Stop Loss Partner Newsletter

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Long COVID is Real: New Chronic Condition Impacts Self-insured Community

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Just when everyone was starting to relax about the impact of COVID-19 on the workplace, it appears that it's a long way from over.

Long COVID is a chronic illness that results from a Covid-19 infection and there are hundreds of potential residual symptoms or medical complications which can be debilitating for many people.

The Centers for Disease Control and Prevention (CDC) reports that millions of people suffer from Long COVID and David Cutler, an economist at Harvard University who projected the $3.7 trillion economic cost of Long-COVID estimates the individual medical costs of the disease to be about $9K+ a year, on average.

This does not include key treatment regimens for hospitalization as well as the indirect costs of workforce absence and potential patient disability.

Paul Fallisi, FSA, MAA, president, Windsor Strategy Partners, a leading actuarial firm, advises, "Long-Covid is basically a new chronic condition requiring ongoing medical attention like high blood pressure, diabetes and obesity. It will affect claims morbidity for the foreseeable future! Fingers crossed that future variants of Covid-19 are mild–but extreme variants are a complete morbidity wild card."

He points out that from 2020 through 2021, COVID-19 claims were offset by fewer doctor visits. Emergency Room visits, elective surgeries and dancer screenings, noting, "But going forward, 2023 total claims

will be impacted by COVID-19 and Long COVID claims not offset by fewer physician office visits. Additionally, medical inflation will be higher due to higher general inflation and the addition of Long COVID claims and cancer claims will be higher due to delayed screenings and treatments. Unfortunately, cancer claims will be more expensive due to later than normal detection."

Long COVID poses a significant business concern with broader workforce implications. It continues to alter the employment landscape, with the American Medical Association (AMA) estimating that 10-30% of the 81 million people diagnosed with COVID will develop long COVID, for months or years to come.

It should be noted that post-COVID conditions are found more often in people who had severe COVID-19 illness, but anyone who has been infected with the virus that causes COVID-19 can experience post-COVID conditions, even people who had mild illness or no symptoms from COVID-19.

While most people with post-COVID conditions have evidence of infection or COVID-19 illness, in some cases, a person with post-COVID conditions may not have tested positive for the virus or known they were infected.

Given these statistics, astute employers need to understand their social and legal obligations to their employees. Failure to do so can be costly to employers directly from discrimination lawsuits, workplace injuries or other liability for other accidents caused by employees or product liability from substandard production.

There's also the indirect costs to re-hire or retrain workers. Long COVID can result in continued disruptions and financial implications long into the future.

Jakki Lynch RN, CCM, CMAS CCFA, director cost containment, Sequoia Reinsurance Services says, "Plan sponsors have become acutely aware of the financial impact that Long-COVID has on their plan spend. Long-COVID is challenging and costly for several reasons; an official Long-COVID diagnosis can be difficult as there is no specific test to diagnose post-COVID conditions and treatment largely consists of symptom management rather than evidence-based treatment protocols which can be labor intensive and long-lasting ranging from three months to a year or more.

She explains that some patients, especially those who had severe COVID-19, have persistent heart, kidney, liver, and nervous system issues and even permanent damage to multiple organs requiring ongoing costly health treatment interventions.

Lynch cites these important studies:

- A study published in 2020 in the journal JAMA Cardiology found 60% of people who had COVID-19 had ongoing signs of heart

inflammation.

- According to C. John Sperati, MD, a kidney specialist at Johns Hopkins Medicine in Baltimore, nearly a third of patients hospitalized for COVID-19 experienced kidney damage that may become chronic; some may need dialysis or a transplant.

- According to United Network for Organ Sharing, the private, non-profit organization that manages the U.S. organ transplantation system, total US transplant volume is trending upward among the working age group during the pandemic (despite a temporary dip in transplants early in 2020) compared to pre-pandemic volume.

- Total costs for organ transplant are also increasing for solid organ transplants year-over-year with claims for a single transplant often exceeding $1 million, in particular lung and heart transplants per Milliman's 2020 triennial report.

"Plan sponsors need affordability solutions to manage Long-COVID high risk expenses and maintain access to timely care," she continues. "The key interventions to help manage this novel financial exposure include:

1) Promotion of best practices for prevention and early intervention strategies for treatment of COVID-19 through proactive patient and provider communication.

2) Access to resources and proactive referrals to multidisciplinary specialist physician teams that focus on the treatment of Long-COVID.

3) Provider contract reimbursement analysis and targeted updates to address the unique risks and nuances of Long-COVID treatments.

4) Claim payment integrity reviews which ensure correct reimbursement and accurate payment of plan benefits."

The Cell And Gene Therapy Sector In 2023: A Wave Is Coming – Are We Ready?

From a scientific perspective, the outlook for patient with rare disease has never been brighter. This year, 13 new cell or gene therapies could be approved in the US, Europe or both by the end of 2023. However, the challenges that stop patients accessing new therapies remain. Could this year be the turning point when our health care systems start to catch up with our science?

The status quo for patients with serious diseases is often death, disability, or poor quality of life. What if I told you that status quo is changing? Ten years ago, Emily Whitehead had run out of treatment options for her leukemia. As a last resort, Emily's parents agreed to an experimental cell therapy never tested in children. Now, 10 years later, Emily is considered cured by this CAR-T therapy.

There are now six FDA-approved CAR-T cell therapies available to patients in both the US and Europe to treat various blood cancers. They are but one part of a growing set of promising cell and gene therapies to address rare and prevalent conditions.

There are over 2,000 clinical trials happening today, with 200 in Phase III – a wave of hope for patients waiting on durable, possibly curative treatments. But investment, policy, and regulatory challenges remain for the sector, and many patients will not benefit unless we modernize our approach to health care.

The Pipeline of Transformative Therapies is Accelerating Rapidly

2022 was a record year for the approval of never-before-authorized gene therapies, with three new therapies approved to treat rare diseases and another approved to treat bladder cancer. Additionally, five therapies that had already been approved in the US or Europe were authorized for the first time in a new geography or for another indication.

But this is just the initial swell of the coming wave. As of this writing, as many as 13 brand new cell or gene therapies could be approved for use in the US, Europe, or both by the end of 2023. We are in reach of the FDA's often-cited 2019 prediction that it would approve 10-20 new cell and gene therapies a year by 2025.

A little over a decade after CRISPR was discovered, the first CRISPR therapy -- from Vertex Pharmaceuticals Incorporated and CRISPR Therapeutics AG to treat sickle cell disease and beta thalassemia -- could be approved for patients in the US, UK, and European Union next year. A gene therapy for Duchenne Muscular Dystrophy – a disease whose R&D path has been beset with disappointment – could receive accelerated approval by the FDA in 2023.

In addition, there were notable clinical advances that will hopefully continue in 2023 – including in prevalent diseases. A brief clinical hold was lifted on Vertex's Phase I/II trial for Type 1 diabetes, setting the stage for potential further readouts in 2023. Intellia Therapeutics, Inc.' in vivo gene-editing approaches for two rare diseases – ATTR amyloidosis and hereditary angioedema – are advancing in the clinic. In fact, clinical data from November showed that the company's gene therapy to treat hereditary angioedema could be a functional cure.

Investment Headwinds Are A Challenge

Investment in cell and gene therapies set records in both 2020 and 2021, aided by low interest rates and global recognition of the importance of innovative health care technologies. In 2022, sector financing has reverted to pre-pandemic levels. While it has been a difficult environment for public financing, we expect total 2022 investment to land somewhere between $9.8B and $13.5B, the sector's performance from 2019 and 2018, respectively.

In public markets, S&P Global's research shows that inflation and interest rate hikes have adversely impacted the valuation of publicly traded companies, particularly those that are smaller and in earlier stages of development, a common attribute of cell and gene therapy companies. What can we expect in 2023?

Market volatility is likely to persist for several reasons, including inflation concerns and geopolitical challenges. Thankfully, venture capital remains a bedrock of funding for the sector. Venture capital was at 40% of full-year 2021 levels through the first half of the year. This indicates continued investor excitement about scientific breakthroughs and new treatment possibilities, despite investment headwinds.

We Must Address Barriers To Patient Access

Currently, while regulators in the US and Europe are taking positive steps to modernize regulatory frameworks in line with scientific advancements, barriers to patient access remain a pressing challenge in both geographies.

Let's start with the US, where modernization efforts championed by Peter Marks, Director for the FDA's Center for Biologics Evaluation and Research, may have a positive impact in 2023 and beyond. The FDA's Office of Tissues

and Advanced Therapies (OTAT) — the office that principally manages the approvals for cell and gene therapies — will become the "Office of Therapeutic Products" (OTP) and be elevated to a "super office." Also, Congress recently approved the seventh iteration of the Prescription Drug User Fee Act (PDUFA), a law first passed by Congress in 1992 authorizing the FDA to collect fees from pharmaceutical developers to fund the review process for new drugs. The authorization contains vital resources and programs to help the FDA review the coming wave of cell and gene therapies.

Standards and expectations around chemistry, manufacturing and controls issues remain a key development hurdle and have led to several program delays. We are working closely with the FDA to address challenges related to potency assays for cell and gene therapies. In October, ARM and the American Society of Gene and Cell Therapy (ASGCT) co-hosted a workshop with the agency to develop a more consistent and clear approach to potency assays, including a whitepaper to identify specific challenges and outline a roadmap for future discussions.

But getting therapies through the approval process is just part of the journey. There is growing concern that our payment systems are not equipped to ensure that patients have access to the coming wave of therapies. And with two therapies to treat sickle cell disease – one of the most prevalent rare diseases – potentially receiving approval in 2023, there will be intense focus on whether the US health care system, and particularly state Medicaid programs, can provide access to these therapies. The proposed Medicaid VBPs for Patients (MVP) Act could help positively modernize our health care system by removing barriers to the use of value-based purchasing arrangements, including outcomes-based agreements, in Medicaid. ARM and its members are working with the bi-partisan co-sponsors of this bill to see how it can be improved and reintroduced into Congress in 2023.

2023 Will Be A Pivotal Year For Europe

There are significant headwinds in Europe, particularly on the access side. In many ways, Europe has been a tremendous leader in the sector, approving the first gene therapy and boasting a world-class regulatory body in the European Medicines Agency. Even so, Europe is now falling behind on several key metrics – likely due to the interplay of complex regulatory and reimbursement challenges. Seven of the 23 advanced therapy medicinal products (ATMPs) approved in the EU have been withdrawn from that market. As of the end of June 2022, the number of developers headquartered in Europe declined by 2% compared to five years ago, while the number in North America increased by 42%, and the number in Asia-Pacific increased by 271%.

Patients are also losing the early access to experimental therapies that they gain from clinical trials. ARM's H1 2022 Report highlights the shrinking clinical trials pipeline in Europe, particularly in early phase trials. This decline in clinical trials may also result in fewer approvals in Europe going forward than would otherwise be the case.How might the region get back on track? For the

first time in a generation, the EU will revize its Pharmaceuticals Legislation – the European Commission's proposal is expected in the first quarter of 2023. The initiative aims to balance affordability and access, among other concerns, and will play a large role in whether European patients will have access to ATMPs for years to come.

Also crucial to patient access is the adoption of joint clinical assessments at the EU level, due to start in 2025 for some therapeutic classes, including ATMPs. This initiative has the potential to streamline the approval process and accelerate access across the EU's 27 member states – but only if it modernizes methodological approaches to reflect the unique characteristics and promise of ATMPs. There is important work to be done in this regard in 2023.

Hope – And Urgency

From a scientific perspective, the outlook for patients who are running out of options – like Emily Whitehead once was – has never been brighter. Five years ago, I would not have imagined the number of potential approvals that are possible in 2023 or the number of clinical trials that are ongoing. But the challenges to ensuring that patients benefit from this science are urgent. I am hopeful that when we look back at 2023, we see it as a turning point for when our health care systems began catching up with our science.

Thoughts on Geographic Considerations of Genetic Disorders

Over the past couple of years, I have seen many presentations on gene therapy and the high cost of associated claims coming down the pipe. While claim frequency and severity were common topics, identifying populations at higher risk than others at a higher level were generally not addressed. As an actuary rather than an underwriter, I tend to look at risk at a macro level rather than at a case-by-case one. This led me to consider how we might identify at risk markets.

It almost seems obvious, but most conditions where gene therapy is being utilized are for genetic disorders. It follows that to the extent that people stay within a region, any genetic disorders that they may pass on also stay within that region. I decided to investigate two blood conditions with a large, expected total spend to see if I could find any patterns. Those two are sickle cell and hemophilia (A and B).

Sickle Cell

Let us begin with clarification on what is meant by sickle cell, and its different types. From sicklecellspeaks.com:

> *"Sickle cell disease" is an umbrella term used to describe a group of genetic diseases that affect the body's hemoglobin. Hemoglobin is the protein in red blood cells that carries oxygen. It is made up of 2 alpha globin chains and 2 beta globin chains. Sickle cell disease is caused by a mutation in the beta globin gene, resulting in an abnormal hemoglobin called sickle hemoglobin, or Hb S. Different types of sickle cell disease arise based on whether the hemoglobin beta S gene is inherited with another beta S gene or with a different beta gene mutation.*

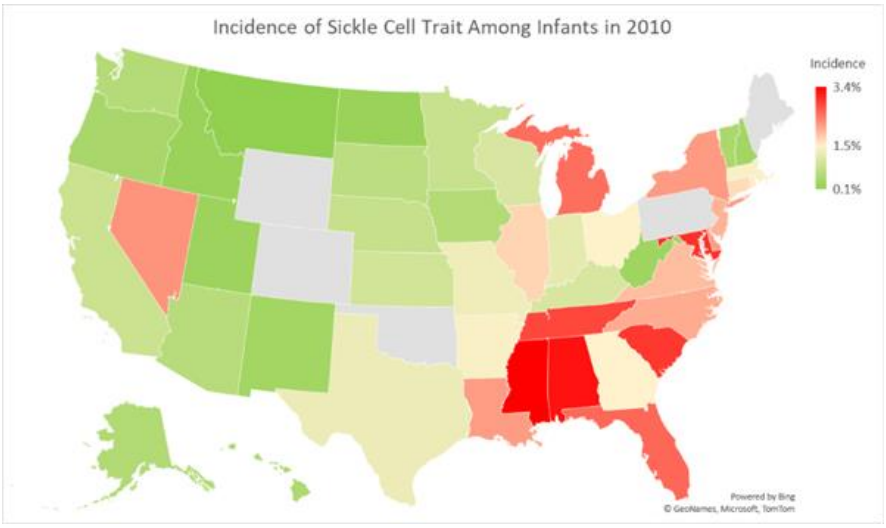
After sickle hemoglobin releases oxygen, it clumps together forming a stiff rod. This causes the red blood cell to become sickled, or banana shaped. These misshapen cells then do not flow as well through the blood vessels, sometimes blocking healthy cells and restricting oxygen to other parts of the body.

The financial impact to insurers over sickle cell disease is of particular concern because of the frequency of the disease. Unlike many of the gene therapies that have been approved so far, which often have only a few thousand estimated potential candidates, there are an estimated 58,000 candidates nationally for this condition. Hemoglobin SS disease is the most common and most severe type of sickle cell disease. Last year, the FDA approved Zynteglo, which is a gene therapy for beta thalassemia. Beta thalassemia is one of the other types of sickle cell disease which is much less frequent (estimated 1,450

potential candidates). This year, the FDA is anticipated to approve a treatment for the more common SS disease under the name LentiGlobin with an expected price tag of $2.0-2.4M.

According to the CDC, the genetic markers for sickle cell are carried by as many as 1.5% of infants born in the United States. However, it is carried much more often by blacks or African American infants at a rate of approximately 7.3%, compared to 0.2% for white infants and 0.5% for Hispanic infants. This likely comes from evolutionary pressures where having the trait could help defend the body against malaria, leading to descendants of regions where the disease is found having a higher chance of carrying the trait.

Unsurprisingly, states with the largest African American populations also have the largest incidence of sickle cell disease, with one notable exception. According to census.gov, at the time of the study (2010) the five states with the highest proportion of black or African American are Mississippi (36.9%), Louisiana (31.8%), Georgia (30.0%), Maryland (29.0%), and South Carolina (27.7%). As can be seen in the map below, all except Georgia have among the highest incidence rates. However, the discrepancy may be due to a difference in methodology since Georgia did not participate in the 2010 study, and the incidence rate shown is from a later 2016 study involving fewer states.



Hemophilia

From the CDC website:

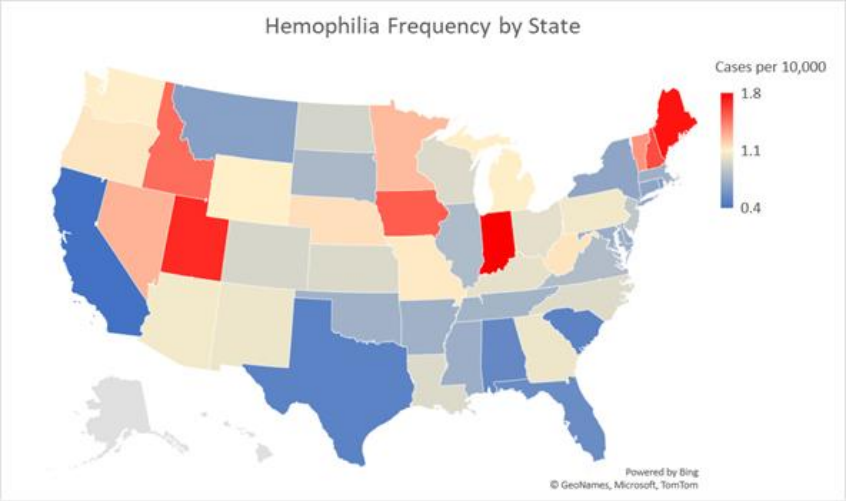
> *Hemophilia is usually an inherited bleeding disorder in which the blood does not clot properly. This can lead to spontaneous bleeding as well as bleeding following injuries or surgery. Blood contains many proteins called clotting factors that can help to stop bleeding. People with hemophilia have low levels of either factor VIII (8) or factor IX (9). The severity of hemophilia that a person has is determined by the amount*

of factor in the blood. The lower the amount of the factor, the more likely it is that bleeding will occur which can lead to serious health problems.

Hemophilia A (Classic Hemophilia) is caused by a lack of clotting factor VIII, while Hemophilia B (Christmas Disease) is caused by a lack of clotting factor IX.

In November 2022, EtranaDez was approved for treatment of Hemophilia B, with an estimated 2,600 potential candidates. In 2023, the FDA is expected to approve Roctavian for treatment of Hemophilia A, which is approximately 3 times more common, with a similar price tag of around $2.5-3M.

I was unable to find exact incidence rates by state. However, the CDC did have information giving ranges of total cases by state. The ranges were given by gender, since males are much more likely to be affected due to the trait being carried on the X chromosome where it is not balanced by the Y. I combined the median of the ranges for both genders and divided by the state populations to get an approximate estimate of the incidence rates.



Hemophilia appears to be more common in New England, as well as parts of the Midwest, particularly Utah, Indiana, Iowa and Idaho. It is worth noting that the estimates for California and Pennsylvania may be skewed to a lower estimate. Both states had case counts for males and females in the top bracket of >1,000 for men and >300 for women. Being unable to put a cap on the ranges, they could be much larger. For California this is likely due to the large population of the state.

Conclusion

Sickle cell appears to be more common in the Southeast, while Hemophilia is more common in the Northeast and Midwest. This certainly supports the idea that there may be a geographic component to the risk of having these claims. More study should be done to look into the levels of risk in different regions for these high cost treatments. Unfortunately (or rather, fortunately), many of the conditions that have a gene therapy being developed for them are so rare that geographic data is hard to come by.

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