SARS-COV-2: The Long Road to Endemicity

After two long years of the SARS-COV-2 virus on the planet, we find ourselves surprised by how uncertain we remain on what the most likely path will be from here. Epidemiologists think we are on the path to endemicity, but also warn that the slow pace of vaccinations in large-populous, low-income developing countries can be fertile breeding grounds for more virulent variants than Delta or Omicron, which can then find their way back into our lives. But with each new wave of the virus, the economic cost has fallen. We seem to be living with COVID today with more manageable disease severity at a relatively low economic cost other than high inflation. The massive rebound of economic activity was met with a shrunken supply of labour as many people have decided to permanently leave the workforce. This has the potential to fuel a wage-price spiral that will draw central bank fire in the form of interest rate hikes that have equity markets giving back much of the 2020-21 small tech-company financial gains. But the earnings behind technology companies still look to have great tailwinds, driven by the systemic growth of the virtual world for work and play.

Question 1:
What is the likely evolutionary path of the virus from here?

Epidemiologists are near unanimous in their belief that SARS-COV-2 is on a path to becoming endemic, joining the ranks of the other four endemic coronaviruses currently in circulation.[1]

This could mean that the virus will eventually become comparable to one of these relatively mild coronaviruses. However, it may well remain more threatening than this and require active mitigants such as those required for influenza A. There will be further variants, but high levels of broad immunity should result in them becoming far less impactful.

In epidemiology terms, an endemic virus is one where the overall rate of infection is relatively static over time, neither rising nor falling[2].In effect, this means that, even with boosters, not enough people will be immune to deny the virus a host, but not enough people will be fully susceptible to allow for a widespread outbreak. Eleanor Murray, an epidemiologist at Boston University School of Public Health, noted that SARS-COV-2 won't be eradicated because "it has other hiding places in the world: not only the bat species that it likely leapt from, but more than a dozen other animal species in which it has found safe harbor. Smallpox and rinderpest, the only two viruses successfully eradicated, had just a single host"[3]. To be very clear, this doesn't mean that there will no further cases, hospitalisations, deaths or variants of concern. SARS-COV-2 is here to stay.

But the colloquial use of the term with Anthony Fauci and other scientific spokespeople, when addressing where SARS-COV-2 is going, suggests a definition of it being at a base level that is tolerable in society, usually requiring certain actions to keep it tolerable. Fauci clarified this by stating that he could see Covid-19 "being on a path to becoming similar to other endemic viruses such as measles and influenza." This implies an end to the highly deadly spikes that require the pandemic-like responses that most of us have all grown to understand and abhor, and a steady state of low-health-impact infections.

Using this definition of endemic, experts believe that SARS-COV-2 will become endemic, rather than

1 The Guardian
2 Nature
3 Wired

eradicated or neutralised, due to vaccines that are imperfect, vaccine coverage that is far from complete and a virus that is continually evolving. But it remains in a pandemic state where vaccination rates are too low.

Question 2:

Could there be another strain of SARS-COV-2 that is more deadly than the Omicron variant?

We cannot rule out a new variant emerging which resets a significant degree of the progress that has been made over the course of the pandemic. However, our base case is that the continued roll out of vaccines, boosters and new and emerging treatments will continue to lower the disease burden and the associated economic costs. A more deadly variant can still emerge, most likely from poorly vaccinated developing countries with large populations such as South Africa, Nigeria, Ethiopia or the Democratic Republic of Congo.

The SARS-COV-2 virus is going to continue to mutate. That is what viruses do. They take over cells and utilise the cell's mechanics to make copies of themselves. During this process, small errors are made. These errors are repeated and will grow naturally over time. Vincent Rancaniello, a professor of microbiology and immunology at the Columbia University Vagelos College of Physicians and Surgeons, notes that "the analogy that is often used is that if you type up notes and make a mistake in a keystroke, you have misspelled a word. That could mar what you've written, but every now and then maybe you'll stumble across a typo that's actually advantageous. That's kind of what happens to the virus. Every now and then, one of these mistakes actually turns out to be advantageous, helping the virus to spread more easily".

The Omicron variant, which is the dominant strain at present, is inherently less severe but there are reasons to be cautious. Sergei Pond, an evolutionary biologist at Temple University, believes that the world got lucky in many ways with this variant. He suggests that it was a chance occurrence that the mutations that made the variant so transmissible also happened to make it less virulent. However, he says "there is no reason to suggest this will always be the case". Sarah Otto, an evolutionary biologist at the University of British Columbia, states that most respiratory viruses are relatively stable from a genetic standpoint and that leads her to a longer-term hypothesis that this stability will also be achieved in SARS-CoV-2. Nevertheless, she notes that "the length of time to achieve this stability is unknown and the next variant could go either way (more or less virulent), or it might chart an entirely new course".

Professor Rancaniello, also noted that the more people that are vaccinated, the fewer opportunities the virus will have to evolve which means "we not only protect people from the disease, we're going to have fewer variants". Dr Anthony Fauci echoed Rancaniello's sentiment saying "the more protection you get with vaccines, the less opportunities the virus has to mutate and the less likely you're going to get a new variant". All of which brings us to the fact that the greatest risk of breeding grounds for new variants is those areas with the lowest vaccination rates which clearly create the most opportunities for significant evolutionary jumps. The Delta variant emerged in India when vaccination rates were low and disease prevalence was high. The Omicron variant is believed to have emerged in an immunocompromised person in South Africa where less than 30% of the population has been fully vaccinated. It is for this key reason, the WHO needs to overcome the many natural impediments many developing countries have to nationwide vaccination reaching 70% of the population.

Question 3:

How will COVID-19 compare to the four relatively mild coronaviruses currently in circulation?

In highly vaccinated areas, experts believe that SARS-COV-2 could become comparable to either a mild coronavirus such as 229E or perhaps something roughly 50% worse than influenza A.

There are two typical ways for a virus to evolve. Firstly, it can change to become more transmissible by replicating more quickly and secondly it can make changes that help it to overcome the host's immune response. At the initial outbreak of a pandemic when a population is fully susceptible, there is little advantage for a virus to mutate in ways that evade immunity. So, the first gains a new virus will make tend to come through enhancements to infectivity or transmissibility. But as population immunity grows, a virus evolves in ways that seek to

evade this immunity as it benefits little from gains in the rate of transmissibility in an immune population. This is precisely what we have observed with the Omicron variant. Adam Kucharski, a mathematical epidemiologist at the London School of Hygiene and Tropical Medicine states "the easiest way for the virus to cause new epidemics is to evade immunity over time. That's similar to what we see with the seasonal coronaviruses".[4]

The speed of viral evolution will largely determine the long-term impact of the virus and the necessity and composition of vaccination programs. The faster the pace of mutation, all else being equal, the more likely we are to require more significant mitigants – more vaccinations in particular.

Exhibit 1, shows four viruses that are currently in circulation, their speed of evolution, impact on the general public and the associated vaccination strategy. Given our knowledge of SARS-COV-2, the empirical path of the measles virus seems too optimistic a scenario. The measles virus today is largely contained thanks to vaccination or prior infection conferring lifelong immunity. Coronavirus 229E, which is one of the coronaviruses commonly associated with the common cold, provides an interesting case study as it has been in circulation for decades. The virus repeatedly infects people throughout their lives, causing mild cold-like symptoms as it slowly evolves to evade antibodies but struggles to evade cellular immunity (T-cells kill infected cells). Evolutionary biologist Jesse Bloom notes that "now that we've had almost two years to see how SARS-CoV-2 evolves, I think there are clear parallels with 229E". Lastly, there is influenza A and B. Influenza B evolves very slowly and primarily infects people during their childhood. Its slow evolution means that infected children can be re-infected later in adult life, but they are largely protected against the worst effects thanks to longer lasting cellular immunity. Influenza A is different as the virus evolves substantially each year leaving large parts of the global population vulnerable. This necessitates the use of annual vaccines against the virus to help shield those most vulnerable. The speed of evolution of SARS-COV-2 over the long-term will determine the mitigants required in the post-pandemic world.

Exhibit 1

Experts believe the virus could eventually be comparable to coronavirus 229E or one of the influenza strains

Virus	Measles	229E (Coronavirus)	Influenza B	Influenza A
Speed of evolution	Exceptionally low	Low	Low - medium	Medium - High
Impact	Infections nearly exclusively in newborn babies	Mild infections throughout life	Slow evolution means that children are vulnerable to infection, adults largely protected via prior infection	Significant evolution each year leaves large parts of the population vulnerable
Vaccines	Single shot	Unnecessary	Unnecessary	Annual booster

Source: *Nature*

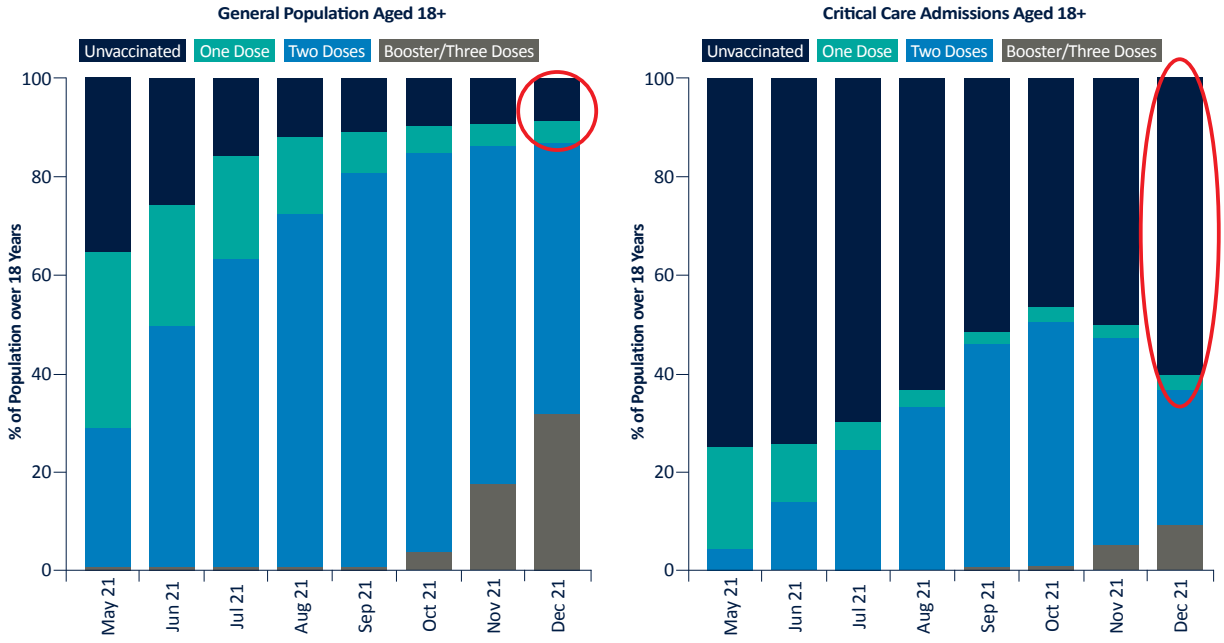
In the UK, it is estimated that the influenza virus (A&B) are responsible for approximately 25,000 deaths per year, over 30,000 hospital admissions and over 800,000 GP consultations.[5] In February 2022 alone, England recorded more than 25,000 hospital admissions for COVID-19, down from 45,000 in January. In just a few months, we should know what the "steady state" level of hospitalisations should be in the UK, but we expect many more than the 30,000 from influenza A&B. The latest data from public health England suggests that COVID-19 (Omicron variant) has an infection fatality rate of roughly 1.5x that of seasonal flu (influenza A).

Crucially, the evidence to date suggests that immunity from prior infection and/or full vaccination continues to provide a strong level of protection against the most severe symptoms of the virus, despite the degree of evolution in the virus that has been observed. Exhibit 2 illustrates this point by showing that 60% of December 2021 UK ICU admissions were unvaccinated individuals who represented less than 10% of the overall population.

4 Nature
5 NCBI

Exhibit 2

In the UK unvaccinated individuals, who represent less than 10% of the population, accounted for over 60% of hospitalisations in December 2021



Source: *Public Health England*

Question 4:

When will vaccinations take the whole planet into the endemic phase?

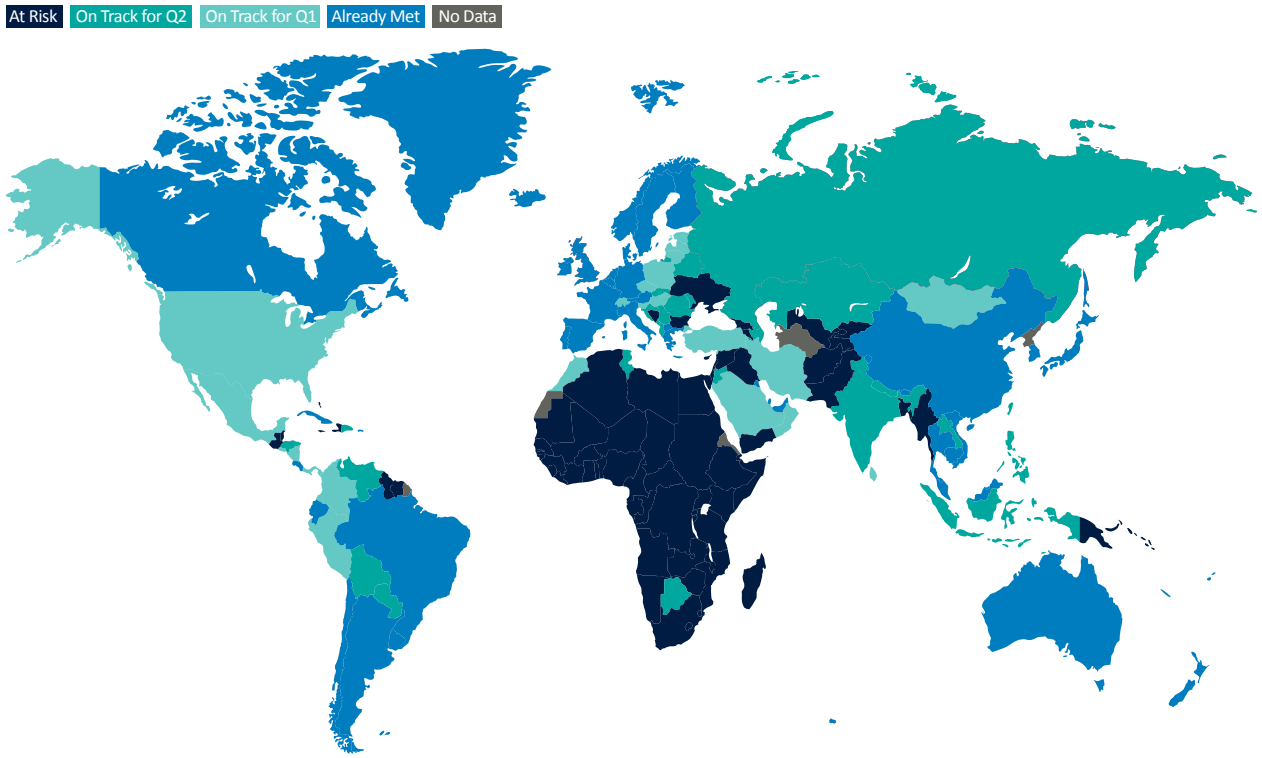
Ultimately, we need to vaccinate at least 70% of the population in each country globally to reach global endemicity. This goal will only be achieved once we see the successful full-scale rollout of vaccines in lower income countries and that is unlikely to be achieved until 2023 at the very earliest. August 2024 is seen as a worst-case scenario by the WHO, but data from Bloomberg suggests that, at the current rate of vaccinations in the developing world, this could be four years away.

There will come a point when the WHO will officially declare that the global pandemic is over, and that SARS-COV-2 has been labelled endemic. This will be a formal announcement, the timing of which will be informed by various statistical benchmarks which measure the stability of the infection rate. What the Omicron variant has shown the world is that as long as vaccine coverage remains insufficient at a global level, the risk of a significant evolutionary jump in the virus' genome remains elevated. This means that vaccinating the world is crucial to transitioning from a pandemic state to an endemic state. Data from the Economist suggests that less than 13% of people in low-income countries have received at least one dose of a COVID-19 vaccine. The WHO's vaccine strategy, published in October 2021, set a goal of 70% vaccine coverage for each and every country across the globe by June 2022. Exhibit 3 overleaf shows that the WHO believe that most regions are on track to meet this objective, with the notable exception of Africa.

6 World Health Organisation

Exhibit 3

IMF-WHO Monitor: Countries on track to reach 70% vaccine coverage by mid-2022



Source: *IMF, WHO*

The pace of vaccination in the developing world continues to be slow and disappointing. Achieving 70% of the population in large populations like Nigeria, Ethiopia and the DR of Congo illustrates the challenges there (Exhibit 4).

Exhibit 4

Many low-income countries still have barely begun vaccinating one year into the global vaccination program

		Vaccinations/100 people		
	Population (M)	31 July 2021	31 Dec 2021	Current
Nigeria	206	2	7	13
Ethiopia	115	2	11	25
Democratic Republic of Congo	90	0	0	0
India	1380	24	104	129
China	1402	114	200	221
USA	330	98	151	165
UK	67	117	198	208

Source: *Bloomberg*

It is important to keep in mind that it takes two or three vaccinations to be fully protected, so the percent of the population vaccinated is likely to be half or less than the number shown above. The Democratic Republic of Congo provides a perfect example of the challenges entailed in rolling out the vaccine across lower-income nations. The country has one of the lowest rates of vaccination out of the 200 nations that are currently tracked by Bloomberg. There have been many issues behind this. Vaccine hesitancy is exceptionally high, the country originally rejected supplies of the AstraZeneca vaccine and politicians were unwilling to endorse vaccination at a high level. The geographic landscape is also one of the most challenging in the world and when coupled with the poor level of infrastructure it has made the distribution of existing supplies to those seeking them exceptionally difficult. “The biggest challenge is distrust of these vaccinations,” said Jean-Jacques Muyembe, a renowned Ebola virus researcher who is leading Congo’s fight against COVID-19. “People here are having difficulty believing in the existence of the disease.” The government is now however attempting to turn the tide. Politicians are officially endorsing the vaccines. DRC’s national television has shown President Felix Tshisekedi receiving his

second dose and they have slowly begun to roll out mobile clinics to the country's 26 provinces. The DRC has set a target of vaccinating 45% of the population by the end of 2023.

There is one positive theory concerning low-income unvaccinated nations which we hesitate to mention in that absence of data to prove it. While accurate reporting in these countries is unlikely, there are almost no cases or deaths being reported in these three African countries relating to COVID. Cases spiked in all three countries mentioned above in January but have dropped off just as in other countries with high vaccination levels. It is possible, that these youthful populations have had high levels of infection without realising it and sit today with high levels of antibodies and may have reached endemicity. South Africa is one of the better African countries for COVID reporting. The South African health minister, Joe Phaahla, told a news conference: "We believe that it might not necessarily just be that Omicron is less virulent, but … coverage of vaccination [and] … natural immunity of people who have already had contact with the virus is also adding to the protection. That's why we are seeing mild illness."

Question 5:
How will the world make this transition to living with the virus?

We expect constant monitoring of variants and outbreaks around the world will carry on for several more years and policy makers will need to have contingency plans built around a wide range of possible outcomes. Societies will carry on being in a position of alertness, but with a reticence to being bounced in and out of restrictions. The reactions to new waves will include everything we have seen before but will be focused on keeping the population vaccinated with an ongoing set of boosters modified to deal with the mutating virus. Economically relevant behaviour modifications will be more self-imposed in terms of a populations' willingness to travel, be in public places and to attend mass events, in particular. Different countries will make different tradeoff decisions regarding acceptable levels of disease and the scale of mitigants. Countries that have invested in strong and ample healthcare infrastructure for dealing with COVID will have the greatest freedom to release movement restrictions in the case of overseas outbreaks or new variants. Tradeoff decisions in favour of more disease and fewer mitigants may impact the degree to which borders stay open to all.

Over the next couple of years, the mitigants that will remain in place will likely exceed those necessary for the seasonal flu. However, the range of scenarios remains vast, from an endemic version of not needing ongoing vaccinations to a return of a more deadly variant that requires some degree of seasonal lockdowns/mobility restrictions.

Living with the virus will involve continued uncertainty around this range of possible outcomes and will require establishing a societal framework which will entail policy makers making difficult trade-offs between an acceptable level of disease burden and the level and bearers of key costs of the mitigants and resulting illnesses. Ultimately experts believe that the burden of the virus will converge to that of something close to the influenza virus and that it can be managed with relatively minimal health and economic impact. In most major Western nations, restrictions are being nearly fully removed but processes for administering ongoing vaccine boosters are being put in place as the principle ongoing mitigant.

To the extent that the removal of restrictions leads to a higher level of illness that is viewed as acceptable, this creates an ongoing economic burden on employers, health care systems and government disability programs. Workforce Intelligence estimates that annual workdays lost to illness pre-COVID averaged 5.8 days. Post COVID, this has increased by 44% to 8.3 days[8].

However, vaccine coverage and broad levels of immunity are continuing to increase and new treatments such as Pfizer's antiviral pills have been shown to reduce the risk of hospitalisation by up to 90% suggesting that, all else being equal, the burden of the disease is likely to continue to fall which should reduce the associated costs of mitigation.

Living with COVID will continue to mean maximising vaccination rates. Segments of the population will continue to fight this. In the US, the proposed vaccine mandate on federal workers has been stymied by the Supreme Court, for now. But as long as 70% or more of a given population keeps their vaccinations up to date, they should achieve a steady state of low-health-impact infections.

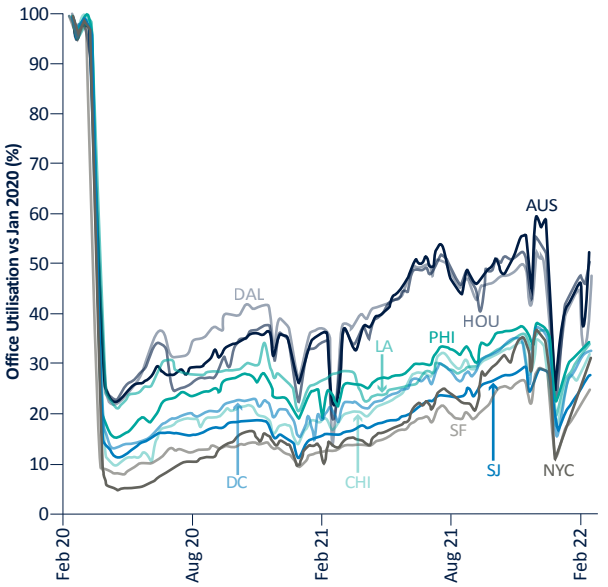
8 Skillsforcare

Global travel is likely to take further time to return to normality. Global airline revenues are still -35% below 2019 levels. Australia, New Zealand, Israel, Japan and Canada are all easing the most severe of their travel restrictions prior to the first of March 2022. Exhibit 5 illustrates that domestic regional air travel is expected to recover by the end of 2022, but inter-continental travel will not recover until the end of 2023 at the earliest. There will continue to be limitations on travel until there is global vaccine equality and as stated previously, the risk of a significant evolutionary jump will linger until we have reached that point.

The new way of working is the biggest legacy of COVID-19. For many sectors, it will be back to the normal way of working. Manual labour, retail workers, public service workers (like transportation), teachers, health care workers will all be back to normal soon, if they are not already. For many other sectors including professional services, IT, white collar management, sales and marketing, etc., expect these to never return to the office five days a week as before. Additionally, the universe of fully remote workers has grown exponentially and is expected to keep growing. Globally, 16% of companies are now fully remote. Exhibit 6 shows that US office utilisation rates are still -50% below their pre-COVID levels.

Exhibit 6

US office utilisation rates are still -50% below pre-COVID levels

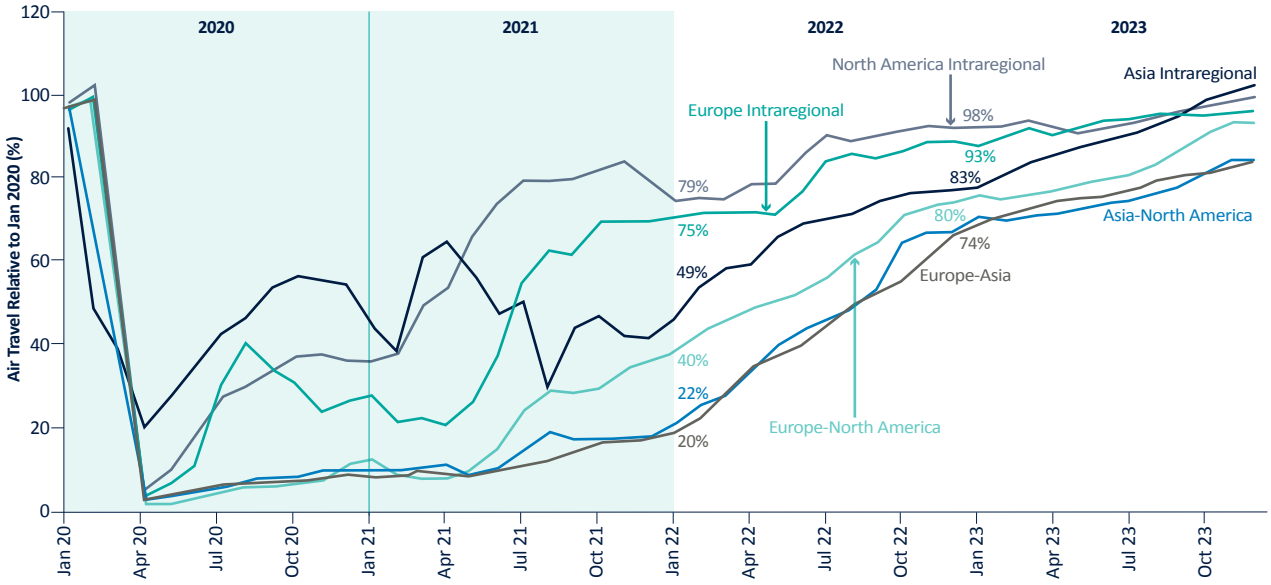


Source: *Kastle*

Overall economic mobility data covering retail, restaurants, transit and workplace movements, suggest activity levels are still -20% below what they were prior to COVID (Exhibit 7). Despite these measures, the overall economic recovery has beaten initial expectations as we discuss below.

Exhibit 5

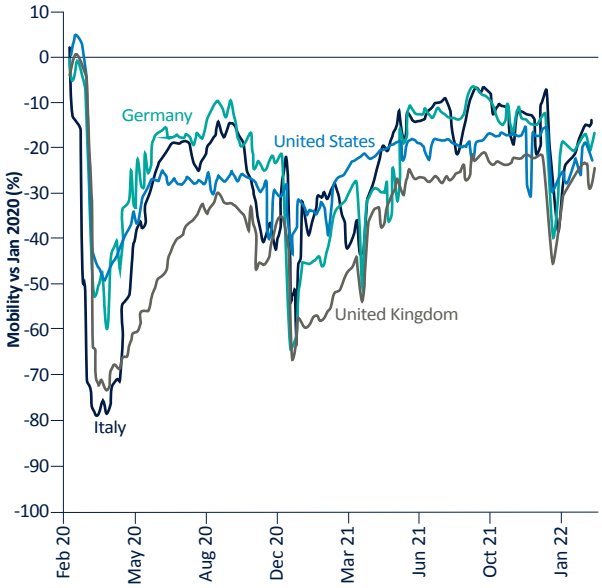
Air travel remains depressed relative to 2019 levels



Source: *Bain & Company*

Exhibit 7

Overall economic mobility data covering retail, restaurants, transit and workplace movements, suggest activity levels are still 20% below what they were prior to COVID



Source: *Google, JPMAM*

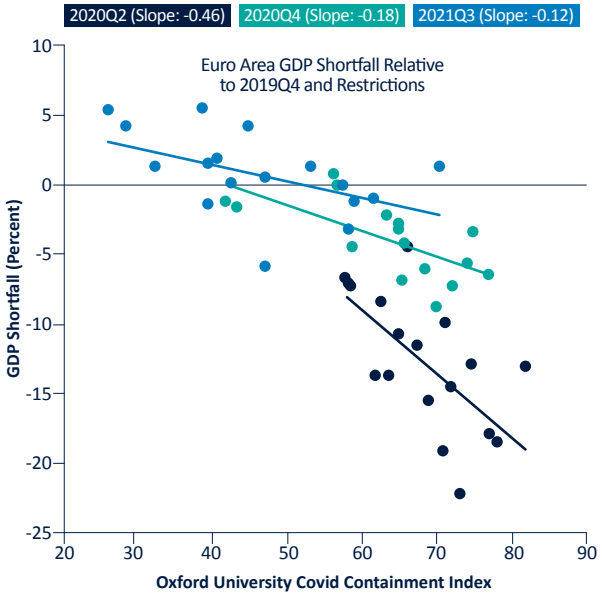
Question 6:
What are the investment implications coming out of COVID with this "long road to endemicity" scenario?

We have no new insights here, but instead look back on the large economic effects of COVID and highlight some interesting observations and implications for what lies ahead. COVID has given a boost to certain technology usage with the huge growth of the virtual working and playing world. Technology asset prices may have gone too far, especially in small cap emerging technology companies with little or no profits. COVID has created an expected spike in global demand and supply chains have not kept up, exacerbated by what appears to be a permanent reduction in the workforce population. This has created a surge in inflation and raises the possibility of a wage price spiral that lasts beyond the COVID rebound period. Inflation is the biggest economic cost of COVID and may be so bad as to require central bankers to put the brakes on economic growth, risking recession. Other sections of Insights 2022 document deal with the explicit investment implications of these COVID economic outcomes.

It is interesting to see data supporting the fact that, with each successive COVID wave, the negative economic impact is less impactful. Exhibit 8 below shows that restrictions have had a smaller impact on GDP in Europe over time. The black line is the economic effect on different European countries (each dot is a European country) of the first wave. The fourth quarter of 2020 saw the Beta variant exploding with less economic effect (green line and dots). Finally, the third wave peaking in October of 2021 saw almost no GDP shortfall (blue line).

Exhibit 8

Euro Area GDP has been less Impacted by restrictions as the pandemic has progressed

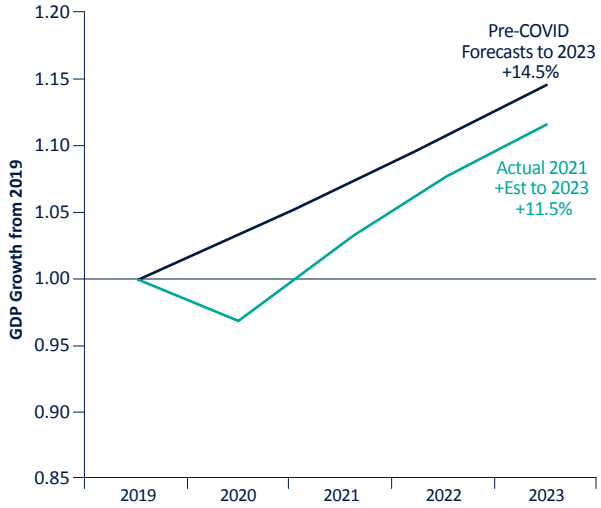


Source: *Goldman Sachs*

At Partners Capital, we always try and take the long-term 30,000 foot view on what has happened out of macro events to help us see what the future brings. Below we have our "look back" on the pre vs post COVID periods comparing economic growth, inflation and earnings impact and try and draw a few conclusions from those.

Exhibit 9

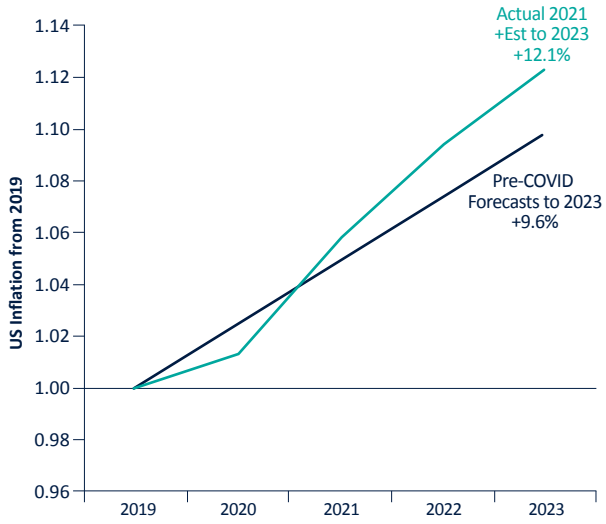
COVID cost the global economy 2.5% in cumulative growth which we expect we will not ever get back



Source: *IMFExhibit 10*

Exhibit 10

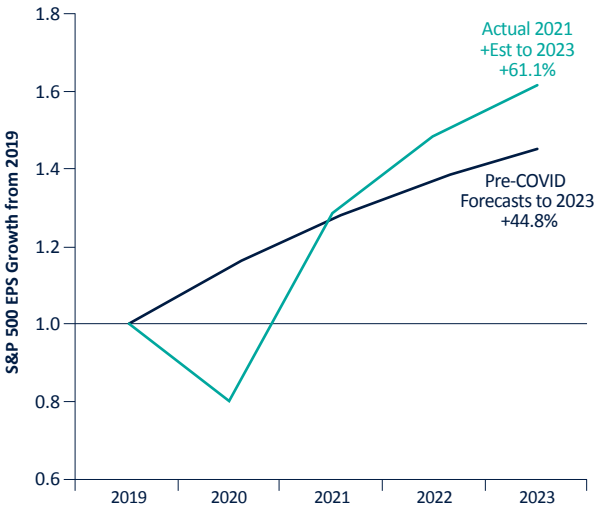
Cumulative inflation is expected to be 2.5% higher than was expected Pre-COVID



Source: *IMF*

Exhibit 11

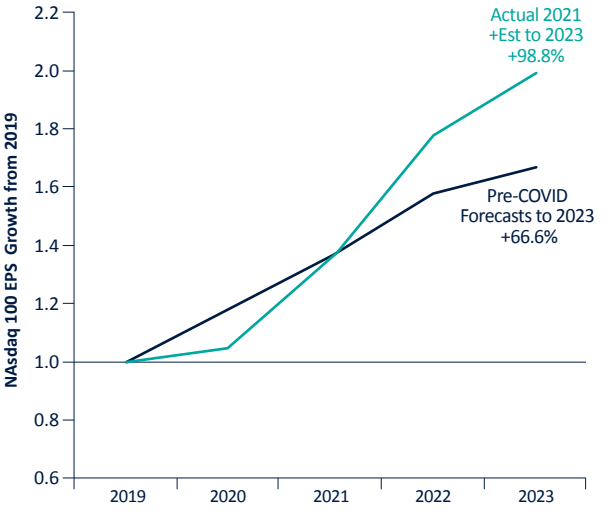
Despite the 2.5% hit to the global economy, corporate earnings are expected to grow cumulatively by 16% more than Pre-COVID EPS forecasts for the S&P 500



Source: *Bloomberg*

Exhibit 12

Despite the 2.5% hit to the global economy, tech sector corporate earnings are expected to grow cumulatively 32% more than Pre-COVID EPS forecasts (Nasdaq 100)



Source: *Bloomberg*

The above analysis ignores the boost that lower interest rates gave risk asset valuations in 2020 and 2021, because 10-year yields today are almost exactly where they were just prior to COVID striking in early 2020. With higher inflation and interest rates, we could see the impact of COVID erasing more of the value derived from tech earnings gains driven by COVID.

This financial retrospective on COVID leaves us with investment implications discussed at length elsewhere in this document around hedging against inflation, and understanding where duration or interest rate risk lies in your portfolio, especially in different public equity sectors or types of companies. All of this points to higher dispersion in equities and other asset classes and the need to have capital placed with the most talented active asset managers who can best assess which companies will weather inflation, interest rate and emerging tech risks which will drive valuations in the years ahead.

Hypothetical return expectations are based on simulations with forward looking assumptions, which have inherent limitations. Such forecasts are not a reliable indicator of future performance.

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