Rare Disease Network

APEC

Life Sciences Innovation Forum

COVID-19 & Rare Diseases: Lessons for Rare Disease Policy and Resilient Health Systems

APEC Life Sciences Innovation Forum (LSIF) Rare Disease Network

April 2021

Executive Summary

- Many people living with a rare disease in APEC economies are vulnerable to COVID-19 infection and complication due to their underlying disease, symptoms, or treatments.
- Patients, families, and caregivers have also faced disruptions to rare disease screening, diagnosis, clinical trials, treatment, and care due to limited healthcare capacity, public movement restrictions, and changes in health-seeking behaviors.
- In a survey of APEC health officials in mid-2020, 60% reported that COVID-19 was having little or no impact to rare disease policymaking or planning.
- At the same time, working-level officials and other non-government stakeholders reported some delays in processes and decisions due to remote work and preoccupation of senior officials.
- Ministries of Health with formal entities focused on rare diseases appeared to report less significant impacts.
- The APEC Rare Disease Network held a series of "Virtual Consultations on COVID-19 and Rare Diseases" in Chile (30 October 2020), Peru (2 November 2020), and Malaysia (10 December 2020) to further explore these issues.
- The following lessons were identified in the findings and feedback from the survey and the virtual consultations:
    - Ensure quarantines, stay-at-home mandates, and other public health measures such as testing and access to personal protective equipment are designed with appropriate prioritization, flexibilities, and support for people living with a rare disease and their families.
    - Ensure the adoption of concrete measures and protocols warranted by the complex needs of rare disease patients in the provision of emergency healthcare during the COVID-19 crisis.
    - Even if temporarily, allow for the transition of at least some hospital-based and/or physician-administered therapies (infusions and injections) to the home setting as appropriate and ensure public and private payment mechanisms reimburse providers for these home-based services.
    - Encourage and facilitate the use of telemedicine by addressing the current reimbursement and licensing regulations and by creating an enabling regulatory environment for digital health technologies, including in the context of monitoring clinical trials.
    - Ensure rare disease patients covered by public or private insurance can obtain a sufficient supply of prescription medication, including specialty drugs, by relaxing restrictions on early refills, out-of-network pharmacies, and coverage for off-formulary prescription drugs if there is not a formulary drug available to treat the insured.
    - Build laboratory and testing capacity to ensure adequate supply for and continuity of newborn screening for rare diseases alongside ongoing PCR and antigen testing for COVID-19.
    - Ensure that pharmacovigilance systems are appropriately resourced and that the available information on risks of adverse reactions, drug interactions and appropriate use of existing chronic treatment are communicated in a clear manner to the patients.
    - Ensure entities responsible for rare diseases within Ministries of Health and high-level advisory committees on rare diseases are formalized, deemed essential personnel, and allowed to continue their activities during public health emergencies to the extent possible.
    - Develop and publish non-binding but comprehensive, whole-of-government, and medium- to long-term plans for addressing rare diseases within the local context in order to mitigate disruptions, postponements, or cancellations of anticipated rare disease programs.
- The APEC Rare Disease Network stands ready to support APEC member economies and other stakeholders if they should decide to consider implementing any or all of the lessons for rare disease policy and resilient health systems.

Introduction

Responding to the COVID-19 pandemic has demanded significant attention and resources of Asia-Pacific Economic Cooperation (APEC) forum leaders and working-level health policymakers alike. Teams have been reassigned, budgets have been reallocated to the extent possible, and the collective focus of APEC governments has narrowed on the urgent task at hand. While these are in many cases necessary actions to manage and eliminate the COVID-19 pandemic considering the local contexts and domestic priorities of APEC member economies, it is also vitally important that APEC health systems continue to provide essential services without disruption or loss of quality.

The resilience of health systems and the continuity of healthcare services is especially critical for people living with a rare disease and their caregivers, who already face a unique and complex journey navigating the many existing barriers to diagnosis, treatment, and care for their often life-threatening, often genetic conditions. At the same time, the momentum built in recent years for comprehensive rare disease policy and planning at the economy-level should not be lost to the urgency and magnitude of the COVID-19 pandemic. Indeed, some shifts are required. But just as health systems in APEC economies should be resilient and ensure continuity of healthcare services, Ministries of Health in APEC economies also should be resilient and work to ensure the continuity of rare disease policymaking and planning while simultaneously responding to public health emergencies now and in the future.

Recognizing this challenge, the APEC Life Sciences Innovation Forum (LSIF) Rare Disease Network (RDN) seeks to support APEC government stakeholders to ensure rare disease diagnosis, treatment, and care is not impeded by the COVID-19 pandemic and future public health emergencies, and to make the case for maintaining and strengthening ongoing rare disease policymaking and planning efforts. To this end, this Discussion Paper is intended to serve as a resource for APEC policymakers by summarizing the key impacts of the COVID-19 pandemic and response (1) on people living with a rare disease, their families, and caregivers, and (2) on rare disease policymaking and planning. The contents of this Discussion Paper were informed and validated by APEC Virtual Consultations on COVID-19 and Rare Diseases in Chile (30 October 2020), Peru (2 November 2020), and Malaysia (10 December 2020). In its conclusion, the Discussion Paper offers recommendations based on multistakeholder feedback and on best practices which have been identified in APEC economies.

Impacts of COVID-19 on people living with a rare disease in APEC economies

Rare disease patient advocacy groups including Rare Diseases International (RDI), Asia-Pacific Alliance of Rare Disease Organizations (APARDO), U.S. National Organization for Rare Disorders (NORD), and Canadian Organization for Rare Disorders (CORD), among others, have surveyed thousands of people living with a rare disease among the +200 million living in the APEC region and +400 million worldwide in order to examine and address the impacts of the COVID-19 pandemic on their health and well-being.

People living with a rare disease and their caregivers in APEC economies already face a unique and complex journey navigating the many barriers to diagnosis, treatment, and healthcare services. The ongoing assessment efforts of patient advocacy groups have revealed how and to what extent the COVID-19 pandemic has further

complicated the journey of patients and caregivers. At the same time, the pandemic itself has exposed the fragility of health systems in APEC economies. In this section, the APEC Rare Disease Network aims not only to highlight the major impacts of the COVID-19 pandemic on people living with a rare disease, but also and more importantly to encourage government officials and health policymakers in APEC economies, especially those working on rare disease policymaking and planning, to identify and implement strategies for ensuring the continuity of healthcare services to the extent possible during public health emergencies.

Vulnerability to COVID-19 infection and complication

Many people living with a rare disease in APEC economies are vulnerable to COVID-19 infection and complication for a number of reasons. Some treatments which are life-saving and essential for the well-being of people living with certain rare disease (e.g., immunosuppressants, chemotherapies) may at the same time render them more vulnerable to viral infections and related complications. As such, rapid diagnosis of COVID-19 in people living with a rare disease is all the more important. Yet current COVID-19 testing guidelines in many APEC economies do not consider children, which comprise the majority of rare disease patients, to be a vulnerable population as is the case for health professionals, elderly, and those with chronic health conditions like diabetes, hypertension, and cardiovascular diseases. (Beyond testing, COVID-19 prevention policies in general tend to exclude children as they have been considered low-risk or asymptomatic until recently.) In effect, people living with a rare disease and their caregivers in many economies still face difficulties accessing COVID-19 testing in a timely manner.

People living with a rare disease who become infected and symptomatic are at increased risk of complication. There are few to no protocols or treatment guidelines in place in hospitals or health systems which address the simultaneous treatment and care for a rare disease and COVID-19. Due to infection control plans, these rare disease patients with COVID-19 may be hospitalized in centers that are not their usual place of care which often lack the required expertise and which often fail to connect with their regular caregivers. In these cases, medical products to treat COVID-19 (e.g., anti-inflammatory, analgesics, anesthetics, mechanical ventilation), which may be effective in the general population, could have severe contraindications for certain rare diseases or lead to severe drug interactions with ongoing rare disease treatments.

Disruptions to rare disease screening, diagnosis, treatment, and care

According to EURORDIS, 90% of people living with a rare disease have experienced interruptions of the care they receive for their rare disease since the beginning of the COVID-19 pandemic; and 30% perceive such interruptions definitely or probably would have a life-threatening impact. Based on qualitative evidence from RDI, APARDO, and domestic patient advocacy groups involved with the APEC Rare Disease Network, this alarming proportion is likely similar for the +200 million rare disease patients in the APEC region.

Given their vulnerability to COVID-19 infection and complication, many people living with a rare disease and their caregivers may face psychological disruption to their normal health-seeking behaviors. Indeed, EURORDIS found that half of those rare disease patients who receive follow-up care through hospitals did not seek care because they were fearful of COVID-19 infection. Many other rare disease patients and caregivers may also fear hospitals for concerns about appropriate care due to their underlying condition. People living with a rare disease

may also face pressure to self-medicate in an attempt to prevent COVID-19 or treat their rare disease, which could increase their risk of using sub-standard or falsified medicines.

In addition to the fear and stress of COVID-19 infection or complication, the material impacts of the pandemic on human and technical capacity are also causing disruptions to rare disease care. Many appointments for rare disease screening and diagnostic tests (e.g., genetic sequencing, medical imaging, blood panels) have been postponed or cancelled due to the lack of medical personnel or the need to use laboratory facilities for COVID-19 testing. Even medical and surgical interventions, especially those that are considered 'elective' or 'non-essential', have been cancelled or postponed. In addition, as surveyed by EURORDIS and RDI:

- Surgeries and transplants have been cancelled or postponed for more than a half of the rare disease patients who need them.

- 80% of patients have had appointments for rehabilitation therapies (e.g., speech, physical) postponed or cancelled; and a recent WHO survey reported that rehabilitation is the most commonly disrupted service among the 120 countries that reported COVID-19 disruptions. They do not have the necessary PPE or sufficient staff to provide them in the home setting.

- Nearly 70% have seen their appointments with the general practitioners or specialists who provide care for the rare disease cancelled.

- Almost 30% of patients reported that the hospital or clinical units that normally provided their care were closed entirely.

- Almost 60% do not have access to medical therapies at home or at the hospital (e.g., infusions, chemotherapy, hormonal treatment).

- More than 60% do not have access to the routine testing (e.g., blood, cardiac) and medical imaging critical to their care.

Lastly, many clinical trials were cancelled or postponed on the basis of the safety of patients who are unable or not willing to travel to the clinical sites, or because healthcare professionals are re-assigned to other tasks. But some of these trials have returned to enrollment, aided significantly by regulatory flexibilities for remote trial monitoring and virtual visits.

Impacts of COVID-19 on rare disease policymaking & planning in APEC economies

Just as patient advocacy groups like RDI are monitoring the impact of the COVID-19 pandemic and response on people living with a rare disease, the APEC Rare Disease Network surveyed its network of government, academic/clinical, industry, and patient/civil society stakeholders from June to August 2020 to examine how and to what extent the pandemic and the response have affected rare disease policymaking and planning in APEC economies.

While a WHO survey earlier this year found that staff at ministries of health in 94% of responding WHO members were partially or fully reassigned from NCDs to COVID-19,[1] the APEC Rare Disease Network survey found results significantly more optimistic for rare diseases in particular. Of the 76 stakeholders[2] surveyed from 15 of the 21 APEC economies[3], 25% said the COVID-19 pandemic and response had a moderate impact or effect on government policymaking/planning related to rare diseases or orphan drugs, while another 25% said it had only a little impact or effect. Among government officials in particular, 60% reported little or no impact to rare disease policymaking/planning related to rare diseases or orphan drugs. These responses for rare disease policymaking and planning were similar for perceived impact to regulatory review and approval of medical products for rare diseases. Thirty percent (30%) of respondents reported a moderate impact or effect, while 22% said that COVID-19 had no impact or effect at all.

The majority of respondents also expected any impacts or effects to rare disease policymaking and planning efforts to dissipate rather quickly. Eighty-two percent (82%) of respondents said that either they or the government was involved in rare disease policymaking and planning in 2019; and while this proportion decreased to 64% during the time of the survey (June to August 2020), 82% of respondents again expect to participate in RD policymaking and planning by the end of 2020. Indonesia, Chinese Taipei, Singapore, and China were among the economies reporting the least perceived impact of the COVID-19 pandemic and response to rare disease policymaking and planning. Chile, Peru, and New Zealand were among the economies reporting the most perceived impact.

Despite the optimistic results of the APEC Rare Disease Network survey, qualitative and anecdotal feedback and evidence suggest a more nuanced situation in APEC economies. While health policymakers responsible for rare diseases may still be formally and/or officially in place within their portfolios or departments, their attention and time still appear to be limited in many cases, demonstrated by a significant increase in response times to APEC Rare Disease Network correspondence. Many if not all working-level officials continue to work remotely, which could impact the efficiency and effectiveness of any ongoing rare disease policymaking and planning efforts. Moreover, many of the newer rare disease initiatives in many APEC economies require more upfront approvals from senior executives in Ministries of Health. While working-level policymakers may still be in place for rare diseases, the senior executives on the other hand remain almost entirely focused on the COVID-19 response. In addition to government officials, patients, families, and caregivers who are essential to and participating in rare disease policymaking and planning are likely unable to maintain a sufficient level of involvement at this time.

In addition, the survey was not designed to measure whether and to what extent Ministries of Health and Finance may be reallocating funds from rare disease programs to the COVID-19 response in the short-term and/or pandemic preparedness in the long-term, where funding for rare disease treatment and diagnosis is not

[1] https://www.who.int/news-room/detail/01-06-2020-covid-19-significantly-impacts-health-services-for-noncommunicable-diseases

[2] Nearly half of respondents were either government officials or academic/clinical experts advising the government, while 25% were patient advocacy group leaders and 26% were industry representatives. The majority of respondents were senior executives: 74% percent were either “Head”, “Director”, “Manager”, “Executive”, or “President”.

[3] APEC member economies that responded to the survey include Thailand, Malaysia, Chile, China, Japan, Peru, Singapore, Chinese Taipei, Republic of Korea, Mexico, United States, Viet Nam, Australia, Indonesia, and New Zealand.

hypothecated or protected by legislation or regulation. At a higher level, in order to pay for economic stimulus now in response to the pandemic, governments may have to reduce spending or increase revenue, which could affect funding for rare diseases programs.

The COVID-19 pandemic has led to one of the steepest and deepest economic declines in recent history. In response, governments have committed fiscal and monetary support which is likely to exceed 10-15% of GDP during 2020 alone[4], which will leave economies facing levels of public debt and fiscal deficits that many will struggle to manage over the coming decade. The economic consequences of COVID-19 will put governments under pressure to contain future healthcare expenditure. In turn, governments will also face calls for more efficient and sustainable use of healthcare resources, which will mean "doing more for less"; calls for greater centralization of decision-making for resource allocation; and increased pressure to "optimize" scarce resources by prioritizing efficiency over effectiveness. Each stated consequence of this economic fallout will place a significant and disproportionate burden on rare disease programs, where cost-effectiveness is an insufficient and inappropriate measure for optimization due to a small number of patients and the life-threatening, debilitating nature of their rare diseases.

All of this said, however, there are some positive long-term impacts of the COVID-19 pandemic and response emerging in a number of APEC economies for rare disease policymaking and planning. COVID-19 has and will continue to force all stakeholders to rethink the delivery of healthcare services. Many components of the pandemic response could be repurposed and utilized to help ensure the continuity of rare disease policymaking, from embracing virtual and hybrid engagements and meetings at all levels of government to protecting the time, attention, and funding of rare disease policymakers by institutionalizing and formalizing rare disease departments and divisions within Ministries of Health.

Lessons for consideration by APEC economies

To support people living with a rare disease during COVID-19 and future public health emergencies

- Ensure quarantines, stay-at-home mandates, and other public health measures such as testing and access to personal protective equipment are designed with appropriate prioritization, flexibilities, and support for people living with a rare disease and their families.

- Ensure the adoption of concrete measures and protocols[5] warranted by the complex needs of rare disease patients in the provision of emergency healthcare during the COVID-19 crisis.

- Even if temporarily, allow for the transition of at least some hospital-based and/or physician-administered therapies (infusions and injections) to the home setting as appropriate and ensure public and private payment mechanisms reimburse providers for these home-based services.

[4] International Monetary Fund

[5] https://download2.eurordis.org/pressreleases/EURORDISstatement_COVID19Triage.pdf#page=2

- Encourage and facilitate the use of telemedicine by addressing the current reimbursement and licensing regulations and by creating an enabling regulatory environment for digital health technologies, including in the context of monitoring clinical trials.

- Ensure rare disease patients covered by public or private insurance can obtain a sufficient supply of prescription medication, including specialty drugs, by relaxing restrictions on early refills, out-of-network pharmacies, and coverage for off-formulary prescription drugs if there is not a formulary drug available to treat the insured.

- Build laboratory and testing capacity to ensure adequate supply for and continuity of newborn screening for rare diseases alongside ongoing PCR and antigen testing for COVID-19.

- Ensure that pharmacovigilance systems are appropriately resourced and that the available information on risks of adverse reactions, drug interactions and appropriate use of existing chronic treatment are communicated in a clear manner to the patients.

To support rare disease policymaking & planning during COVID-19 and future public health emergencies

- Ensure entities responsible for rare diseases within Ministries of Health and high-level advisory committees on rare diseases[6] are formalized, deemed essential personnel, and allowed to continue their activities during public health emergencies to the extent possible.

- Develop and publish non-binding but comprehensive, whole-of-government, and medium- to long-term plans for addressing rare diseases within the local context in order to mitigate disruptions, postponements, or cancellations of anticipated rare disease programs.[7]

[6] See Recommendation 2.2 in the *APEC Action Plan on Rare Diseases*
[7] See Recommendation 10.1, *APEC Action Plan on Rare Diseases*