International Journal of Rehabilitation & Disability Studies
Vol 2 Issue 1 (2026)
Pages 43 - 51
Available at
www.emiratesscholar.com

Long COVID as a Mass Disability Event: Biological Mechanisms, Economic Consequences, and the Rehabilitation Imperative

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ARTICLE INFO

KEYWORDS

long COVID; post-COVID-19 condition; disability; rehabilitation; economic burden; labour supply; global health

HOW TO CITE

Chikanda, T., & Miller, J. A. (2026). Long COVID as a Mass Disability Event: Biological Mechanisms, Economic Consequences, and the Rehabilitation Imperative. International Journal of Rehabilitation & Disability Studies, 2(1), 43-51.
https://doi.org/10.54878/dgn8jd93

ABSTRACT

The COVID-19 pandemic left behind a chronic condition whose scale qualifies it as one of the largest disability events in modern history. Long COVID, or post-COVID-19 condition, affects a meaningful fraction of those infected with SARS-CoV-2 and produces fatigue, cognitive impairment, and respiratory limitation that can persist for years, fluctuate unpredictably, and remove otherwise healthy adults from work at the peak of their productive lives. This paper joins a biological and an economic reading of the phenomenon and asks what both imply for rehabilitation and disability policy. We first synthesise the mechanistic evidence, viral persistence, immune dysregulation, endothelial injury, and autonomic dysfunction, that has moved long COVID from contested syndrome to documented multi-system disease. We then assemble the economic evidence: population-level estimates of symptom-cluster prevalence, labour-market withdrawal on the order of millions of workers in the United States alone, and aggregate cost estimates in the trillions of dollars once foregone earnings, medical spending, and lost wellbeing are counted. A simple accounting framework formalises these components, and we discuss what its terms look like in low- and middle- income countries, where surveillance is weakest, rehabilitation capacity thinnest, and the condition largely invisible in official statistics. We argue that long COVID exposes a structural mismatch between episodic, fluctuating disability and rehabilitation and benefit systems built for stable diagnoses, and that the response, multidisciplinary rehabilitation, paced self-management, telehealth, and disability recognition, is affordable relative to the cost of inaction. Recommendations are offered for health systems, employers, and researchers.

Double-blind peer review by independent reviewers.

Received: 25 Jan 2026, Accepted: 15 May 2026, Published: 17 Jun 2026

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1. Introduction

Every pandemic leaves two epidemics behind it: the deaths that are counted, and the disability that mostly is not. Six years after SARS-CoV-2 emerged, the second epidemic has a name, a case definition, and a research literature of unusual size, yet it remains strikingly under-served by the systems meant to respond to it. The World Health Organization's Delphi consensus defines post-COVID-19 condition as symptoms arising or persisting three months after infection, lasting at least two months, and not explained by an alternative diagnosis (Soriano et al., 2022). The Global Burden of Disease collaboration estimated that in 2020 and 2021, 6.2 per cent of people with symptomatic infection developed at least one of three persistent symptom clusters, fatigue with pain or mood disturbance, cognitive problems, or respiratory problems, at three months, and that among them roughly fifteen per cent still had symptoms a year after infection (Wulf Hanson et al., 2022). Applied to billions of cumulative infections, percentages of this size stop being clinical statistics and become demography.

The condition sits at an awkward junction of disciplines, which is partly why policy has lagged. To biologists, long COVID is a puzzle in post-viral pathophysiology, with mounting evidence implicating viral persistence, immune dysregulation, and vascular injury (Davis, McCorkell, Vogel, & Topol, 2023; Klein et al., 2023). To economists, it is a labour-supply shock and a large, slow-moving cost; Cutler (2022) put the aggregate burden for the United States alone at approximately 3.7 trillion dollars. To rehabilitation professionals and disability scholars, it is a mass-onset chronic illness whose episodic character fits poorly into eligibility systems designed for fixed impairments. Each discipline holds a piece; the pieces are rarely assembled.

This paper attempts the assembly, with particular attention to a question the high-income literature mostly neglects: what long COVID means for developing regions, where infection was widespread, vaccination arrived late, surveillance of chronic sequelae barely exists, and rehabilitation systems were already unable to meet pre-pandemic need (Cieza et al., 2020; WHO, 2017). Writing from the vantage points of economics and biology, we make three arguments. First, the biological evidence now supports treating long COVID as an organic multi-system disease, with direct implications for how rehabilitation should and should not be delivered. Second, the economic magnitudes involved justify substantially larger investment in rehabilitation and income protection than any country has yet made, on conventional cost-benefit grounds alone. Third, the condition's invisibility in low- and middle-income countries is a measurement artefact with distributional consequences, and correcting it is among the cheapest high-value investments available to global health.

Section 2 reviews the biology. Section 3 assembles the epidemiological and economic evidence and sets out a simple cost-accounting framework. Section 4 examines the rehabilitation response and its fit with the condition's clinical character. Section 5 turns to developing regions. Section 6 discusses implications and limitations, and Section 7 concludes.

2. The Biology of Long COVID: From Contested Syndrome to Multi-System Disease

2.1 Clinical picture and case definition

Long COVID encompasses more than two hundred reported symptoms, but its clinical core is consistent across cohorts: profound fatigue frequently accompanied by post-exertional malaise, cognitive impairment colloquially called brain fog, dyspnoea and reduced exercise capacity, and a long tail of cardiovascular, gastrointestinal, and neurological complaints (Davis et al., 2023). Controlled cohort studies were essential in separating the condition from background symptom prevalence. In the Dutch Lifelines cohort, matched pre- and post-infection symptom data indicated that about one in eight infected adults developed persistent somatic symptoms attributable to COVID-19 (Ballering, van Zon, olde Hartman, & Rosmalen, 2022), a design that answered early scepticism more effectively than any advocacy could. Meta-analytic work confirms that fatigue and cognitive impairment persist in a substantial minority of patients twelve weeks or more after infection, irrespective of hospitalisation status (Ceban et al., 2022).

Two features matter disproportionately for everything that follows. The condition is episodic and fluctuating, symptoms relapse under physical or cognitive exertion, which complicates both employment and the exertion-based rehabilitation that suits other deconditioning syndromes. And it strikes working-age adults predominantly, including those whose acute illness was mild, which is why its economic footprint is so large relative to its mortality.

2.2 Mechanisms

The mechanistic literature has converged on a small set of interacting hypotheses, summarised in Table 1. Analyses of national healthcare databases established early that survivors carried elevated burdens of incident

disease across virtually every organ system six months after infection, an observation incompatible with a purely psychogenic account (Al-Aly, Xie, & Bowe, 2021). Immune profiling has since identified objective biological signatures: Klein and colleagues (2023) found distinguishing features in circulating immune cell populations, exhausted T cells, altered cortisol, and evidence consistent with reactivation of latent herpesviruses, in people with long COVID relative to matched convalescent controls. Persistence of viral antigen in tissue reservoirs, endothelial dysfunction with microvascular clotting abnormalities, and autonomic nervous system dysregulation, most visibly postural orthostatic tachycardia syndrome, complete the current mechanistic map, and the overlap with myalgic encephalomyelitis/chronic fatigue syndrome is now taken seriously rather than dismissed (Davis et al., 2023).

Table 1. Principal mechanistic hypotheses for long COVID and representative supporting evidence.

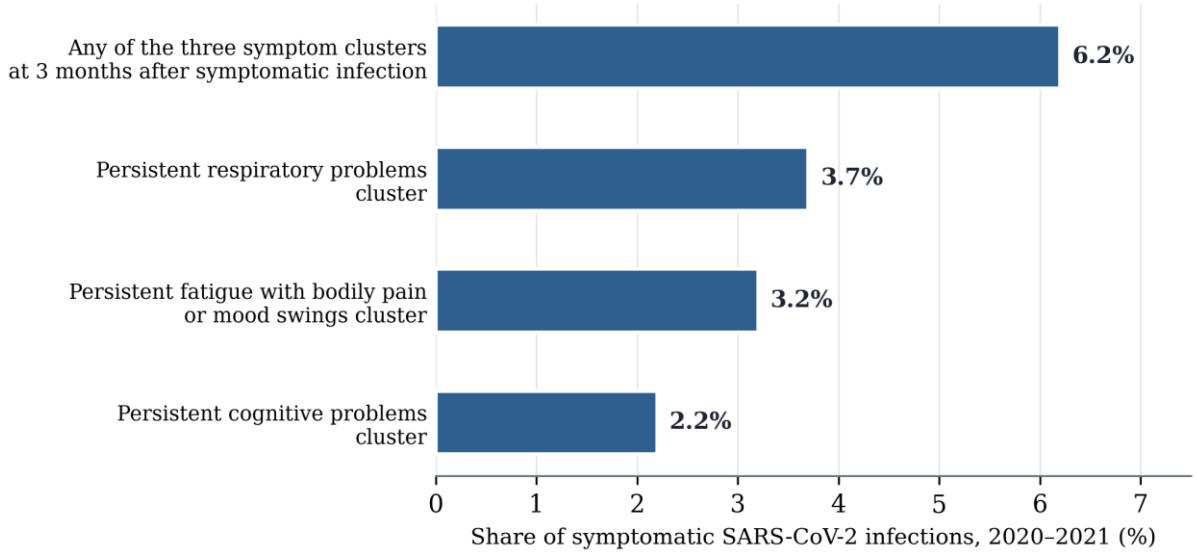
Mechanism	Core evidence	Clinical correlate	Key sources
Viral persistence / antigen reservoirs	Viral protein and RNA detected in tissues and plasma months after infection	Relapsing symptoms; potential target for antiviral trials	Davis et al. (2023)
Immune dysregulation	Distinct immune-cell phenotypes, T-cell exhaustion, altered cortisol; herpesvirus reactivation signals	Fatigue, flu-like relapses, unrefreshing sleep	Klein et al. (2023)
Endothelial & microvascular injury	Widespread multi-organ sequelae in national cohort data; clotting abnormalities	Exercise intolerance, chest pain, organ dysfunction	Al-Aly et al. (2021)
Autonomic dysfunction	Orthostatic intolerance and POTS documented in large fractions of clinic cohorts	Tachycardia, dizziness, exertional collapse	Davis et al. (2023)
Overlap with ME/CFS	Symptom architecture including post-exertional malaise mirrors ME/CFS diagnostic criteria	Requires pacing; graded exercise can harm	Davis et al. (2023); Ceban et al. (2022)

For rehabilitation, the mechanistic evidence carries a practical warning. Where post-exertional malaise is present, therapy built on progressive exertion, appropriate for deconditioning, can trigger relapse; guidelines therefore emphasise symptom-titrated pacing, and the National Institute for Health and Care Excellence explicitly cautions against fixed incremental exercise programmes in this population (NICE, 2022; WHO, 2021). A rehabilitation system that has not absorbed this point can do harm at scale.

3. The Economic Anatomy of a Mass Disability Event

3.1 Prevalence at population scale

Figure 1. reproduces the central prevalence estimates from the Global Burden of Disease analysis. The proportions look modest until multiplied by the base. With cumulative symptomatic infections in the billions, a 6.2 per cent three-month rate implies a stock of tens of millions of people who have experienced at least one persistent symptom cluster, and the twelve-month persistence estimate implies many millions in whom the condition is long-lasting (Wulf Hanson et al., 2022). These are conservative bounds on the phenomenon's true footprint: the clusters capture three symptom groups, not the full clinical picture, and reinfections, each carrying fresh risk, continue.



Note: clusters overlap, so cluster-specific shares sum to more than the 6.2% total. Among those with symptoms at 3 months, an estimated 15.1% continued to experience symptoms at 12 months. Data: Wulf Hanson et al. (2022), JAMA 328(16).

Figure 1. Estimated proportions of symptomatic SARS-CoV-2 infections resulting in persistent symptom clusters at three months, 2020–2021 (Wulf Hanson et al., 2022).

3.2 Labour markets and aggregate cost

The labour-market evidence is the clearest place where biology becomes economics. Analysing United States survey data, Bach (2022) estimated that long COVID was keeping the equivalent of two to four million full-time workers out of the labour force, an annual earnings loss she placed around 170 billion dollars, at a time when employers were reporting historic labour shortages. Survey measures introduced into national statistical systems since then consistently find a meaningful share of working-age adults reporting activity limitation from long COVID. The condition also erodes labour supply on the intensive margin, reduced hours, reduced intensity, abandoned promotions, in ways standard statistics capture poorly.

Cutler's (2022) aggregate accounting for the United States, an update of the framework in Cutler and Summers (2020), reached approximately 3.7 trillion dollars: roughly 2.2 trillion in lost quality of life, about one trillion in foregone earnings, and something over half a trillion in additional medical spending. The number is an estimate built on contestable assumptions, as its author is careful to say, but even under aggressive discounting the order of magnitude survives, comparable to the output loss of a major recession, attached to a single chronic condition. Table 2 collects the principal published magnitudes.

Table 2. Selected published estimates of long COVID's scale and economic burden.

Quantity	Estimate	Scope	Source
Symptomatic infections with ≥1 persistent cluster at 3 months	6.2%	Global, 2020–2021	Wulf Hanson et al. (2022)
Of those, still symptomatic at 12 months	15.1%	Global, 2020–2021	Wulf Hanson et al. (2022)
Adults with persistent symptoms attributable to COVID-19	≈1 in 8 infected	Netherlands (Lifelines cohort)	Ballering et al. (2022)
Full-time-equivalent workers out of work	2–4 million	United States, 2022	Bach (2022)
Associated annual lost earnings	≈ $170 billion	United States, 2022	Bach (2022)

Aggregate economic burden (earnings + medical + wellbeing)	≈ $3.7 trillion	United States, cumulative	Cutler (2022)
Full pandemic cost benchmark	≈ $16 trillion	United States	Cutler & Summers (2020)

3.3 A simple accounting framework

It is useful to make the structure of such estimates explicit, both to compare countries and to see what data are missing where. Write the aggregate burden of long COVID in a population as

$$C_{total} = C_{med} + C_{prod} + C_{well} \quad (1)$$

where C_{med} is excess medical and care expenditure, C_{prod} is the value of lost market and non-market production, and C_{well} is the monetised value of lost health-related quality of life. The production term for a cohort of N affected workers can be written

$$C_{prod} = \Sigma_{i=1..N} \Sigma_t \delta^t w_{it} (h_{itpre} - h_{itpost}) \quad (2)$$

with w_{it} the wage, h_{it} hours supplied before and after onset, and δ a discount factor; the wellbeing term is conventionally $C_{well} = \Sigma \Delta QALY_i \times V$, the sum of quality-adjusted life-year losses valued at a chosen threshold V. The framework is elementary, but its emptiness in most of the world is the point: for the majority of countries, not one of the three terms can currently be computed from national data, because neither prevalence nor labour-market attachment of people with post-COVID condition is measured. Equation (1) is thus less a calculation than a data agenda.

4. The Rehabilitation Response

4.1 What appropriate care looks like

Guidance has stabilised around a multidisciplinary, symptom-led model: structured assessment across systems; management of specific treatable phenotypes such as orthostatic intolerance; energy-management and pacing for post-exertional malaise; cognitive rehabilitation strategies; gradual, symptom-titrated return toward activity where tolerated; and psychological support offered as support rather than as implied aetiology (NICE, 2022; WHO, 2021). The WHO's self-management materials, designed for delivery without specialist infrastructure, are significant precisely because most of the world's patients will never see a specialist clinic. The model's centre of gravity, in other words, sits close to community-based rehabilitation practice long familiar in low-resource settings (Tadyanemhandu, Shava, Chengetanai, & Mkandla, 2024), a convergence Section 5 returns to.

4.2 The structural mismatch

Long COVID collides with three design assumptions embedded in most rehabilitation and disability-benefit systems. Systems assume stable impairment, but long COVID fluctuates, a claimant capable of work in a good week may be bedbound the next, and episodic disability fits badly into binary fit-for-work determinations. Systems assume objective verification, but long COVID still lacks a routine diagnostic biomarker, leaving claimants dependent on clinical judgement in an atmosphere of residual scepticism. And systems assume small inflows, whereas long COVID arrived as a cohort of millions within two years. The predictable result, documented across high-income countries, is high claim-denial rates, long appeals, and exit from the labour force by people who wanted accommodation rather than benefits. The condition's naming history is itself instructive: the term long COVID was coined by patients themselves, who organised online to force recognition of persistent illness that early clinical frameworks had no category for (Callard & Perego, 2021). Rarely has the social construction of disability categories been so visible in real time.

4.3 Technology and monitoring

Because long COVID care is longitudinal, fluctuating, and largely home-based, it is a natural candidate for the digital-health infrastructure that the pandemic itself accelerated. Reviews of regional health systems note that COVID-19 acted as a catalyst for telemedicine, remote monitoring, and AI-assisted diagnostics in the management of chronic respiratory disease in older adults, exactly the toolset long COVID monitoring requires (Sulthan et al., 2025). Looking further ahead, machine-learning approaches to multi-modal biological data of the kind reviewed by Alshamsi and Alhammadi (2025) in the neurodevelopmental context offer a plausible route to the objective diagnostic signatures long COVID currently lacks, though the same authors' cautions about small cohorts, cost, privacy, and algorithmic bias apply with full force here. Wearable-derived measures of heart-rate variability and activity are already used informally by patients for pacing; formalising them into validated monitoring tools is a tractable near-term research goal.

5. The Invisible Burden: Long COVID in Developing Regions

Almost everything quantitative in Section 3 comes from high-income countries. This is not because long COVID respects income boundaries, seroprevalence studies showed infection rates in many low- and middle-income countries as high as anywhere on earth, but because the instruments that make chronic illness visible, longitudinal cohorts, insurance claims, labour-force surveys with health modules, are concentrated in rich countries. The Global Burden of Disease estimates are global in ambition but thin in LMIC primary data (Wulf Hanson et al., 2022). What exists suggests the burden is real and unmeasured rather than absent.

Three considerations make the developing-region case urgent rather than merely incomplete. First, exposure was less mitigated: vaccination arrived later and reached less deeply, and infection-acquired immunity came at the price of repeated unprotected infection waves. Second, the labour-market consequences bind more tightly where work is physical, informal, and uninsured. A market trader or smallholder farmer with post-exertional malaise has no sickness benefit to claim and no desk job to be redeployed to; the household absorbs the shock directly, through the same disability-poverty channel long documented in this literature. Third, rehabilitation capacity was already overwhelmed before the pandemic, with rehabilitation need rising everywhere (Cieza et al., 2020) and services in much of sub-Saharan Africa dependent on community-based programmes whose funding is fragile (Tadyanemhandu et al., 2024; WHO, 2017).

The response need not wait for specialist infrastructure that will not arrive soon. The convergence noted above, between recommended long COVID care and community-based rehabilitation practice, is an opportunity: trained community workers can deliver screening, pacing education, and WHO self-management support at low cost through structures that already exist (WHO, 2021; Tadyanemhandu et al., 2024). The binding constraint is measurement. Adding a brief post-COVID module to existing national surveys, the demographic and health survey platforms most obviously, would cost little and would convert an invisible burden into a governable one. Table 3 summarises the contrast and the near-term options.

Table 3. Long COVID system readiness: high-income versus low- and middle-income settings, and near-term LMIC options.

Dimension	High-income settings	LMIC settings	Near-term LMIC option
Surveillance	Cohorts, claims data, survey modules	Largely absent; condition invisible in statistics	Post-COVID modules on existing national surveys
Diagnosis	Specialist clinics; exclusion-based diagnosis	Scarce specialists; competing acute priorities	Primary-care case definition (Soriano et al., 2022) with training
Rehabilitation	Multidisciplinary clinics, variable capacity	Pre-existing unmet need; fragile CBR funding	Deliver WHO self-management via CBR workers
Income protection	Sickness/disability benefits, imperfect fit	Informal employment; no benefit channel	Social-protection pilots; disability recognition
Data & research	Large trials, biobanks, immune profiling	Minimal primary research	South-led cohorts; shared protocols; telehealth follow-up

6. Discussion

6.1 Reading the two literatures together

Joining the biological and economic evidence changes the policy arithmetic in a way neither literature achieves alone. The biology establishes that long COVID is an organic disease with measurable signatures and mechanisms, which forecloses the temptation, visible early in the pandemic, to treat the problem as somatised anxiety to be managed by reassurance. The economics establishes that the stakes are macroeconomic: when a condition subtracts millions of full-time workers and trillions of dollars of value, interventions costing a fraction of that, rehabilitation services, benefit reform, research into treatments, clear conventional cost-benefit tests easily. The two together yield the paper's central claim: under-investment in long COVID response is not fiscal prudence but an accounting error, in which costs shifted onto patients and households are booked as savings.

6.2 The framework applied: what figure 2 organises

Figure 2. summarises the argument as a causal chain with a policy feedback. Biological injury produces functional impairment whose signature feature, episodic fluctuation, drives economic consequences through labour supply, expenditure, and wellbeing; the scale of those consequences is what justifies, and should motivate, the rehabilitation and policy response; and the response, if well designed, feeds back by restoring function and limiting chronicity. Every element of the chain is documented in the sources reviewed here; what remains weak is the feedback arrow, in rich countries because systems fit the condition poorly, in poor countries because the condition is not yet measured at all.

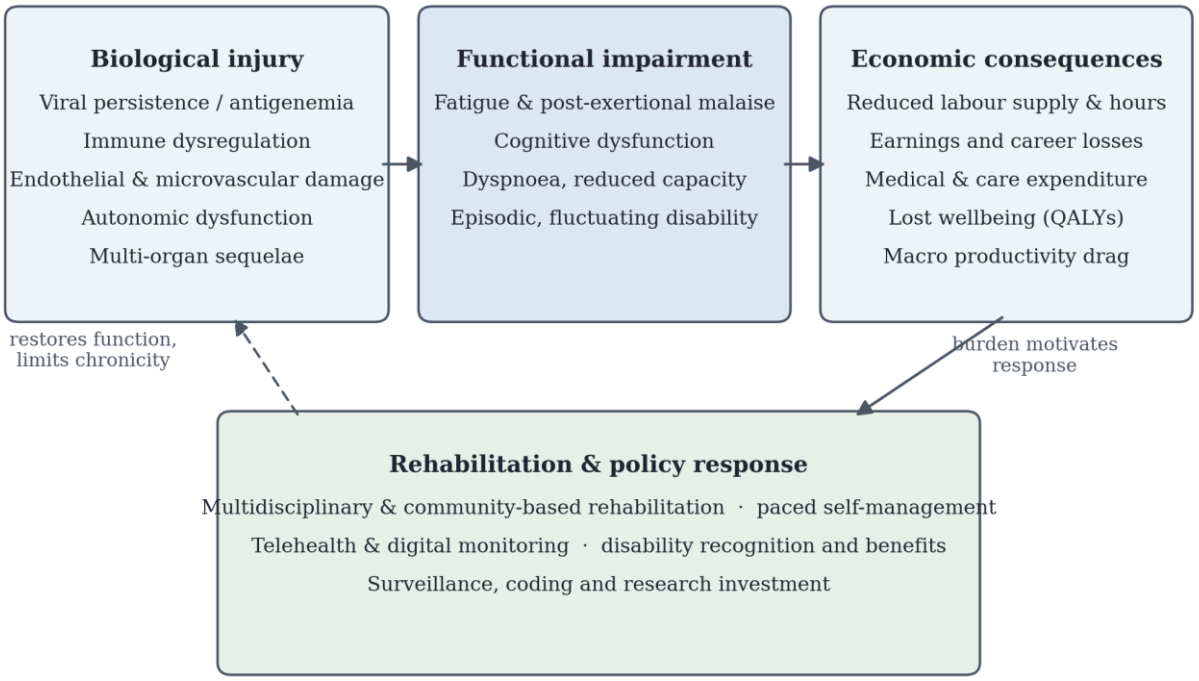


Figure 2. Long COVID as a mass disability event: from biological injury to economic consequences and the rehabilitation feedback.

6.3 Limitations

Our synthesis inherits the limitations of its sources. Prevalence estimates for long COVID span a wide range across definitions and study designs, and the Global Burden of Disease figures we foreground, though the most systematic available, rest on modelling assumptions and sparse LMIC data. The economic estimates are dominated by a single country and include a wellbeing valuation that is methodologically contested. The mechanistic literature, while converging, has not yet produced a validated diagnostic biomarker or an approved disease-modifying treatment, and some current hypotheses will not survive. Finally, we have argued from the convergence between long COVID care and community-based rehabilitation without direct trial evidence that CBR-delivered long COVID support improves outcomes; that trial is precisely the study we would most like to see conducted, and conducted in Africa.

7. Conclusion and Recommendations

Long COVID is what a mass disability event looks like in the twenty-first century: biologically real, economically enormous, unevenly measured, and met by systems designed for a different kind of patient. The evidence reviewed here supports five actions. Health systems should establish symptom-led, pacing-aware rehabilitation pathways, using community-based delivery where specialist capacity is absent, and should stop deploying exertion-based protocols where post-exertional malaise is present (NICE, 2022; WHO, 2021). Statistical agencies, especially in developing countries, should add post-COVID condition to routine surveys, because none of the policy machinery works on an unmeasured problem. Benefit systems should build episodic-disability categories, so that fluctuating illness does not force a false choice between full work and full exit. Employers should treat flexible hours, remote arrangements, and phased return as the cheap productivity investments the labour-supply numbers show them to be. And research funders should back the search for diagnostic biomarkers and disease-modifying treatments at a scale commensurate with a trillion-dollar problem, with

cohorts that include the populations of the global South rather than treating them as an afterthought.

The pandemic's acute phase ended; its disability phase did not. Whether long COVID is remembered as the moment health and economic systems learned to handle chronic, fluctuating, mass-onset illness, or as another burden quietly transferred onto the disabled and the poor, is a policy choice still open. It should be made deliberately.

Declarations

Conflict of interest. The authors declare no conflict of interest.

Funding. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgements. The authors thank colleagues at their respective departments for helpful comments on an earlier draft.

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