allow researchers to compare them fully with real embryos, and test them as feasible stand-ins for research, says Lovell-Badge.

Not everyone agrees that the shift to the rule is justified. Kirstin Matthews, a legal and policy scholar at Rice University's Baker Institute for Public Policy in Houston, Texas, says there is unexplored science to be done with embryos that are two weeks or younger, and that given the public scrutiny of studies of human embryos, the ISSCR should have engaged the public while considering changes to the guidelines. "It doesn't feel like we've exhausted our knowledge in this space," she says.

Lovell-Badge acknowledges that the review and redrafting steps did not include public-engagement exercises, in part because of the cost and time involved. Also, an international public-comment period would probably receive varied responses from different jurisdictions, he says. "You'd have to make it a huge exercise, and we can't do that."

Shifts in genetic science

Some of the other key changes to the ISSCR's ethics guide reflect advances in genetics.

For example, the guidelines now describe terms under which mitochondrial-replacement therapy could be used in medical research. Some metabolic diseases are caused by genetic mutations in the mitochondria, the power generators in cells, which children receive from their mothers. In cases where a mother's mitochondria carry these mutations, doctors can now swap the nucleus from the mother's egg cell into a donor cell with healthy mitochondria, whose nucleus has been removed, before *in vitro* fertilization (IVF).

In 2016, US physician John Zhang announced that he had attempted such a procedure, and delivered in Mexico what news reports called a 'three-parent baby'. Since then, researchers in the United Kingdom have won approval to begin clinical trials of the method.

The ISSCR guide also weighs in on whether it's okay to edit the genes of human embryos or egg or sperm cells intended for implantation, and concludes that this science is still too risky. In 2018, scientists were alarmed by an announcement from Chinese biophysicist He Jiankui that he had used CRISPR–Cas9 technology to edit genes in human embryos that he then implanted in a woman's uterus, resulting in the birth of twin girls. Since then, other expert panels have debated how to regulate gene editing that introduces heritable changes. They have pointed out that the procedure, still fairly nascent, can cause unintended changes to genes and has other technical flaws.

The ISSCR allows that the concept might be valuable in the future, for scientifically defensible reasons, once the science has advanced. "As a matter of absolute principle, we do not say that heritable editing is absolutely wrong in every possible circumstance," says Charo.

HOLLIE ADAMS/BLOOMBERG/GETTY

A street in Bolton, UK, where COVID-19 cases caused by variant B.1.617.2 have been identified.

THE RUSH TO STUDY FAST-SPREADING CORONAVIRUS VARIANTS

Questions remain about how quickly B.1.617 variants can spread, and whether they can evade immunity.

By David Adam

Since the SARS-CoV-2 variant known as B.1.617 was first reported in India late last year, it has spread to dozens of other countries — including the United States, Singapore and the United Kingdom, where it has become dominant in some regions.

Researchers have identified three subtypes, known as B.1.617.1 (the 'original' B.1.617), B.1.617.2 and B.1.617.3, each with a slightly different genetic make-up.

They are now rushing to investigate these variants and work out how they might affect the trajectory of the pandemic in countries where they have gained a foothold. Key questions remain about how quickly the variants can spread, their potential to evade immunity and whether they cause more severe disease.

A lot of this research takes the form of standard epidemiology — confirming COVID-19 cases through testing, identifying the variants responsible for infections and cross-referencing these data to people's clinical symptoms and vaccination statuses. Scientists can also glean insights from genomic-sequencing data, identifying which mutations are present in the B.1.617 subtypes and comparing these with mutations in earlier variants whose behaviour is better understood.

More transmissible

"I look at individual mutations because they each have individual properties that we think might confer higher transmissibility," says Julian Tang, a consultant virologist at the Leicester Royal Infirmary, UK. Increased transmissibility — a measure of how quickly variants can spread from person to person — could accelerate outbreaks, which could put more pressure on health-care systems and counter-measures such as vaccination programmes. For example, the B.1.617.2 variant has mutations called 452R and 478K, which Tang says are linked to increased transmissibility. Both mutations alter the spike protein, which the virus uses to enter human cells.

Researchers have also been able to rapidly track the spread of B.1.617.2, because its genome contains a marker not present in B.1.1.7, a variant now established in the United Kingdom and many other countries. The presence of this marker — known as the 'S gene target' — can be seen in the results of some of the PCR tests used to confirm cases of COVID-19,

so researchers can use positive S-target hits as a proxy to quickly map the spread of B.1.617.2, without needing to sequence samples fully. Both S-gene tests and more detailed sequencing data from virus samples collected in the United Kingdom indicate that B.1.617.2 is outcompeting the two other B.1.617 subtypes, and replacing B.1.1.7 – a variant identified in southeast England in late 2020 – as the most common variant driving new infections in the country.

"Across all of England now, we would expect that 50% of infections would be the [B.1.617.2] variant," says Tom Wenseleers, a biologist at the Catholic University of Leuven in Belgium who is tracking the figures. An analysis of UK sequencing data that he shared online suggests that numbers of B.1.617.2 infections could be growing 13% faster than B.1.1.7 infections each day (see go.nature.com/3wav3bx).

In a report published on 12 May, A UK government advisory committee called the Scientific Pandemic Influenza Group on Modelling, Operational subgroup said there is a "realistic possibility" that B.1.617.2 is 50% more transmissible than B.1.1.7, according to the available data (see go.nature.com/3oyxtgz).

"The prediction of 50% more transmissible sounds entirely plausible," says Sharon Peacock, a microbiologist at the University of Cambridge, UK, who leads the COVID-19 Genomics UK consortium. "I think as data goes up more, we'll get more confidence in that, but you can't really ignore what's happening."

Immune escape

Another question researchers are keen to resolve is whether vaccines will remain effective against the B.1.617 variants. If any of these strains can evade the immune protection conferred by vaccination, or by previous exposure to the virus, they could derail plans to relax lockdowns and other restrictions.

In theory, the accelerated spread of B.1.617.2 in the United Kingdom – where more than 50% of the population has received at least one dose of a COVID-19 vaccine – could indicate an ability to escape vaccine protection. But Wenseleers says there is little evidence that vaccine escape is driving the increase in cases. Preliminary data from Bolton, an outbreak hotspot in northwest England, from mid-May showed that most people there who were hospitalized with COVID-19 caused by B.1.617.2 had not been vaccinated.

Separate data analysed by Wenseleers showed that infections with the B.1.617.2 variant in northwest England were initially clustered in teenagers, who are not routinely vaccinated. Although the variant subsequently spread to people in their thirties and forties, those in their fifties – who are more likely to have had both vaccine doses – experienced lower rates of infection. "That is reassuring," he says.

Genetic-sequencing data suggest that the rapid spread of B.1.617.2 is less likely to pose a problem to vaccination efforts than is the spread of B.1.617.1. The 452R and 478K mutations identified in B.1.617.2 are both linked to vaccine escape as well as increased transmissibility, says Tang. But B.1.617.1 also carries a different mutation called 484Q, which is more strongly associated with vaccine escape (D. A. Collier *et al. Nature* **593**, 136–141; 2021). This mutation isn't found in B.1.617.2.

"Saying the vaccine is 'effective' isn't very helpful, because there's a range of effectiveness."

Reassuringly, no mutation in any of the B.1.617 variant subtypes is associated with increased disease severity, Tang says.

Researchers can also conduct laboratory tests to check how well antibodies neutralize different viral variants. Some of these lab studies indicate that vaccines could be less effective against the B.1.617.1 subtype. Results from similar experiments with B.1.617.2 have not yet been published, but data released by Public Health England on 23 May suggest that the Pfizer–BioNTech and Oxford–AstraZeneca vaccines are effective against B.1.617.2 after two doses (go.nature.com/34rlclo).

Some key uncertainties remain, including how much more transmissible B.1.617.2 is than other variants, such as B.1.1.7. "It's plausible that it could be 50% greater, but it could also be 10% greater, or 60–70% greater," says Christina Pagel, a health-care researcher at University College London. Establishing this will allow scientists to build more accurate models of the effects the variants could have on outbreaks in countries where they are becoming dominant, including the United Kingdom. "It makes a massive difference in terms of what will happen in the summer," says Pagel. "The difference from 20% to 50% is like the difference between a moderate wave and a January-style surge. So that really needs pinning down."

Pagel also questions whether the results on vaccine effectiveness are reassuring. "Saying the vaccine is 'effective' isn't very helpful, because there's a range of effectiveness," she says. Vaccine-efficacy studies tend to focus on the ability to prevent severe disease and death. But it's also important to know whether vaccinated people could catch the B.1.617.2 variant without getting ill, and pass it on, she says. If that is the case, "you don't get the same level of population immunity than you would otherwise".

Peacock says continuing to gather epidemiological data from the UK outbreak will help to answer those questions. It will also help to forecast the potential impact of B.1.617 variants in other countries, particularly developing nations, which do not yet have widespread access to vaccines. "It's important that we provide a service to the world by making those measurements," she says.

CONTROVERSIAL FOREST STUDY WILL BE LARGEST IN UNITED STATES

In an Oregon forest, researchers will explore how best to balance timber production with conservation.

By Jeff Tollefson

Despite lingering tensions between environmentalists and loggers, a plan to launch the largest forestry experiment in the United States – and perhaps the world – has cleared a major hurdle. Controversially, the study would allow logging in a new research forest, in an attempt to answer a grand question: in a world where wood remains a necessary resource, but biodiversity is declining, what's the best way to balance timber production with conservation?

"We all love wood, and we all need wood," says Thomas DeLuca, dean of the College of Forestry at Oregon State University (OSU) in Corvallis. "We have to find ways to produce it sustainably, and this project could help us do that."

If the project – proposed by DeLuca and other researchers at OSU – launches successfully, the newly created Elliott State Research Forest in southwestern Oregon would occupy a roughly 33,000-hectare parcel of land. This would be divided into more than 40 sections, in which scientists would test several forest-management strategies, some including extensive logging. The advisory committee for the project, which comprises environmentalists, hunters, loggers and