

to whether they received the vaccine or a placebo. But once a vaccine has been shown to work, it becomes harder to ask participants to remain in the placebo arm unprotected, says Paul Offit, a vaccine researcher at the Children's Hospital of Philadelphia in Pennsylvania. "It is a question of ethics," he says.

On 10 November, Pfizer sent a letter to participants, seen by *Nature*, which states that the company is exploring ways to allow interested participants in the placebo group who meet eligibility criteria for emergency access to cross over into the trial's vaccine arm. A Pfizer spokesperson wrote in an e-mail that the company would have "an ethical responsibility to inform all study participants about the availability of an Emergency Authorized Vaccine".

Nature heard from around a dozen participants in the Pfizer–BioNTech or Moderna trials, most of whom said that if they learnt they had received a placebo, they would take the vaccine if offered. "One reason I participated was my understanding that the standard for blinded studies is to unblind the study if the vaccine is highly effective, and offer all groups the vaccine," says Moderna trial participant Emma Bernay, from Cincinnati, Ohio.

Ethical crossover

But if too many people cross over, the trials might not have sufficiently large control groups to gather statistically significant results for some long-term goals, says Stöhr. These include ruling out any long-term safety issues, and conclusively establishing whether the vaccine prevents people getting infected with SARS-CoV-2, or whether it simply protects infected people from getting the disease. There's also the risk of people in trials other than the Pfizer–BioNTech and Moderna ones dropping out to get vaccinated under emergency-use provisions, says Larry Corey, a vaccinologist at the Fred Hutchinson Research Center in Seattle, Washington.

The Pfizer spokesperson said the company will discuss with the FDA how it will gather data to comprehensively measure safety and efficacy if participants cross over. The company's clinical-trial plan says it intends to monitor participants for two years after their final vaccine dose. Moderna did not respond to questions about how an EUA might affect its trial.

Other COVID-19 vaccine developers are also grappling with these issues. Eduardo Spitzer, the scientific director of the Elea Phoenix Laboratory in Buenos Aires, which is running trials in Argentina of a Chinese vaccine from Sinopharm in Beijing, is sure that the country will start an emergency-use vaccination programme. If that happens, doctors, nurses and other essential workers, many of whom have been enrolled in the trial, might be given mandatory vaccinations and therefore no longer qualify for participation in the trial. Other participants in the placebo group might drop out

to get a shot they know is the vaccine. "I am 200% sure that an EUA will affect the trial," says Spitzer.

There are ways of managing such disruptions without jeopardizing the trial outcome, says Kathleen Neuzil, director of the Center for Vaccine Development and Global Health at the University of Maryland in Baltimore. She is also co-chair of the US National Institutes of Health's COVID-19 Prevention Trials Network,

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which arranges clinical trials for companies including Pfizer and Moderna. Participants who initially received a placebo but crossed over to get the vaccine could be monitored as a separate group, and a comparison of the vaccine's long-term efficacy and safety could be made between those groups, she says. Neuzil used a similar set-up to determine the length of protection offered by the first shingles vaccine.

Before unblinding the trials, companies could also ask volunteers to remain in the study and receive the vaccination as soon as

the trial is over, says Corey.

Christian Smerz from Houston, Texas, a participant in the Pfizer trial, told *Nature* that he understands the importance of the placebo group for further testing and would consider staying in the trial.

Companies and regulators can also gather safety and efficacy data on people in the high-risk groups who purchase the vaccines, says Eng Eong Ooi, an infectious-disease researcher at Duke–NUS Medical School in Singapore.

But such data can be biased because they cannot be compared with data from a control group, says Ooi. However, they can still provide useful insights into safety and efficacy, he says. "We cannot have the best of both worlds. The world is in need of what we have now."

Nevertheless, once a COVID-19 vaccine receives emergency authorization, trials of subsequent vaccines will become more complicated, says Ooi, who is developing a vaccine that is in early trials. Companies starting new trials might have to show that their vaccines are better than those granted emergency approval, making trials more expensive, he says. "Any vaccine approved, even if only for emergency use, will change the landscape of how vaccines get into the market."

Additional reporting by Smriti Mallapaty.

NATURE JOURNALS REVEAL TERMS OF OPEN-ACCESS OPTION

The titles will charge authors up to €9,500 to make research papers free to read.

By Holly Else

Publisher Springer Nature has announced how scientists can make their papers in its most selective titles free to read as soon as they are published – part of a long-awaited move to offer open-access publishing in the Nature family of journals.

From 2021, the publisher will charge €9,500, US\$11,390 or £8,290 to make a paper open access (OA) in *Nature* and 32 other journals that currently keep most of their articles behind paywalls and are financed by subscriptions. It is also trialling a scheme that would halve that price for some journals, under a common-review system that might guide papers to a number of titles.

OA advocates are pleased that the publisher has found ways to offer open access to all

authors, a commitment it first made in April. But they are concerned about the price. The development is a "very significant" moment in the movement to make scientific articles free for all to read, but "it looks very expensive", says Stephen Curry, a structural biologist at Imperial College London.

The change was spurred by the 'Plan S' movement, in which funders are mandating that their grant recipients must make their work OA as soon as it is published; the funders will generally cover researchers' costs for this in journals that meet their requirements. Last month, Springer Nature signed a deal that allowed some German scientists to publish openly in Nature-branded journals for free, with a €9,500-per-article price baked into their institutions' subscription fees. But today's announcement reveals the options for any author who wants to publish OA. (*Nature* is

News in focus

editorially independent of its publisher.)

Publishers of extremely selective journals, such as *Nature* and *Science*, have been trying to work out how to switch from subscriptions to OA since Plan S was announced. A large proportion of their production costs come from evaluating manuscripts that are ultimately rejected; when revenue can be collected only from the few articles that get published, the fee per article is high.

High price

No other journals charge as much as €9,500 per OA paper: the highest fees elsewhere are less than \$6,000 (about €5,000). Some OA advocates criticize Springer Nature's fee as too high. Peter Suber, director of the Harvard Office for Scholarly Communication in Cambridge, Massachusetts, says it is a "prestige tax", because it will pay for the journals' high rejection rates, but will not, in his opinion, guarantee higher quality or discoverability. "I think it would be absurd for any funder, university or author to pay it," he says. But Lisa Hinchliffe, a librarian at the University of Illinois at Urbana-Champaign, says that the fees are not necessarily too high for authors. "I think many authors will find this to be an acceptable price for value," she says.

Juan Pablo Alperin, a communications scholar at Simon Fraser University in Vancouver, Canada, says that although the announcement "signals that universal open access is inevitable", the costs are out of reach for researchers in poorer countries.

A Springer Nature spokesperson responds that costs are higher than at other titles because Nature-branded journals review many more papers than are published, and because they employ in-house editors and press officers, whose work is of "huge value"

to researchers. "Making comparisons is difficult, as no other highly selective journal portfolio is offering OA on this scale," they say. Authors who don't choose OA can continue to publish their research behind a paywall, the spokesperson notes. These papers are available to subscribers, and authors can make their accepted manuscripts available online after a delay; for *Nature*, that is six months after publication.

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The group of funders backing Plan S, called cOAlition S, says publishers should provide data to break down how publishing fees relate to the services provided. "Once this information is available, the research community will be better placed to decide whether the fees levied by publishers are fair and reasonable," says coalition coordinator Robert Kiley, who is also head of open research at the biomedical-research funder Wellcome in London.

'Guided' OA pilot

Springer Nature is also introducing a scheme that would roughly halve OA fees for some journals, which it is trialling with *Nature Physics*, *Nature Genetics* and *Nature Methods*. Under the scheme, called guided OA, authors submit manuscripts and – if they pass a suitability screen – pay a non-refundable fee of €2,190 to cover an editorial assessment and the peer-review process. In return, they get a detailed review document, and they are told which Springer Nature title

their work is recommended for.

Authors who submit to *Nature Physics*, for instance, might be accepted at that journal or told what revisions they need to make to reach it; they might be guided to the less-selective journals *Nature Communications* or *Communications Physics*; or their manuscript might be rejected. They can then walk away with their report or, if accepted, can pay a top-up fee of €2,600 to publish in *Nature Physics* or *Nature Communications*. The total fee of €4,790 is half the standard OA fee for *Nature Physics*, and a slight increase on the price of publishing in *Nature Communications*, the only Nature-branded title that is already fully OA. The top-up fee is €800 for *Communications Physics*, again making the total cost a slight increase on the current price in that OA journal; the increase is to cover the extra editorial work involved in the guided OA route compared with direct submissions, the publisher says.

This mechanism "shares the cost more evenly over multiple authors" and will save time by avoiding multiple rounds of review in different journals, says James Butcher, vice-president of journals at the Nature Portfolio and BMC, an imprint owned by Springer Nature. Hinchliffe sees it as "a creative experiment" to manage financial risk.

The scheme could be tempting to researchers hoping to publish in a Nature-branded journal, says Alperin. Compared with the full-price OA option, it "offers a lower initial barrier of entry with a higher threshold of success", he says. But peer reviewers who have appraised the manuscript under this scheme might feel that Nature titles are "essentially selling their free labour to authors" if a reviewed paper is not eventually published, says Curry.

Test run

Kiley will watch the idea with interest. "Ultimately, we believe that publishing costs need to be split so that they reflect the different services publishers provide, and this experiment by [Springer Nature] will help inform this approach," he says.

Journals in the Nature family have committed to increasing their OA content over time, so most Plan S funders have said they will pay their OA fees, despite a general reluctance to support hybrid journals (which keep some papers behind a paywall and make others open). But some, including the European Commission and the Dutch Research Council (NWO), have not yet agreed to this.

Other publishers of highly selective journals haven't yet announced policies in response to Plan S. Cell Press (owned by Elsevier in Amsterdam) says that the journal *Cell* is finalizing its approach: it currently offers OA publishing at \$5,900, but only to authors whose funding agency "has an appropriate agreement" with the journal. That policy doesn't suit Plan S, Kiley says.



Nature and 32 other subscription titles in the Nature family will offer open-access publishing.