GENOME EDITING TECHNOLOGIES

The patient perspective

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ABOUT US

Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic conditions. We are an alliance of over 180 patient organisations. Our aim is to ensure that high quality services, information and support are provided to all who need them. We actively support research and innovation across the field of genetic medicine.

Genetic Alliance UK undertakes various projects and programmes that add evidence and knowledge to improve health service provision, research and support for families. These initiatives include:

Rare Disease UK, a stakeholder coalition brought together to work with Government to develop the UK Strategy for Rare Diseases.
www.raredisease.org.uk

SWAN UK (syndromes without a name), a UK-wide network providing information and support to families of children without a diagnosis.
www.undiagnosed.org.uk

Download a copy of this report here:
https://www.geneticalliance.org.uk/our-work/medical-research/public-perspectives-on-neuro-enhancement/

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The Genetic Alliance UK team

EXECUTIVE SUMMARY

Patients are interested in genome editing technologies, and would like to learn more about them.

Two thirds of patient respondents had thought about the implications of genome editing technologies, and over 80% were interested in finding out more about these technologies. We received over 200 responses to the survey in the five weeks that it was live, suggesting that genome editing technologies are a topic of great interest to those living with genetic conditions. Patients and families are open to engaging in conversations that will enable them to learn more about the potential of these technologies.

Patients welcome the use of genome editing technologies in research and clinical settings, but are clear that such uses should be limited to treating medical conditions and not for the enhancement or alteration of physical or cognitive attributes of healthy people.

Respondents overwhelmingly support the use of genome editing technologies in research, where that research is focused on treating medical conditions. Respondents were equally welcoming of the use of genome editing technologies in a clinical setting, but again, a clear distinction was drawn between acceptable uses in a medical context, and the use of technologies to enhance physical attributes in healthy people, which was deemed unacceptable by most.

Patients call for a multiple stakeholder approach to regulatory decisions to ensure ethical use of genome editing technologies, and want to be involved in this process.

Patients want a say in the regulation of genome editing technologies, but as part of a multi-stakeholder approach involving government, researchers and clinicians. Patients see the role of patient groups as important in representing their views.

Patients are clear that consent must be obtained in a way that ensures the recipient of any genome editing process understands the risks.

Most respondents see a need for clear consent guidelines in the administering of genome editing technologies in clinical settings. Most respondents feel that if such technologies were available to patients, they should only be offered via referral by a specialist clinician, and that it should be confirmed that patients understand the risks and benefits of the process being used.

Overall, patients feel the future of genome editing technologies offer more potential benefits than risks, if tightly regulated and used in the treatment of medical conditions.

Over 200 people responded to our survey, with 163 respondents completing the survey from beginning to end. 152 of these completed responses came from patients, or their families or carers. The remaining responses came from people who did not identify as either of these groups, but did not state the capacity in which they answered the survey. The responses from these patients highlighted five key points to consider when making decisions about genome editing technology use and regulation.

CASE STUDIES

Charlotte, mother to Elsa, who was born with SMA

On the 24 of June 2014 our second beautiful daughter Elsa was born. We had no indication of any problems at birth and there was no reason why my husband or I would be tested for genetic conditions as we have a healthy daughter already.

Just before Christmas 2014 Elsa became very ill with bronchiolitis and then never seemed to get over her cough or gain any strength. We spent many hours talking to GPs and health visitors trying to get a diagnosis, and struggled many times to get an answer as to why she was still not developing her strength to sit or roll like other babies her age.

On the 1 of March 2015 Elsa was admitted to hospital suffering pneumonia and a collapsed lung. It was only at that point that we were given any help, when consultants became concerned. On the 8th of March we finally had the diagnosis of Spinal Muscular Atrophy (SMA) type one.

We soon found out the devastating effect of the condition, including that Elsa would lose her capability to swallow (which she did) and would need to be fed through a tube. She lost most of her movements and we were told it was highly unlikely she would ever sit up unaided. We were to learn that most children with type one SMA do not live beyond 12 months old. We hoped and prayed that this was not the case with Elsa. Sadly, on the 20of April 2015, Elsa lost her battle and gained her angel wings.

SMA as a genetic condition has had a huge impact on our family. Not only because of Elsa passing away, but because we have found out that we're carriers of the condition which will impact on any further pregnancies for us. Our other daughter may also be a carrier, and in years to come she will find this out. Other family members have had awareness raised and are being tested prior to trying for children themselves.

So for us a family we firmly believe that gene editing is incredibly important in the future.

> **If, by genome editing, genetic conditions such as SMA could be eradicated that would be a great legacy for us. To think that in the future other families may not have to suffer like ours; to watch your daughter in pain and to see her take her final breath is something I would never want another family to go through.**

But I do think as important as gene editing is, there is scope for misuse and I firmly believe it should only be used in cases like ours, where there is the likelihood of carrying a child with the life limiting genetic condition. It should not be used as a means to determine eye colour or just cosmetic reasons. I think it is very important that

patients and families have a say in how genome editing is regulated in the future to ensure that it is being used to help families and not for purely cosmetic reasons.

Carole, a patient with multiple rare and genetic conditions

Developing multiple, complex conditions has had a massive impact on my life. I can't look after my grandchildren over long periods of time, I had to retire early from my job as a medical secretary, and I now rely on many medications. In fact, I sometimes realise that I have forgotten what it was like to be the person I was before the onset of my conditions. As much as I would welcome any breakthrough that could ease my symptoms, I realise that much of the work in the area of genome editing will not benefit me, and I think it is important for patients to be involved in research and discussions now in order to make things better for future patients.

However, I also think it's important that genome editing should only be used for illnesses that have significant impact on a person's life, not for cosmetic reasons.

When it comes to genome editing, there needs to be a meeting in the middle of patients and experts. We need the clinical knowledge of experts, but we should remember patients have the experience of living with conditions.

We also need to make the expert knowledge accessible to patients so that they can understand the research, but also not expect too much of these new technologies. Even though I have worked as a medical secretary, and I try to research as much as possible the treatments that I receive, I still find some information difficult to understand. Understanding complex treatments will help patients, and not leave them disappointed with the limits of new research. Experts are important to communicating new treatments, just as patients are important to communicating the reality of living with a rare condition.

Patricia, grandmother of a PKU patient

As a retired nurse and nurse teacher of 42 years, I have always been aware of genetic diseases, especially when I have cared for, and taught student nurses about, people living with Huntington's disease, breast cancer, and other conditions. However, when my 2nd eldest grandson was diagnosed at a few days old with phenylketonuria (PKU) it changed the life of our immediate family. Some years later we received a distressed phone call late at night from an elderly uncle of my husband's to say he too had a new grandson diagnosed with PKU. We then realised that a recessive gene was present in my husband's maternal relatives.

Cooking with protein-free ingredients, getting children to drink bad tasting supplements, and frequent blood tests have been just some of the trials we have had over the last 20+ years. Treatment, screening, genetic testing, and dietary supplements are very important to us, so that children, adolescents, and now adults can live better and more normal lives.

PKU is a metabolic genetic disease. Until the Guthrie blood test and low protein diet were formulated in the late 1960's, children were born who developed learning difficulties, skin problems, smelt musty, could have seizures and skeletal problems and often died young. Even today, women who do not have strict dietary compliance can give birth to babies with microcephaly or miscarry, although many, if not most, treated people lead very happy, healthy lives.

My hopes for genome editing are that the faulty gene can be removed from carriers so that they cannot have children who are affected, or who are carriers of the disease. My concerns, however, are those often raised in the media of unscrupulous people using genome editing to affect the gender of babies, or their physical attributes. I would want genome editing to be very strongly monitored, and be used only for the prevention of disease.

> **There must be proper control of practices and use of the large amounts of money poured into research.**

Patients and their families need proper controls of research data from their blood and DNA samples, and test results should not be used for research unless patients fully consent. Patients want to see that tax-payers' money is spent for developing services and alleviating symptoms of medical conditions, and, if possible, finding a 'cure'.

Regulation is all about prevention of wrong doing, whether it is financial, morally or ethically wrong or for illegal purposes. Patient voices must be heard in this discussion.

BACKGROUND

Most genetic conditions have no cure, where treatment is available this is normally with the intention of managing symptoms or slowing deterioration rather than stopping the disease all together. Genome editing technology presents a promising way of addressing the cause not just the symptoms of genetic conditions.

This technique holds a few major potential strands of benefit to patients and families affected by genetic conditions: as a research tool, as a technique for the development of treatments and as a potential reproductive choice technique.

Genetic Alliance UK, as an organisation striving to improve the lives of patients and families affected by all types of genetic conditions, aimed to gather patient perspectives on the ethical use and regulation of genome editing technologies. The survey that informed this report was developed as part of the European Commission funded Neuroenhancement: Responsible Research and Innovation (NERRI) project.

In line with the work of the NERRI project, we questioned respondents on the ethical use of genome editing technologies in a treatment *versus* an enhancement scenario. Participants were asked to reflect upon different case scenarios and to discuss whether those would be acceptable and should be allowed. Those scenarios aimed to contrast two situations; the one in which these technologies would be used to improve cognitive abilities in individuals living with a genetic conditions and those of healthy individuals.

The survey was developed in-house, within the Public Engagement and Research teams of Genetic Alliance UK. We used a mixture of structured and unstructured questions. Structured questions tended to use a multiple choice format, while unstructured questions provided an open box for responses to questions. A draft version of the survey was sent to two patient organisations, and member groups, the AKU Society and Action Duchenne, who in turn shared the survey with a small number of patients for testing. Feedback from the patients and patient groups was incorporated into the survey before a final version was launched online, using the third party online service, SurveyMonkey. On the first page of the survey we included an information video about genome editing, using CRISPR as an example of this technology given its recent attention within the media. The aim of the video was to ensure that all respondents had a basic understanding of genome editing, and the types of technologies discussed in the survey. Between the open and close date of the survey, there were 90 views of the video.

Our survey was made freely available online. The link to the survey was disseminated though social media and direct mails to the 184 member organisations of Genetic Alliance UK, to members of the SWAN UK support network (parents of undiagnosed children) and to supporters of the Rare Disease UK campaign which includes individual patients, patient groups, patient

families, academics, and industry members. We also asked our members to share the survey through their own media outlets, and received an enthusiastic response to this request. The survey was live for five weeks.

It should be noted that by recruiting participants through our member groups, we mainly reached those patients who were already engaged to some level with that patient group. It is likely, then that many of the participants are likely to already be engaged in or interested in biomedical research in some way, hence seeking out opportunities to engage in projects like these.

Respondents to the survey

We received 223 respondents to our survey, with 163 participants completing the survey from beginning to end.

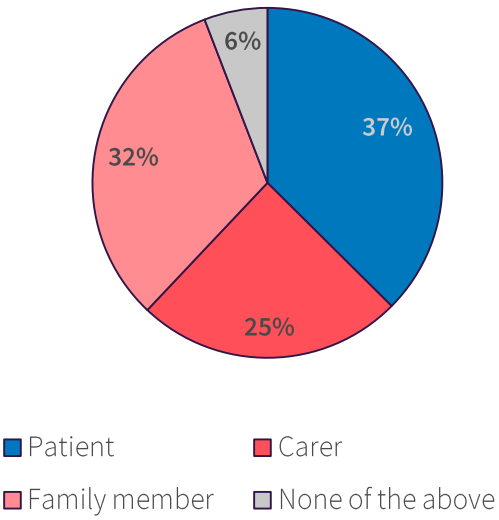
In our analysis of responses we have excluded those that did not complete the full survey.

Patients and non-patients showed interest in the survey

The largest group of respondents (70 out of 163, 42%) reported that they were patients with medical conditions, and mostly rare and/or genetic conditions. The second largest group of respondents described themselves as family members of patients, followed by those identifying as carers of patients. Respondents were able to identify as having more than one role, and many family members also identified as carers, while some patients were also family members of, and carers to, others with genetic conditions.

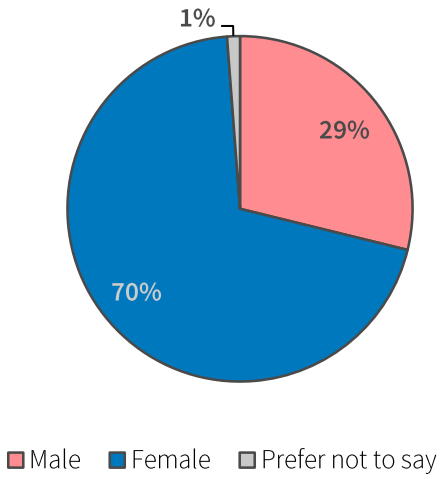
A small proportion of respondents were not patients, carers, or family members. We did not provide these respondents with space to note their role. Understanding who is interested in these issues beyond those directly affected by genetic conditions is of interest to patient groups seeking to raise awareness and knowledge among the general public, and those in healthcare related professions.

However, for the rest of this report, we have only included patients, families, and carers in our analysis, (making up 152 respondents) as these are the main constituents of Genetic Alliance UK membership.



Women were more likely to complete the survey

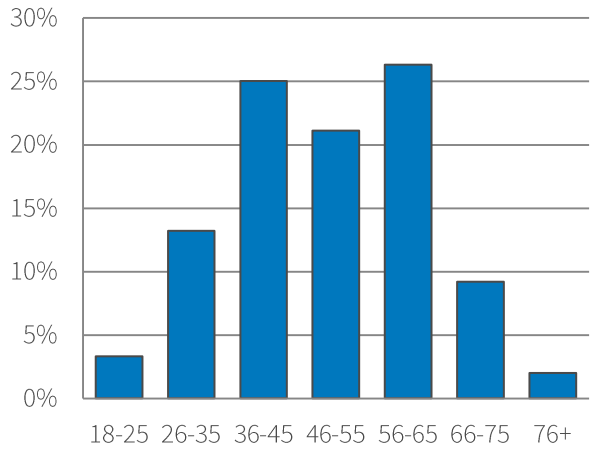
Making up 106 out of the 152 respondents (69.7%), women were more than two times as likely to respond to the survey as men (44 male respondents). Of the female respondents, 39 (36.8%) described themselves as carers, while 7 out of the 44 (15.9%) male respondents described themselves as carers.



Respondents spanned a broad range of age groups

The age of respondents was fairly evenly spread, with most respondents aged between 36 and 65, but with 20 out of 152 respondents (13.2%) falling in the 26-35 age bracket, and 14 out of 152 (9.2%) falling in the 66-75 bracket. A small proportion, just 5 out 152, (3%) were between 18 and 25. This may suggest a lack of interest among the youngest and oldest age groups, or a lack of reach by Genetic Alliance UK and its membership. Alternatively, or in addition, it may reflect a smaller number of patients existing within these age groups, owing to a lack of early diagnosis in younger people and a reduced life expectancy for some conditions.

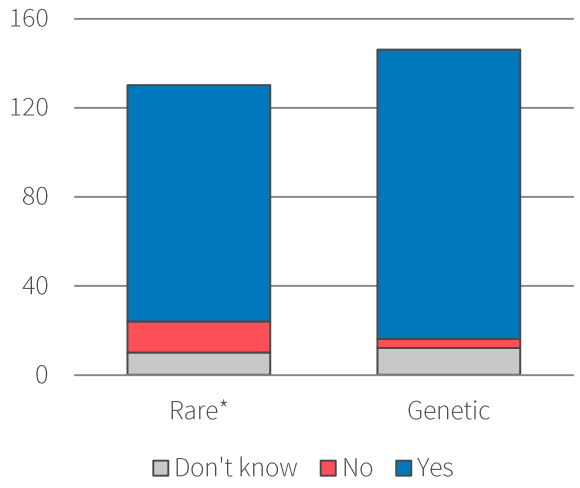
Respondents age:



Patient and carer respondents have been diagnosed with a range of conditions

Most patient or family/carer respondents reported having a rare genetic condition. 106 out of 152 (69.7%) of respondents reported that they, or their family member, had a genetic condition, while 103 out of 152 (85.5%) reported that they, or a family member, had a rare condition. Respondents represented a broad range of genetic conditions, including cerebellar ataxia, Duchenne muscular dystrophy, Huntington's disease, and sickle cell anaemia. This is a reflection of the broad scope of Genetic Alliance UK and its membership, and suggests there is interest in genome editing technologies from a wide range of groups, not just those where potential for use of this technology has been shown in early studies.

Is your condition/your family member's condition:



* We included in our survey a note informing respondents that the European Union (EU) defines a rare condition as affecting fewer than fewer than 5 in 10,000 people across the EU

AWARENESS AND INTEREST

Genome editing is not new – scientists have been working with different techniques to modify genes for 30 years – but the pace at which the technology is advancing, and the accessibility of the technology, has put genome editing high up the agenda for scientists and bioethicists. Additionally, with the granting of the first UK license in February 2016, this subject has been brought to the centre of media attention and to the public eye.

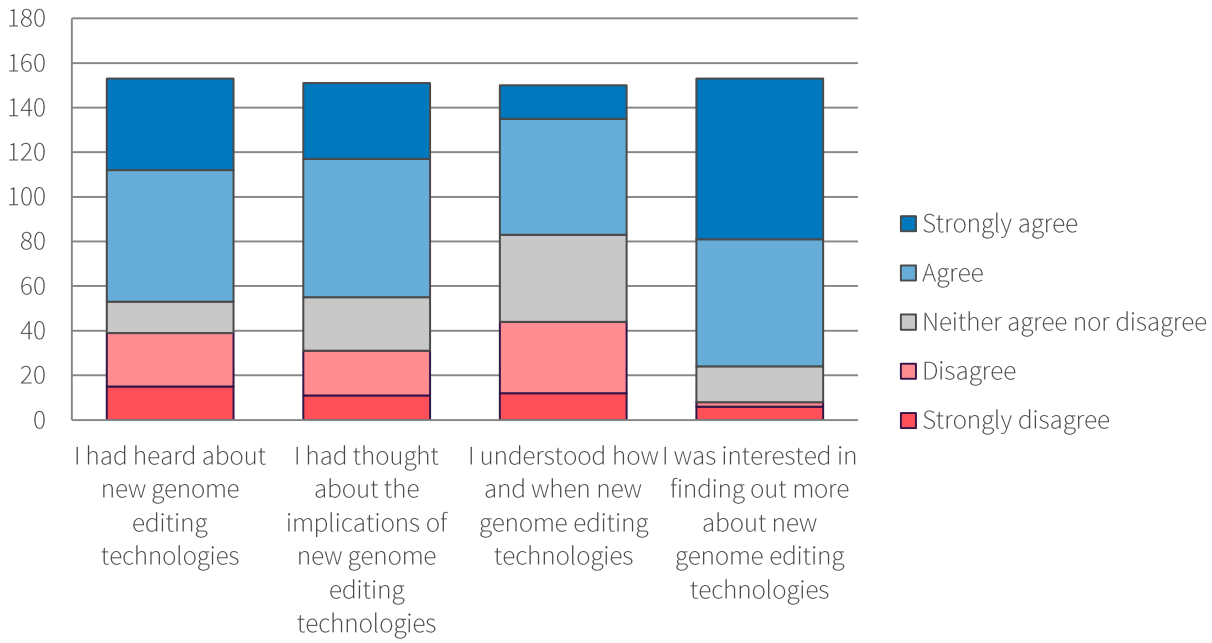
We asked respondents how much they knew about genome editing technologies prior to watching our video primer, and how interested they were in learning more about such technologies.

Patients are interested in genome editing technologies, and would like to learn more about them.

Two thirds of patient respondents had thought about the implications of genome editing technologies, and 129 out of 152 (80%) were interested in finding out more about these technologies. We received over 200 responses to the survey in the five weeks that it was live, suggesting that genome editing technologies are a topic of great interest to those living with genetic conditions. Patients and families are open to engaging in conversations that will enable them to learn more about the potential of these technologies.

While selectively biased (those choosing to take a survey on genome editing are likely to already be interested in genome editing), the

Before today, to what extent would you agree with the following statements:



responses showed that the majority of respondents (100 out of 152: 66.2%) had heard of genome editing technologies, while 129 (84.9%) respondents were interested in finding out more about new genome editing technologies. This result, combined with the 39 out of 152 (54.6%) respondents who felt unsure of their knowledge of genome editing technologies, suggests there is interest from patients and families/carers in genome editing technologies but a lack of knowledge, or a perceived lack of knowledge.

More work into this area would be helpful in revealing why respondents feel they have a lack of knowledge about genome editing technologies. Is it, for example, a lack of access to information sources, or a lack of understanding of the information provided?

The high number of people taking the survey and reporting an interest in genome editing technologies, however, suggests that opportunities to learn more about genome editing technologies, and to share thoughts about these technologies, are needed and welcomed. Further work on this subject would also help address the level of understanding and possible misconceptions around genome editing.

Genome editing is surrounded by complex language. As the methodology and research develops, this language might become increasingly complex. Previous work, regarding mitochondrial donation and human admixed embryos, strongly highlights the importance of a clear language and useful analogies.

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Total
I had heard about new genome editing technologies	41	59	14	24	15	151
I had thought about the implications of new genome editing technologies	34	62	24	20	11	149
I understood how and when new genome editing technologies might be used	15	52	39	32	12	148
I was interested in finding out more about new genome editing technologies	72	57	16	2	6	152

USES OF GENOME EDITING TECHNOLOGIES

Genome editing could have many different applications for patients in the future. In the short term, the most likely application is to better understand human biology. In the longer term, researchers may be able to develop clinical applications both as a technique in the manufacturing process of treatments and as a potential addition to the range of reproductive choice techniques available to avoid the birth of children affected by genetic conditions. Uses of genome editing technologies in research and clinical contexts certainly overlap in that we may need the former before we can have the latter. As we work to better understand the technique we should work to keep the uses separate, not least because they are at different stages of feasibility and implementation.

As part of our survey, we seek to gather patients' views on the use of genome editing technologies in the context of both research and clinical use.

Overall, patients welcome the use of genome editing technologies in research and clinical settings, but are clear that such uses should be limited to treating medical conditions and not for the enhancement or alteration of physical or cognitive attributes of healthy people.

Respondents overwhelmingly supported the use of genome editing technologies in research, where that research is focused on treating medical conditions. Respondents were equally welcoming of the use of genome editing technologies in a clinical setting, but again, a clear distinction was drawn between acceptable uses in a medical context, and the use of technologies to enhance physical attributes in healthy people, which was deemed unacceptable by most. Sections below describe in further detail patients perspectives on the use of genome editing technologies in research and clinical settings.

Genome editing technologies in research

It is hoped that genome editing could have many different applications for patients in the future. In the short term, developments are likely to happen in the research context. Genome editing research is likely to happen for several different reasons: to promote a better understanding of human biology; to try to make the technique more accurate; to develop treatments for application on humans who already have a genetic condition; and finally, research into the use of the technique in human reproduction.

Most respondents in our survey approved of the use of genome editing technologies in research. 127 out of 152 (83.6%) respondents said that they would be happy for their tissue samples to be used in research that applied genome editing technologies, with just 5 (3.3%) respondents saying no, and the remainder of the respondents was unsure.

While most respondents responded positively to the idea of using their tissue samples for research using genome editing technologies, the option for respondents to explain their answer showed that respondents often felt that their positive response would depend on appropriate consent and regulation:

> 'I am sure that such research if properly controlled could lead to new treatments'

> 'I am the parent and it would not be my decision'

> 'I would be happy for you to use mine, but I couldn't speak for my son if you were to need his tissue'

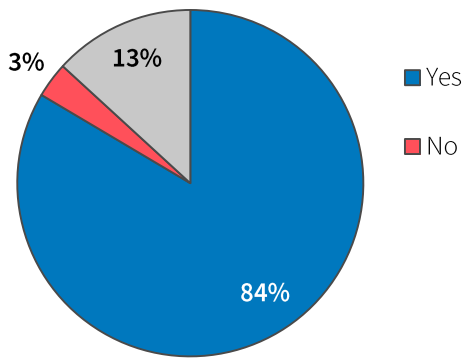
> 'If used in a very controlled and regulated way these technologies could be transforming for many people with serious rare and debilitating illnesses'

There were also a large number of respondents who commented that they would be happy for their tissue samples to be used for research, with the specific purposes of developing a treatment or cure for a genetic condition:

> 'If it was for the greater good, then yes I would be pleased to help this research'

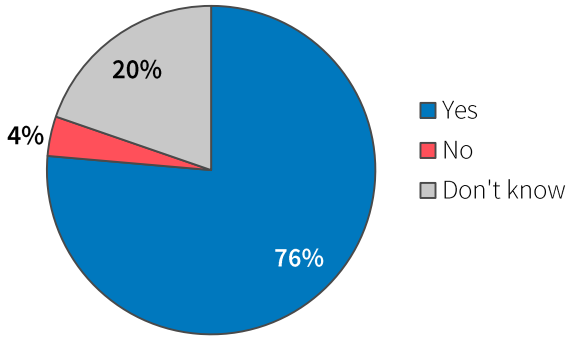
> 'If it helps alleviate the pain of patients and carers or bring a cure, I'm down!'

Would you be happy for your tissue samples to be used in research applying genome editing technologies, such as CRISPR?



There was similar response to the question of benefiting from genome editing technology use in research. 116 out of 152 (76.3%) respondents would be happy to use a treatment devised at least partly through the use of genome editing technology, while 6 (3.9%) would not, and 30 (19.7%) respondents were unsure.

Would you be happy to use a treatment that might have been partly discovered using this method?



This rate of approval is similar to that observed in existing literature (Blendon, RJ, 2016)[1]. In our previous genome sequencing project, My Condition, My DNA, we worked with patients living with rare conditions. 93% of participants in this earlier project said that they would want their genome sequences to be used for research purposes, and 92% of participants would like to make their genetic data available to research. This mirrors broader findings that show that patients, when informed as to the potential use of their data, are usually willing to share their data for research purposes.

Progress in genome editing research aimed at better understanding human biology is already taking place. In February 2016, the first licence to allow a research team to genetically alter human embryos using the CRISPR-Cas9 method was issued in the UK. The research team, based at the Francis Crick Institute, proposed to modify genes to explore why some women have repeated miscarriages (Callaway, E, 2016)[2].

[1] Robert J. Blendon, Sc.D., Mary T. Gorski, Sc.M., and John M. Benson, The Public and the Gene-Editing Revolution, *N Engl J Med* 2016; 374:1406-1411DOI: 10.1056/NEJMp1602010

[2] Ewen Callaway, UK scientists gain licence to edit genes in human embryos, Nature 2016; 530 DOI: 10.1038/nature.2016.19270

Genome editing technologies in the clinic

Currently, genome editing techniques are used only occasionally in a clinical setting and usually in infrequently used procedures for serious conditions where few options exist, and in a trial context.

In November 2015, Great Ormond Street Hospital and the UCL Institute of Child Health used, for the first time in the world, genome edited immune cells to treat a one-year-old with relapsed acute lymphoblastic leukaemia[3]. This treatment involved using CRISPR-Cas9 system – molecular scissors – to edit genes and design immune cells programmed to hunt out and kill drug resistant leukaemia. While these are still very early days and this was a highly experimental treatment for which researchers and clinicians had to get special permission, if replicated, it could represent a step forward in treating leukaemia and other cancers.

It is important to recognise the difference between these legal techniques, and potential future techniques that are not currently legal, specifically techniques to edit the genomes of sperm cells, egg cells or human embryos as part of an artificial reproductive technique. Since egg and sperm cells are called germ cells (from germline cells), and other cells that are not related to these cells are called somatic cells, the two types of use can be differentiated as germline genome editing and somatic genome editing.

As research progresses, it is likely that more developments will be brought into a clinical setting. These clinical applications will come with further ethical challenges such as judging in which situations genome editing would be acceptable.

As part of our survey, we described four hypothetical scenarios and asked participants to decide whether, in their view, the use of genome editing technologies would be acceptable. The scenarios suggested some potential future uses of genome editing technologies that raised ethical questions. Respondents strongly approved of the use of somatic genome editing technologies in treating medical conditions, but were very strongly against the use of the same technologies for purely cosmetic reasons.

Respondents were heavily in favour of the use of genome editing technologies in a clinical setting to treat those living with genetic conditions. Just two respondents disapproved of the use of genome editing technologies to treat an adult with a genetic condition which would cause cognitive decline.

There was a less strong approval rate where the scenario suggested applying germline genome editing technology to a fetus carrying a faulty gene, but still the majority of respondents approved of this use.

A similar response was seen when respondents were asked about the use of germline genome editing technologies to alter the genome of an embryo prior to implantation in a woman, where this would result in changes being passed onto future generations.

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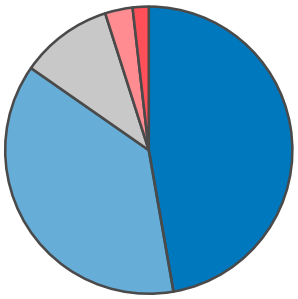
[3] World first use of gene-edited immune cells to treat 'incurable' leukaemia (2015). [online] Available at: http://www.gosh.nhs.uk/news/press-releases/2015-press-release-archive/world-first-use-gene-edited-immune-cells-treat-incurable-leukaemia [Accessed 06 June 2016]

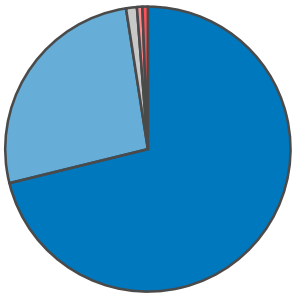
The opposite was found when respondents were asked about introducing cosmetic changes through germline genome editing technology. Just 7 out of 152 respondents (5.2%) of respondents approved of this type of use, compared to 131 of 152 respondents (86.2%) who disapproved to some degree. This was a theme that recurred throughout the survey, with patients clear about their acceptance, and encouragement, of genome editing technology use in clinical settings to treat conditions, but rejection of its use to make cosmetic changes, or changes that would enhance performance of otherwise healthy individuals.

Patients were asked in later questions about the use of such technologies to enhance cognitive abilities in healthy individuals, and the same reluctance was seen. This suggests that patients would view the use of neuroenhancement technologies in healthy individuals as problematic.

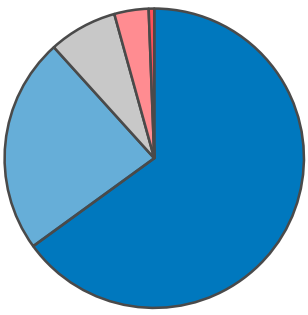
Use of genome editing technologies to correct a faulty gene in an embryo pre-implantation



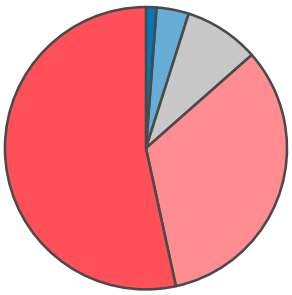
Use of genome editing technology to correct a faulty gene in an adult man

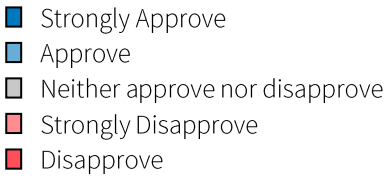


Use of genome editing technologies to correct a faulty gene in a fetus



Use of genome editing to make cosmetic changes to a fetus





Acceptable use of genome editing technologies

We asked respondents to choose any combination of genome editing application and recipient that they approved of. Hypothetical applications range from improving motor abilities, to improving attractiveness. Hypothetical recipients included, but were not limited to, patients with genetic conditions, fetuses with an inherited condition, and athletes.

It is of note here that we did not specify whether these would be somatic or germline changes, although in the case of an 'unborn child' changes could be, hypothetically, made at the early stages of embryo development, leading to germ line changes.

In line with answers to previous questions in the survey, respondents tended to approve of the use of genome editing technologies for the improvement of motor and cognitive abilities in people with medical conditions, but were much less likely to approve of the same use in healthy adults. There was also a greater level of approval for the use of genome editing technology to improve cognitive and motor abilities, and less support for its use in improving attractiveness or lifespan. These results were qualified by comments from respondents.

We gave respondents the option to explain their choices, and to also give any circumstances not included where the use of genome editing would be either acceptable or unacceptable. In line with previous answers, it was made clear that only those with genetic conditions, or other health problems, should have access to genome editing technology. It was also made clear that those who are healthy should not be able to improve aspects of their physiology using such technologies:

> 'I feel any person with a life changing or life limiting condition should be given the chance of a normal life'

> 'Any suffering patient with a disease who may benefit [should have access to genome editing technologies]'

> 'Older people with health related issues which affect physical or mental capacity such as Parkinson's disease, fibromyalgia or multiple sclerosis [should have access to genome editing technologies]'

> '[Genome editing technologies should not be used for] the purpose of enhancement or increasing any ability (mental or physical) if a person has no medical condition'

> '[Genome editing technologies should not be used] unless for a rare medical condition which cannot be treated any other way. Should not be used as a life choice or for purely cosmetic reasons'

	To improve cognitive abilities e.g. memory, concentration	To improve attractiveness	To improve motor abilities e.g. coordination, physical strength	To increase length of life
People with life limiting genetic conditions	128	16	117	109
People with genetic conditions for which other treatments are available	86	14	77	78
People with genetic conditions for which no other treatments are available	130	17	115	107
Military personnel with no known condition	8	4	6	5
Athletes with no known genetic condition	5	2	4	4
Parents seeking to use genome editing technologies for their born or unborn child, who has no known condition	14	3	11	11
Anybody	8	2	3	7
If none of the above, please explain why	26			

With respect to germline genome editing there were frequent mentions of 'designer babies' in the comments, with a number of respondents citing this as a risk of developing such technologies. In contrast to this, it is of note that one respondent wrote that it would be dangerous to allow 'misrepresentation by media that could lead to delays in medical treatments due to "designer baby" [scares]'.

With the developments in germline genome editing research, this subject is likely to receive an increased profile in media attention, both for the general public as well as to specialists. A series of landmark developments have already driven this subject into the public eye. Developments such as the pioneering of the CRISPR approach to genome editing in June 2012, the announcement that Chinese researchers had used CRISPR in human embryo research in April 2015, and the granting of the first UK licence to use CRISPR in human embryo research in February 2016 have lead to widespread media coverage and a range of reactions, including some critics warning that allowing embryos to be edited opens the door to designer babies and genetically modified humans.

With different types of reproductive technology the argument has been made that parents could be offered the opportunity to pick and choose traits in their child, and while this is, in theory, scientifically possible, there is some way to go before techniques used to allow babies to be born free from genetic disease, can be used to create 'enhanced' humans.

Some people might consider this a 'slippery slope to designer babies'. Our view is that there is an obvious line, already drawn, between the use of reproductive technology for therapeutic purposes, and the use of such techniques for human enhancement. There has been no implication that public opinion has changed with respect to the ethics of crossing this line. We expect this treatment/enhancement distinction will remain fundamental to the way that technology such as this is regulated.

Some of the respondents felt the answer to the question of when would genome editing be acceptable, wasn't an easy one. One respondent commented that where a medical condition resulted in facial disfigurement, patients should have access to treatments that could prevent or lessen this effect. There was also a small minority of respondents who approved of life lengthening treatments for anyone, regardless of health status, noting that many public health and other medical interventions that have become common place have extended life in recent decades. Two respondents felt that it is inevitable that such technologies will become widely available anyway, and adapting to this development to make access as fair as possible is advisable:

> 'If it can be done, I'm sure someone is already doing this to build their own perfect human … even if it's not approved. And of course we don't live in a perfect world, so people that can really benefit from this are suffering due to all these surveys and safety procedures'

> 'I believe the only way to keep genome editing ethical is to make it accessible to everyone. Everyone should be allowed to have the same health benefits that come of it, regardless of age, ethnicity, or economic standpoint. However, I do not believe that genome editing should be used on something as superficial as attractiveness.'

Further work on raising awareness about genome editing technologies, both regarding its research and possible future clinical applications, would be beneficial to promote an informed societal dialogue around this topic.

ACCESS TO TREATMENTS USING GENOME EDITING

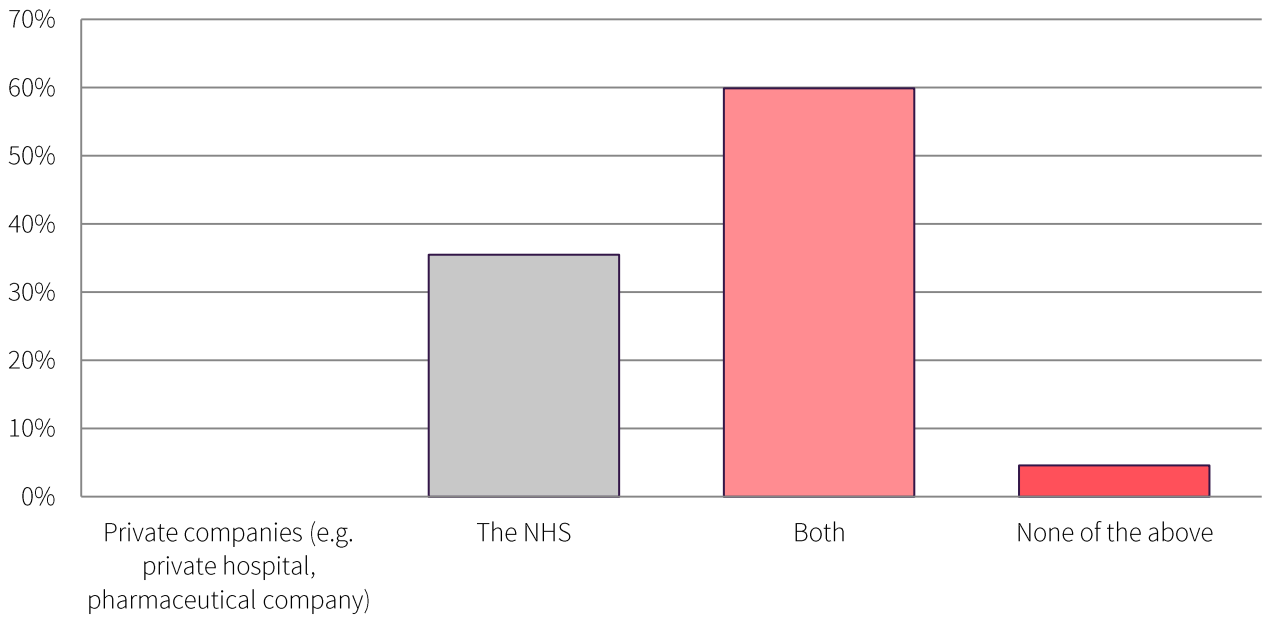
We asked participants what they considered the best route of access for individuals to obtain genome editing technologies. It was clear that most respondents felt that access to genome editing technologies should only be available as part of a health service and through referral by a specialist.

114 out of the 152 respondents (75.0%) agreed that this should be the case, while just 10 (6.6%) thought self referral was appropriate, and 20 (13.2%) approved of referral by a GP. Of the 8 (5.3%) respondents that selected 'other', it was suggested all of the above would be appropriate, or respondents wanted to emphasize the need for referral by a highly specialist clinician.

Who should be able to offer genome editing technologies?

There was obvious concern from respondents about the motive of private companies wanting to offer therapies using genome editing technologies. However most respondents (91 out of 152, 59.9%) felt that if they were to be accessible in a clinical setting, genome editing technologies should be offered by both the NHS and private healthcare or research centres. This finding is in line with our previous work on the

Who should be able to offer new genome editing technologies to individuals?

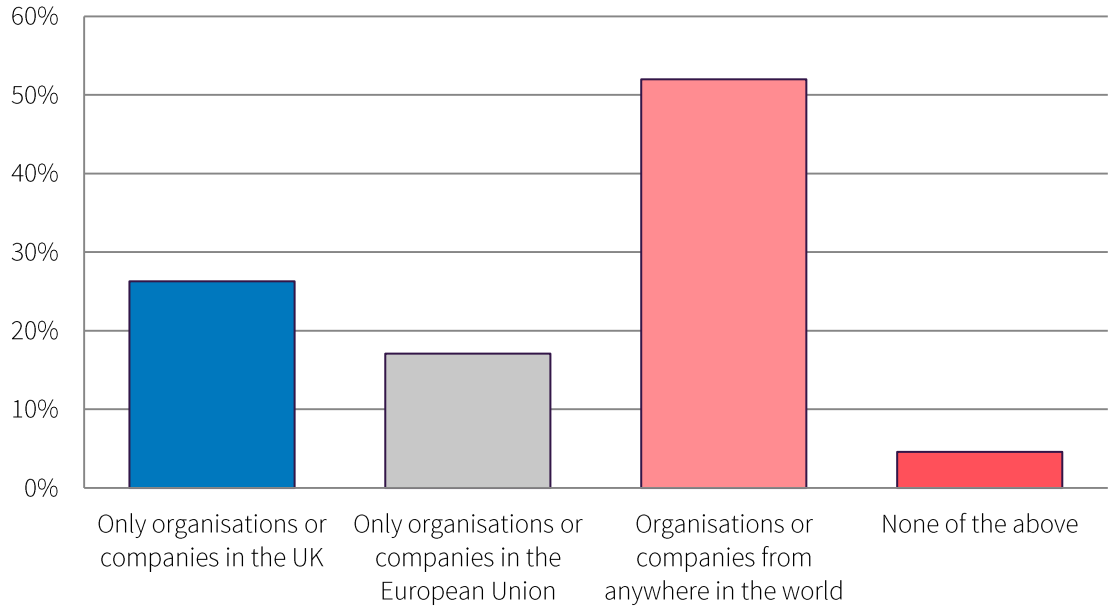


implementation of novel technologies. Patients tend to be worried about private companies having access to their health information. Our previous work also suggests that patients are willing to reconsider, provided the aim of the application and potential of such technologies are made clear. Our report on genome sequencing in rare genetic conditions, *My Condition, My DNA,* showed that just 38% of respondents felt comfortable with private companies using their data, where the term private companies was not defined, and included pharmaceutical companies and other privately funded organisations.

Comparatively, in later project investigating cancer patient views of genome sequencing, 61% of participants were supportive of providing their genetic data to, specifically, pharmaceutical companies. Where it is clear that private companies are using data for development of treatment or diagnostic tools, then, it seems there is a greater willingness from patients to share information and data. As somatic genome editing technologies develop we are likely to see the technology applied more and more to clinical scenarios. Initial developments are likely to continue to be implemented within research studies and clinical trials, before they become part of mainstream clinical care. When considering who should offer such technologies it is important to highlight that different stakeholders will bring different benefits to the development of such technologies. Research development does not happen in isolation and the future of these technologies is likely to benefit from a conversation between both the private and the public sector. Similarly, respondents were mostly happy for genome editing technologies to be provided by organisations outside the UK, as long as there would be in place some level of regulation (further information on page 29).

79 out of 152 (52.0%) respondents approved of organisations from around the world offering services using genome editing technologies, compared to 40 out of 152 (26.3%) respondents who felt provision of such services to UK patients should only be by UK organisations, and 26 out of the 152 (17.1%) who felt services should be restricted to EU based organisations.

Who should be able to offer new genome editing technologies to individuals living in the UK?



When asked to explain any concerns about providers of services using these technologies, the focus of most respondents concern was not on where in the world providers were based, but their motives in offering the services, and the extent to which they would be regulated. 23 out of 152 respondents mentioned a concern about provision through commercial organisations set to make a profit:

'I would have concerns about private companies offering the technology, because of the associated profit motive: ethical behavior may not figure largely in their consideration'

'The strictest of protocols need to be adhered to and there has to be concern that any private company will put profit before morals'

'NHS ideally [should provide genome editing technology based services]. Other providers more likely to be unethical because of the profit motive'

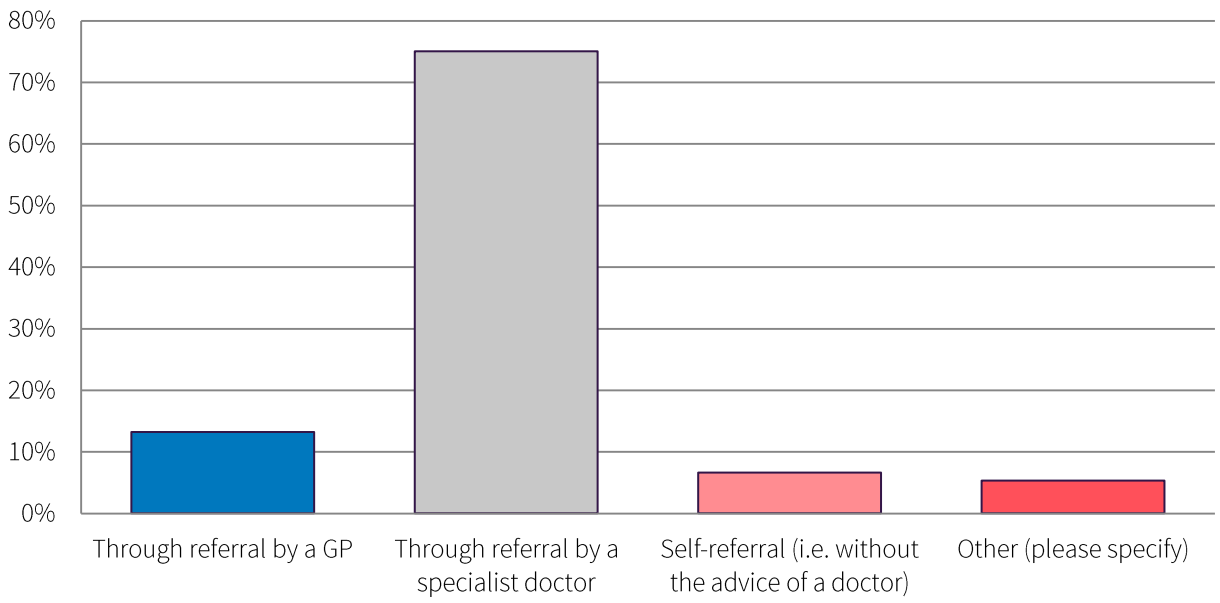
Another recurring theme from respondents was regulation. 63 out of the 152 respondents had concerns about regulation, noting that they would only be comfortable using or granting others access to providers that were regulated, or had been given an accreditation. One respondent mentioned the European Medicines Agency as a good judge of suitable providers, and others felt standards should be set by a UK body for UK patients (further information on page 31).

'It should only be commissioned under tight regulations in cases of medical need and this needs to be a global undertaking'

'It would need to be a well regulated process and be well restrained by laws and procedures to stop bad use of the technology and unethical practices'

'I feel it should be kept under the strictest of guidelines at all times. Yet let's not hinder the progress as in so many cases because of so called red tape taking too long!

How should people obtain access to genome editing technologies such as CRISPR?



How should consent be provided?

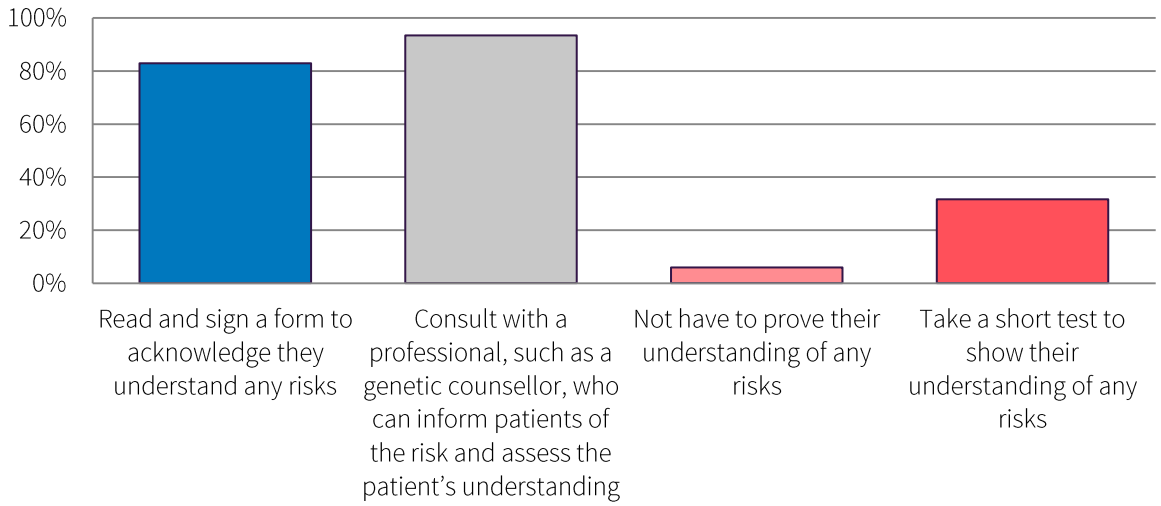
Consent to treatment is the principle that a person must give their permission before they receive any type of medical treatment or examination. Consent is required from a patient regardless of the intervention – from a physical examination to organ donation.

When questioned on the method of giving consent, our respondents were almost unanimous that any individual making use of genome editing technology should demonstrate an understanding of the process and the risks. Most respondents, 142 out of 152 (93.4%), believed that individuals should consult with a specialist, such as a genetic counselor, who would inform the patient of the risks and assess the patient's understanding. An almost equally high percentage of respondents thought that patients should in addition to, or instead of, consulting a professional, read and sign a form to acknowledge their understanding of the risks. Just 9 (5.9%) of respondents were comfortable with individuals not being compelled to prove their understanding of the risks of utilising genome editing technologies, and a third of respondents would be satisfied with patients, solely or in addition to other consent processes, taking a short test to show understanding of the risks.

As part of the current routine practice, patients are not normally compelled to prove their understanding of risks of existing complex medical treatments – consent forms state that the patient understands an intervention, but they are not tested on that understanding. Further work would help address if this call for testing of understanding is a call for the specific case of genome editing or if patients would feel the need of this procedure for existing complex medical treatments.

In a previous question, regarding the use of genome editing for research, some respondents raised concerns about consent, with four respondents noting that they could not make that decision for their child, and respondents frequently commented that such treatments would need to be regulated. Eight respondents stated that they would need more information about the procedure and its risks before consenting, suggesting that patients have a desire to be well informed about, and involved in, decision making about new treatments.

Before being given genome editing, individuals must:



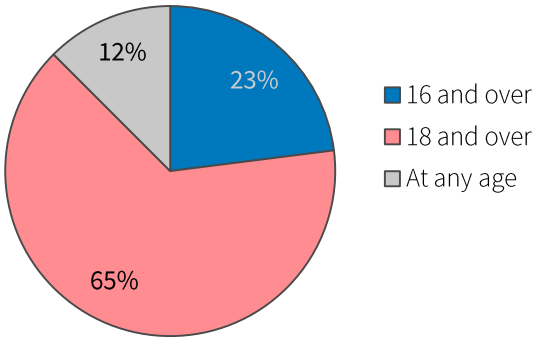
At what age should patients have access to genome editing?

When receiving treatment, patients are required to provide consent. Children under the age of 16 are presumed to lack capacity, but can consent to their own treatment if it is thought that they have enough intelligence, competence and understanding to fully appreciate what is involved in their treatment. Otherwise, someone with 'parental responsibility' can consent for them.

Most respondents, 98 out of 152 (64.5%), felt an individual seeking to use genome editing technologies (with their motivation not specified) should be at least 18 years of age to access this technology without consent from a parent or guardian.

A smaller proportion 35 out of 152 (23.0%) felt individuals could give consent at 16, and a minority of 19 (12.5%) felt a person could give consent at any age. One respondent noted that where young people disagree with parents or guardians about the ethics or morality of a certain treatment, and where that treatment could improve their lives in the long term, access could be granted without parental consent.

At what age should access be given to genome editing technologies without a parent/guardian's consent?



REGULATION OF GENOME EDITING TECHNOLOGIES

We asked our respondents about regulation of genome editing technologies, and how this regulation should be implemented . We have removed the 'don't know' responses to this question in our analysis.

Genome editing technologies should be regulated

Our respondents were almost unanimously supportive of regulation of genome editing technologies. 123 out of 152 respondents (81.5%) strongly agreed that genome editing technologies should be regulated, climbing to 147 out of 152 (97.4%) respondents when including those that agree.

The UK political and regulatory systems have in the past dealt effectively with controversial new research tools and reproductive choice techniques. Examples include human admixed embryos, mitochondrial donation, and the regulation of preimplantation diagnosis and research on human embryos.

Though there are new topics to discuss in the case of genome editing, such as the potential for germ line alteration, there is no reason to suppose that the approaches that have been successful in the past, including good quality engagement, open debate, ethical consideration of the pros and cons of the activity weighed against the pros and cons of not permitting the activity, and prudent and appropriately timed regulatory and political decisions, should not be successful again.

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
New genome editing technologies should be regulated	123	24	1	1	2

Patients prefer a multi-stakeholder approach to regulation in which they would have involvement

Where it is agreed that these technologies should be regulated, most respondents felt that the general public should have input into decision making about regulation. Most respondents were in favour of scientists and doctors being involved in such decisions. The opposite was seen with the statement that government alone should have responsibility for deciding how genome editing technologies should be regulated, with 78 out of 148 respondents (45.2%) against this proposal, 32 out of 148 respondents (22.1%) in favour, and the remainder being unsure.

There was general approval of a combination of stakeholders making these decisions, with strong agreement with the statements that doctors, scientists, and the government should make regulatory decisions together, and that the public should input into this process. It is clear that for respondents to this survey, no single group should have sole responsibility for regulatory decision making.

Genome editing in somatic cells is legal in the UK and, as discussed above, to a small extent it is already happening. This use of genome editing in this context is regulated by the Medicines and Healthcare Regulatory Authority (MHRA) and the European Medicine Agency (EMA).

In the UK the undertaking of research on human embryos is heavily regulated under the Human Fertilisation and Embryology Act (2008). The Act permits researchers to use donated embryos (usually 'spare' embryos left over after a couple has undergone IVF) for research purposes up until the embryo is 14 days old, at which point it must be destroyed. To conduct such research the scientist must be given a licence

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
The general public should have a say in how we use new genome editing technologies	25	51	38	20	13
Scientists and doctors should make decisions about how we use new genome editing technologies	49	63	17	12	6
It is the responsibility of governments to decide how we use new genome editing technologies	9	23	35	45	33
Scientists, doctors, and governments should work together to decide how we use new genome editing technologies	63	52	14	8	9
Scientists, doctors, and the general public should work together to decide how we use new genome editing technologies	54	42	25	16	8

by the Human Fertilisation and Embryology Association (HFEA). Once an embryo has been altered in any way it is not allowed to be implanted into a woman.

Any use of genome editing for reproductive purposes is not permitted in the UK, and would require Parliament's approval before it is possible. If reproductive techniques using genome editing are made legal by Parliament, then the HFEA would be the most likely of existing regulatory bodies to have the responsibility of governing this activity.

Our respondents call for a multiple stakeholder approach to regulatory decisions to ensure ethical use and applications of genome editing technologies.

This is broadly speaking compatible with the regulatory approach that is taken by the MHRA and the HFEA currently, though the extent to which representatives of the patient community have a voice in their decision making is relatively lower than other arm's length bodies of the Department of Health, such as NHS England and the National Institute for Health and Care Excellence (NICE), and lower too than the European Medicines Agency.

UK patients call for an international approach to regulation

Most respondents felt that some level of international regulation of genome editing technologies is important. Most respondents either strongly agreed, or agreed, that the UK should regulate UK organisations, and that the EU should regulate genome editing technology use in the EU, and, finally, that a worldwide governing body should regulate genome editing technologies internationally. Very few respondents disagreed with these statements, which suggest that overall, users or providers of genome editing technologies would not gain support for self regulation, and a higher body would be trusted by patients to regulate these technologies. While these responses reflect participants' views, further work would help assess if these views are the reflection of lack of awareness or misunderstanding of the regulatory landscape at the international level.

This call is not compatible with the means by which similar reproductive techniques, treatments or research techniques are regulated around the world. Though there is European level regulation of many treatments, research involving human embryos and artificial reproduction techniques are firmly a competence of individual member states of the EU.

Further research would help evaluate whether, once provided with a more detailed explanation of how similar ethically complex subjects – such as research involving human embryos and artificial reproduction techniques – are managed at the international level, patients' views would remain the same.

Patients value the work of patient groups as mediators

Respondents varied in how they would most like to be involved in decision making about genome editing technology regulation, with 120 (80%) of 152 respondents wanting to be involved in this type of decision making. When asked how they would want to be involved, around a sixth of respondents saw voting for an MP that aligned with their views as an important method of involvement, and a similar percentage of respondents felt that writing to their MP on the issues was also a good way to be involved. 75 (49.3%) of respondents would be interested in taking part in government-run focus groups, but the majority, 89 of 152, or 58.6% would like to be involved through consultations with charities or independent think tanks. These responses together suggest a clear call for patient groups and charities to represent patients to the UK government, and other governing bodies, in decision making processes around new technologies.

Would you like to be involved in decision making about how new genome editing technologies are used and applied in the future, if given the opportunity?	
I wouldn't like to be involved	32
I would like to take part in focus groups run by the government	75
I would like to take part in consultations with charities or think tanks who will then influence government	89
I would like to be involved by voting for an MP who best represents my views	25
I would like to be involved by writing to my MP	24
I would like to take part in a nationwide vote on the issue, for example, by referendum	58
Other (please specify)	8
Total respondents	152

THE BIG PICTURE

In a final question, respondents were asked whether they felt that genome editing technology offered more benefits than risks to patients and the general public. Respondents were provided with an open box to explain their response. Using thematic analysis[4], we were able to pull out six recurring themes from the open text responses.

Most respondents concluded that there is overall potential benefit offered by genome editing technologies. Many of the 75 out of 152 respondents (49.3%) who answered in this way, mentioned the benefit such technologies could have for their children who had, or might have, a genetic condition. 32 out of the 152 (21%) respondents felt there was more potential for benefit, but that this would only be the case if there existed tight regulation, while 20 out of 152 respondents (13.1%) felt there was potential for benefit and risk. 15 out of 152 (9.9%) respondents felt they needed more information to make a decision, and just 2 respondents felt there was greater risk posed by such technologies, with one of these respondents noting that this could change in the future, and the other stating that they would worry about such technologies being in the 'wrong hands'.

Overall, do you feel that genome editing technologies offer greater benefit or pose greater risk to patients and the wider public?	
Overall benefit	75
Beneficial with regulation	32
Beneficial if used for medical ('right reasons')	20
Both	9
Need more information to make a decision	15
Greater risk	2
Total respondents	153

[4] A thematic analysis approach involves selecting a group of common themes emerging from a set of answers to a question, and grouping answers according to these themes in order to suggest commonalities or differences in responses

LOOKING FORWARD

Overall, we found that patients feel the future of genome editing technologies offers more potential benefits than risks, if regulated appropriately and used in the treatment of medical conditions.

Respondents showed a clear support for the use of genome editing technologies in research, provided that research is focused on treating medical conditions. Respondents were equally welcoming of the use of genome editing technologies in a clinical setting, but again, a clear distinction was drawn between acceptable uses in a medical context, and the use of technologies to enhance physical attributes in healthy people, which was deemed unacceptable by most.

There is significant discussion and debate as to where the distinction between treatment and enhancement lies, and as to whether the distinction is valid. In the case of the membership of Genetic Alliance UK, it is perhaps an easier distinction to make given the profound unmet need that our members face and the type of treatment that they might imagine.

While the technology may not be safe to use in clinical applications right now, it holds potential to be revolutionary in research – to help inform our understanding of human biology. The wealth of knowledge that can be gained from studying genes in this way, without any intention to use it for reproductive purposes, is invaluable to our understanding of genetic conditions and might hold answers to the management of those conditions.

Moving forward, further work to examine the patient community's understanding of genome editing technologies, including defining best practice in communicating about this subject, and defining a set of analogies to explain complex topics would be beneficial. An informed patient community, particularly those with most to gain from the potential innovative treatments that might arise from ongoing research into and using genome editing, is a crucial part of an effective societal dialogue which will be vital if the potential benefits are to be realised in the UK.

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