“strong protection against hospitalization, death and disease”, says Macartney.

AstraZeneca’s interim trial data suggest that the vaccine is 80% effective at preventing COVID-19 among those aged 65 or older, who made up 20% of participants. The press release does not state how many cases of COVID-19 were found in this cohort, but Falsey said there were enough infections in the older age group to enable a statistically significant comparison.

What is the optimal timing of doses?

The optimal dosing schedule has been unclear since the first results were announced in November, revealing that a subset of participants who had accidentally received less vaccine in their first dose were less likely to develop COVID-19. A later analysis suggested that the increased protection resulted not from a dosing error, but from the longer time between doses.

Early trials were originally designed for a one-dose regimen, but researchers decided to add a booster after data showed that a single dose didn’t produce a strong enough immune response. They tried a range of intervals between doses, from 4 to 12 weeks.

The interim results from AstraZeneca do not add more clarity on how to optimize dosing, because all participants were given two doses four weeks apart. Falsey says that a longer gap would probably induce a stronger immune response, but a briefer interval is more practical in the middle of a pandemic. The WHO recommends an interval of 8 to 12 weeks.

What will be the impact of this week’s confusion on the US roll-out?

Falsey said on Monday that AstraZeneca planned to file for emergency-use authorization with the US Food and Drug Administration (FDA) in the coming weeks, and hopes to gain approval in April.

Stephen Evans, a biostatistician at the London School of Hygiene & Tropical Medicine, hopes that the FDA will put the vaccine’s reputation back on track. In contrast to other regulators, the FDA uses raw trial data to conduct its own analysis. “I think the way that the ship will be righted is by having the FDA’s scrutiny,” says Evans, who expects the agency to authorize the vaccine eventually.

It is unclear whether the vaccine will be widely rolled out in the United States, which is flush with doses of vaccine from Pfizer, Moderna and Johnson & Johnson. But researchers worry that confusion over the AstraZeneca vaccine’s efficacy will dent global uptake. “What I’m most distressed about is the effect in low- and middle-income countries — that they will lose confidence,” says Evans.

This uncertainty only adds to any fallout from the pauses in Europe last week. “Decisions made in the global north can have substantial consequences,” warns Madhi.

How does the Oxford–AstraZeneca vaccine perform against variants?

A big question facing all vaccines since new virus variants started emerging last year — some more transmissible than earlier variants — is how well vaccines work against them. Preliminary analysis in one UK trial of the AstraZeneca vaccine found that it provided a similar level of protection against the B.1.1.7 variant, first detected in the United Kingdom, as it did against pre-existing variants.

But the situation with the variant B.1.351, first detected in South Africa, is more complicated. A small study there, of some 2,000 adults aged under 65, found that it didn’t protect against mild-to-moderate COVID-19 from that variant. South Africa has suspended roll-out of the vaccine, but the WHO still recommends it in regions where variants of concern are circulating.

Soon, AstraZeneca will start trials on next-generation vaccines that will work against all current variants of the virus SARS-CoV-2, said Mene Pangalos, the company’s executive vice-president of biopharmaceuticals research and development, at a virtual press briefing on 23 March. He added that he hopes they will become available for use in late 2021.

Additional reporting by Heidi Ledford.

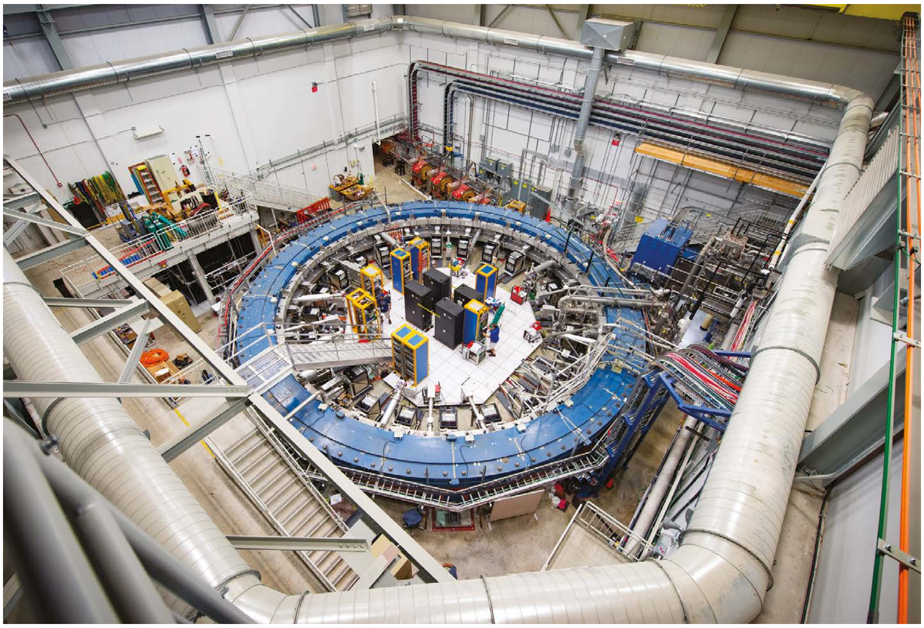
LONG-AWAITED MUON PHYSICS EXPERIMENT NEARS MOMENT OF TRUTH

Results could reveal the existence of new particles, and upend fundamental physics.

By Davide Castelvecchi

After a two-decade wait that included a long struggle for funding and a move halfway across a continent, a rebooted experiment on the muon — a particle similar to the electron but heavier and unstable — is about to unveil its results. Physicists have high hopes that its latest measurement of the muon’s magnetism, scheduled to be released on 7 April, will uphold earlier findings that could lead to the discovery of new particles.

The Muon *g*−2 experiment, now based at the Fermi National Accelerator Laboratory (Fermilab) in Batavia, Illinois, first ran between 1997 and 2001 at Brookhaven National Laboratory on Long Island, New York. The original results, announced in 2001 and then finalized in 2006 (ref. 1), found that the muon’s magnetic



The storage-ring magnet used for the *g*−2 experiment at Fermilab.

REIDAR HAHN/FERMILAB

moment — a measure of the magnetic field it generates — is slightly larger than theory predicted. This caused a sensation, and spurred controversy, among physicists. If those results are ultimately confirmed — in next week's announcement, or by future experiments — they could reveal the existence of new elementary particles and upend fundamental physics.

"Everybody's antsy," says Aida El-Khadra, a theoretical physicist at the University of Illinois in Urbana-Champaign.

Magnetic measurements

Muon $g-2$ measures the muon's magnetic moment by moving the particles around in a 15-metre-diameter circle (see 'The hunt for new physics'). A powerful magnet keeps the muons on their circular track, and at the same time makes their magnetic north–south axis rotate. The stronger the particles' magnetic moment, the faster the axis will spin.

"What we measure is the rate at which the muon rotates in the magnetic field, like a [spinning] top that precesses," says Lee Roberts, a physicist at Boston University in Massachusetts, who has worked on Muon $g-2$ and its predecessor since 1989.

The discrepancy from theoretical expectations that the original experiment found was tiny, but big enough to cause a stir among theoreticians. To first approximation, quantum physics predicts that elementary particles such as the muon and the electron have a magnetic moment exactly equal to 2 (in units of measurement that depend on the particle). But a fuller calculation reveals a deviation from this perfect value, caused by the fact that empty space is never truly empty. The space around a muon seethes with all kinds of 'virtual particles' — ephemeral versions of actual particles that continuously appear and disappear from the vacuum — which alter the muon's magnetic field.

The more types of particle that exist, the more their virtual versions affect the magnetic moment. This means that a high-precision measurement could reveal indirect evidence for the existence of previously unknown particles. "Basically what we're measuring is a number that's the sum of everything nature has got out there," says Roberts.

Tiny discrepancy

The resulting magnetic moment is only slightly different from 2, and that tiny difference is commonly denoted by $g-2$. At Brookhaven, the physicists found $g-2$ to be 0.0023318319. At the time, this was slightly larger than theoreticians' best estimates of the contributions from known virtual particles.

The precision of the measurement was not high enough to claim with confidence that the discrepancy was real, but it was large enough to cause excitement. The results also came at a time when the field seemed poised for an explosive period of discovery. The Large Hadron Collider (LHC) was under construction on the Swiss–French border, and theorists believed it would discover scores of new particles. But apart from the historic 2012 discovery of the Higgs boson, the LHC has not found any other elementary particles. Moreover, its data have ruled out many potential candidates for virtual particles that could have inflated the muon's magnetic moment, says Michael Peskin, a theoretical physicist at the SLAC National Accelerator Laboratory in Menlo Park, California.

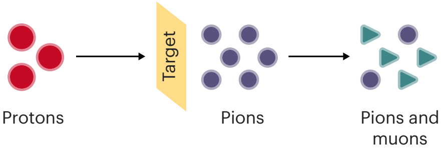
"What we're measuring is a number that's the sum of everything nature has got out there."

But the LHC did not rule out all possible explanations for the discrepancy, Peskin says. Among them, says theoretical physicist Dominik Stöckinger at the University of Dresden in Germany, is that there is not just one type of Higgs boson, but at least two.

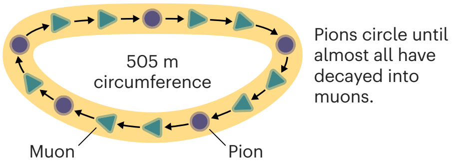
THE HUNT FOR NEW PHYSICS

The Muon g - 2 experiment has been looking for virtual particles by measuring how muons wobble in a magnetic field.

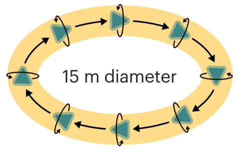
1. Protons from the Fermilab accelerator hit a target, creating pions. Some of these pions decay into muons.



2. Pions travel around a delivery ring.



3. Muons speed around a second ring, with a doughnut-shaped magnetic field.



Muons act like tiny magnets spinning on an axis like tops. As they circulate, their spin axis tilts, or 'precesses' in a way that relates to their magnetic moment.

Measuring the muons' spin direction, combined with a precise measurement of the ring's magnetic field, reveals the muon's anomalous magnetic moment — the part caused by interaction with the virtual particles.

SOURCE: ADAPTED FROM GO.NATURE.COM/39SQ9NF

At the time of the Brookhaven experiment, the experimental value for the muon's magnetic moment had to be compared with theoretical predictions that themselves came with relatively large uncertainties. But whereas the best experimental measurement of $g-2$ has not changed in 15 years, the theory has evolved. Last year, a large collaboration co-chaired by El-Khadra brought together several teams of researchers — each specializing in one type of virtual particle — and published a 'consensus' value for the fundamental constant[2]. The discrepancy between theoretical and experimental values did not budge.

Also last year, a team called the Budapest-Marseille-Wuppertal Collaboration posted a preprint in which the team suggested a theoretical value for $g-2$ that is closer to the experimental one[3]. The team focused on one particularly stubborn source of uncertainty in the theory, coming from virtual versions of gluons, the particles that transmit the strong nuclear force. If its results are correct, the gap between theory and experiment might turn out to be non-existent. The preliminary findings, which are currently undergoing review for publication, "caused a big splash" and have since been fiercely debated, says El-Khadra.

Increased accuracy

Since the results from Brookhaven came out, researchers have continued to show intense interest and to produce elaborate explanations for its findings.

The results to be unveiled on 7 April might not settle the issue quite yet. Thanks to upgrades to the apparatus, the team ultimately expects to improve the accuracy of $g-2$ fourfold compared with the Brookhaven experiment. But it has so far analysed only one year's worth of the data collected since 2017 — not enough for the margin of error to be narrower than for the Brookhaven experiment. Still, Roberts says, if the measurement closely matches the original one, confidence in that result will improve.

"My personal opinion is, when the smoke clears, the discrepancy will go away," Peskin says. Other physicists are more optimistic that the gap between theory and experiment is genuine. If Fermilab ultimately confirms the Brookhaven surprise, the scientific community will probably demand a further, independent confirmation. That could come from an experimental technique being developed at the Japan Proton Accelerator Research Complex (J-PARC) near Tokai, which would measure the magnetic moment of the muon in a radically different way.

Additional reporting by Elizabeth Gibney.

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2. Aoyama, T. *et al. Phys. Rep.* **887**, 1–166 (2020).
3. Borsanyi, S. *et al.* Preprint at https://arxiv.org/abs/2002.12347 (2020).