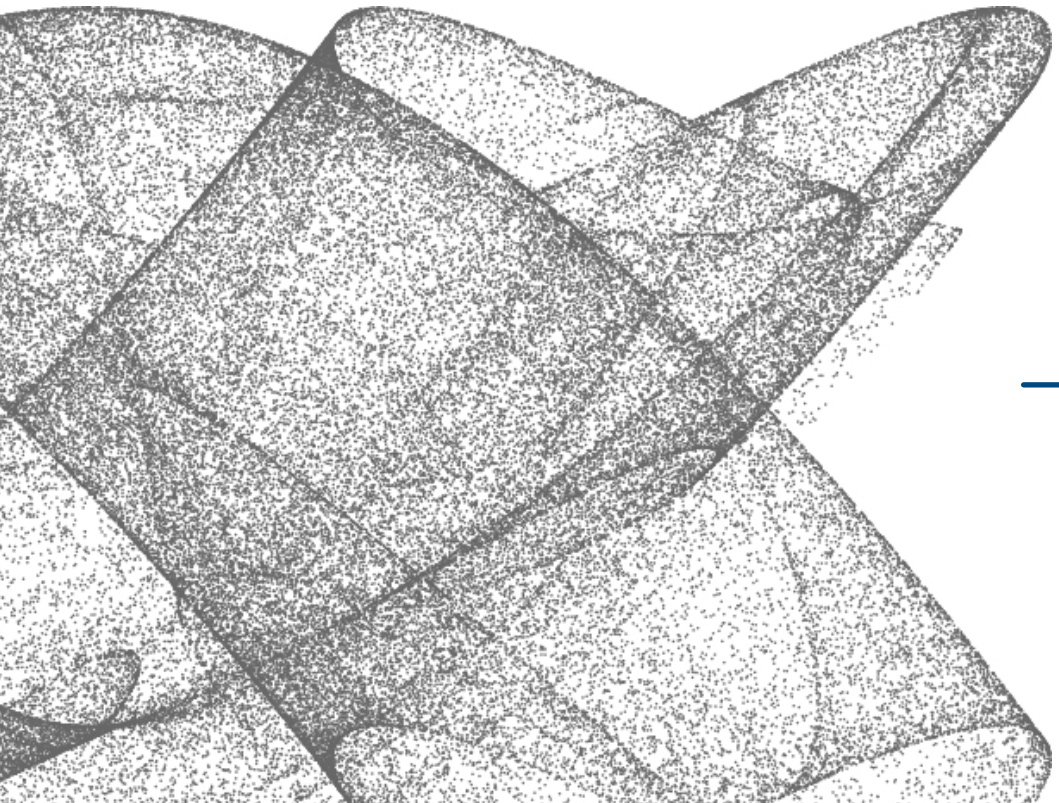
IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

Assessing the Global Burden of Post-COVID-19 Conditions

MODELING THE INCIDENCE OF POST-COVID CONDITIONS WORLDWIDE BASED ON REAL-WORLD EVIDENCE (RWE) AND CLINICAL LITERATURE REVIEW



DECEMBER
2021

Introduction

As the number of reported cases of COVID-19 exceeds 250 million globally and deaths exceed 5 million, there is growing awareness and concern about those who suffer long-term conditions which appear to be associated with the virus. These long-term conditions are likely to impose a large burden on the healthcare system and require careful examination and understanding. However, the breadth of these conditions and their incidence remains unclear.

The objective of the research reflected in this report is to quantify the magnitude of patients with post-COVID-19 conditions based on analysis of medical open claims data and a review of the growing body of literature globally. The research also models the potential demand for medicines required to treat these patients with the post-COVID conditions, even as optimal treatment for these patients is currently based on existing therapeutics.

This report discusses the varying definitions of post-COVID conditions that have been proposed in the literature. The report also profiles the different conditions that have been identified as falling under the umbrella of post-COVID conditions. These conditions are then used as the basis for assessing the number of patients with post-COVID conditions globally as well as the therapeutic costs of treating these conditions, as per existing therapeutics and treatment paradigms. Finally, the report also proposes some future areas of research and management that are needed to further enhance our knowledge of these conditions and to ensure that people with these conditions are given the best treatment.

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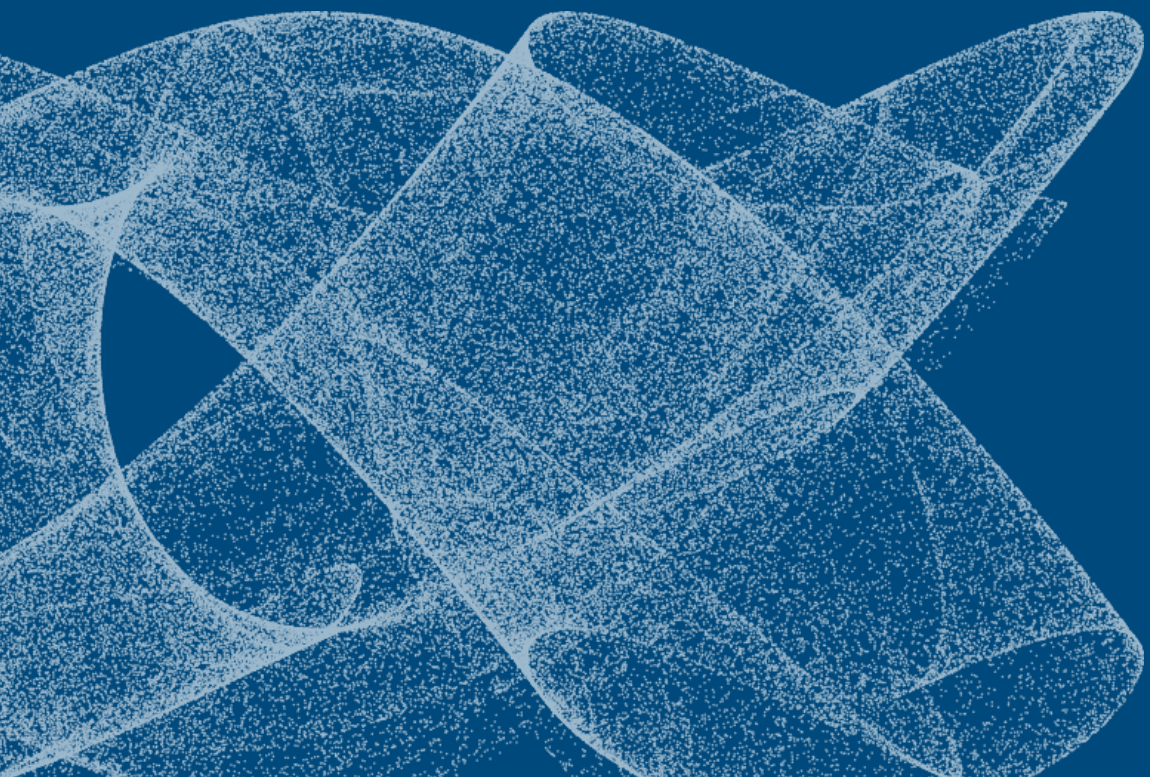


Overview

COVID-19 has disrupted human life since early 2020, causing heavy burdens on individuals, communities, businesses, and healthcare systems globally. Out of the consequences of COVID-19, "post-COVID conditions" pose a long-term challenge with potentially severe implications for healthcare systems. While there are multiple definitions of post-COVID conditions, it generally refers to an umbrella term for the wide range of physical and mental health consequences that are present after at least four weeks of infection with SARS-CoV-2.

Despite a growing volume of research, post-COVID conditions remain insufficiently studied, with a lack of consensus on the definition, epidemiology, underlying causes, and the effective therapeutics and treatment strategies for patients. To enhance the understanding of post-COVID conditions and their impact on healthcare systems, this report presents a model to analyze the burden of these conditions in the U.S. and across the globe by leveraging the IQVIA proprietary U.S. medical open claims database and an extensive clinical literature review. Using this analysis, this report presents estimated incidence rates for post-COVID conditions overall and for specific conditions.

Based on IQVIA U.S. medical open claims data as of June 2021, at least 22% (2.2 million) of the 9.7 million COVID-19 tagged patients in the database had one or more conditions (newly diagnosed or persistent) even after 90 days since their COVID-19 diagnosis. For these 2.2 million patients, 4.3 million claims for various post-COVID conditions were identified – 64.7% of the claims for post-COVID conditions were recorded in people aged 50 and above while the CDC data suggests only 32% of the COVID-19 reported cases in U.S. were reported in this age group. Females had a higher proportion (58.9%) of the claims for post-COVID conditions in comparison to men, owing to the higher rates of COVID-19 infection rates (52.3%) seen in females as reported by the CDC.
The organ systems most frequently affected by these post-COVID conditions as per the claims data include central nervous, cardiovascular, and respiratory systems. Within the central nervous system (CNS), anxiety (2.0%), fatigue (1.5%) and depression (1.4%) were the top conditions. Apart from CNS, general bone/joint pain (3.7%), hypertension (2.6%), hyperlipidemia (2.3%), abdominal pain (2.0%) and arrythmias (1.9%) were the most common conditions. Although renal conditions such as acute kidney failure (0.7%) and chronic kidney failure (0.7%) had lower rates of incidence as per the claims data, they have been of interest for researchers, owing to their serious implications for both patients and healthcare systems.

Using a global modelling approach and considering the total population diagnosed with COVID-19, at least 104.6 million newly diagnosed conditions were estimated among the reported COVID-19 survivors as of September 15, 2021. If undiagnosed cases are considered, this number would rise to at least 167.3-334.6 million conditions, assuming a factor of 3.2 undiagnosed cases for every 1 reported case in the U.S. and 50% of this factor as a conservative estimate. This additional pool of 62.7-230 million patients, including the total and 50% undiagnosed patients, is termed 'shadow post-COVID' patients — people that never received a COVID-19 diagnosis but may develop post-COVID symptoms. Globally, CNS (28.7 million), respiratory (22.5 million) and CVS (18.4 million) were the organ systems most frequently affected by post-COVID conditions. A higher burden of post-COVID conditions was estimated in the U.S. (19.1 million), Brazil (9.7 million) and India (15.5 million) due to their high volume of COVID-19 infections. Using average treatment costs, the estimated cost of therapeutics needed to treat these patients and conditions at a 100% treatment rate would reach $13.5– $43.2 billion annually, including the shadow post-COVID conditions, and $3.9–$12.4, assuming only the 1st priority conditions are treated in all patients. This incremental cost represents about 0.3–3.4% of total pharmaceutical expenditure. Additional diagnostic, clinician and facility costs would also be significant and suggest a major incremental potential costs for health systems globally.

While this research provides an assessment of the incidence of post-COVID conditions overall and by therapeutic condition, additional research and discussion is needed to gain clarity on an exact definition and therapeutic regimens. Understanding of post-COVID conditions remains limited, and further research coupled with multi-stakeholder collaboration will be necessary to ensure that knowledge of these conditions continues to grow and that appropriate care strategies are developed for patients.

Defining Post-COVID Conditions

+ **Various healthcare bodies have been working to define post-COVID conditions; however, these definitions still lack clarity on the exact conditions which can be considered a part of the post-COVID.**
+ **Post-COVID conditions are known to affect several organ systems in the body including the central nervous system (CNS), cardiovascular system, respiratory, gastrointestinal, renal, and other systems.**
+ **The public impact of post-COVID conditions is being increasingly recognized by the public health bodies around the world as these groups undertake several initiatives to advance the research and understanding of post-COVID conditions.**

The COVID-19 pandemic has created a lasting impact on all parts of the global healthcare sector by testing the capacity of healthcare systems while simultaneously accelerating innovation and collaboration needed to efficiently find a cure or vaccine for the associated infection and illnesses. Despite the best efforts and remarkable successes on these fronts, more than 253 million people have been affected by COVID-19 as of November 15, 2021[1], and there is growing evidence to suggest that COVID-19 is beginning to enter into an endemic phase in certain geographies. According to a survey conducted by 'Nature,' ~90% of scientists expect SARS-CoV-2 to become endemic and continue to create outbreaks in different parts of the world.[2]

While most of those infected have recovered, an emerging population of COVID-19 survivors are developing a wide range of new, recurring, or ongoing health problems at least four weeks after being first infected with COVID-19. Even a proportion of asymptomatic patients (i.e., patients that did not experience COVID-19 symptoms in the days or weeks after they were infected) appear to be experiencing some long-term or newly diagnosed conditions post-COVID.

These post-COVID conditions do not have a single definition yet and are referred to by different names by different health bodies (see Exhibit 1).

Exhibit 1: Post-COVID Conditions Definitions by Various Health Bodies

HEALTH BODY, COUNTRY	DEFINITION
World Health Organization (WHO)[3]	Post-COVID conditions occur in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.
Center for Disease Control and Prevention (CDC), USA[4]	Post-COVID condition is an umbrella term for the wide range of physical and mental health consequences that are present four or more weeks after infection with SARS-CoV-2.
The National Institute for Health and Care Excellence (NICE), UK[5]	The term 'long COVID' is a combination of the ongoing symptomatic COVID-19 and 'post-COVID-19 syndrome' Ongoing symptomatic COVID-19: Signs and symptoms from four to twelve weeks Post-COVID-19 syndrome: Signs and symptoms beyond twelve weeks
Haute Autorité de santé (HAS), France[6]	HAS specifies following 3 criteria for patients suffering from prolonged symptoms of Covid-19: • Presented a symptomatic form of Covid-19 • One or more initial symptoms 4 weeks after the onset of the disease • None of these symptoms can be explained by another diagnosis

Source: "A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021", World Health Organization (WHO), published on October 6, 2021; Centers for Disease Control and Prevention. COVID-19. Post-COVID Conditions: Information for Healthcare Providers, accessed on September 6, 2021

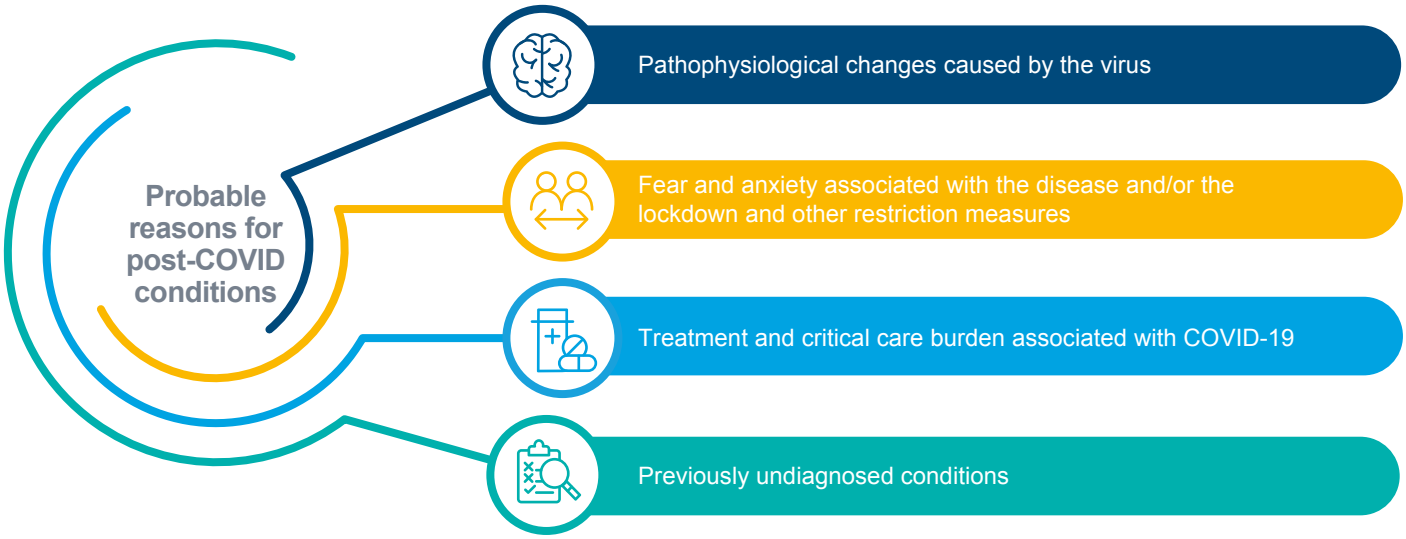
"COVID-19 rapid guideline: managing the long-term effects of COVID-19". NICE guidelines, published on December 18, 2020; "Long Covid: the recommendations of the High Authority for Health". The Haute Autorité de Santé (HAS), published on February 16, 2021

While terms such as post-acute COVID syndrome, chronic COVID, long-haul COVID, late sequelae, etc., are also being used, the term 'post-acute sequalae of SARS-CoV-2 infection (post-COVID)' is used most commonly for research purposes.[4]

Probable causes of post-COVID conditions: While the time frame defining post-COVID conditions has been fairly consistently defined by various organizations between four weeks to three months post the diagnosis of COVID-19, the conditions which are a part of the post-COVID definition are still not well established. This may be driven by the variety of potential reasons for the genesis of these conditions (see Exhibit 2). These conditions could arise due to the pathophysiological changes caused by the virus itself and can be seen in patients with a diagnosis of COVID-19, irrespective of whether they were symptomatic or asymptomatic. People who never received COVID-19 testing and diagnosis, or did not have access to testing, can also develop these long-term symptoms and form part of this patient segment as so-called "shadow post-COVID" patients. Some mental and psychological conditions such as depression can arise due to the fear and anxiety because of the COVID-19 infection or the lockdown and other restriction measures. Another reason for these conditions to appear post-COVID could be the treatment burden, including the therapeutic treatment, e.g., indiscriminate use of certain treatments such as steroids have led to increase in black fungus cases in India and perhaps an increase in incidence of acute vascular necrosis of bones in the post-COVID period , and intensive care, including intubation. Along with these causes, some of these conditions could be due to the unmasking of previously undiagnosed conditions.[4]

Spectrum of post-COVID conditions: Irrespective of the terms used to describe post-COVID conditions, they appear to be affecting multiple organ systems (see Exhibit 3). Post-COVID conditions are now understood as a multi-organ disorder or syndrome that consist of a constellation of different conditions that are acute, chronic or both, and vary in terms of severity. Emerging evidence highlights the post-COVID conditions as dynamic and evolving, with the latest studies reporting more than 200 conditions, which is an increase from the ~100 conditions that were being reported previously.[9]

Exhibit 2: Probable Cause for Post-COVID Conditions



Source: Centers for Disease Control and Prevention. COVID-19. Post-COVID Conditions: Information for Healthcare Providers, accessed on September 6, 2021; IQVIA intellectual property

Exhibit 3: Spectrum of Various Post-COVID Conditions Affecting Multiple Body Systems

Neurological complications
Brain fog, Fatigue, Headache, Strokes, Seizures, Encephalopathies, Nerve disorders, Disturbance in smell and/taste, POTS, Parkinson's disease, Dementia, dry eyes, pink eye.

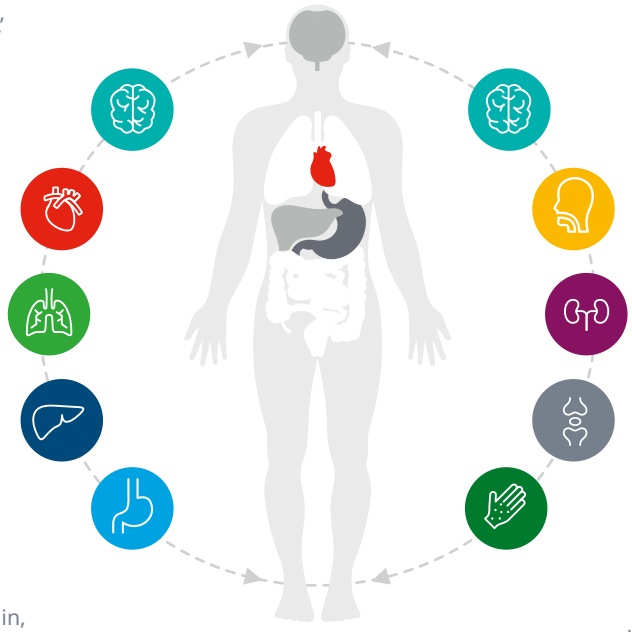
Cardiovascular complications
Dysrhythmias/ Arrhythmias, Hypertension, Dyslipidemia, Myocardial injury, Myocarditis, Heart failure, Acute Coronary Syndrome, VTE, Cardiomyopathy, Hypercoagulation, DIC, Cardiogenic shock, Cardiac arrest, Low Blood pressure.

Respiratory complications
Chronic cough, Pulmonary fibrosis, Bronchiectasis, Pulmonary vascular disease, Worsening of pre-existing respiratory conditions (asthma/COPD), Shortness of breath.

Endocrine complications
New onset diabetes mellitus.

Gastrointestinal disorders
Post infectious dysmotility, Abdominal pain, Nausea, Diarrhea, Anorexia, GI vascular diseases, Gastroesophageal reflux.

In pediatric age-group: Multi system inflammatory syndrome



Psychiatric complications
Depression, Anxiety, Psychotic disorders, Mood disorders, Sleep disorders, Substance misuse, Post Traumatic Stress Disorder, Delirium, Suicidality.

ENT complications
Tinnitus, sore throat, Earache, Hearing loss, Inner ear disorder.

Renal complications
Renal damage, Acute renal injury, Chronic Kidney Disease, Accentuation of post hypertension/Diabetes Mellitus renal disorders.

Musculoskeletal complications
Myositis, Chest pain Rhabdomyolysis, Muscle pain, Joint pain, Muscle disorders including increase severity of pre-existing diseases.

Dermatological complications
Vasculitis rash, Urticaria, Chilblains, Vesicular Purpura, Irritant dermatitis, Hair loss.

Note: POTS – Postural orthostatic tachycardia Syndrome; VTE – Venous Thromboembolism; DIC – Disseminated Intravascular Coagulation; List is indicative and not exhaustive.

Source: Centers for Disease Control and Prevention. COVID-19. Post-COVID Conditions, accessed on September 6, 2021; "Coronavirus: Kidney Damage Caused by COVID-19". Johns Hopkins Medicine, accessed on July 10, 2021; "COVID-19 (coronavirus): Long-term effects". Mayo clinic, accessed on July 10, 2021; "The lasting misery of coronavirus long-haulers". Nature, published on September 14, 2020; BMJ best practices. Coronavirus disease 2019 (COVID-19). Complications, accessed on July 14, 2021; "New-Onset Diabetes in Covid-19". The New England journal of medicine, published on August 20, 2020; "Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study". The Lancet, published on October 1, 2020; "Neurological and Musculoskeletal Features of COVID-19: A Systematic Review and Meta-Analysis", Frontiers, published on June 26, 2020; "COVID-19: Cutaneous manifestations and issues related to dermatologic care", UpToDate, accessed on December 5, 2020; "Impact of COVID-19 on the GI System", Rochester regional health, accessed on December 15, 2020; "COVID-19 rapid guideline: managing the long-term effects of COVID-19", National Institute for Health and Care Excellence, accessed on January 5, 2021; "Patient History and Physical Exam". Centers for Disease Control and Prevention. Evaluating and Caring for Patients with Post-COVID Conditions: Interim Guidance, accessed on June 16, 2021

Although less severe, post-COVID conditions are also being detected in children. According to the data published by the UK Office for National Statistics, ~13% of UK children aged 2 to 11 and ~15 % of children aged 12 to 16, still have symptoms five weeks after their first infection.[10] A specific condition called Multisystem Inflammatory Syndrome in Children (MIS-C), where different body parts can become seriously inflamed, is noted in children infected with COVID-19.[11]

Vaccination and post-COVID conditions: Rigorous vaccination drives are underway around the globe to reduce the spread of COVID-19. However, the 80–90% efficacy of the vaccines suggest that there will be breakthrough cases of SARS CoV-2.[12] Additionally, the majority of vaccines are available for people aged 18 years and above and some vaccines have started becoming available for children between 5–17 years only recently and in certain parts of the world.[13]

Vaccines may reduce the number of people suffering from SARS CoV-2 infection and as a result, reduce the number of post-COVID conditions; however, as breakthrough cases will continue, they will not fully reduce the disease burden of new post-COVID conditions. Recent studies indicate that nearly 30-40% of vaccinated post-COVID patients have experienced a respite in their symptoms post vaccination.[14]
A study published by the CDC suggests around 28.7% patients with a positive COVID test result reported believing that receiving a COVID-19 vaccine made their long-term symptoms better.[15] Another UK based study reported only 5 % of those who were infected with COVID-19 post vaccination experienced symptoms for four weeks or more.[16] There are multiple theories about how these vaccines could help patients with post-COVID conditions. It may be due to clearing of the virus remnants, or by stopping a harmful immune response, or by resetting the immune system.[14] However, there is no conclusive evidence yet that supports the hypothesis that vaccination can reduce the post-COVID symptoms.

Variants and post-COVID conditions: Similar to other viruses, SARS-CoV-2 has mutated multiple times with some strains such as the delta variant, which is a highly contagious strain, leading to sustained increase in the COVID-19 cases worldwide. Certain variants such as alpha, beta, gamma and delta have been designated as 'variants of concern' and are being closely watched by the WHO.[17] Whether different SARS-CoV-2 variants have different propensities to cause post-COVID conditions is still unclear.

Public health bodies and post-COVID conditions: The public health impact of post-COVID conditions is increasingly being recognized by the public health bodies across the globe, e.g. in U.S., UK, Canada, and Germany.

The National Institutes of Health (NIH) in the U.S. has initiated an initiative called '*RECOVER*', to understand, prevent, and treat post-COVID conditions by engaging people impacted by the COVID-19 infection.[18] In the UK, the '*post-hospitalization COVID-19 study (PHOSP-COVID)*' consortium comprised of leading researchers and clinicians has been established to increase the understanding of the impact of COVID-19 on longer term health outcomes.[19]

In Canada, 'CANCOV' is a prospective study, conducted by University Health Network (Funded by Ontario Ministry of Health and Long-Term Care) to evaluate early to one-year outcomes in patients with COVID-19 and their family caregivers.[20] The German Federal Ministry of Research has provided funding for 10 projects focusing on outpatient care, rehabilitation and care and for the cooperation between specialized long COVID outpatient clinics and primary care.[21] The Institut National de la Santé et de la Recherche Médicale (Inserm) funded French COVID study is aimed at developing a better understanding of the short and long-term outcomes and mechanisms behind the persisting symptoms over months following diagnosis.[22] Understanding various aspects of post-COVID conditions can help in providing the required care and support to patients.

Profiling Post-COVID Conditions

+ **In the U.S., at least 22% of COVID-19 tagged patients in a large open claims database were identified to have at least one condition newly diagnosed or persistent even after 90 days following their COVID-19 diagnosis**
+ **In these patients, 4.3 million open claims were recorded for various post-COVID conditions, with an average of at least two conditions being experienced per patient**
+ **Globally, at least 104.6 million conditions were estimated using a modelling approach, with a higher number of conditions seen in countries such as the U.S., India, and Brazil due to high COVID-19 burden**
+ **CNS, respiratory and CVS organ systems emerged as the most commonly affected systems in the U.S. and globally**
+ **Anxiety, fatigue, and depression were identified as the top CNS conditions; bone/joint pain, hyperlipidemia and hypertension were some of the other conditions with high incidences**

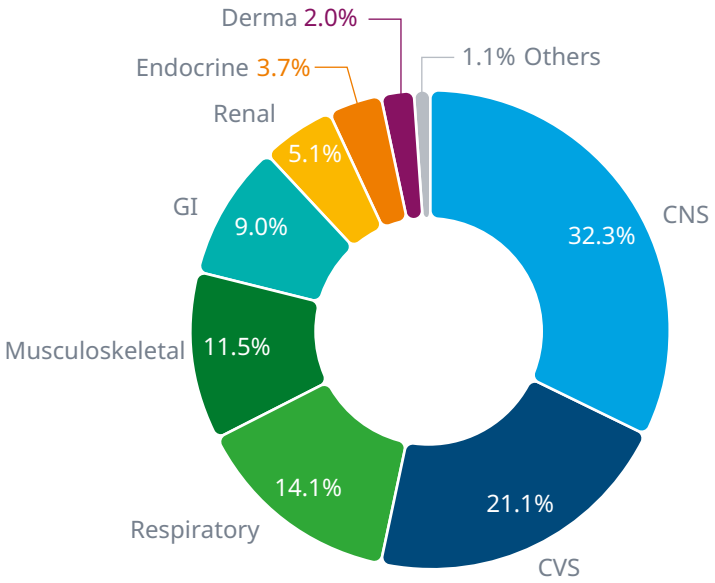
POST-COVID CONDITIONS IN U.S.

IQVIA U.S. medical open claims data was analyzed by considering newly diagnosed and/or persisting conditions after COVID-19 infection was documented, which were not present during the 12 months look back period (see Appendix for details on methodology and data sources). For the purposes of this research, newly diagnosed and/or persisting conditions beyond 90 days after COVID-19 infection was documented and which were not present during the 12 months look back period (post-COVID condition patients) have been in line with the new WHO working case definition.[3] Due to the nature of the open claims database, the full universe of all claims associated with all patients may not be captured, thus the conditions shown in this analysis represent a minimum number and additional post-COVID conditions may also be possible.

Out of 9.7 million COVID-19 tagged patients on the IQVIA medical open claims database, 2.2 million patients had a claim for at least one post-COVID condition, indicating that at least ~22% of the COVID-19 tagged patients in IQVIA claims data were post-COVID condition patients. In these 2.2 million patients, ~4.3 million claims for various post-COVID conditions were identified, indicating presence of an average of at least 2.0 conditions per patient, which is consistent with the studies identified in the literature review for the U.S.[23-25]

Within the 4.3 million newly diagnosed conditions identified as per the claims data, 32.3% of the conditions were related to the CNS organ system, followed by CVS (21.1%) and respiratory (14.1%). These three organ systems together represented 67.6% of all post-COVID conditions (see Exhibit 4), which validates that post-COVID is a multi-organ system disorder and that it is not restricted to respiratory symptoms such as cough, breathlessness, and related symptoms. Exhibit 4 shows the split of these conditions by organ systems.

Exhibit 4: Percentage of Post-COVID conditions by Organ System in the U.S.



Note: Others include Ear nose and throat (ENT) indications like otalgia, tinnitus and multi system inflammatory syndrome.
Source: IQVIA medical open claims database, June 2021

Within CNS, anxiety disorder, fatigue and depression were the top conditions. Other organ systems including musculoskeletal, gastrointestinal, renal, endocrine, dermatology, ENT, and pediatric together contributed for the remaining 32.4% to this pool. Exhibit 5 shows the incidence rates of top post-COVID conditions based on IQVIA claims data.

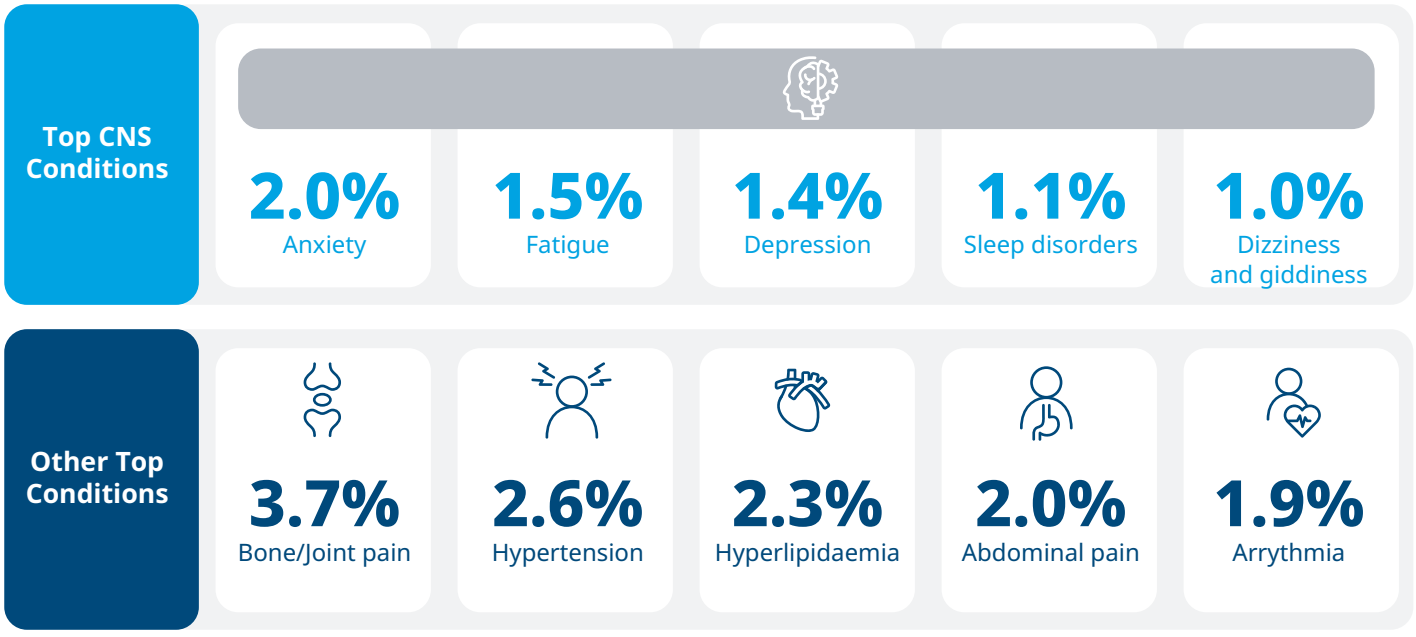
Although renal conditions contributed only 5.1% to the total post-COVID conditions as per the claims database, some of these conditions can be severe, such as acute and chronic kidney failure, which were found to be 1.6% and 1.7% respectively. Based on the literature, researchers are currently looking to understand the reasons for severe renal issues as post-COVID conditions. A potential rationale suggests a bi-directional nature, i.e., pre-existing renal comorbidities, increase risk of SARS-COV-2. SARS COV-2 causes renal pathologies as well. Potential direct effects on the kidney include endothelial damage from viral entry, complement activation, local inflammation, and collapsing glomerulopathy. However, indirect mechanisms that injure the kidney, such as sepsis, use of nephrotoxic medications, systemic inflammation, hypercoagulability, and thromboembolic disease, might also be a factor. Although it is well known that acute kidney failure can lead to chronic kidney disease (CKD), knowledge of the long-term effects of COVID-19 on the kidney remains limited.[26] These long-term impacts of post-COVID conditions may take place at the hospital level and may not be fully captured in the open claims database.

Further investigation of the data was conducted to provide a better understanding of the demographics of post-COVID conditions. Overall a higher percentage of women had post-COVID conditions compared to men. The number of post-COVID conditions also increased with age (see Exhibit 6).

According to the CDC, 52.3% of total COVID-19 cases have been reported in females while ~58.9% of all the claims for post-COVID conditions were recorded in women.

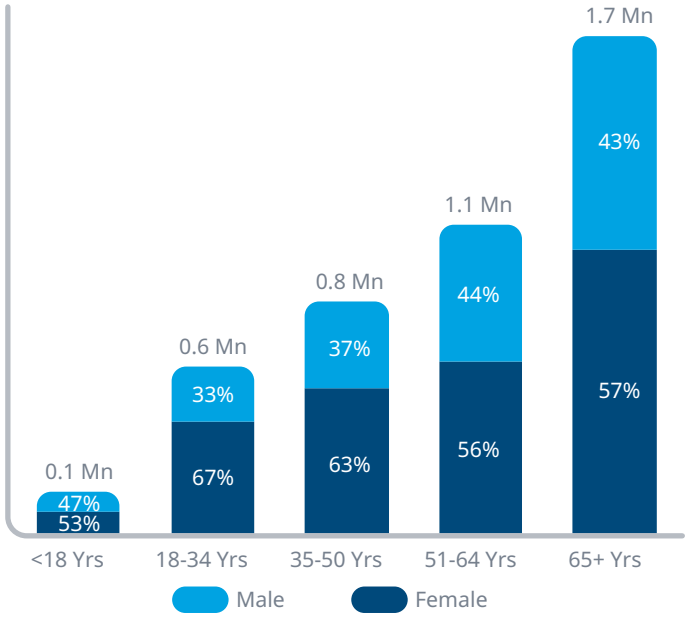
According to U.S. CDC data, 32.0% of all COVID-19 cases are reported in people more than 50 years of age, while the claims for post-COVID conditions recorded for the 50 plus age groups were 1.8 times greater as

Exhibit 5: Incidence of Various Post-COVID Conditions Based on IQVIA US Claims Data



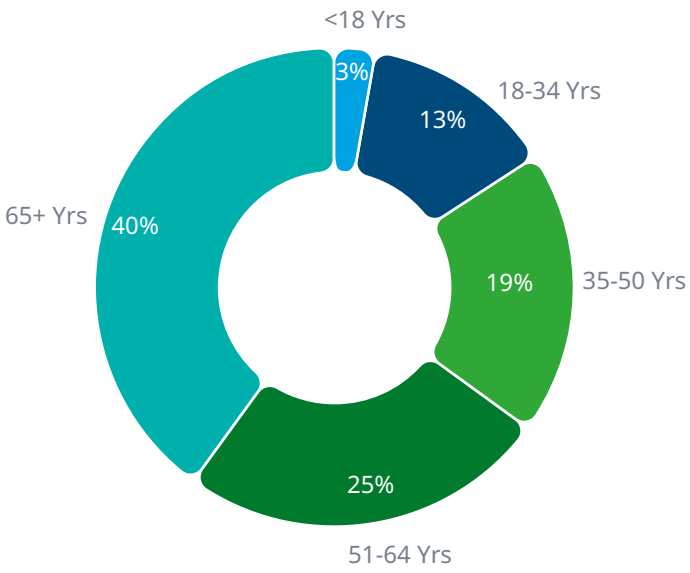
Source: IQVIA medical open claims database, June 2021

Exhibit 6: Split of Post-COVID Conditions by Age and Gender in the U.S.



Source: IQVIA medical open claims database, June 2021

Exhibit 7: Split of Post-COVID Conditions by Age in the U.S.

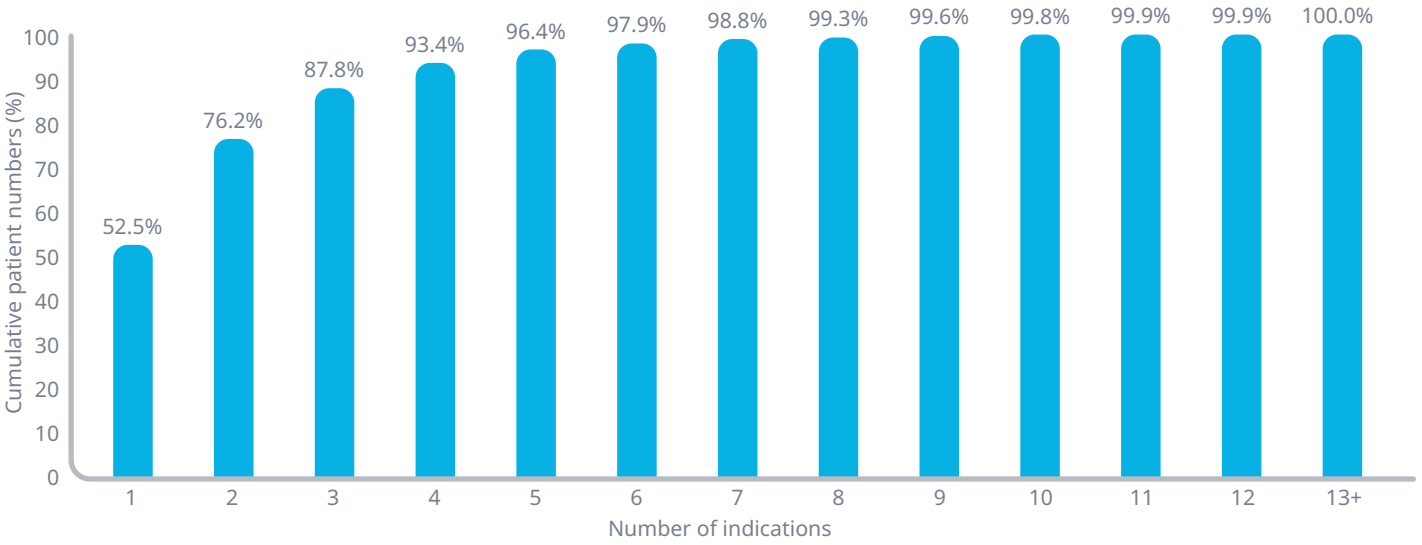


Source: IQVIA medical open claims database, June 2021

compared to the under 50 age group. This suggests a higher occurrence of post-COVID conditions in this age group.[27] Also, 64.7% patients in the post-COVID pool were observed to be within the age group of 50+ years, a trend that has also been seen in other studies (see Exhibit 7)[23,28]

Out of the cohort of 2.2 million patients who tested positive for COVID-19 as per the open claims database and subsequently received one or more new diagnoses in the database, 52.5% had only one new diagnosis, 23.8% had two new diagnoses, 11.5 % had three new diagnoses, and 12.2% had more than three new diagnoses (see Exhibit 8).

Exhibit 8: Indication Count per Patient (U.S.)



Source: IQVIA medical open claims database, June 2021

Exhibit 9: Indication Combinations in Post-COVID Patients (U.S.)

INDICATION 1	INDICATION 2	INDICATION 3	INDICATION 4
Anxiety disorder	Depression		
Acute Kidney Failure	COPD		
Depression	Hyperlipidemia		
Hypertension	Type 2 DM		
Anxiety disorder	Breathlessness	Arrythmia	
Acute Kidney Failure	Acute Myocardial Infarction	Encephalopathy	
Acute Kidney Failure	Hyperlipidemia	Hypertension	Type 2 DM

Note: Exhibit highlights only few indication combinations and not necessarily the top ones.
Source: IQVIA medical open claims database, June 2021

Some of the indication combinations suggest a mix of predominantly chronic and acute conditions affecting different organ systems in patients post-COVID (see Exhibit 9)

POST-COVID CONDITIONS – GLOBAL VIEW USING MODEL

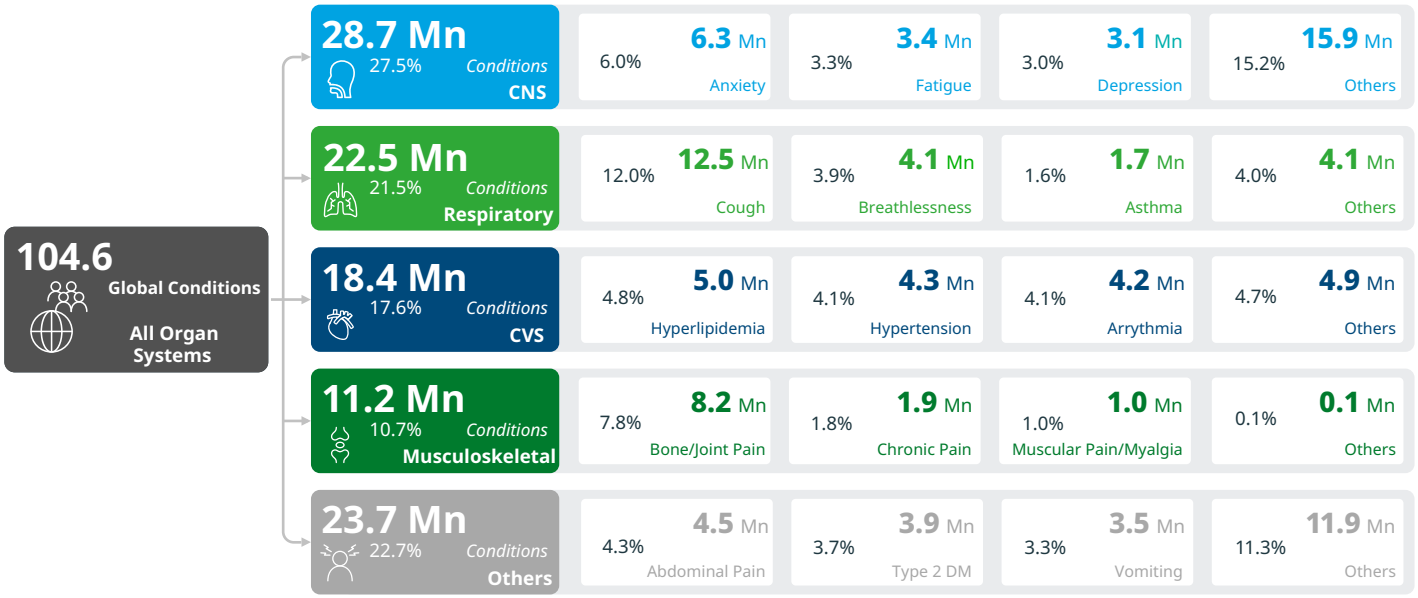
As indicated earlier, a model was designed by integrating the inputs from IQVIA medical open claims data for U.S. (as of June 2021) and detailed clinical literature search to quantify the incidence rates of 73 post-COVID conditions around various geographies. These incidence rates were combined with the reported COVID-19 survivors across various geographies (221 million as of September 15, 2021) to estimate the emerging segment of post-COVID patients worldwide. Based on general literature estimates, around 10%-30% of COVID-19 survivors are at risk of becoming post-COVID patients (22–66 million as of September 15, 2021). Also, the U.S. claims data analysis described earlier suggests proportion of post-COVID patients as 22.2%. Hence, 20% as the percentage of COVID patients having post-COVID conditions has been used in the model.

Based on the model calculations, a total number of at least 104.6 million conditions was estimated among the 44.2 million post-COVID patients (i.e., 20% of the report COVID-19 survivors), with an average of 2.4 conditions per patient.

In order to account for the undiagnosed COVID-19 cases, CDC estimates that for every single COVID-19 reported infection, more than three COVID-19 infections are not reported were assumed for all the countries.[29] These additional number of so-called “shadow post-COVID” patients could bring the total number of post-COVID conditions to 167.3 million-334.6 million, assuming 50% and total shadow post-COVID patients.

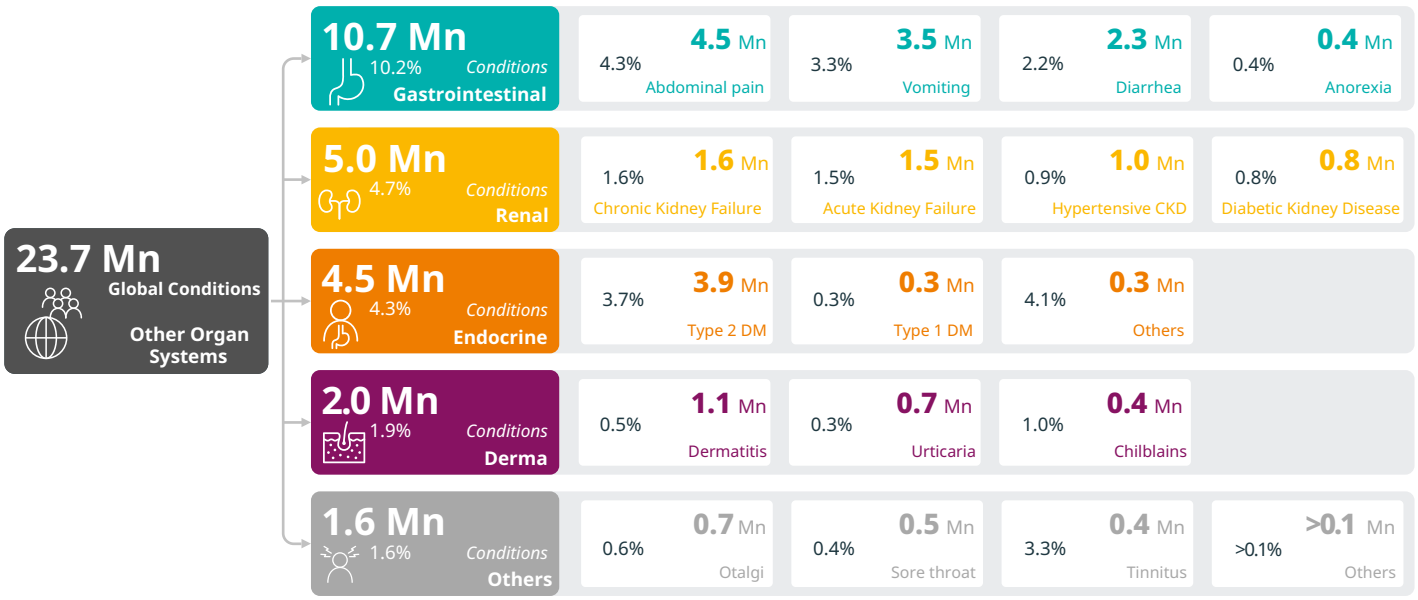
Within the estimation of 104.6 million newly diagnosed conditions, the majority was represented by CNS organ system totaling nearly 28.7 million, followed by respiratory organ system totaling nearly 22.5 million, and 18.4 million newly diagnosed CVS conditions.

Exhibit 10: Major Organ System Conditions: Global Model



Source: IQVIA medical open claims database, June 2021

Exhibit 11: Other Organ System Conditions: Global Model

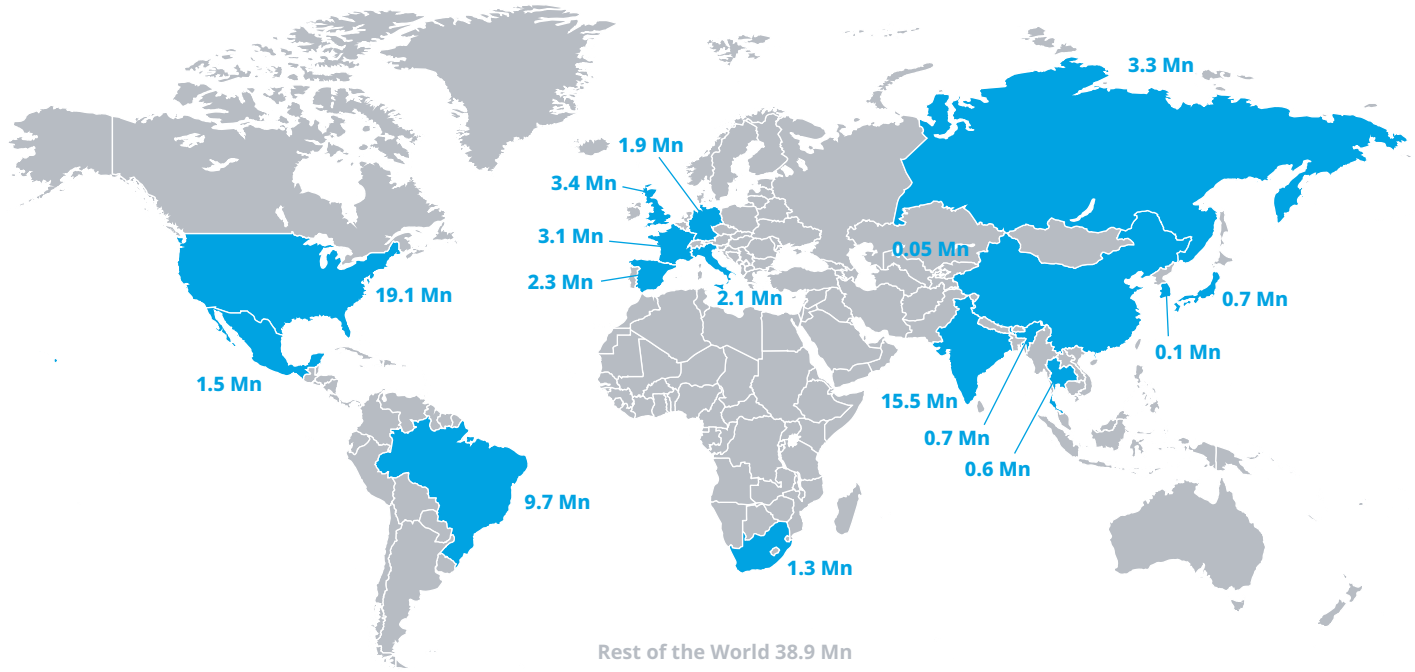


Source: IQVIA medical open claims database, June 2021

Other organ systems including musculoskeletal, gastrointestinal, endocrine, dermatology, ENT and renal together contributed about 34.9 million to this pool.

Exhibits 10 and 11 represent the top conditions in every organ system.

Exhibit 12: Post-COVID Conditions Worldwide



Source: IQVIA medical open claims database, June 2021

Around the globe, ~30% of the burden of the post-COVID conditions was estimated to be in high income countries including the U.S. (19.1 million), UK (3.4 million) and EU4 (9.4 million). Middle income countries including India (15.5 million) and Brazil (9.7 million) are estimated to have the highest number of post-COVID conditions after the U.S., owing to the high number of COVID-19 survivors (see Exhibit 12).

As the cases of COVID-19 continue to rise, the post-COVID patient segment is expected to increase along with a growing need to identify and understand this segment to devise care and support strategies for them. The costs involved in caring for patients with post-COVID conditions will also need to be assessed to help governments, healthcare providers and health insurers take informed decisions in managing this group of patients.

Therapeutic Management of Post-Covid Conditions

+ **The current therapeutic recommendations by various health bodies highlight the need for a multidisciplinary approach to the assessment and management of post-COVID patients**
+ **Estimated therapeutic cost for treating these conditions with the already existing standard of care is expected to create a potential burden of $3.8 to $43.2 billion**
+ **Investigation of the clinical trials for the post-COVID patients suggests very few ongoing interventional trials currently evaluating drugs and supplements in the post-COVID space**
+ **Among these studies, 16 are focused on respiratory organ systems, 7 on CNS organ systems and 4 on CVS and others**
+ **Some newly emerging and ambiguous conditions such as brain fog demand further research to understand the cause and potential treatment strategies**

Currently, no specific treatment has been approved to prevent or treat post-COVID conditions, and patient treatment guidelines are evolving. In the UK, a guideline has been developed jointly by NICE, the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners (RCGP), and proposes a holistic assessment followed by a two-pronged approach for management as below:

1. Self-management
2. One of the following, depending on clinical needs:
   - Support from integrated and coordinated primary care, community, rehabilitation, and mental health services
   - Referral to an integrated multidisciplinary assessment service
   - Referral to specialist care for specific complications

The guidelines also suggest that the core team for management of such patients could include, but not be limited to, occupational therapy, physiotherapy, clinical psychology and psychiatry, and rehabilitation medicine.[5] The proposed primary care clinical guidelines published by the Catalan Society of Family and Community Medicine (Spain) also endorse the key points proposed by the NICE guidelines.[30]

The U.S. CDC interim guidance suggests symptomatic management of the conditions using the already established treatment protocols with the goal to optimize the function and quality of life for the patients. Exhibit 13 summarizes the management strategies for some conditions from the CDC interim guidance[31]:

Exhibit 13: Management Strategies for Some Conditions from the CDC Interim Guidance

CONDITION	INTERVENTION
Dyspnea	Breathing exercise
Cognitive symptoms	Comprehensive rehabilitation including physical and occupational therapy, speech and language therapy, vocational therapy, as well as neurologic rehabilitation
Post-exertional malaise	Conservative physical rehabilitation, activity management (pacing)
Headache, anxiety	FDA-approved or over the counter medications, vitamin, or electrolyte supplements

Source: Centers for Disease Control and Prevention. General Clinical Considerations. Evaluating and Caring for Patients with Post-COVID Conditions: Interim Guidance, accessed on September 21, 2021

The Association of the Scientific Medical Societies in Germany recommends strategies for different post-COVID conditions (translated from German) (see Exhibit 14).

The Haute Autorité de Santé (HAS) published rapid response guidelines for help healthcare professionals to identify and manage patients with post-COVID symptoms, emphasizing personalized treatment strategies for every patient. The guidelines recommend symptomatic treatment, rehabilitation, psychological support and self-management for the care of such patients. The HAS also published 10 technical sheets specifying the clinical and paraclinical explorations required and the elements of first-line treatment of the most common post-COVID symptoms. (fatigue, dyspnea, chest pain, taste and smell disorders, pain, hyperventilation syndrome, functional somatic disorders, neurological manifestations and dysautonomia disorders, and exercise retraining).[33]

A Delphi study conducted with a panel of 33 clinicians representing 14 specialties recommends involvement of physicians with cross-specialty knowledge and experience to enable individualized investigations, management, and rehabilitation for patients in long COVID clinics. It recommends following interventions for management of some specific conditions[34] (see Exhibit 15).

Out of the 73 conditions for which incidence data was quantified, cost was estimated for 59 conditions, covering around 94% of the cases. These costs were modelled based on the general costs associated with treating these conditions currently. The combined therapeutic cost for these conditions was estimated at a lower range of $3.9 billion, assuming treatment of only the first priority conditions. (See Methodology section for details. Cost of hospitalization may be underestimated as hospital data is potentially underrepresented in the data.) If a 100% treatment rate is assumed, this could rise up to around $13.5 billion. Taking into consideration the shadow post-COVID patients, the costs could be in the range of $6.2–43.2 billion, representing about 0.3–3.4% of total pharmaceutical expenditure. These additional treatment costs along with the diagnostic, clinician and facility costs can create an unexpected additional burden for health systems globally.

Exhibit 14: Management Strategies for Different Post-COVID Conditions Recommended by the Association of the Scientific Medical Societies, Germany

CONDITION	INTERVENTION
Fatigue	Promotion of sleep, pain therapy, circulatory support, measures for Stress reduction and relaxation, controlled instructions on physical activity, psychotherapeutic or psychopharmacological treatment, Occupational therapy
Dermatological aspects	Symptomatic treatment using Antihistamines, corticosteroids etc.
Smell disorders	Structured “smell training”
Cardiac disorders	Symptomatic therapy based on existing guidelines
Neurological aspects	Physiotherapy, occupational therapy, neuropsychological and socio-educational Assistance (Neurorehabilitation for cognitive disorders)
Pain	Symptomatic therapy based on existing guidelines
Dyspnea, sleep disorders, cough	Symptomatic therapy based on existing guidelines along with supportive breathing and physical therapy
Psychological aspects	Psychopharmacological treatment, rehabilitation etc.

Source: “S1 guideline Post-COVID / Long-COVID”. Association of the Scientific Medical Societies in Germany, published on July 7, 2021

Exhibit 15: Delphi Study Recommendations for Management of Some Specific Conditions

CONDITION	INTERVENTION
Cardiac symptoms	Limiting heart rate to 60% of maximum
Autonomic dysfunction including PoTS	Increased fluids, salts, compression hosiery, and specific rehabilitation. Pharmacological treatment including beta-blocker, ivabradine, or fludrocortisone
Possible mast cell disorder	1-month initial treatment with antihistamines and dietary advice, followed by second-level treatment with montelukast and referral to allergy or immunology specialist
Breathing pattern disorder	Specialist physiotherapy and/or alternative therapies such as pranayama breathing and meditation
Distress, significant low mood, anxiety, or symptoms of post-traumatic stress disorder	Mental health assessment

Source: "Prolonged symptoms following an adult Covid-19 - Diagnosis and management". The Haute Autorité de Santé (HAS), published on February 12, 2021

LOOKING AHEAD

While a majority of the conditions can be treated using existing therapeutic approaches, some less understood conditions such as brain fog demand more research to understand the cause and devise an appropriate treatment strategy.

There has been significant interest in post-COVID conditions from governments and the medical research community. However, an analysis of the clinical trial activities suggested relatively few studies around development of therapeutic interventions for the post-COVID conditions. Exhibit 16 highlights the current interventional trials activity.

Exhibit 16: Current Clinical Trials Activity

40 interventional trials have been categorized, analyzed and added in tabular format

CNS	Respiratory	CVD	PASC	Others
7	16	1	13	3

Source: Clinical trials.gov

Source: "S1 guideline Post-COVID / Long-COVID". Association of the Scientific Medical Societies in Germany, published on July 7, 2021

Out of the total pool of 476 trials for post-COVID conditions, 40 studies were identified as interventional, the majority of which were focused on assessing the efficacy of existing approved therapeutics in treating post-COVID patients. Exhibit 17 highlights the various interventions being studied for the post-COVID conditions.

Exhibit 17: Interventional Study Objectives

Interventional	Cognitive symptom/ Neurocognitive	Post COVID-19 fatigue	Post-COVID	Respiratory diseases	CVS and others
# of studies	3	4	13	16	4
Study Objective	• Role of Niagen supplement in recovery • Statin treatment to optimize neurological recovery • Role of Hyperbaric Oxygen Therapy	Evaluate the benefit of • Anhydrous Enol-Oxaloacetate (AEO) • RUCONEST drug • Treatment with Bioarginin C supplement • Transcranial direct current stimulation	Evaluate the benefit of • Drugs like Naltrexone, Sodium Pyruvate, RSLV-132, Coenzyme Q10, PD-1 and ACE2 Knockout T Cells, Remdesivir • Supplements like ADAPT-232, CBDRA60, Microbiome Immunity Formula and Wellness Formula • Cannabidiol	Evaluate the benefit of • Biologics like Ampion, stem cells and monocytes • Drugs like Montelukast, S-1226, LYT-100, Pirfenidone, corticosteroids like prednisone • Supplements like Taxifolin Aqua, Omni-Biotic	Role of • Ivermectin in Post COVID-19 Anosmia • Apixaban in COVID-19 thrombosis prevention • Transcranial direct current stimulation in rheumatic diseases • Trans retinoic acid in anosmia and sense of smell

Source: Clinical trials.gov

Future Research and Management

+ **A number of short- to long-term actions by healthcare stakeholders are needed in order to strengthen the understanding of post-COVID conditions and to develop assessment and management strategies to provide better care for these patients**
+ **While several aspects associated with the post-COVID conditions are still not clear, future research in this direction should continue to refine the understanding and estimation of post-COVID conditions through further robust analysis and discussion**

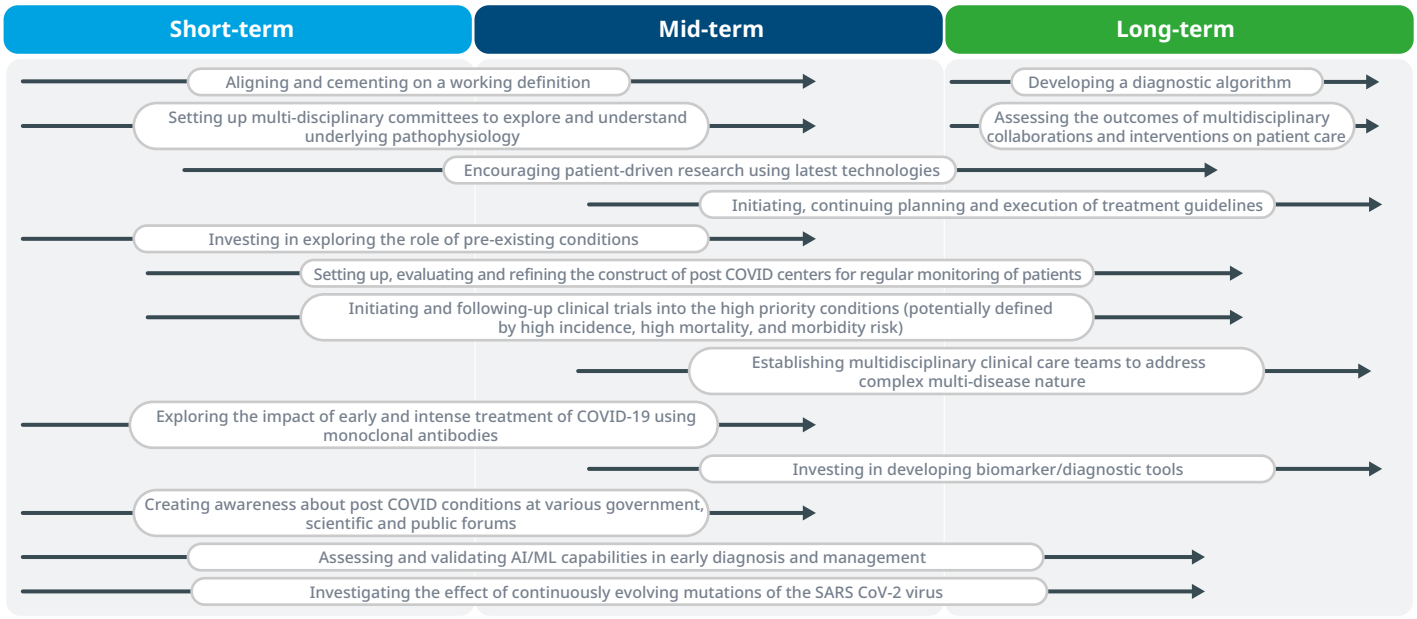
Despite the high volume of ongoing research, understanding of post-COVID conditions continues to be limited and evolving. Unclear impact of the pathophysiology, lack of consensus around the definition, and limited concrete evidence around identification, prevention, and management of post-COVID conditions can lead to increased burden on an already overwhelmed community.

Exhibit 18 presents some short-term, mid-term and long-term directional actions that the governments, public health/research bodies and the life sciences industry can take to address some of these challenges. Enhancing understanding and devising an approach to manage patients with post-COVID conditions will require multi-stakeholder, multi-specialty collaboration over a long time period. Given the potential large impact of these conditions, it is important that stakeholders across the healthcare spectrum come together to provide solutions for this patient population (see Exhibit 18).

FUTURE RESEARCH PRIORITIES

Subsequent research on post-COVID conditions should aim to rule out alternative diagnoses and diagnoses of conditions that may have been pre-existing but not yet uncovered. Assessing the conditions directly linked to COVID-19 infection would require estimating the general rate of diagnoses of these conditions without COVID-19 in a control group of patients with similar characteristics as the patients that had COVID-19. Additional research should also take into consideration the time limit of conditions occurring for at least two months as mentioned by the WHO. Conditions missed due to discontinuation of treatment and/or lack of follow-up visits to providers by patients after certain time would also need to be accounted for. As post-COVID conditions are known to occur in asymptomatic patients as well, it is important to consider the presence of these conditions in the population that never received the COVID-19 diagnosis. Finally, a closed claims database that can account for the full universe of a patients' claims would provide a more complete assessment of all of the post-COVID conditions.

Exhibit 18: Short- to Long-Term Actions for Healthcare and Life Sciences Industry



Just an indicative list and not exhaustive

Note: An indicative list and not exhaustive.
Source: IQVIA intellectual property

Methodology

STUDY DESIGN – USA

An analysis of IQVIA proprietary U.S. medical open claims database was conducted to profile the conditions diagnosed and treated in patients during the post-COVID period.

IQVIA proprietary medical open claims Database analysis: Within U.S. open claims data, 9.7 million unique patients with positive diagnosis for COVID-19 (as of June 2021) were identified and analyzed. Based on the literature review, 86 post-COVID conditions were identified. ICD codes for these were defined and claims with at least one of these conditions were identified. To be considered as a post-COVID condition, the condition must have been newly diagnosed and/or persisting beyond 90 days after COVID-19 infection was documented and these conditions were not present during the 12 months look back period prior to the documentation of COVID-19. Patients with new or persisting diagnosis of these conditions 90 days post COVID-19 diagnosis were considered in line with the WHO's case definitions for post-COVID conditions. Incidence rates of the new conditions were calculated by dividing the number of claims by the total unique COVID-19 patients identified in the database. Due to the nature of the open claims database, the full universe of all claims associated with a patient may not be captured, likely resulting in an underestimation of the conditions. The database may not capture all of the claims for every patient in case a provider/hospital that the patient visited is not included in the database. In particular, the data's ability to capture claims at the hospital level may be limited.

While some of the literature studies suggests presence of more than 200 symptoms as post-COVID conditions, this report quantifies 86 conditions, which club together several symptoms to form one condition, e.g., bone pain and joint pain has been combined as one condition bone/joint pain, all sleep disorders excluding insomnia have been clubbed together as sleep disorders.

STUDY DESIGN – GLOBAL MODEL

Along with the analysis of proprietary IQVIA data on the U.S., a global model was also developed to assess the potential prevalence of post-COVID conditions across the world. The global model had inputs from two sources, the IQVIA proprietary medical claims database analysis and the literature review.

IQVIA proprietary medical open claims database analysis: Results from the IQVIA open claims data, (details mentioned in above section) were synthesized with the clinical literature analysis for the global modelling of post-COVID conditions.

Clinical literature review: PubMed was searched for follow-up studies regarding long-term consequences of COVID-19 up to any time frame. Only studies in English language were captured for analysis and open searches were conducted to capture any supplementary studies for follow-up on long-term consequences. Search terms such as COVID-19, SARS-CoV-2, Coronavirus disease 2019, 2019-nCoV, PASC, Post-Acute Sequalae, survivor, recover, persistent, follow up, discharge, long-term, sequelae etc. were used to conduct the search. The geographies in focus were U.S., UK, EU 4 (Spain, Germany, Italy, France), rest of the world (India, Korea, China, Brazil, South Africa, Russia, Bangladesh, Thailand, Mexico and others). The search focused on organ systems including central nervous system (CNS), cardiovascular system (CVS), respiratory, musculoskeletal, endocrine, derma, ear, nose and throat (ENT), gastrointestinal and renal.

The studies captured were screened for long-term manifestations of COVID-19 in COVID survivors. Further, these studies were segregated based on the following:

Methodology

- Setting type: outpatient and inpatient (with information around intensive care – if available)
- Outcome reporting: whether a study is based on patient reported outcomes or physician/provider reported outcomes
- Symptom persistence: follow-up time for patients such as 0.5-3 months, 3-6 months, or 6-9 months

Based on the above segregation criteria, the studies were divided into nine scenarios. Mean, median incidence and range were calculated for each

- A1: Only Outpatient and 0.5-3 Months
- A2: Only Outpatient and 3-6 Months
- A3: Only Outpatient and 6-9 Months
- B1: Only In-patient and 0.5-3 Months
- B2: Only In-patient and 3-6 Months
- B3: Only In-patient and 6-9 Months
- C1: Both in and outpatient and 0.5-3 months
- C2: Both in and outpatient and 3-6 months
- C3: Both in and outpatient and 6-9 months

The incidence rates for conditions across various organ systems were collected from physician/provider reported studies with a focus on a minimum of three to six-month period, considering post-COVID conditions are commonly defined as a long-term condition occurring at least 90 days post-COVID-19 diagnosis.

Global Modeling: A model was designed and applied to estimate the emerging segment of post-COVID patients worldwide using inputs from clinical literature review and U.S. medical claims data (as of June 2021).

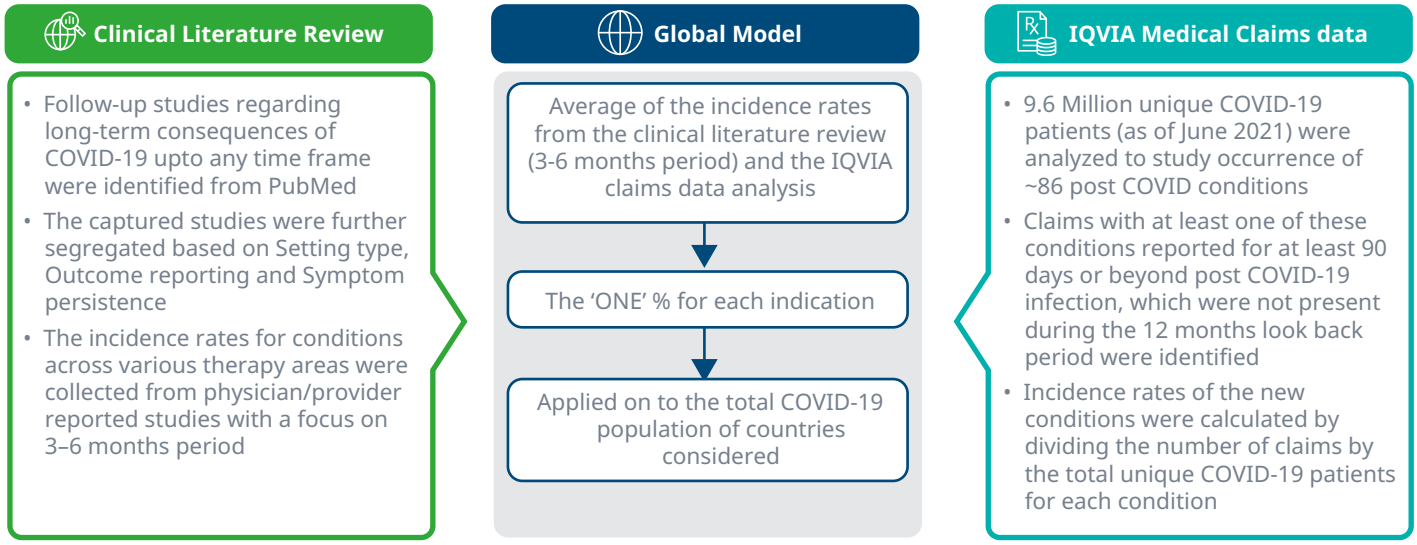
The model provides split of post-COVID conditions by various parameters such as:

- Organ systems namely CNS, CVS, respiratory, musculoskeletal, endocrine, derma, ENT, gastrointestinal and renal
- Conditions such as depression, cough, breathlessness, abdominal pain, etc.
- Geographies, namely the U.S., UK, EU 4 (Spain, Germany, Italy, France), rest of the world (India, Korea, China, Brazil, South Africa, Russia, Bangladesh, Thailand, Mexico, and others)

Results from the detailed clinical literature search and the U.S. medical open claims data were combined to arrive at a single incidence percentage for each condition. Average of the incidence rates from the clinical literature review (three to six-month period) and the claims data analysis was used. Out of the 86 conditions quantified using the U.S. medical open claims data, incidence rate for 73 conditions which were either seen on claims data or secondary research was quantified and applied on COVID-19 survivors in each geography to estimate the number of emerging post-COVID conditions in COVID-19 survivors (see Exhibit 19).

Therapeutic cost estimations: For the estimation of therapeutic costs, the patient numbers for each condition were multiplied by average price for the treatment for that indication per day and the days of therapy in one year. For price calculations, a weighted average approach was applied using the IQVIA MIDAS database. Each indication was tagged to one or more ATC3/ATC4 classes or molecules used for treatment.

Exhibit 19: Snapshot of Methodology for the Global Model

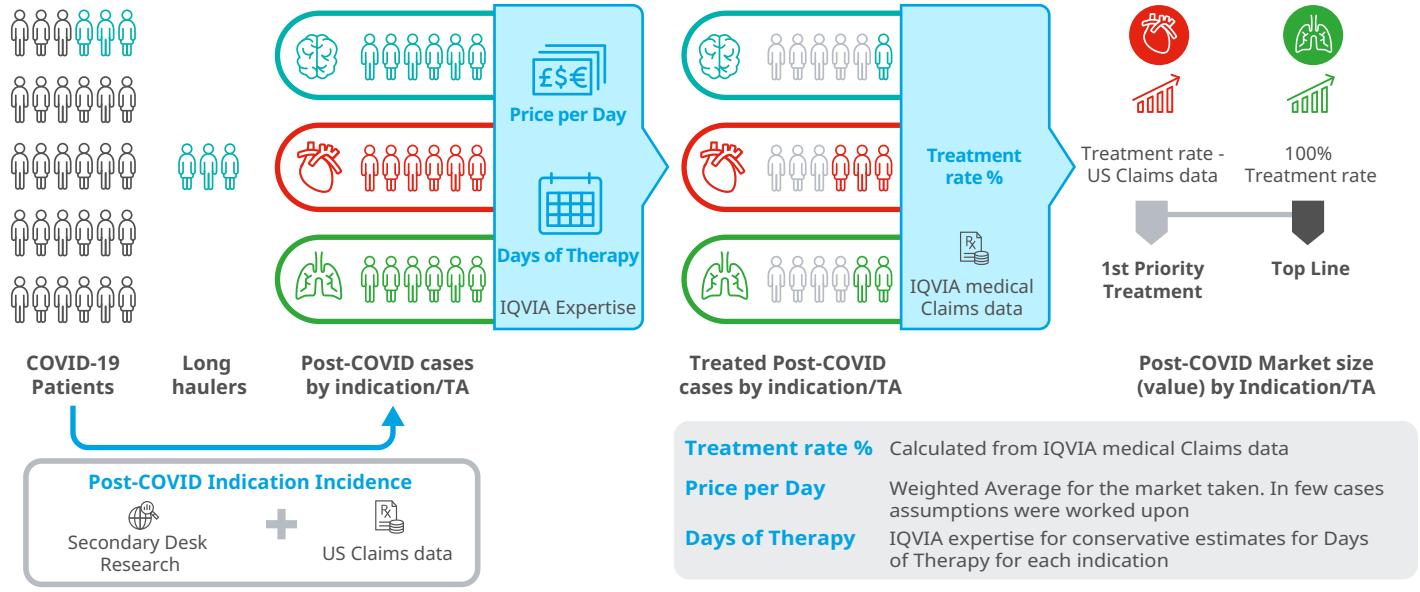


Source: IQVIA intellectual property

For each indication, the price per SU for all international products within the tagged ATC classes were multiplied by the market share (by volume, 2020) of respective international product within the tagged ATC classes. The price per SU for all the products was then summed and multiplied with factor of minimum daily dosage to arrive at the price per day for the indication. Certain adjustments were made across a limited number of classes when calculated prices, e.g., for pulmonary hypertension, brands which are possibly marketed for erectile dysfunction were removed; for chronic kidney disease, erythropoietin (EPO) has not been considered as not all patients are treated with this drug. To account for the geographical differences, average prices were considered for three groups: U.S., other selected high-income countries such as UK, EU4, Japan and Korea, and selected middle-income countries including Russia, Brazil, Mexico, South Africa, China, India.

In cases of multiple post-COVID conditions, the patient may not be treated for all the conditions. To account for this while estimating the market size, most commonly occurring indication combinations were studied and treatment rate was derived for the conditions. Exhibits 20 and 21 elaborate the methodology for treatment rate. A lower range of market size was estimated by using these treatment rates.

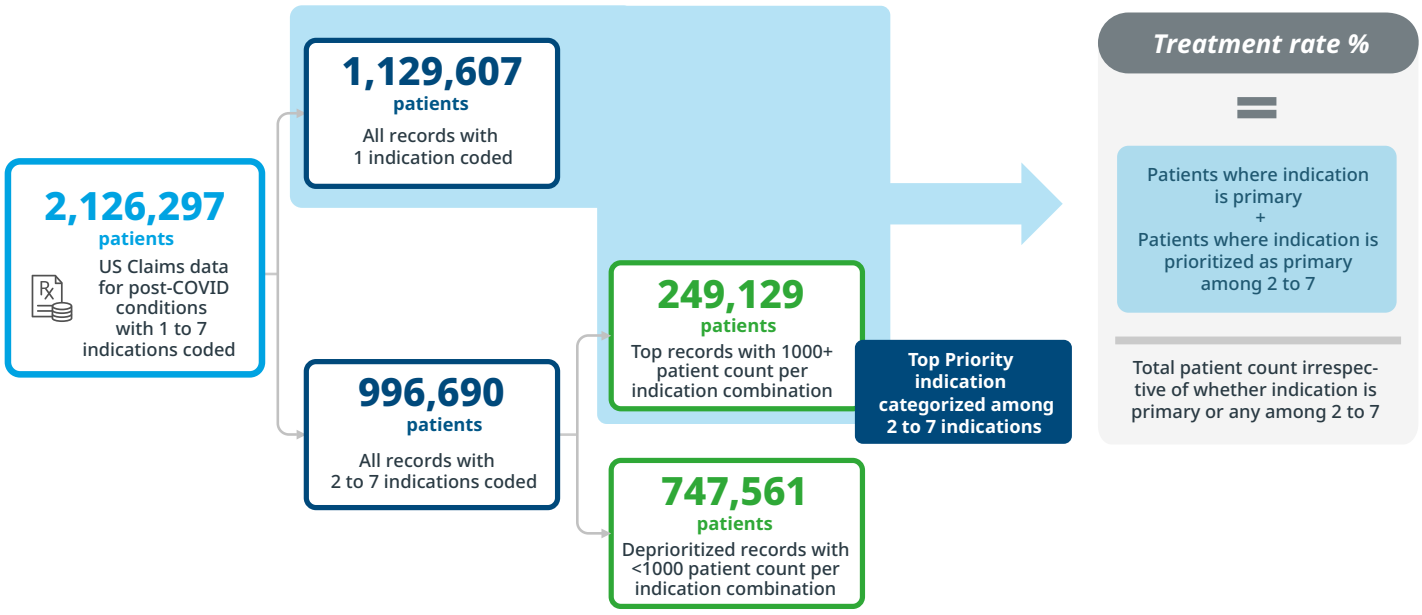
Exhibit 20: Methodology for Therapeutic Cost Estimation



Treatment rate %	Calculated from IQVIA medical Claims data
Price per Day	Weighted Average for the market taken. In few cases assumptions were worked upon
Days of Therapy	IQVIA expertise for conservative estimates for Days of Therapy for each indication

Source: IQVIA intellectual property

Exhibit 21: Treatment Rate for Post-COVID Conditions



Source: IQVIA intellectual property; IQVIA medical open claims database, June 2021

Notes on sources

IQVIA medical open claims database provides insights into what takes place during a patient's visit with their physician. IQVIA receives more than 1.7 billion electronic medical claims per year including information on patient level diagnosis, procedures, and in-office treatments for visits to U.S. office-based professionals, ambulatory and general healthcare sites. All data is anonymous at the patient level but contains an encrypted yet persistent patient code that permits analytics to be conducted.

MIDAS® is a unique platform for assessing worldwide healthcare markets. It integrates IQVIA's national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes, and provides estimated product volumes, trends, and market share through retail and non-retail channels. MIDAS data is updated monthly and retains 12 years of history.

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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

CHAITALI PHADKE
Associate Consultant,
Business Strategy and Insights Center Of Excellence,
IQVIA

Chaitali is a pharmacist by education and has more than four years of experience in pharma/ life sciences consulting. She currently works as an associate consultant in Business Strategy and Insights Center Of Excellence based in Bangalore, India. She is well versed in data analysis and interpretation, market estimation and landscape assessment, competitive intelligence and KOL identification.

Chaitali did her post-graduation in pharmacy from National Institute of Pharmaceutical Education and Research, NIPER and graduation from Nagpur University.

SURAJ PRASAD
Principal, Business Strategy & Insights CoE,
IQVIA

Suraj Prasad has more than 19 years of experience working with life sciences and consulting firms, and currently leads the Business Strategy and Insights Center of Excellence. He also is part of the innovation ventures team. He has a strong understanding of strategic planning and business development and has executed projects in a range of therapy areas and markets, including onsite delivery in U.S., Europe, South East Asia, Middle East and Africa. He is also involved in development of AI-based products and solutions in collaboration with multi-disciplinary teams across IQVIA

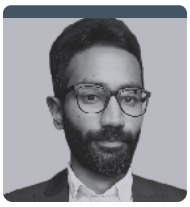
Suraj did his postgraduate in Management from Indian Institute of Management, Kozhikode and is a Pharmacy Graduate from NGSMIPS, Mangalore University.

DR. KUNAL PURI
Senior Consultant,
Business Strategy & Insights CoE,
IQVIA

Dr. Kunal Puri is a clinician by training with more than eight years of academic, clinical and health consulting experience. He currently works as a Senior Consultant in the Business Strategy & Insights Center of Excellence based in Bangalore, India.He provides clinical expertise for varied spectrum of projects across multiple teams.

Dr. Puri specializes in the study of hematological disorders including bleeding disorders such as hemophilia and von Willebrand Disease. He also has a keen interest in the study of cancers as well as rare metabolic, genetic and emerging diseases like COVID-19, Ebola Virus

He graduated as an MBBS and received his doctorate from the Rajiv Gandhi University of Health Sciences, Bangalore.



VIBHU TEWARY
Project Director, IQVIA Institute for Human Data Science

Vibhu Tewary is a Project Director at the IQVIA Institute for Human Data Science and is based out of New York, NY. His key areas of interest include healthcare policy, global market access, and economic modeling. Vibhu has authored multiple reports on global healthcare policy and market access. Prior to joining IQVIA, he worked as a researcher in a policy think tank in India. Vibhu did his undergraduate studies at the Indian Institute of Technology, Madras, and holds an MBA from Duke University.

About the Institute

The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry and payers.

Research Agenda

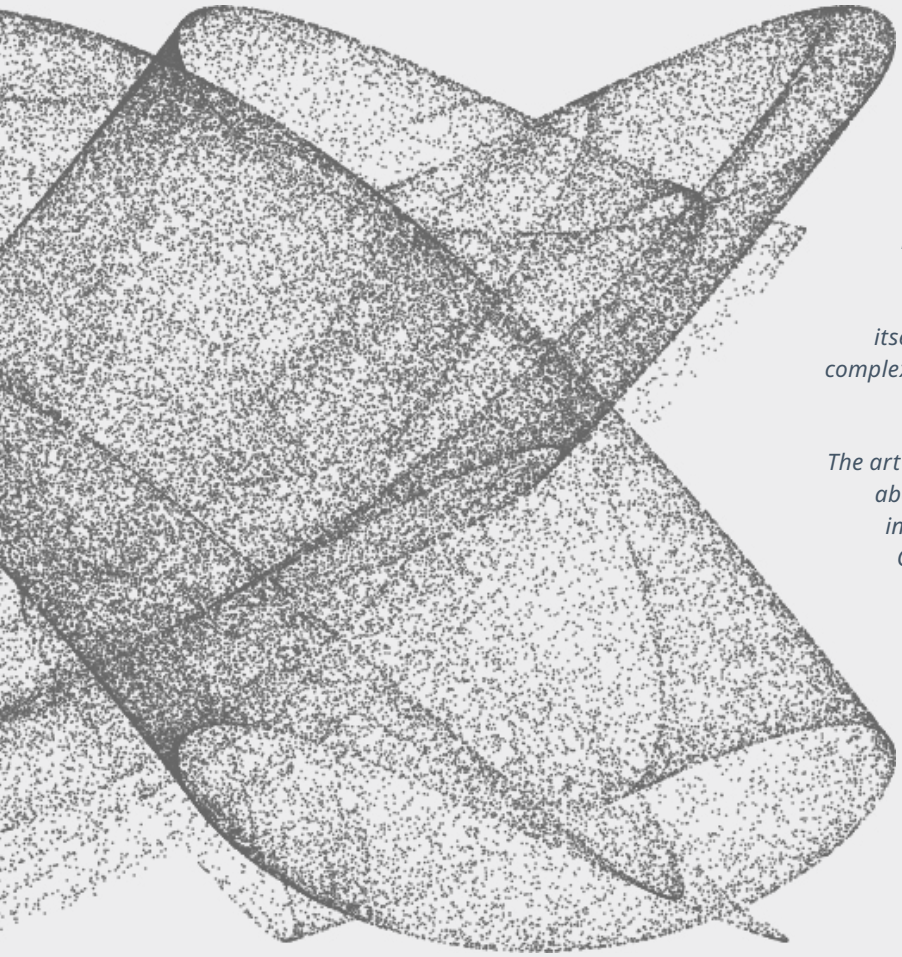
The research agenda for the Institute centers on 5 areas considered vital to contributing to the advancement of human health globally:

- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

Guiding Principles

The Institute operates from a set of guiding principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.



The IQVIA Institute for Human Data Science is committed to using human data science to provide timely, fact-based perspectives on the dynamics of health systems and human health around the world. The cover artwork is a visual representation of this mission. Using algorithms and data from the report itself, the final image presents a new perspective on the complexity, beauty and mathematics of human data science and the insights within the pages.

The artwork on the report cover is created from information about incidences of post-COVID conditions. The dataset includes information about incidences of various post-COVID conditions by indication and associated organ system in the U.S. and globally.

IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

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