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ADDRESSING THE DUAL BURDEN OF LONG COVID AND NONCOMMUNICABLE DISEASES IN ARMENIA: A STRATEGIC POLICY APPROACH

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Abstract

In the post-COVID-19 era, Armenia faces a dual epidemiological challenge: the persistent health burden of long COVID and a concurrent rise in noncommunicable diseases, such as obesity, diabetes, hypertension, oncological diseases, and mental health disorders. National health surveillance reports, including the Health System Performance Assessment (2022) and Health and Health Care Yearbooks (2022–2024) indicate a steady increase in noncommunicable disease-related morbidity and mortality, particularly among middle-aged and elderly populations.

A nationwide observational study assessing public knowledge, attitudes, and practices regarding long COVID, as well as its burden among adults, revealed significant post-COVID sequelae. Approximately 26.6% of respondents reported seeking medical care for long COVID symptoms, while 36% experienced persistent fatigue, 51.4% reported musculoskeletal pain, 27.8% experienced memory disturbances, and 43% reported anosmia/ageusia. Notably, 24.7% self-medicated, often with antibiotics, frequently without physician guidance, highlighting critical gaps in public awareness and healthcare access. These findings underscore the urgent need for an integrated response.

This paper applies the Grading of Recommendations Assessment, Development, and Evaluation framework together with Evidence-to-Decision framework to translate observational evidence into policy. We propose a digitally enhanced, multidisciplinary care model for long COVID management within the primary healthcare system in Armenia. A central innovation is the integration of artificial intelligence tools for real-time triage, personalized care pathways, and predictive analytics to improve surveillance, treatment precision, and overall health system efficiency.

Policy recommendations include establishing a standardized long COVID case definition, adopting national clinical protocols, integrating artificial intelligence-driven tools into the e-health infrastructure in Armenia, and expanding rehabilitation and mental health services. By aligning long COVID management with noncommunicable diseases prevention strategies and digital health transformation through a unified, person-centered approach, Armenia can strengthen system resilience, improve quality-adjusted life years, and accelerate progress toward the 2030 global health agenda.

Keywords: *long COVID, SDG 3, noncommunicable diseases, burden, DALYs, QALYs, health policy, artificial intelligence.*

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has posed an unprecedented challenge to public health systems globally, particularly in low- and middle-income countries. More than 777 million cases of COVID-19 and over 7.1 million fatalities have been documented since the outbreak [*WHO, 2025*]. In Armenia, the pandemic has not only strained acute care services but also aggravated pre-existing health burdens, most notably the high prevalence of noncommunicable diseases, which account for over 90% of all-cause mortality [*NIH, 2023, 2024, 2025*].

COVID-19 is an infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It can be asymptomatic or produce mild symptoms such as fever, cough, sore throat, malaise, fatigue, nausea, vomiting, and diarrhea, with critical manifestations including respiratory failure, septic shock, and/or multiple organ dysfunction [*Da Rosa Mesquita R. et al., 2021; NIH 2023; Gulick R et al., 2023*]. In addition, many people may exhibit chronic alterations associated with neuropsychiatric, endocrine, gastrointestinal, and musculoskeletal symptoms - even several months after disease onset - developing long COVID or post-acute COVID-19 syndrome [*Wang B. et al., 2022; Nalbandian A. et al., 2021*] (*Fig. 1*).

Long COVID or post-acute sequelae of SARS-CoV-2 infection (PASC) refers to symptoms of COVID-19 that persist for between 4 and 12 weeks or a post-acute syndrome at over 12 weeks after the onset of acute symptoms that cannot be attributed to any other illnesses (*Fig. 2*).

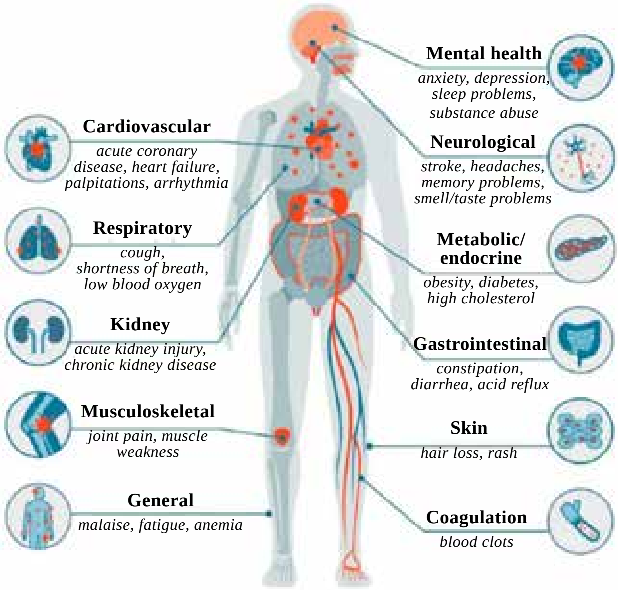

FIGURE 2. *Long COVID symptoms grouped by affected organ systems and functions.*

Furthermore, long COVID has been observed in a diverse spectrum of COVID-19 regardless of whether the initial illness was mild or severe. Thus, it could be reasonably hypothesized that a more devastating effect could occur in the long COVID period than in the acute period of COVID-19. The incidence is estimated at 10–30% of non-hospitalized cases, 50–70% of hospitalized

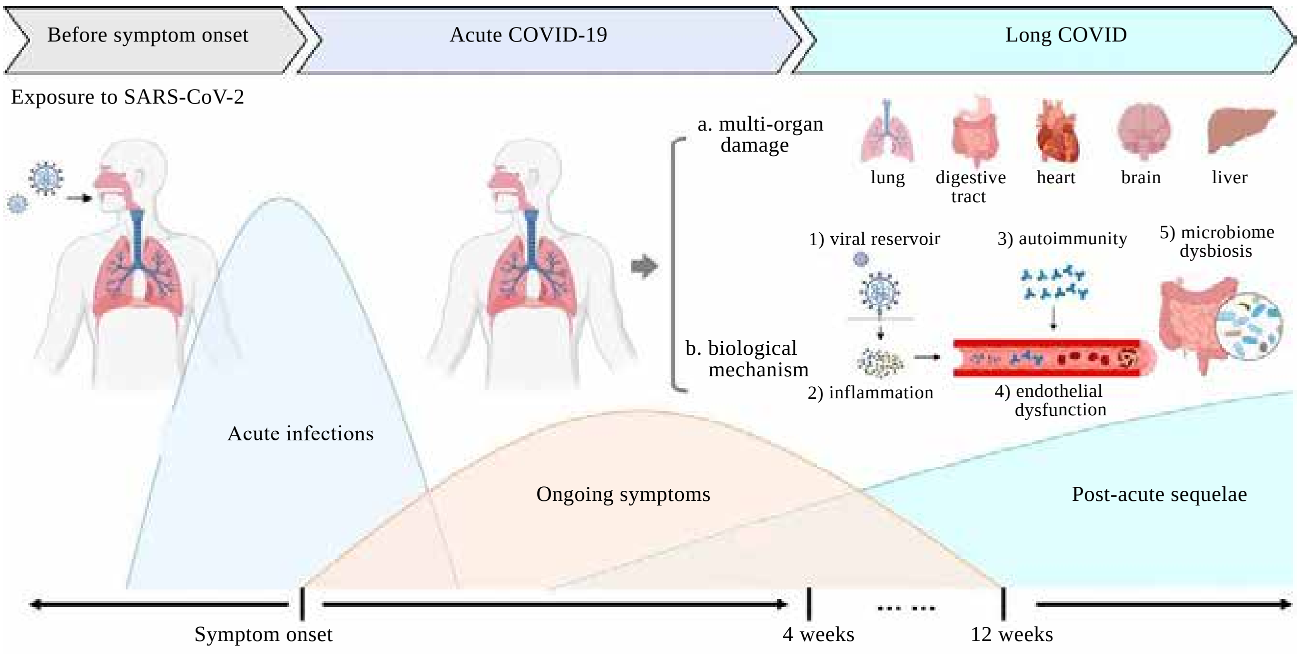

FIGURE 1. *Timeline and multi-organ damage in Long COVID. The diagram illustrates potential pathophysiological mechanism underlying Long COVID.*

cases [*Bull-Otterson et al., 2022; Ceban F. et al., 2022*] and 10–12% of vaccinated cases [*Al-Aly Z. et al., 2022; Ayoubkhani D. et al., 2022*]. This multifaceted condition presents a significant and emerging burden on the primary health care system in Armenia [*HSPA, 2022*].

The pathogenesis of Post-acute COVID-19 syndrome is unclear and may be multifactorial, involving prolonged inflammation, immune-mediated vascular dysfunction, thromboembolism, and nervous system dysfunction (*Fig. 2, 3, 4*). Persisting reservoirs of SARS-CoV-2 in tissues [*Proal A. D. et al., 2021; Swank Z. et al., 2022*]; immune dysregulation [*Proal A. D. et al., 2021; Klein J. et al., 2023; Glynne P. et al., 2022; Phetsouphanh, C. et al., 2022*]; with or without reactivation of underlying pathogens, including herpesviruses such as Epstein–Barr virus (EBV) and human herpesvirus 6 (HHV-6) among others [*Proal A. D. et al., 2021; Klein J. et al., 2023; Zubchenko S. et al., 2022; Peluso M. J. et al., 2022*]; impacts of SARS-CoV-2 on the microbiota, including the virome [*Yeoh Y. K. et al. 2021; Liu Q. et al., 2022; Li et al., 2023*].; autoimmunity [*Proal A. D. et al., 2021; Wallukat G. et al., 2021; Su Y. et al., 2022*] and priming of the immune system from molecular mimicry [*Proal A. D. et al., 2021*]; microvascular blood clotting with endothelial dysfunction [*Proal A. D. et al., 2021; Charfeddine S. et al., 2021; Pretorius E. et al., 2022*]; and dysfunctional signaling in the brainstem and/or vagus nerve [*Maltezou H.C. et al., 2021; Proal, A. D. et al., 2021; Spudich S. et al., 2022*].

Among the above factors, a special role is given to aliphatic polyamines. It is generally accepted that the normal level of polyamines in mammals is controlled in three ways. The first is due to the de novo metabolism of the cells of the macroorganism; the second is due to resident microorganisms (bacteria, fungi, viruses) persisting in bioeconics and the third is due to the active absorption and assimilation of polyamines that have entered the gastrointestinal tract with food.

Polyamines were detected in human viruses much later than in bacteriophages. In bacteriophages polyamines were found by the end of the 1950s [Kay D, 1959], and in human viruses since 1971. The presence of individual representatives from the groups of aliphatic polyamines or all of them were simultaneously detected in a very wide range of human viruses, with a very different structure of organization, functional activity, both in vitro and their persistence in the human body. A range of aliphatic polyamines is found in enteroviruses, alphaviruses, flaviviruses, rhabdoviruses, coronaviruses, and bunyaviruses [Mounce B et al., 2016a]. The role of polyamines in the progression of viral infections was first established in bacteriophages [Pererva TP, 2008]. (Fig 5)

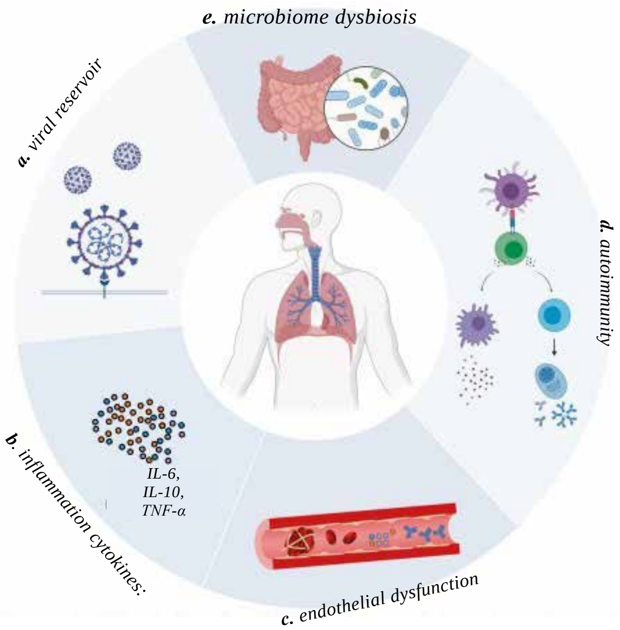

***FIGURE 3.** Potential pathophysiological mechanisms of long COVID. The main hypothesized mechanisms include (a.) viral reservoir, (b.) inflammation, (c.)endothelial dysfunction, (d.) autoimmunity, , and (e.) gut microbiome dysbiosis.*

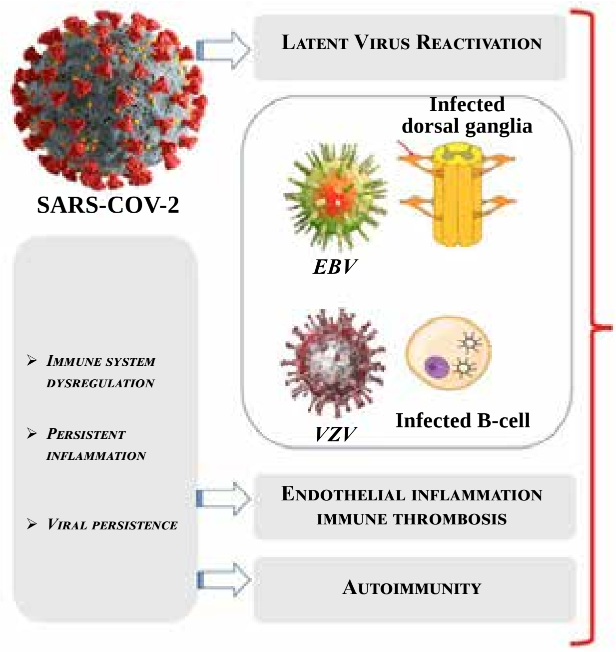

***FIGURE 4.** Immune dysregulation with reactivation of underlying dormant pathogens, including herpesviruses such as Epstein–Barr virus (EBV) and human herpesvirus 6 (HHV-6).*

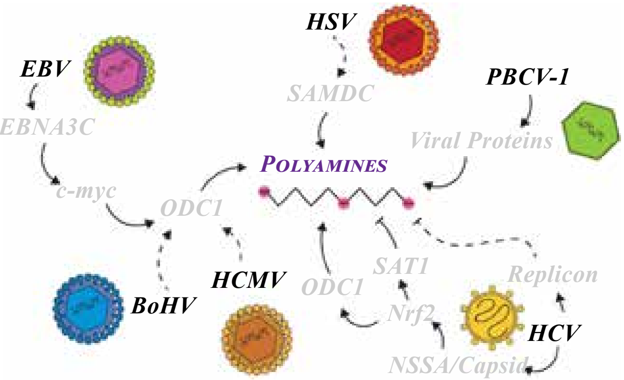

FIGURE 5. Viral manipulation of polyamines in infected cells [Fipro M, Mounce C, 2020]. EBV - Epstein-Barr herpes virus, HSV - herpes simplex virus), BoHV - bovine herpes virus, HCMV - human cytomegalovirus, HCV - hepatitis C virus, PBCV-1 - Paramecium bursaria chlorella virus.

Optimal levels of aliphatic polyamines including putrescine, spermidine, spermine, and cadaverine present in mammals, bacteria, fungi, and viruses contribute to various integrative cellular functions. These include transcription, translation, nucleic acid structuring, nuclear chromatin packaging, genome incorporation into virions, ion channel regulation, and receptor apparatus modulation [*Basu HS et al., 1992; Kalac P., 2014; Gómez GC et al., 2017; Muñoz-Esparza NC et al., 2019; Miller-Fleming L, 2015*].

Polyamines serve a crucial yet relatively unexplored function in viral mechanisms, particularly in coronaviruses, where their presence in virions has not yet been documented. Emerging research indicates polyamines are critical facilitators of viral attachment and penetration into host cells [*Avagyan S.A. et al., 2020*]. Besides their essential role in genome packaging, polyamines also stimulate viral protein activity [*Yoshida S et al., 1976; Osland A, Kleppe K, 1978; Ostrander M, Cheng YC, 1980; Wallace HM et al., 1980, 1981; Kenyon TK et al., 2001*].

A newly identified function of polyamines is their role in viral attachment to mammalian host cells [*O'Hara SD et al., 2014; Kicmal TM, 2019*]. Several human pathogenic viruses, including enteroviruses, flaviviruses, and bunyaviruses, utilize polyamines to facilitate their adhesion to target cells [*Kicmal TM, 2019*]. The initial stage of virus-cell interaction occurs through attachment to the cytoplasmic membrane, where receptor-mediated factors govern the earliest steps of viral entry [*Jolly CL, Sattentau QJ, 2013*]. A key factor in this process is the viral S-glycoprotein, which binds to host-cell receptors such as angiotensin-converting enzyme 2 (ACE2) [*Tipnis SR et al., 2000*] and CD147 [*Zhou Y et al., 2020*].

The significant role of polyamines in viral attachment is further reinforced by the inhibitory effect of difluoromethylornithine (DFMO), an ornithine decarboxylase inhibitor that disrupts polyamine-dependent viral infection pathways (Fig. 5. DFMO, approved by the U.S. Food and Drug Administration (FDA), exhibits notable antiviral activity against multiple RNA viruses [*Mounce BC et al., 2016*] while maintaining low toxicity and causing only mild, transient side effects [*Milord F et al., 1992*] (Fig. 6).

Polyamine depletion strategies serve as a protective mechanism by host cells, curbing viral attachment and replication while remaining well tolerated in most human tissues. A novel therapeutic approach is emerging that involves employing polyamine-blocking agents or incorporating polyamine-deficient diets to limit viral spread.

Coronaviruses, among other human pathogens, exploit polyamines to enhance cellular attachment. The crucial role of polyamines is evident in the suppression of this attachment mechanism upon DFMO treatment [*Mounce B et al., 2016a; Milord F et al., 1992*].

Fundamental research has established that polyamine depletion significantly disrupts the early stages of the viral life cycle in mammalian hosts. This mechanism represents a defensive strategy that mammalian cells employ to mitigate viral infection risks. A crucial conclusion drawn from these studies suggests that polyamine deficiency in mammalian organisms restricts this essential

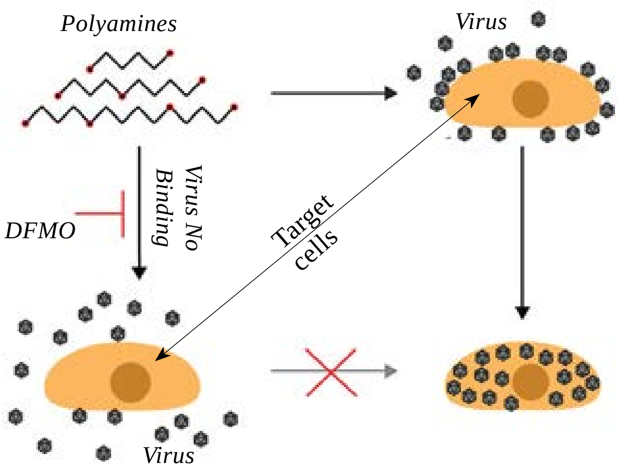

FIGURE 6. Polyamines promote binding virus to cell surfaces and initiate infection, while polyamine depletion via DFMO decreases binding [Kicmal T, 2019]

stage required for nonstructural protein expression, thereby markedly inhibiting viral replication [Mounce B et al., 2016a; Milord F et al., 1992; Firpo MR, Mounce BC, 2020; Wang K, 2020].

To achieve polyamine depletion, three approaches can be utilized either independently or in combination:

- ➢Pharmacological intervention using drugs containing natural or synthetic polyamine inhibitors
- ➢Antibacterial agents that suppress polyamine synthesis in microbial cells
- ➢Dietary modifications, incorporating polyamine-deficient foods (commonly known as a "polyamine-deficient diet") [Avagyan et al., 2021, 2022, 2023].

Risk factors potentially include female sex, type 2 diabetes, EBV reactivation, the presence of specific autoantibodies [*Su Y. et al., 2022*], connective tissue disorders [*Renz-Polster H. et al., 2022*] attention deficit hyperactivity disorder, chronic urticaria and allergic rhinitis [*Merzon E. et al., 2022*] , although a third of people with long COVID have no identified pre-existing conditions [*FAIR Health, 2022*].

While comprehensive national statistics on long COVID remain limited, clinical reports and patient follow-ups indicate a growing number of cases presenting with persistent fatigue, respiratory symptoms, cognitive impairments, and cardiovascular complications. These symptoms often overlap with pre-existing or emerging chronic conditions, leading to delays in diagnosis and fragmented care. Significant disruptions were observed in primary health care (PHC) essential services [*Dupraz J et al., 2022*] provided to patients living with chronic conditions such as cancer [*Riera R. et al., 2021; Jones D. et al., 2020; WHO Rapid Assessment, 2020*], cardiovascular diseases [*WHO 2023; Mafham M.M. et al., 2020*], diabetes [*WHO Rapid Assessment, 2020*], chronic respiratory diseases [*WHO, 2020*] and other noncommunicable diseases - leaving patients at increased risk of severe illness from COVID-19, and worsening morbidity related to these conditions [*Matenge S. et al., 2022; Yadav U.N. et al., 2021; Parkinson A. et al., 2021*].

This disruption had the potential to result in adverse effects on individual and population health by negatively impacting preventable and treatable diseases [*Bilinski A. et al., 2020; Wu J. et al., 2021; Dupraz J et al., 2022; WHO, 2020, 2022*]. During the pandemic, countries encountered various challenges and were obligated to make difficult decisions to maintain essential health services through strategic planning and coordinated actions [*WHO 2020, 2021, 2022*].

Primary healthcare (PHC) is the cornerstone of healthcare systems, serving as the basis for universal health coverage; any disruption of services provided in this setting can be associated with a major impact on health outcomes and public health [*WHO 2021, 2022; Kumpunen S et al., 2022*]. PHC plays a decisive role in the prevention and treatment of diseases, especially for vulnerable populations: children, older adults, and people living with chronic conditions and disabilities [*WHO 2021, 2022*].

Additional advantages for better health care are potential by incorporating digital health technologies (DHTs) in PHC [*WHO 2021; Abdulazeem H.M. et al., 2025*]. DHTs are transforming healthcare delivery, enabling more precise diagnostics and personalized treatment plans and saving providers time and effort [*WHO 2021; Abdulazeem H.M. et al., 2025*]. A wide variety of DHT modalities using simple technologies, such as teleconsultations, or complicated ones, such as those utilizing artificial intelligence artificial intelligence (AI), enables this transformation. Active engagement of physicians in digital health transformation through education opportunities, collaboration with AI developers in developing AI-assisted DHTs, and interaction with policymakers to support efficient integration strategies in primary care is of crucial need [*Borges do Nascimento I, et al., 2023*].

In Armenia, PHC service utilization declined remarkably in 2020 (1 388 724 visits) compared to 2019 (2 055 102 visits) [*Andreasyan D. et al., 2021*]. According to experts, underutilization of PHC services, especially for chronic conditions such as cardiovascular and respiratory diseases, could lead to excess deaths in Armenia [*Andreasyan D. et al., 2021*]. One of the reasons for the underutilization of PHC services were the COVID-19 restrictions. Another reason for underutilization of services was the 44-day war with Azerbaijan, which caused displacement, injury and death of thousands of people in Armenia and diverted attention away from COVID-19 prevention and control measures, additionally exacerbating the pandemic situation [*Markosian C. et al., 2022*].

When viewed through the lens of Sustainable Development Goals (SDG), especially SDG 3, Armenia faces a double challenge - managing Long COVID while containing the escalating noncommunicable disease (NCD) epidemic [Kluge *HH, et al., 2020; WHO* 2023].

The lack of structured protocols, designated rehabilitation services, and consistent follow-up strategies for long COVID patients in Armenia presents significant challenges to the delivery of quality care. With nearly 30% of COVID-19 patients reporting persistent symptoms lasting beyond 12 weeks, the need for a coordinated, multidisciplinary approach is urgent.

In the early stages of the COVID-19 pandemic, Armenia experienced widespread overuse of antibiotics and corticosteroids, particularly during the acute phase of infection. Data from WHO (2024) indicate that while only 8% of hospitalized patients with COVID-19 had bacterial co-infections requiring antibiotics, three out of four (approximately 75%) of hospitalized COVID-19 patients received antibiotics in the absence of confirmed bacterial co-infection, just in case, and 30% were administered corticosteroids outside the scope of WHO clinical management guidelines [*WHO, 2021*].

This indiscriminate use of medications contributed to the growing threat of antimicrobial and adversely impacted patient outcomes, particularly among those experiencing Long COVID.

The inappropriate administration of corticosteroids also heightened susceptibility to latent infection reactivation, further complicating the clinical management of Long COVID cases.

Emerging evidence highlights the broader consequences of this pharmacological overuse. Excessive use of antibiotics and corticosteroids has been shown to disrupt the gut microbiome, potentially triggering immune dysregulation and promoting a state of chronic low-grade inflammation known as "inflammaging" [*Bonafè M. et al., 2022; Zazzara M. B. et al., 2022*], which is increasingly recognized as a contributor to the persistence and severity of Long COVID. These findings underscore the interconnection of medication stewardship, immune resilience, and the burden of chronic diseases in the post-pandemic era.

MATERIALS AND METHODS

To evaluate the impact of various factors on the risk of new-onset noncommunicable diseases in the context of PASC and Long COVID, and to inform policy recommendations, a comprehensive methodological approach was used:

Evidence to Decision (EtD) Framework [*WHO 2014; Ham C., 1997; Niessen L.W. et al., 2012; Alonso-Coello P. et al., 2016*]. This framework facilitates transparent and systematic decision-making by considering factors such as the balance of benefits and harms, resource use, equity, acceptability, and feasibility. It ensures that recommendations are grounded in evidence while also considering contextual factors relevant to Armenia. When applied well, these EtD frameworks can help identify and integrate the criteria of relevance for a given decision-making process, even if the voices of all relevant stakeholders were not heard. Therefore, EtD frameworks should be as comprehensive as possible, which often is at odds with the constraints, and needs to be balanced against the resources and time available for developing an informed decision.

GRADE Approach (Grading of Recommendations Assessment, Development, and Evaluation) . The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology is utilized to assess the quality of evidence and the strength of recommendations. This approach provides a structured process for evaluating the certainty of evidence across studies and determining the confidence in effect estimates. The GRADE uses specific approaches to presenting the quality of the available evidence, the judgments that bear on the quality rating, and the effects of alternative management strategies on the outcomes of interest [*Baltussen R. et al., 2006, Gordon G, 2011*].

Disease Burden Estimation **[***WHO, 2019*]. The WHO methodology for estimating disease burden, including metrics such as Disability-Adjusted Life Years (DALYs) and Quality-Adjusted Life Years (QALYs), is applied to quantify the impact of Long COVID and associated noncommunicable diseases. This allows for the assessment of health loss due to both mortality and morbidity, facilitating comparisons across diseases and informing resource allocation.

Integration of National and Global Data. National statistics on COVID-19 cases in Armenia, hospitalizations, and comorbidities are integrated with global data on Long COVID prevalence and risk factors, observational study using the structured e-questionnaire assessing the Long-COVID burden. This synthesis enables the contextualization of international evidence within the Armenian healthcare landscape.

By employing this multifaceted methodological framework, policymakers can derive evidence-based, context-specific recommendations to address the challenges posed by Long COVID and its intersection with noncommunicable diseases.

Results

Nationwide Assessment of Knowledge, Attitudes, Practices, and Burden of Long COVID in Armenia: A nationwide observational study which employed a custom-designed electronic questionnaire was conducted to assess the knowledge, attitudes, practices, and public health burden of Long COVID among the adult population (aged 18+) in Armenia. Among 99 respondents, approximately 22% reported newly diagnosed health conditions following their COVID-19 infection. Symptomatically, fatigue was reported by 36% of participants, musculoskeletal pain by 51.4%, and remitting headaches by 25%. Cognitive impairments, including memory issues (27.8%) and difficulty concentrating (15.3%), were prevalent, alongside neurological complaints such as dizziness (12.5%) and sleep disturbances (12.5%). Anosmia and ageusia (loss of taste and smell) were reported by 43% of respondents. Other persistent symptoms included cough (18.1%), cardiac palpitations (12.5%), chest pain (11.1%), gastrointestinal disorders (4.2%), persistent fever (4.2%), rhinitis (2.8%), dermatological manifestations (1.4%), and psychological symptoms such as anxiety or depression (~6%). Hair loss was also reported by 12.5% of participants.

Approximately 26.6% of respondents pursued medical care for symptoms consistent with Long COVID. However, access to care was limited: 24% of respondents cited financial constraints as a barrier to seeking healthcare services, 15.2% noted the absence of specialized Long COVID clinics, and 13% expressed concern that healthcare professionals did not take Long COVID symptoms seriously.

Medication usage patterns further illustrated the burden of unregulated care. Over 24.7% of participants reported self-administering medications, including antibiotics without a prescription. When asked about the rationale for self-medication, 56.3% cited previous experience with similar symptoms, 18.8% expressed fear that their condition might worsen, and another 18.8% relied on advice from friends or family members. Significant proportion of respondents expressed their willingness to engage in Long COVID management programs. Alarmingly, only 55.2% of respondents reported physicians had inquired about patients' self-treatment practices prior to hospitalization. Moreover, 24.2% of hospitalized patients confirmed receiving antibiotics during their hospital stay, regardless of microbiological confirmation.

Despite relatively high public awareness of the dangers of antibiotic overuse 90.6% of respondents acknowledged potential harm; a significant proportion (33.8%) continued to believe incorrectly that antibiotics are effective against viral infections. This discrepancy between perceived awareness and accurate biomedical understanding highlights a critical gap in public health education. The data suggest that awareness campaigns alone are insufficient and must be supplemented by targeted interventions that correct deeply rooted misconceptions and promote rational antimicrobial use, particularly in the context of viral illnesses like COVID-19.

The findings of this observational study were systematically incorporated into an evidence-based policy development framework. To support national decision-making, comparative evidence tables were developed using the GRADE approach alongside EtD frameworks. These tools were employed to assess the certainty of evidence for each identified risk factor and to align recommended health interventions with national capacity, equity considerations, and cost-effectiveness thresholds. The analysis provides a structured foundation for prioritizing responses to Long COVID within the broader health system strengthening and recovery strategy in Armenia.

Rising NCD Trends and Risk Factors in the Post-Pandemic Context

According to the *Health and Health Care Yearbooks of Armenia* (2022, 2023, 2024), Armenia has exhibited an increasing trend in the prevalence of noncommunicable diseases, notably obesity (affecting over 21.7% of the adult population), diabetes mellitus (9.2%), arterial hypertension, and cardiovascular morbidity. These conditions are especially prevalent among older adults and residents of rural areas [*NIH 2022, 2023, 2024*]. The COVID-19 pandemic has further contributed to the deterioration of public health by disrupting daily routines, limiting access to preventive health services, and elevating levels of psychosocial stress, collectively exacerbating the risk factors for noncommunicable diseases.

The *Health System Performance Assessment* [*HSPA*, 2022] documented a notable increase in multimorbidity, particularly among individuals who recovered from COVID-19, accompanied by considerable healthcare utilization in post-discharge settings. In 2022, the most frequently diagnosed conditions by healthcare professionals included cardiovascular diseases (15.8%), arterial hypertension (15.2%), visual impairments (14.0%), neurological disorders (12.0%), gastrointestinal diseases (11.9%), and COVID-19 (11.0%). That year, the total number of diagnoses recorded across all major disease categories increased significantly.

The most substantial relative increases among physician-diagnosed conditions in 2022 were observed in diabetes mellitus (3.27-fold increase), liver diseases (2.00-fold), bronchial asthma (2.00-fold), gastrointestinal disorders (1.98-fold), ear, nose, and throat (ENT) conditions (1.95-fold), and thyroid disorders (1.94-fold). According to evidence-based medical literature, the development of noncommunicable diseases is predominantly associated with lifestyle factors and modifiable risk elements. Data from the World Health Organization (WHO) further emphasize that tobacco use, alcohol misuse, unhealthy dietary patterns, physical inactivity, and elevated blood pressure are critical contributors to NCD burden.

In terms of metabolic risk factor trends, the prevalence of high blood pressure steadily declined from 33.8% in 2012 to 22.7% in 2022. Conversely, the proportion of individuals aged 35 years and older with blood cholesterol concentrations exceeding 6.2 *mmol/L* rose from 8.5% in 2016 to 11.6% in 2022. Similarly, the percentage of individuals in the same age group with fasting blood glucose levels above 6.1 *mmol/L* increased from 17.5% to 24.9% over the same period.

The proportion of the population classified as overweight or obese reached 55.1% in 2022, a slight increase compared to 52.1% in 2012 and 51.2% in 2016. Among men, the rate of daily tobacco smoking remained relatively unchanged - 53.2% in 2022 compared to 53.4% in 2016. Notably, harmful alcohol consumption among men, defined as the intake of ≥20 grams of pure alcohol per day, declined significantly from 16.3% in 2016 to 6.2% in 2022. Physical inactivity also showed a decrease, with rates dropping from 21.3% to 17.4%, based on the WHO STEPS methodology [*WHO, 2017*].

In addition to revealing the number of diseases diagnosed by the doctor during the last 12 months, the number of prescribed medicines by the doctor in the case of diagnoses was also calculated. The chart shows that 80 percent or more of patients diagnosed with a stroke, arterial hypertension, diabetes, COVID-19, heart disease, anemia, asthma, and chronic bronchitis were prescribed medication. Furthermore, 70-80% of patients diagnosed with thyroid, ears nose throat diseases, gastrointestinal diseases, visual diseases, and nervous system diseases were prescribed drug treatment. During the COVID-19 pandemic, significant disruptions in access to primary healthcare services in Armenia led to widespread delays or omissions in routine cancer screenings and essential vaccinations, including those for HPV. These gaps in preventive care likely contributed to the increased detection of late-stage malignancies (*Fig. 7a*), particularly malignancies of the trachea, bronchi, and lungs (*Fig. 7b*), colorectal (*Fig. 7c*), breast (*Fig. 7d*), cervical (*Fig. 7e*), and prostate cancers (*Fig. 7f*), in the post-pandemic period [*Health and Healthcare Yearly Book, 2024*]. Compounding this issue was a notable rise in self-treatment practices among the population, driven by fear of infection and healthcare inaccessibility. Of particular concern was the widespread and often inappropriate use of corticosteroids which were frequently prescribed without adequate clinical indication [*Niazyan L.G.et al., 2020, 2021*]. The over prescription of corticosteroids by healthcare providers, in the absence of strict clinical protocols, may have further compromised patients' immune responses, potentially contributing to tumor progression or susceptibility to oncogenic processes. These trends underscore systemic challenges in pandemic-era care delivery and highlight the critical need for strengthened regulatory oversight, public health education, and robust post-pandemic recovery strategies in primary care and oncology.

The review of the national health statistics data [*Health and Health Care Yearly Book*, 2024] has shown a high prevalence of neuropsychological disorders (*Fig. 8a*, particularly anxiety, depression, cognitive impairments, and sleep disturbances has been documented in the post-COVID Armenian population, likely exacerbated by prolonged psychosocial stress, social isolation, and the neuroinflammatory effects of SARS-CoV-2 (*Fig. 8a, 8b*). These conditions not only impair quality of life but may also influence treatment adherence, healthcare-seeking behavior, and long-term outcomes in patients with chronic diseases, including cancer.

DALY Estimation for Long COVID in Armenia

Using the revised life expectancy of 73 years for Armenia, the burden of Long COVID is estimated using DALYs and QALYs, as described below in 1and 2 sub-points.

1. Disability-Adjusted Life Years (DALYs)

DALYs are calculated by combining Years of Life Lost (YLL) due to premature mortality and

Years Lived with Disability (YLD) due to the chronic health effects of the disease.

YLL Calculation: For individuals with Long COVID who die prematurely, we used a life expectancy of 73 years for Armenia. A global estimate suggests that 10% of Long COVID cases may result in death. Given that 148,920 individuals in Armenia are expected to experience Long COVID, approximately 14, 892 individuals may die prematurely due to Long COVID complications. Assuming these individuals die at an average age of 60 years, the Years of Life Lost would be:

$$YLL=14,\ 892\times(73-60)=193,596$$

YLD Calculation: The average disability weight for Long COVID is estimated at 0.3.

Assuming that symptoms persist for 6 months (0.5 years), the YLD can be calculated as follows:

$$YLD = 148,920x0.3x0.5 = 22,338$$

Total DALYs for Long COVID:

$$DALYs=YLL+ YLD= 93,596 +22,338=215,934$$

Thus, the total DALYs due to Long COVID in Armenia is estimated to be 215,934 annually.

2. ***Quality-Adjusted Life Years (QALYs)***

Quality-Adjusted Life Years (QALYs) are a measure that accounts for both the quantity and quality of life lived. One QALY equates to one year of life in perfect health. Health states less than perfect health are assigned a utility value between 0 (equivalent to death) and 1 (perfect health). The QALY loss is calculated as the product of the time spent in a health state and the degree to which the health state is less than perfect.

Assumptions:

- Population affected by Long COVID: 148,920 individuals
- Average duration of illness: 6 months (0.5 years)
- Health utility weight for Long COVID: 0.7 (based on global estimates)
- This implies a quality-of-life reduction of 1 − 0.7 = 0.3, or 30%
- Premature deaths due to Long COVID: 14,892 individuals

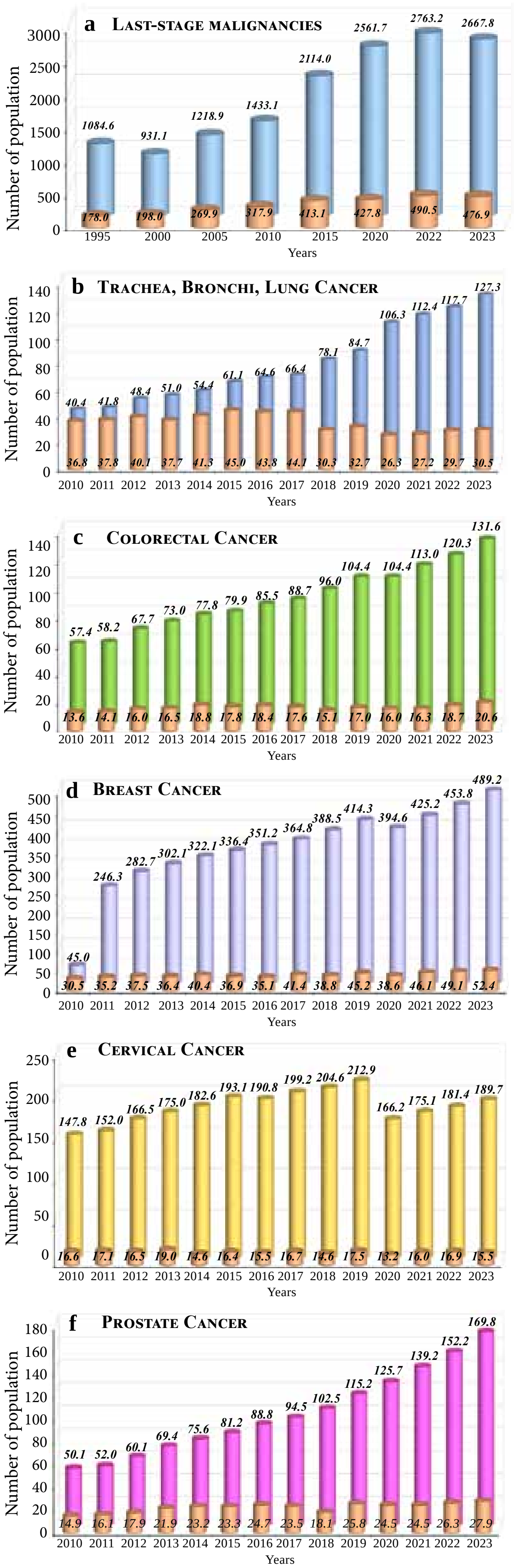

Figure 7. Prevalence and incidence of malignancies among 100,000 populetion in Armenia, 1995-2023. In this figure, the anterior cylinders indicate incidence, the posterior ones indicate prevalence. Different types of cancer in population a) last-stage malignancies, b) trachea, bronchi, and lung cancer, c) colorectal cancer, d) breast cancer, e) cervical cancer, and f) prostate cancer are observed.

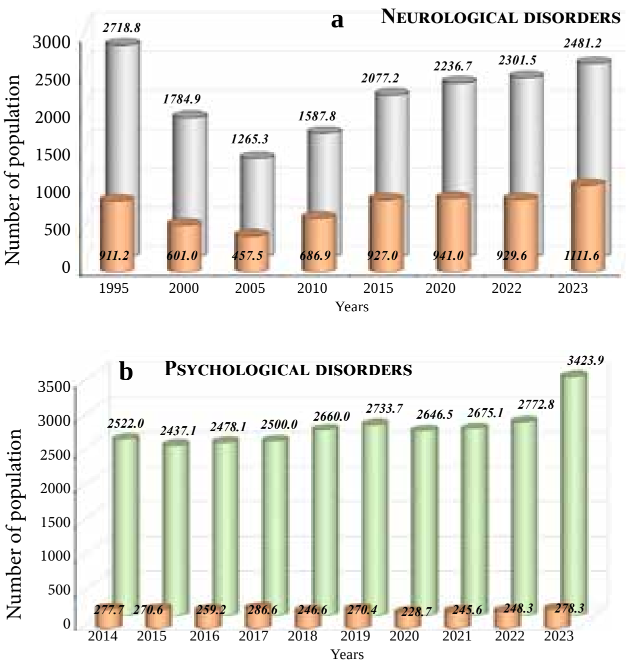

FIGURE 8. *Prevalence and incidence of neurological (a) and psychological(b) disorders among 100,000 popule-tion in Armenia, 1995–2023. In this figure, the anterior cylinders indicate incidence, the posterior ones indicate prevalence.*

➢Remaining life expectancy at average age of death (60 years): 13 years (based on revised life expectancy of 73 years)

QALYs lost due to morbidity (non-fatal Long COVID)

These are QALYs lost due to reduced quality of life during the illness period among those who survive Long COVID.

➢Number of survivors with Long COVID = 148,920 − 14,892 = 134,028

➢Utility loss per person over 0.5 years = 0.3 × 0.5 = 0.15 QALYs lost per person

QALYs lost (morbidity) =134,028×0.15=20,104

Based on 451,272 confirmed COVID-19 cases in Armenia applying a 30% Long COVID prevalence rate yields an estimated 135,382 individuals with Long COVID. Adjusting for 10% underreporting, the infection count increases to 496,399, leading to approximately 148,920 Long COVID cases with 215,934 DALYs and 20,104 QALYs lost in Armenia. These numbers highlight an underappreciated dimension of the pandemic's legacy. Long COVID is increasingly linked to the onset or worsening of noncommunicable diseases - diabetes, cardiovascular and kidney disease, and neurological disorders [*MOH NIH 2023, 2024, 2025*].

RESULTS AND COMPARISON USING GRADE AND ETR FRAMEWORK

This section presents a comparison of key factors in the context of the GRADE approach [*Gordon G. et al., 2011*] and EtD framework. Table 1 summarizes how evidence is graded according to GRADE, and Table 2 explains the rationale for decisions made based on the EtR framework, providing a clearer insight into the policy recommendations for addressing the burden of Long COVID in Armenia.

DISCUSSION

The results of an observational study aimed to assess the burden of long COVID within the Armenian population indicate a growing number of cases presenting with persistent fatigue, respira-

TABLE 1.

GRADE assessment for the impact of long COVID on noncommunicable diseases in Armenia

Factor	Evidence Type	Quality of Evidence	Confidence in Effect Estimate	Strength of Recommendation
Risk of developing NCDs (e.g., diabetes, cardiovascular diseases)	Observational studies, meta-analyses	Moderate to High	Moderate to High	Strong for urgent interventions
Impact of Long COVID on mortality and YLL	Long-term cohort studies, mortality data	High	High	Strong for healthcare prioritization
Post-COVID fatigue and cognitive dysfunction (brain fog)	Systematic reviews, cohort studies	Moderate to High	Moderate	Conditional for policy emphasis
Use of corticosteroids in post-COVID treatment and NCD risk	Observational studies, meta-analyses on randomized controlled trials, cohort studies	Moderate	Low to Moderate	Conditional depending on resource availability
Effect of obesity and comorbidities on Long COVID severity	Meta-analyses, cohort studies	Moderate	Moderate to High	Strong recommendation for preventive strategies

NOTE: *NCD noncommunicable disease, YLL- Years of Life Lost*

TABLE 2.

Evidence-to-Decision (EtD) Framework: Policy Implications for Long COVID and Noncommunicable Diseases in Armenia

Domain	Consideration	Evidence Synthesis	Recommendation Strength	Rationale
Balance of Benefits and Harms	The long-term benefits of preventing or mitigating Long COVID outweigh the harms of resource allocation.	Strong evidence from meta-analyses on post-COVID sequelae	Strong	Long COVID significantly impacts quality of life and leads to long-term health complications.
Resource Use	Availability of healthcare resources in Armenia, focusing on the most impactful interventions.	High-cost interventions are more resource-intensive	Conditional	Targeted strategies (e.g., corticosteroid use and chronic disease management) can optimize healthcare use.
Equity	Long COVID disproportionately affects vulnerable populations, including those with comorbidities.	Strong evidence from international studies	Strong	Policy should focus on reducing health disparities, with special emphasis on at-risk groups (elderly, obese, etc.).
Acceptability	The general public willingness to engage in Long COVID management programs	Surveys on public health programs	Strong	The public generally accepts policies aimed at reducing the impact of Long COVID, especially if proven effective.
Feasibility	The capacity of Armenian healthcare system to implement interventions based on available resources	High feasibility for outpatient care and health monitoring	Moderate to Strong	Armenia can implement scaled interventions, but more resources may be needed for comprehensive care.
	Digital tracking, provider training, and clinical protocols essential	High	Strong	Armenia has ongoing e-health projects that can integrate prescribing tools.

tory symptoms, cognitive impairments, cardiovascular complications, and others. These symptoms often overlap with pre-existing or emerging chronic conditions, leading to delays in diagnosis and fragmented care.

The GRADE approach provides an objective means of evaluating the quality of evidence, while the EtD framework systematically evaluates the context and feasibility of recommendations. Both methodologies underscore the critical need for policies that address the long-term impact of long COVID, especially in the context of noncommunicable diseases that emerge as sequelae.

Evidence from global meta-analyses and national statistics and observational study data in Armenia supports the urgent need for the policy implications:

INTEGRATED MODEL FOR MANAGING LONG COVID AND NONCOMMUNICABLE DISEASES

To address these intersecting burdens, we propose a multidisciplinary, PHC-based model supported by interoperable digital infrastructure and stratified by patient risk levels.

Key components include:

Multidisciplinary Teams: Composed of general practitioners, specialists (cardiology, neurology, endocrinology), rehabilitation therapists, and mental health professionals to enable coordinated care.

E-Health Integration: Interoperable platforms for patient tracking, triaging, referral, and algorithm-based decision support to guide care pathways across long COVID categories (e.g., cardiovascular, neurological, autoimmune).

Community Rehabilitation: Strengthening rehabilitation services especially in underserved rural areas - focused on physical therapy, pulmonary rehab, mental health, and social reintegration.

Integrated NCD Services: Embedding routine screening for hypertension, diabetes, and mental health within long COVID care, alongside counseling for healthy lifestyles and behavioral risk factors.

High-Risk Patient Prioritization: Structured triage systems to prioritize follow-up for elderly patients, those with multiple organ conditions, and individuals with a history of ICU admission during acute COVID.

Risk of infection by COVID-19 and dietary: Long COVID outcomes are heavily influenced by age-related immune decline, chronic inflammation, and microbiota health. Prevailing dietary deficiencies in Armenia exacerbate these immunological vulnerabilities, necessitating targeted nutritional interventions.

The polyamines spermine, spermidine, and putrescine are involved in various biological processes, notably in cell proliferation and differentiation, and also have antioxidant properties. Dietary polyamines have important implications in human health, mainly in the intestinal maturation and in the differentiation and development of immune system. The antioxidant and anti-inflammatory effect of polyamine can also play an important role in the prevention of chronic diseases such as cardiovascular diseases.

A number of very informative studies provide data according to which, at all stages of COVID-19 infection, there are significant changes in the metabolism of polyamines localized in virus-sensitive target cells of the macroorganism [*Muñoz-Esparza N et al., 2019; Avagyan S et al., 2020; Zilfyan A et al., 2020; Xu X et al., 2022*].

Significant amounts of polyamines enter into the macroorganism with various food products that SARS-CoV-2 infected patients consume daily, without taking into account the content of polyamines in them. Thus, the situation is much more complicated, since SARS-CoV-2 is in dire need of polyamines for its activation and long-term persistence. Avagyan and Zilfyan (2022) proposed a phase-specific diet: restrict polyamines during acute viral replication (to reduce viral replication substrates) and increase intake during recovery to promote immune repair and microbiota restoration.

Polyamine-rich foods include aged cheeses, wheat germ, fermented soy, mushrooms, and cruciferous vegetables. These foods are largely absent in the standard Armenian diet, creating a polyamine-deficient baseline.

Artificial Intelligence Integration for Long COVID Case Management: An essential enhancement to this model is the integration of Artificial Intelligence (AI)-based tools to support real-time triage, risk stratification, and clinical decision-making. AI technologies offer unique potential to optimize Long COVID care, particularly in resource-constrained and geographically fragmented health system in Armenia. Key benefits include:

- ➢AI-Supported Triage and Stratification: Machine learning algorithms can analyze clinical inputs such as symptom clusters, comorbidities, demographic profiles, and historical health data to stratify patients into appropriate care pathways. This enables prioritization of complex or high-risk cases for early intervention.
- ➢Personalized Care Recommendations: AI-driven clinical decision support systems can tailor rehabilitation or pharmacological plans based on patient-specific variables, enhancing therapeutic efficacy and minimizing unnecessary referrals.
- ➢Remote Monitoring and Predictive Analytics: Integration of AI-enabled digital tools, such as mobile apps or wearable biosensors, can support continuous symptom tracking, detect clinical deterioration, and notify providers automatically, enhancing continuity of care.
- ➢Resource Optimization: By automating elements of diagnosis and follow-up, AI platforms reduce workload for healthcare providers and improve the allocation of scarce resources especially in underserved or rural areas.
- ➢Data Integration and Surveillance: AI tools integrated within national e-health systems can support real-time analysis and forecasting of long COVID trends, informing health policy and system preparedness.

The incorporation of AI tools not only improves clinical decision-making but also aligns with digital health transformation goals in Armenia and supports achievement of SDG 3 by reducing disability, improving quality-adjusted life years (QALYs), and enhancing system resilience.

POLICY RECOMMENDATIONS FOR ARMENIA

To implement this integrated model, key actions are recommended for policymakers and health authorities:

1. Introduction of a Long-COVID Case Definition: It is crucial to establish a clear and standardized Long-COVID case definition in Armenia. This will help healthcare providers identify and diagnose Long-COVID more effectively. The case definition should include the range of symptoms, duration, and diagnostic criteria, ensuring that patients with persistent symptoms post-COVID infection are appropriately identified and treated.
2. Criteria-Based Triaging of Patients: Implementing a criteria-based triaging system will help prioritize patients based on the severity and complexity of their symptoms. This system should include clear diagnostic thresholds and risk stratification based on factors such as age, pre-existing noncommunicable diseases, comorbidities, and symptom severity. Such

triaging will allow healthcare systems to allocate resources more efficiently and ensure that those most at risk receive timely care.

3. Integration of Long-COVID Data into e-Health Platforms: To streamline patient management and improve the quality of care, Long-COVID data should be integrated into the e-health platform in Armenia. This will allow for better monitoring of patients' progress, track treatment outcomes, and facilitate communication between healthcare providers. Ensuring that patient records are accessible across the healthcare system will help coordinate care and reduce delays in treatment, leading to better clinical outcomes.
4. Multi-Disciplinary Approach to Case Management: Long-COVID requires a multi-disciplinary approach, involving primary care physicians, specialists, rehabilitation experts, and mental health professionals. This collaborative approach will ensure that all aspects of Long-COVID care, including physical, cognitive, and emotional health, are addressed. Early referral systems and case conferencing should be implemented to facilitate coordinated care and shorten time to diagnosis and management.
5. Development and Implementation of National Clinical Protocols for Long-COVID: Armenia should adopt national clinical protocols for the management of Long-COVID, developed in accordance with international best practices. These protocols should outline diagnostic guidelines, treatment pathways, and rehabilitation strategies to standardize care across the country. Protocols should be regularly updated as new evidence on Long-COVID emerges.
6. Training of Healthcare Workers: Health workers need comprehensive training on Long-COVID recognition, diagnosis, and management. Training should be part of continuing professional education, ensuring that healthcare providers are equipped to identify Long-COVID early and apply the appropriate clinical pathways.
7. Rehabilitation Services for Long-COVID Patients: Long-COVID patients should have access to comprehensive rehabilitation services as part of the Universal Health Coverage (UHC) package. These services should include physical, cognitive, and psychological rehabilitation to help patients recover their quality of life. Rehabilitation specialists, including physical therapists, speech therapists, and psychologists, should be integrated into the care team to support functional recovery.
8. Enhance Surveillance and Research: Establish a national registry for long COVID cases and conduct longitudinal research on outcomes and associations with noncommunicable diseases.
9. Integrate with National Health Strategy and SDGs: Align long COVID interventions with National Health Strategy and SDG 3 indicators in Armenia, including targets for reducing premature NCD mortality and achieving universal health coverage.
10. Designing tailored strategies within the larger vision to implement DHTs will promote healthcare practice and patients' quality of life.

CONCLUSION

The convergence of Long COVID and the rising burden of noncommunicable diseases presents a complex public health challenge in Armenia. However, it also offers a critical opportunity to strengthen the health system through integrated care, digital innovation, and a renewed focus on primary care and prevention, including clinical and policy recommendations on integrating immunonutrition into rehabilitation protocols and public health strategies. By operationalizing multidisciplinary, e-health-enabled Long COVID management within PHC, leveraging a digitally enhanced, AI-supported PHC model, Armenia can modernize its care infrastructure, improve triage accuracy, strengthen chronic disease prevention, and ensure equitable access to care. These innovations can play a pivotal role in reducing the long-term burden of COVID-19 and advancing the national health agenda in alignment with global development goals, ensure equitable health outcomes, and build resilience against future health crises.

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