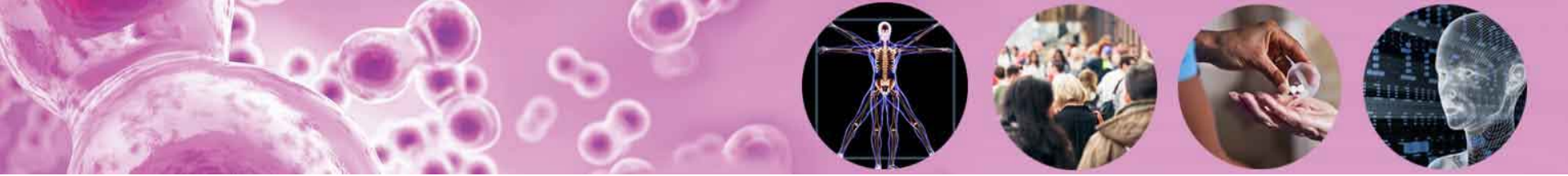
Comparing cost and risk for HGE vs SGE

Somatic genome editing

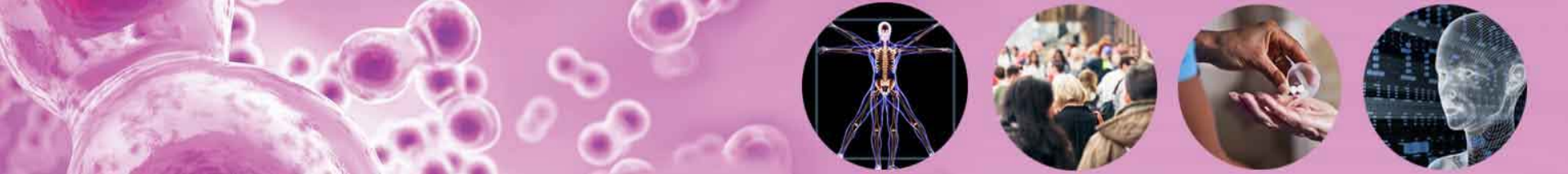
- Side-effects not passed on to future generations
 - But will still affect genomes of future children
- Need to repeat in each generation
 - depending on reproductive options
 - Note: currently no screening for carrier status
- Costs and harms of somatic treatment
 - Cost to patient / health system
 - Harm and suffering during treatment procedure
- Repetition multiplies risk

Heritable genome editing

- Side-effects potentially passed on
 - depending on reproductive options and choices made
- If successful, no need to repeat
- Single instance of risk to a given individual
 - Trade-off against multi-generational instances of repeated risk, plus harms to multiple subsequent generations
 - At some point the trade-off becomes unfavourable to SGE
- Distribution of risk across current and future generations?
- What is at stake for the first generation?



- Heritable genome editing is not *automatically* more risky
- Avoid conflating ‘moral risks’ with ‘physical risks’
- Consideration of risks of HGE should incorporate comparison with somatic genome editing as possible alternative
- This comparison needs to take into account intergenerational distribution of risk and consider what is at stake for each generation



Rights of future generations?

Who are these future generations?

- Future people
 - who not only do not exist yet, but who *will not* exist unless GE procedure is carried out
 - (or, they will be *different* people if no GE)
 - (A right to non-existence?)
- This is also a feature of SGE:
 - Different people will exist depending on our choices

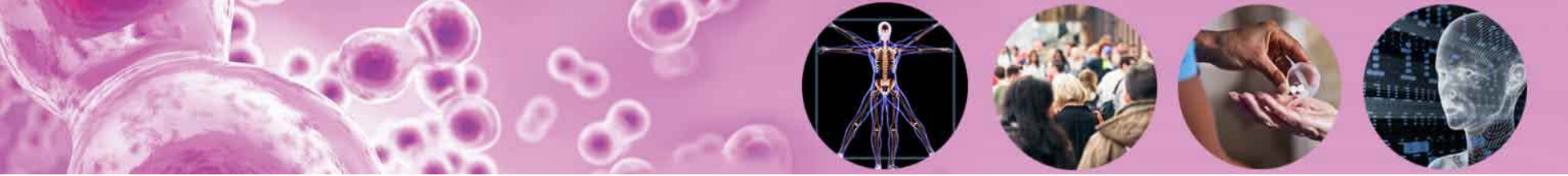
What rights are at stake?

- A right to an unmodified genome?
 - Unmodified by what?
- A right not to have been born as the consequence of a HGE procedure?
- A right to a healthy genome?
- A right to be born free from disease?
- A right to pass on an unmodified genome to descendants? Or a healthy genome?



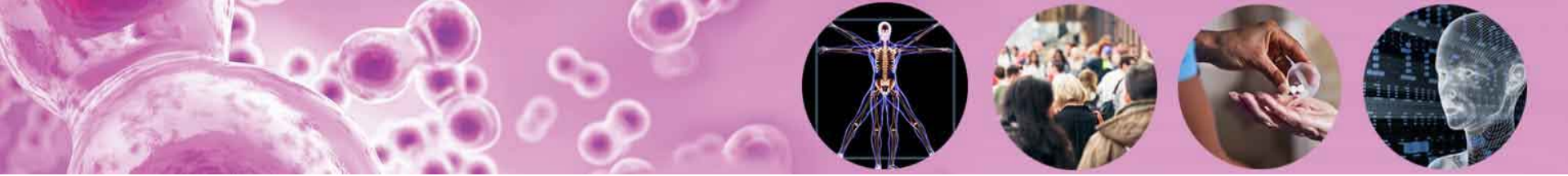
Genome editing and reproductive rights

- Who bears the burden of mitigating reproductive risks in relation to genetic disease and genome editing?
- In HGE, if a heritable adverse event occurs, the editee would face a difficult reproductive choice over whether or not potentially to burden their children with the effects of this
- But this is a similar choice already faced by current would-be parents who carry a burden of genetic disease
- Why prioritise reproductive rights of future people over current people?
- And if SGE used instead, the editee would still carry the known existing genetic disease and hence face choices over what to pass on to their own children



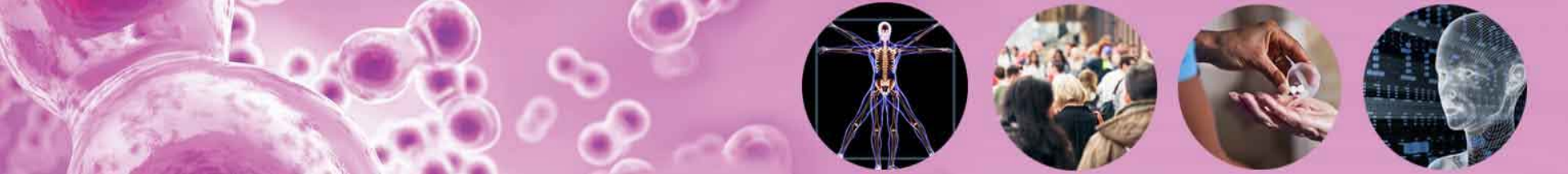
Global dimensions in assessing HGE

- Socio-culturally relative differences in risk assessment?
- Assumptions about alternative options and their availability
 - E.g. PGT
- Resource considerations in evaluating alternative treatment options
- Burden of genetic disease in LMICs
 - E.g. sickle cell anaemia
 - Alternatives: address using PGT – cost, availability; or somatic therapy – cost, including repeating over multiple generations
- Possibility for genetic therapies to address non-genetic diseases?
 - E.g. resistance to infectious disease
 - Alternatives? Not available via PGT
- Caution in deploying this argument
 - Realism about likelihood of these treatments being widely available in LMICs?
- But if HGE could achieve significant public health gains in these contexts, we should not allow 'squeamishness' to prevent this being realised
 - (Moral vs physical risks again)



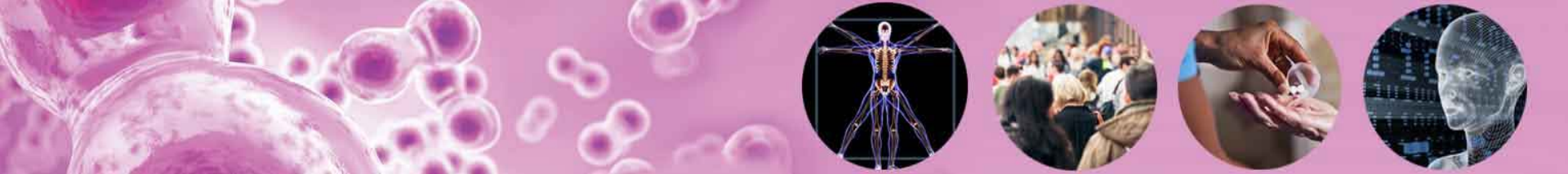
Precaution and risks of the unknown

- Rights of future generations discussed particularly with respect to environmental policy
- ‘Precautionary principle’
 - “lack of scientific certainty shall not be used as a reason for postponing cost-effective measures...” (Rio 1992)
 - “... the proponent of an activity... should bear the burden of proof” [of safety] (Wingspread Statement, 1998)
- Pro-action vs precaution?
- PP against HGE: 2 claims
- 1) Empirical: balance of risk in HGE & what it would therefore be responsible to do
 - consequences of HGE likely to be detrimental
 - ‘wisdom of nature’ / Master Engineer Analogy (Powell & Buchanan)
 - Not necessarily!
 - Comparative: better-than or worse-than... serious disease?
- 2) Moral: for which consequences we should be held responsible
 - more responsible for causing vs allowing; acts vs omissions?
 - ‘responsibility of nature’??
 - conflating causal vs moral responsibility



What's the worst that could happen?

- Worst-case scenario:
 - Whole-species 'genetic time-bomb': unknown / unpredictable effect that spreads through entire population, with indefinitely delayed effect so we don't realise until it's too late?
- How likely is it...
 - That this would occur in actuality?
 - What mechanisms could we envision that could cause this?
- ... that we wouldn't become aware of and be able to address it before then?
- ... that we wouldn't already have been wiped out by some (anthropogenic) climate disaster well before then??
- In terms of genes + environment → phenotype...
 - We are already full of 'natural' genetic time-bombs!
- Do we need 'Cassandra science'?



Thank you!



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