frontiers in Medicine

TYPE Policy and Practice Reviews
PUBLISHED 02 November 2026
DOI 10.3389/fmed.2026.1957295

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OPEN ACCESS

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RECEIVED 03 August 2026
REVISED 07 October 2026
ACCEPTED 20 October 2026
PUBLISHED 02 November 2026

CITATION
Brand M, Bellmann-Strobl J, Franke C, Scheibenbogen C and Wittke K (2026) Recommendations for the primary care management of post COVID and post acute infectious syndrome: a comparative analysis of international guidelines.
Front. Med. 13:1957295.
doi: 10.3389/fmed.2026.1957295

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Recommendations for the primary care management of post COVID and post acute infectious syndrome: a comparative analysis of international guidelines

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The medical care of people with post COVID syndrome (PCS) and other post-acute infectious syndromes (PAIS) remains a major challenge as dedicated care structures are scarce, diagnostic evaluation is often complex, and curative therapies are largely lacking. General practitioners play an essential role in initial assessment and the coordination of care and treatment. However, standardized and evidence-based recommendations specifically tailored to primary care are scarce. This study aimed to analyze and compare diagnostic and therapeutic recommendations for primary care of PCS from international guidelines. Six guidelines and recommendations were included, originating from Germany, Switzerland, the United Kingdom, the United States, the WHO, and a European scientific society. The analysis revealed considerable variation in scope, level of detail and practical applicability. Most guidelines recommend symptom-based or exclusionary diagnostic approaches. Non-pharmacological interventions such as rehabilitation, self-management and psychological support are commonly addressed. In contrast, pharmacological options are rarely specified due to limited evidence. While the importance of general practitioners is acknowledged across documents, specific support structures and implementation strategies vary. To date, structured care recommendations for patients with Long COVID and other PAIS in primary care remain limited.

KEYWORDS
clinical guidelines, general practitioners, long covid, PAIS, PCS, post COVID syndrome, post-acute infection syndrome, primary care

Introduction

Post COVID syndrome (PCS) is a complex condition that affects a growing number of patients worldwide. Symptoms are diverse and may fluctuate or persist over time, making comprehensive care challenging. PCS is defined by the World Health Organization (WHO) as a set of symptoms that occur within three months of a confirmed or

suspected SARS-CoV-2 infection, last for at least two months, cannot be explained by an alternative diagnosis, and impair everyday functioning (1).

Estimates of PCS prevalence vary considerably depending on the definition applied and the population studied. In a nationwide population-based survey conducted in France, the prevalence of post-COVID-19 condition according to the WHO definition was estimated at 4.0% in the general adult population and 8.0% among individuals reporting a probable or confirmed SARS-CoV-2 infection more than three months previously (2). In some patients, symptoms persist beyond six months and may follow a chronic or relapsing course (3, 4). A subset of affected individuals develops severe conditions such as myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS, ICD G93.3) and postural orthostatic tachycardia syndrome (POTS, ICD G90.80), both of which may also occur following other, predominantly viral, infections (5, 6).

PCS is associated with substantial impairments in quality of life (5), daily functioning and work capacity. The WHO also highlights challenges related to returning to everyday activities and work (7). This underscores the urgent need for structured diagnostic and therapeutic approaches.

Care structures for PCS and PAIS vary considerably between countries. While some have established national guidelines and specialized outpatient clinics, in many regions coordinated care strategies are still lacking.

General practitioners play a central role in the care of PCS patients. They are usually the first point of contact, coordinate diagnostic assessments, monitor the course of illness and initiate treatment. Despite this key role, there is still a lack of standardized, evidence-based and practical guidelines tailored specifically to primary care. A recent German study highlighted substantial challenges in the primary care management of post COVID patients, identifying barriers across all areas of care, including diagnosis, treatment, continuity of care, and coordination, with particularly high information needs regarding therapy, pathophysiology, and rehabilitation (8). Existing national and international guidelines differ in methodology, target audience, level of detail, and overall purpose. Many are based on expert consensus or adopt findings from related conditions (7). A comparative assessment of these documents with regard to their practical relevance for primary care is still lacking.

While the comparative guideline analysis in this review focuses specifically on PCS, PAIS is considered as a broader post-infectious context. Recommendations identified for PCS are therefore not assumed to be directly transferable to other PAIS.

In Germany, the Joint Federal Committee (G-BA) has issued a guideline on coordinated and interdisciplinary care for patients with Long COVID and conditions with similar causes or manifestations (9). Within the PAIS CARE project, these recommendations are operationalized in a structured primary care model. The PAIS CARE model integrates general practitioners and specialized Charité outpatient clinics into a coordinated care network, with general practitioners serving as the primary point of contact and coordinating further diagnostic and therapeutic measures. Depending on functional impairment and clinical indications, patients may be referred to specialized outpatient services for further evaluation and treatment (10).

This review was conducted within the framework of the PAIS CARE project, with the aim of comparing national and international guidelines with regard to their recommendations on the diagnosis and management of PCS in general practice. The goal was to identify areas of agreement, gaps, and practical implications for primary care. The PAIS CARE model was considered separately as an example of a structured approach to implementing guideline-based recommendations in primary care.

Methods

Study design

This review employed a qualitative analysis of clinical guidelines to compare international recommendations on the diagnosis and management of PCS in general practice. A formal systematic literature review was not conducted, as documents were selected purposively.

Selection of guidelines and documents

Six international guidelines and recommendations published between 2020 and 2025 were included in the analysis. The documents originated from Germany (DGP), Switzerland (BAG), the United Kingdom (NICE), the United States (CDC), the World Health Organization (WHO) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Documents were selected purposively from major national and international guidelines and clinical guidance documents on Long COVID available at the time of the review. Selection focused on guidance issued by major international health organizations and professional societies (WHO and ESCMID), as well as national guidance from countries with established Long COVID care frameworks relevant to the European healthcare context (Germany, Switzerland, the United Kingdom, and the United States). The aim was to include major and widely used guidance documents representing international, European, and national perspectives rather than to provide an exhaustive systematic review of all available national guidelines. Inclusion criteria were relevance to primary care, availability as full text, and recency. The selection was restricted to documents published in German or English. Relevance to primary care was based on the inclusion of recommendations applicable to initial assessment, diagnostic evaluation, symptom management, follow-up, or referral in a primary care setting. The documents were not required to be guidelines specifically developed for general practitioners. Guidelines or recommendations specifically addressing pediatric populations were excluded.

Table 1 provides an overview of the publishers, countries of origin, and the year of the most recent update of the analyzed guidelines and recommendations.

Data extraction and analysis

The documents were thematically analyzed using a structured, qualitative approach. The analysis focused on four key domains:

TABLE 1 Overview of the included guidelines and recommendations.

No.	Abbreviation	Publisher	Country of origin	Year
1	**WHO**	*World Health Organization*	*international*	2023
2	**ESCMID**	*European Society of Clinical Microbiology and Infectious Diseases*	*Europe*	2022
3	**DGP**	*Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin*	*Germany*	2024
4	**BAG**	*Bundesamt für Gesundheit*	*Switzerland*	2023
5	**CDC**	*Centers for Disease Control and Prevention*	*USA*	2025
6	**NICE**	*National Institute for Health and Care Excellence*	*UK*	2024

diagnostic recommendations, non-pharmacological interventions, pharmacological treatment options, and the role of general practitioners. Pharmacological recommendations were differentiated into symptom-oriented treatment and specific pharmacological treatment targeting PCS. The term symptom-oriented treatment refers to the therapeutic purpose and does not imply a specific regulatory on- or off-label status, which may depend on the individual drug, indication, and patient population. Recommendations regarding off-label or experimental pharmacological treatment were initially considered as a separate category; however, no specific guideline recommendations for such treatment were identified. All relevant content was categorized and summarized. The findings were presented in tabular form. In addition, the identified recommendations were compared with the content of the PAIS CARE manual, which was considered separately and was not included among the six analyzed guidance documents. The aim was to identify areas of alignment or divergence, as well as practical implications for primary care.

Assessment of guidelines and implications for primary care

Overview of guideline content

As part of the analysis, guidelines were examined with regard to their recommendations on the diagnosis and management of post COVID syndrome in the context of general practice. The core content analysis focused on three main areas: diagnostics, non-pharmacological treatment, and pharmacological treatment. The role of general practitioners was additionally analyzed in a separate section, as relevant statements in the guidelines were often implicit or only briefly mentioned. Table 2 provides a structured overview of key primary care-relevant recommendations on diagnosis and treatment of PCS derived from the analyzed documents. Selected contents are presented below, with a more detailed assessment provided in the following sections. The PAIS CARE model of care, which is not a guideline but a structured approach to the organization and implementation of primary care for patients with PAIS, is described separately below.

Diagnostic recommendations

All guidelines emphasize the importance of a thorough medical history and physical examination (3, 4, 7, 11–13). Regarding laboratory testing, the recommendations vary in scope and are generally guided by clinical presentation. The DGP, ESCMID, BAG and NICE provide specific guidance on basic laboratory assessment, including a complete blood count, inflammatory markers such as C-reactive protein, and renal and liver function tests (3, 4, 11, 12). Depending on the clinical indication and presenting symptoms, these guidelines also describe additional laboratory investigations, which may include thyroid function, ferritin, glucose metabolism, creatine kinase, and cardiac biomarkers, among other symptom-specific parameters (3, 4, 11, 12).

Several guidelines recommend the use of structured assessment tools such as symptom diaries, functional scales or validated questionnaires (3, 4, 7, 11–13), primarily to assess severity and monitor progress. These include the Post-COVID-19 Functional Status Scale, mentioned by the WHO (7), the Fatigue Scale for Motor and Cognitive Functions (FSMC) (14), or the DePaul Symptom Questionnaire for screening post-exertional malaise (PEM) (15). The latter two are recommended by the BAG, which lists specific questionnaires and scales for assessing many of the most common symptoms of PCS (11). In all diagnostic procedures, the exclusion of potential differential diagnoses is prioritized, as PCS remains a diagnosis of exclusion due to the lack of specific confirmatory tests (4).

More complex or technical procedures, such as imaging diagnostics, pulmonary function testing or specialist evaluations, are often not feasible within general practice. Several of the analyzed guidelines recommend referral to specialist services when clinically indicated (3, 4, 7, 11, 12).

Overall, there is a considerable overlap across the guidelines with regard to basic diagnostic measures. However, differences emerge in the level of detail and systematic presentation. The guidelines issued by the DGP (3), ESCMID (4), and BAG (11) provide particularly detailed recommendations, whereas the information provided by the CDC remains rather general (13).

Several guidelines recommend advanced diagnostics, such as imaging procedures or functional tests, on a symptom-specific basis when clinically indicated (3, 4, 11–13). For example, the ESCMID guideline refers to instrumental diagnostics such as pulmonary function testing or echocardiography in patients with persistent symptoms (4). The NICE guideline likewise recommends additional diagnostics, including exercise tolerance tests or imaging procedures such as chest x-rays for patients with respiratory symptoms and appropriate clinical indications (12).

TABLE 2 Key recommendations on diagnosis and treatment of PCS in selected guidelines and recommendations.

Document	Diagnosis	Non-pharmacological treatment	Pharmacological treatment
WHO (7)	- Medical history - Symptom-related scales/tests - Self-observation - Follow-up consultations	- Multidisciplinary treatment - Stress management - Physical and memory training - Pacing	Symptom-oriented pharmacotherapy (e.g., NSAIDs, corticosteroids, antidepressants)
ESCMID (4)	- Medical history - Exclusion of differential diagnoses (DD) - Laboratory tests, functional diagnostics, and imaging as necessary	- Multidisciplinary rehabilitation - Olfactory training if necessary - Smoking cessation	Consideration of extended anticoagulation prophylaxis in selected patients based on individual thrombotic and bleeding risk
DGP (3)	- Medical history - Physical examination - Symptom-related scales/tests - Basic laboratory diagnostics	- Symptom-oriented, multidisciplinary - Pacing - Coping - Basic psychosomatic support	Symptom-oriented pharmacotherapy; no specific PCS therapy
BAG (11)	- Medical history - Physical examination - Symptom-related scales/tests - Laboratory tests	- Multidisciplinary treatment with focus on energy management - Meditation, mindfulness exercises - Assistive devices	Symptom-oriented pharmacotherapy
CDC (13)	- Medical history - Physical examination - Symptom-related tests	- Rehabilitation plan - Treatment of underlying conditions - Preventive measures	Symptom-oriented pharmacotherapy
NICE (12)	- Medical history - Physical examination - Exclusion of differential diagnoses (DD)	- Personalized plan - Multidisciplinary treatment - Rehabilitative medicine	Symptom-oriented pharmacotherapy according to existing guidance

Recommendations for treatment

Non-pharmacological approaches

Across the analyzed guidelines, treatment recommendations generally follow an individualized, symptom-based, and functionally oriented approach (3, 4, 7, 11–13). Non-pharmacological measures form the core of care. These include educational elements, rehabilitative services such as physical or occupational therapy, psychosocial support (3, 7, 11, 12), and supportive interventions such as breathing therapy, relaxation techniques, or mindfulness exercises (3, 7, 11). Several guidelines emphasize the importance of pacing strategies for fatigue and PEM, which should be individually tailored and closely aligned with symptom dynamics (3, 7, 11).

The recommendations differ in their level of detail: while some guidelines refer more generally to the importance of interdisciplinary management, others (e.g., BAG, DGP, ESCMID) provide more differentiated information on specific measures. The importance of cross-sectoral cooperation, especially in complex cases, is emphasized in several documents (3, 4, 7, 12).

Pharmacological therapies

There is currently no established causal pharmacological therapy for PCS. Pharmacological recommendations in the analyzed documents primarily concern symptom-oriented treatment of individual symptoms or comorbid conditions. The WHO, DGP, BAG, CDC, and NICE address such symptomatic treatment to varying degrees (3, 7, 11–13). The WHO, for example, mentions short-term anti-inflammatory treatment for arthralgia and antidepressants for depression (7). ESCMID does not provide evidence-based pharmacological treatment recommendations for Long COVID but suggests considering extended anticoagulation prophylaxis in selected patients based on individual thrombotic and bleeding risk (4).

Role of general practitioners

Several of the guidelines explicitly recognize the central role of primary care. It is addressed in detail in the guidelines of the DGP and the BAG with regard to initial diagnosis, follow-up assessments and coordination of further measures (3, 11).

In guidelines where no specific references to general practitioners are included, we inferred potential primary care tasks from the described care pathways. These include the initial classification of symptoms, the assessment of functionality, and referral to specialized structures (4, 7). Some guidelines emphasize the importance of shared decision-making and the consideration of patients' individual needs and preferences (3, 7, 12, 13). From a primary care perspective, these aspects underline the potential importance of general practitioners due to continuity of care and their established relationship with patients.

Implications for primary care: the PAIS CARE study

Building on the guideline-based recommendations, the PAIS CARE model provides a structured framework for their implementation in routine care. Based on the G-BA guidelines, the PAIS CARE study operationalizes the role of primary care more clearly, with general practitioners playing a central role from the initial visit to the coordination of further care. Diagnostic and therapeutic measures are initiated and coordinated using a standardized manual based on current scientific evidence. Functional symptom severity is assessed using the Klok scale, which informs the subsequent care pathway within the PAIS CARE model. Patients with more

severe functional impairment (Klok grades 3-4) and specific clinical indications, such as suspected ME/CFS, POTS, or neurological symptoms, may be referred to specialized Charité outpatient clinics for further diagnostic evaluation and treatment (10). While the Klok scale has been validated for assessing functional limitations in adults with PCS, its use as part of this referral pathway is specific to the PAIS CARE model (3, 10). PAIS CARE integrates both pharmacological and non-pharmacological options into a graded treatment pathway based on the functional limitations of the patient. For common symptoms, the manual refers to the Therapy Compass of the German Federal Institute for Drugs and Medical Devices (BfArM) expert group, which lists potential medications according to key symptoms within their licensed indications (6, 10). Patient organizations and self-help groups are an integral part of the care structure.

Actionable recommendations

Based on the common principles identified across the reviewed guidelines, primary care management of PCS should follow a structured, symptom-oriented, and individualized approach. General practitioners should serve as a central point of contact, coordinating initial assessment, follow-up, and referral to specialized care where required. Diagnostic assessment should include structured history taking, symptom-oriented diagnostics, assessment of functional impairment, and consideration of relevant differential diagnoses.

Given the limited evidence for disease-specific pharmacological treatment, management should emphasize individualized, symptom-oriented care and appropriate non-pharmacological interventions. Functional limitations and PEM should be considered when planning therapeutic interventions.

For future guideline development, we suggest that greater emphasis should be placed on actionable recommendations for daily practice. Examples include flowcharts, stepwise care concepts, and standardized assessment tools for general practitioners.

Discussion

This paper provides a comparative analysis of international guidelines and recommendations for primary care of patients with PCS. The analysis identified common principles across the guidelines, particularly regarding structured history taking, symptom-oriented diagnostics, and individualized treatment. However, the recommendations differ in their level of detail, specificity, and practical applicability, reflecting differences in the available evidence and national healthcare structures. In Switzerland, for example, Long COVID contact points are centrally coordinated (11), while other countries have more decentralized structures.

Non-pharmacological therapy is described in detail, while pharmacological recommendations are largely limited to symptom-oriented treatment, reflecting the limited evidence base. No established causal pharmacological treatment for PCS was identified across the included guidelines, and no specific recommendations for experimental or off-label pharmacological treatment were identified.

The role of general practitioners is emphasized in several guidelines, but usually only outlined in general terms. Detailed statements on the specific structure of general practitioner care, such as the structuring of follow-up checks or cooperation with other levels of care, are rare. In contrast, the PAIS CARE model of care provides a more structured approach to the organization of primary care. In the guidelines, the direct incorporation of the patients' perspective into guideline development or the recommendation of specific participatory tools is largely absent (3, 7, 12, 13). From our perspective, especially in the context of a complex and often elusive clinical condition such as PCS, a stronger emphasis on patient-centered care concepts would be beneficial.

The scientific literature to date contains only a limited number of studies or review articles examining the role of primary care or addressing the delivery and management of care in primary care settings for patients with PCS and related post-infectious conditions. The article by Kingdon et al. focuses on the NICE guidelines for ME/CFS and their implications for primary care physicians (16). The review by Brode and Melamed proposes a pragmatic, structured framework for the management of Long COVID in primary care (17). Their stepwise approach emphasizes energy management and prevention of post-exertional malaise, symptom-oriented treatment, and cautious consideration of experimental therapies, highlighting both the opportunities and current limitations of primary care-based management in this complex condition.

Limitations

This work has some methodological limitations. The selection of guidelines was targeted and does not claim to be exhaustive. A systematic literature search was not conducted. Other relevant concepts or country-specific recommendations may therefore not have been captured. The evaluation of the content was based on a descriptive and qualitative approach. A methodologically critical case-by-case analysis of the guidelines was not planned. The results therefore do not permit conclusions on the effectiveness or superiority of specific approaches; instead, they provide a context-based comparison. Furthermore, it should be taken into account that the evidence base of the guidelines is limited, and numerous recommendations are based on expert opinions rather than reliable study data (4, 7). This applies, among other things, to pharmacological therapies, which are often suggested on a symptomatic basis without confirmed efficacy. Despite these limitations, the analysis provides important impetus for the further development of care. It highlights where national concepts such as PAIS CARE align with international guidance and where further additions could be beneficial.

Conclusion

The comparison of internationally relevant guidelines on PCS identified substantial overlap in key aspects of care, such as

symptom-oriented diagnostics and individualized therapy planning, while the role of primary care is addressed to varying degrees. At the same time, there are clear differences in the depth, specificity, and practical applicability of the recommendations. Overall, clear practical guidance for primary care remains scarce.

The PAIS CARE model provides a structured approach that incorporates central aspects of international guidelines and supplements them with a practical, tiered framework for the primary care context. The clear operationalization of primary care tasks within this model offers valuable approaches for the further development of primary care for patients with PCS.

Future directions

Given the large number of affected individuals and the still limited evidence base, there is an urgent need for scientifically sound and practice-oriented care concepts. Future research should evaluate the effectiveness of integrated care models such as PAIS CARE and how these structures can be adapted to different healthcare systems. The aim is to establish standardized, quality-assured, and cross-sectoral care that supports patients effectively while making efficient use of resources.

The social and health-economic consequences of PCS also require attention. Persistent functional limitations, reduced quality of life, and loss of work capacity also place a substantial burden on society and the labor market. Early, coordinated, and needs-based care is therefore of central importance not only in the interest of patients, but also from a health economics perspective.

Author contributions

MB: Conceptualization, Writing – original draft. JB-S: Writing – review & editing. CF: Writing – review & editing. CS: Conceptualization, Writing – review & editing. KW: Conceptualization, Writing – review & editing.

Funding

The author(s) declared that financial support was received for this work and/or its publication. This work was carried out as part of the PAIS CARE project, which is funded by the German Federal Ministry of Health (BMG) (Grant No. ZMII2-2524FSB105). The funding body had no role in the design of the study; in the collection, analysis, and interpretation of data; or in writing the manuscript.

Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was used in the creation of this manuscript. Generative AI was used to assist with language editing and improving the clarity and readability of the manuscript. All scientific content, interpretation, analyses, and conclusions were developed and verified by the authors, who take full responsibility for the manuscript.

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