Structuring knowledge on Long Covid: a bibliographic approach based on 3CGP (Core Content Classification in General Practice)

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Abstract

Long Covid represents a multidimensional challenge. Even in a reputedly high-level healthcare system, patients feel lost and abandoned when faced with this unknown disease and doctors who don't understand them because they can't find their usual nosographic framework. And if they do want to venture out and find out, the rapidly expanding scientific literature (over 7,000 articles listed on PubMed in just 4 years) overwhelms them. A structured organization of knowledge is essential to manage this complexity. To this end, an open bibliography has been developed based on the use of 3CGP (Core Content Classification in Primary Care), integrating ICPC (International Classification of Primary Care) and Q-Codes. ICPC-2 classifies references by body systems and medical themes, the Q-Codes integrate conceptual dimensions. Both tools are accessible via the HeTOp server. (https://www.hetop.eu/hetop/3CGP/en).   This bibliography is freely available on the Zotero platform under the name *Long Covid Open Library*. (https://www.zotero.org/groups/4929325/long_covid_open_library/library)   It provides a structured and evolving resource for exploring bodily systems and the concepts used to describe the long-term consequences of SARS-CoV-2 infection. This tool serves as a strategic starting point for organizing and prioritizing research on Long Covid, with opportunities for continuous improvement.

Résumé

Le Long Covid représente un défi multidimensionnel. Même dans un système de santé réputé de haut niveau les patients se sentent perdus et abandonnés face à cette maladie inconnue et des médecins qui ne les comprennent pas parce qu'ils ne retrouvent pas leur cadre habituel nosographique. Et s'ils veulent s'aventurer à savoir, une littérature scientifique en rapide expansion (plus de 7 000 articles répertoriés sur PubMed en seulement 4 ans) les débordent complètement. Une organisation structurée des connaissances s'avère essentielle pour gérer cette complexité. À cet effet, une bibliographie ouverte a été développée en s'appuyant sur l'usage de la classification 3CGP (Core Content Classification in Primary Care), intégrant l'ICPC (International Classification of Primary Care) et les Q-Codes. ICPC-2 classifie les références par systèmes corporels et thématiques médicales, les Q-Codes intègrent des dimensions conceptuelles. Ces deux outils sont accessibles via le serveur HeTOP (https://www.hetop.eu/hetop/3CGP/fr).   Cette bibliographie est librement disponible sur la plateforme Zotero sous le nom *Long Covid Open Library* (https://www.zotero.org/groups/4929325/long_covid_open_library/library) Elle constitue une ressource structurée et évolutive permettant d'explorer les systèmes corporels et les concepts utilisés pour décrire les conséquences à long terme de l'infection par le SARS-CoV-2. Cet outil représente un point de départ stratégique pour organiser et prioriser les recherches sur le Long Covid, avec des perspectives d'amélioration continue.

Context

Long COVID is a novel condition characterized by a pattern of symptoms previously unknown to both patients and physicians. This pattern is not part of the popular health culture, and while Long COVID has been assigned the code *RA02 Post Covid-19 condition* in ICD-11[1], it does not fit into known nosological frameworks[2]. It shares similarities with chronic fatigue syndrome and fibromyalgia but also with burnout syndrome. As a result, Long COVID is often overlooked or misidentified by physicians[3]. Patients, of which more than 65% are women, feel unrecognized or abandoned[4] and navigate from one doctor to another, often seeking solutions outside the medical system for a condition that overwhelms them and disrupts their lives.[5] Long COVID induces significant medicolegal challenges and leads to work loss for many individuals[6], often misclassified under misleading diagnoses such as burnout or anxiety-depression.[7]

An Inoperative Medical Nosology

The challenge of integrating Long COVID into medical nosology becomes apparent when examining the medical terminologies referencing this condition. This exploration was enabled using the multi-terminology server HeTOP from the University of Rouen.[8] Managing health data does not rely solely on definitions of Long COVID, whose limitations are well-known [9], but on the concepts and terms representing them. A striking heterogeneity in terminologies used by major medical sources is notable. Multiple categories are used to describe Long COVID, including "condition," "disease," "disorder," "diagnosis," "symptom," "syndrome," and "sequelae." Most terminologies categorize Long COVID as a general disease, except for ICPC and MedDRA, which specifically include the term "respiratory." The Human Phenotype Ontology (HPO), a symptom ontology, does not incorporate Long COVID within its conceptual framework.[10]

In 2021, Deer et al. developed an ontology based on HPO to examine the content of 47 articles on Long COVID, leading to the creation of the Long COVID Phenotype Ontology (LCPO).[11] The LCPO, comprising 286 entries, was mapped by the author and a colleague to the International Classification of Primary Care, third revision (ICPC-3).[12] This mapping highlighted the prevalence of neurological and psychiatric issues identified by healthcare professionals in the analyzed articles (Fig.1).

By 2021, it was not yet possible to classify accurately Long COVID within medical nosology. A shift in approach was required, focusing on symptoms as clinical indicators. The exceptional symptom distribution, with a notable emphasis on neuropsychiatric symptoms, paved the way for meticulous observation
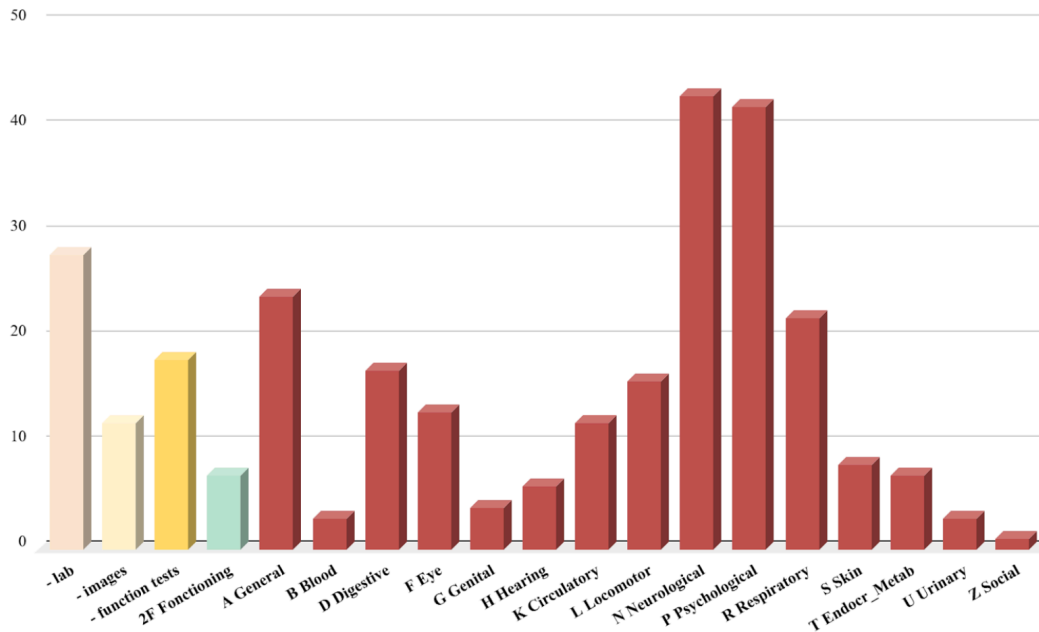
Fig. 1; The 286 entries of the ontology developed by Deer et al. (2021) have been mapped to ICPC-3 chapters (work carried out by the author and Prof. Kees van Boven, University of Nijmegen - unpublished). The distribution of all ontology concepts across ICPC-3 chapters reveals a striking pattern, with a notable prevalence of neurological and psychological symptoms. (A general, B Blood, D Digestive, F Eye, G genital, H Hear, K cardio, Locomotor, N neuro, P Psycho, R, Resp, S Skin, T Metabol, U Urinary, W Pregnancy , Z Social)

Utilization of the Human Phenotype Ontology

Numerous studies attempted to describe the symptoms of the disease as early as 2021. The symptom profile is highly unexpected, with more than 60 symptoms identified to date.[13–15] The disease affects all bodily systems and has severe psychological, familial, social, and economic repercussions.

The Human Phenotype Ontology (HPO)[11] is a structured vocabulary designed to describe human phenotypic abnormalities in a standardized and machine-readable manner. Each HPO term corresponds to a specific clinical feature, such as "dyspnea" or "muscle weakness," and is associated with a unique identifier (e.g., HP:0002094). The ontology is hierarchically organized, with general categories encompassing more specific phenotypes.

Figure 2 shows the distribution of the top 20 symptoms among the first 50 patients seen in 2021 in a general practice clinic in Charleroi, Belgium, classified according to the Human Phenotype Ontology (HPO). An unusual symptom pattern emerges, necessitating information from diverse domains such as memory issues, respiratory problems, sleep disturbances, or cardiac symptoms. These first 50 patients underwent transcriptomic investigation strongly suggesting viral persistence, published elsewhere.

Top 20 Long Covid Symptoms By Prevalence

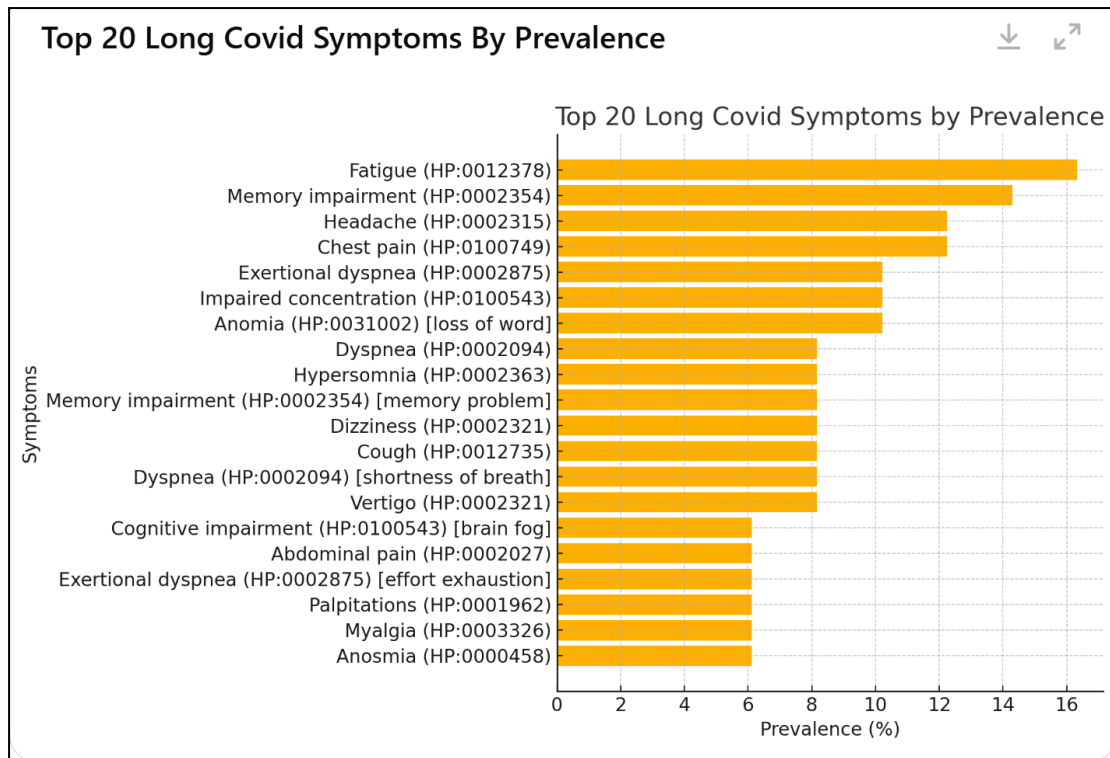### Top 20 Long Covid Symptoms by Prevalence

Fig 2; Distribution of symptoms in the first 50 patients seen in 2021 (MJ personal practice) in Long Covid patients, identified in the Human Phenotype Ontology (HPO) on analysis of patient verbatim and consultation notes.

These symptoms frequently occur in individuals with no prior experience of illness, whose acute COVID-19 infection disrupted their life narratives. Even patients with pre-existing comorbidities often feel much more altered than before. Their functional state has become a struggle, often concealed, internalized as guilt, or misinterpreted as depression. When a long-standing relationship exists between the patient and their physician, the change may be quickly noticed. The family doctor, recognizing the change, may question its cause. However, in healthcare systems without access limitations to specialists, patients often consult wherever their symptoms lead them.[16] Pulmonologists, cardiologists, rheumatologists, and other specialists are consulted for symptoms they fail to recognize. Lab results appear normal, and imaging techniques remain silent. The patient eventually ends up in psychiatry, excluded from known diagnoses.

Hence, physicians must adapt their relationship with patients, take the time to listen and record, and become an explorer, the Humboldt [17] of this new disease, where the patient is the expert.

This type of doctor-patient relationship, termed partnership [18], requires tools to manage knowledge from both the patient's experience and peer expertise. Regarding patient experience, automated interview transcription and symptom identification using HPO through large language model (Fig.2) are employed—a topic to be discussed in another article.

In this document, we focus on managing knowledge from peers, commonly referred to as a bibliography, but driven by the patient's experiences.

Scientific Knowledge Management of Long COVID through Bibliography

Post-COVID syndrome does not fit into known categories, confusing both physicians and patients.[2] In this context, maintaining an operational bibliography is a critical challenge within the broader framework of research, as previously described. A simple PubMed query using the term *Long COVID* currently returns over 7,400 articles (January 2025), a volume that is challenging to manage without a structured tool.

Since July 2021, weekly compilation and organization of knowledge on Long COVID have led to the development of a structured bibliography dedicated to this complex and evolving subject. Zotero, a free and open-source software,[19] has been used for this purpose. Zotero facilitates the collection, organization, and citation of sources from various online platforms. The bibliography thus created remains an evolving project.

References are primarily retrieved using monitoring systems on PubMed and Google Scholar with simple descriptors like *Post-Acute COVID-19 Syndrome [Mesh]* or *Long COVID [tw]*, generating an average of two to five new citations per week. Social media platforms, such as X (formerly Twitter) and LinkedIn, are also valuable sources consulted regularly. Abstracts of identified articles are systematically reviewed, and relevant elements are stored in Zotero using its integrated Google Chrome save feature. The selection of retained items is performed by a single observer, based on clinical, epidemiological, diagnostic, or therapeutic interest and aligned with ongoing research areas (multi-omics, neurobiology, advanced imaging).

Patient demands, as they too can become formidable Internet experts, also require particular attention.

Structuring Bibliographic Data

Long COVID spans all bodily systems, social interactions, and professional issues, making a methodical approach essential to organizing the exponentially growing scientific literature. To manage this information overload, a knowledge organization framework has been established using the **Core Content Classification in General Practice (3CGP)**.[20,21]

This classification system is designed to structure and organize essential content in general practice or primary care. Its main goal is to create a standardized database for describing competencies, activities, and fundamental knowledge in this domain, integrating the ICPC (International Classification of Primary Care) and Q-Codes.

International Classification of Primary Care (ICPC)[22] **;** The ICPC, developed by the World Organization of Family Doctors (WONCA), categorizes consultation reasons, diagnoses, and interventions in primary care. It is divided into 17 chapters, each representing a body system or theme (e.g., A for general, N for neurology, Z for social issues). (See Fig.3) For example, neurological aspects are grouped under the code LC-N (neuro), corresponding to the ICPC neurology chapter. Societal and labor-related issues are classified under LC-Z (Social), corresponding to the ICPC

social chapter. Procedural codes are used for immunology (-33), imaging (-41), pharmacological therapy (-50), physical therapy (-51), and psychological therapy (-58).
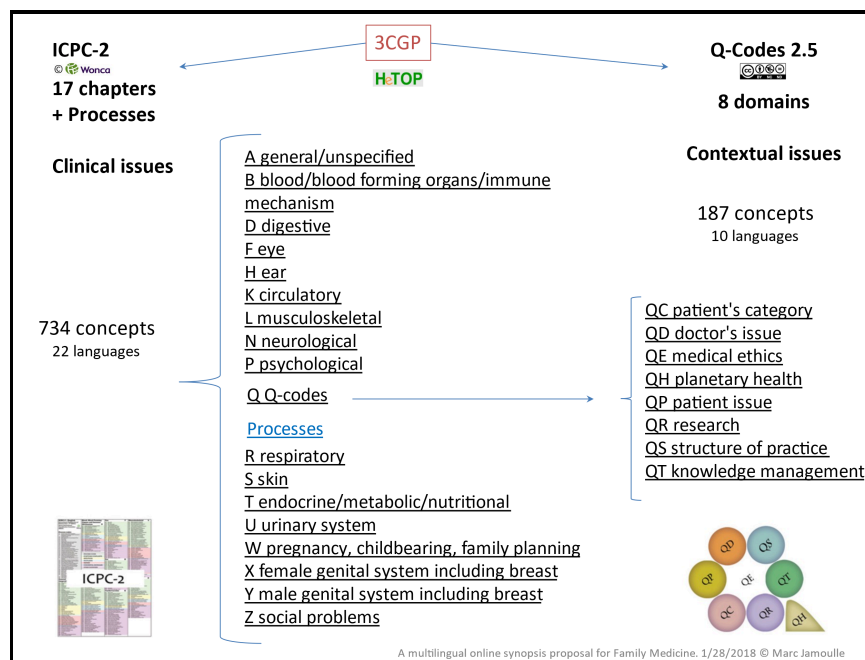

ICPC-2 © Wonca 17 chapters + Processes	3CGP HeTOP	Q-Codes 2.5 8 domains

Clinical issues

A general/unspecified
B blood/blood forming organs/immune mechanism
D digestive
F eye
H ear
K circulatory
L musculoskeletal
N neurological
P psychological

734 concepts
22 languages

Q Q-codes

Processes

R respiratory
S skin
T endocrine/metabolic/nutritional
U urinary system
W pregnancy, childbearing, family planning
X female genital system including breast
Y male genital system including breast
Z social problems

ICPC-2

Contextual issues

187 concepts
10 languages

QC patient's category
QD doctor's issue
QE medical ethics
QH planetary health
QP patient issue
QR research
QS structure of practice
QT knowledge management

A multilingual online synopsis proposal for Family Medicine. 1/28/2018 © Marc Jamoulle

Fig 3; General Practice Core Content Classification (3CGP) showing the 17 chapters of ICPC-2 and the process as well as the 8 usual concept domains (Q-Codes) used in daily practice. Most of these are used in the Long covid bibliography.

The Q-Codes; Q-Codes are an extension of ICPC classification, designed to integrate cross-cutting and conceptual dimensions into primary care.[23] They allow coding of themes that do not strictly fall under symptoms or diagnoses but reflect contextual, social, or methodological aspects of medical practice. Examples include qualitative research, palliative care, patient education, epidemiology, ethics, epistemology, or social determinants of health. This classification is particularly useful for structuring complex issues like Long COVID, providing a conceptual framework complementary to ICPC chapters.

These tools are integrated to form **3CGP**, accessible in 14 languages on the HeTOP (Health Terminology/Ontology Portal) server. Developed by the CISMeF team at CHU Rouen, France, HeTOP includes major health terminologies and ontologies with over 3 million concepts in 55 languages across 100 terminologies.[8]
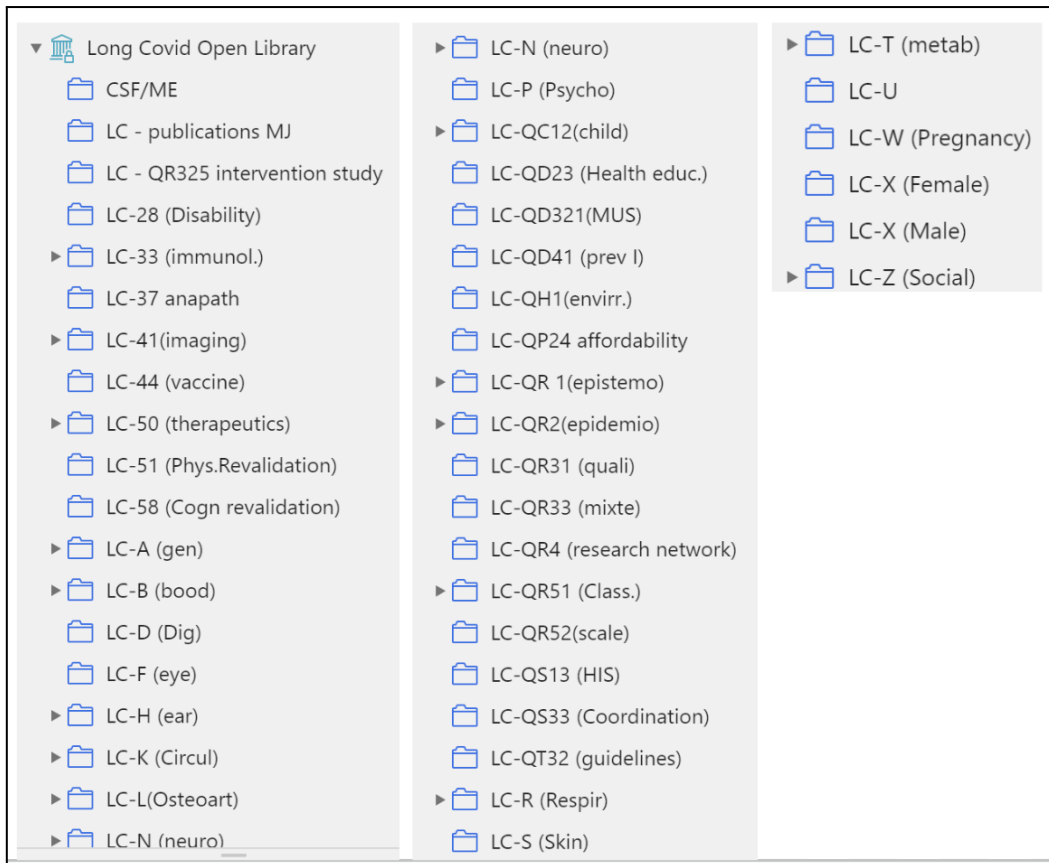
Fig 4 ; Bibliography headings on the Long Covid bibliography freely available on Zotero. The Letters refer to body systems (A general, B blood, K cardiovascular, Z social etc.) The Letter Q identifies concepts necessary for conceptual organization.

Using HeTOP, corresponding items can be identified, and relevant references grouped into an open-access Zotero library: the Long COVID Open Library. As of January 2025, this library contains 1,479 entries, including 1,167 articles, 169 web pages, and 10 books.

Some citations may belong to multiple categories due to the cross-cutting nature of Long COVID issues.

Progressive Development and Practical Examples

Some current uses of the bibliography are described here

Investigating Unusual Symptoms

Encountering new symptoms is common even when Long COVID is strongly suspected.[24] A young woman may develop post-COVID organic anorexia, another reports fever with exertion, while someone else notes blue discoloration of fingers. Why does a particular patient experience previously unknown digestive issues, visual disturbances, tinnitus, memory loss, anomia or dysphasia? These symptoms or their associations are often unknown even to seasoned clinicians, necessitating peer consultation.

Addressing the issue of Long covid in children and teenagers

In our tool, the issue of long covid in children is managed in the LC-QC12(child) and LC-QC13 (adolescent) directory. This library has been useful to the Association Long Covid Belgium, which has published a remarkable informative document on this issue.[25] This disaster affecting the very young[26] goes unnoticed and parents feel despised and denied when they ask for help.

Responding to specific patient queries

Abandoned by the healthcare system, patients turn to the Internet and social network (27) and arrive with proposals, ideas, or questions—sometimes odd, sometimes insightful, but always marked by their struggle with uncertainty. As patients, they expect professionals to address their concerns with authority. The Fig. 5 illustrates the subdirectories of LC-50 (therapeutics) (-50 address pharmacology in ICPC) where documents were actively searched to answer both practitioner and patient questions. Themes range from ancestral remedies to monoclonal antibodies.

Trust cannot be gained through denial. If a patient reads in peer groups about a miraculous treatment, dismissing it outright is insufficient. It is crucial to reveal the uncertainty behind such claims, often hidden in fake news. This is even more critical if a colleague endorsing unconventional medicine offers definitive opinions. The Brandolini Principle—"It takes more effort to refute misinformation than to produce it"—is particularly apt here.[28]
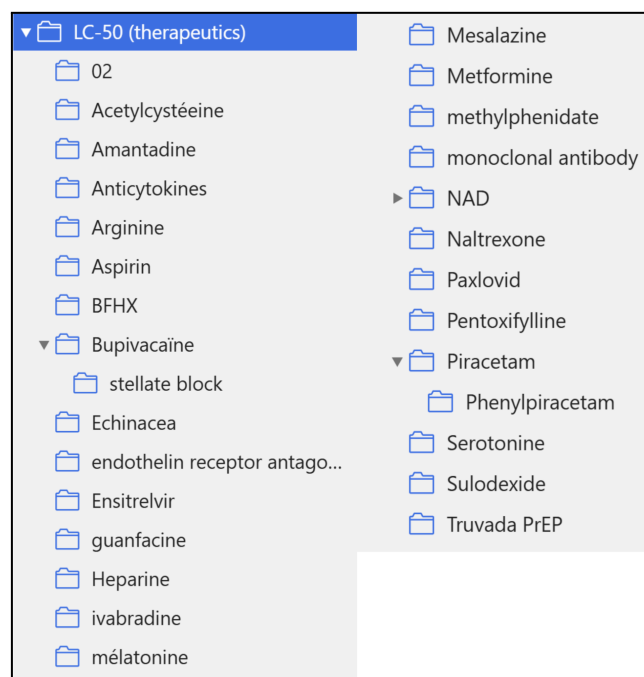

Fig 5 ; Open the LC-50 (Therapeutics) directory of the Long Covid online bibliography on the Long Covid website. Products studied.

Learning Entirely New Fields

Given the silence of cellular biology and conventional imaging in Long COVID cases, it became necessary to turn to advanced molecular biology or imaging techniques. With support from the COVID Human Genetic Effort network and Professor Casanova (Necker & Rockefeller), resources like transcriptomics,[29] proteomics, metabolomics, advanced immunology, and genomics became essential tools (refer to LC-33 (immunol)). Scintigraphy with technetium,[30] 8FDG PET scans, functional magnetic resonance imaging (fMRI), and magnetic resonance spectroscopy (SMR) (refer to (LC-41(imaging)) all reveal the extent of brain damage caused by SARS-CoV-2.

Documenting Referrals to Specialists or Insurance Physicians

For Long COVID, it is essential to highlight and explain the disease to both the patient and the various specialists to whom they are referred. Knowledge distribution remains uneven. For example, a gastroenterologist preparing for a colonoscopy should be informed that it is possible to search for viral RNA in colon biopsies.[31,32]

All specialties are affected, but convincing insurance physicians of the disease's reality remains particularly challenging.[33] Detailed reports, accompanied by tailored bibliographies, can support patients in being recognized for their suffering, adequately compensated, or assisted with work accommodations or school arrangements for children.

Educating Medical Students

A general practice clinic serves as a pedagogical training ground. Since 2021, numerous trainees have had the opportunity to work with and understand Long COVID patients or conduct thesis projects on the topic. Whether through traditional observation,[34] qualitative research [35], or learning to manage data professionally,[36] students have found valuable information through this open-access bibliography. Thus, this bibliography becomes a dynamic and living tool, which also helps document this very article.

Discussion

The development of a structured bibliography dedicated to Long COVID represents an essential response to the multidimensional complexity of this condition. Faced with a new invisible disease,[37] poorly understood by both physicians and patients, this initiative provides a methodological framework to organize and prioritize knowledge. The organization of references using 3CGP—the combination of ICPC-2 and Q-Codes, accessible via the HeTOP platform facilitates the exploration of bodily systems and conceptual dimensions. Integrating this bibliography into the Zotero platform makes it a collaborative and evolving resource, well-suited to the ongoing evolution of Long COVID research.

It is striking to note that all 17 chapters of the ICPC and several Q-Codes are required to cover the knowledge field needed for Long COVID. Indeed, it is known that the virus affects all bodily systems [38] and has severe social, psychological, and economic consequences.[39] This new disease also highlights a double epistemological gap: between patients and doctors on the one hand,[3] and between doctors and scientists on the other.[40] The latter are

fascinated by the multiplicity of the attacks caused by this new virus, while the former seem relatively indifferent to the avalanche of new knowledge generated by studying the disease.

The distribution of concepts across ICPC-3 chapters in Deer et al work [11] already highlights, as early as 2021, the prevalence of neurological and psychiatric symptoms, illustrating the profound impact of Long COVID on these systems. Simultaneously, the use of the HPO to document symptoms enriches diagnostic approaches by capturing the diversity of clinical manifestations.

This structured knowledge management meets not only scientific needs but also provides a valuable tool to assist patients in their care journey, often marked by diagnostic uncertainty and feelings of abandonment.

Standardizing Long COVID in Medical Nosology

Several researchers have investigated the integration of Long COVID into medical nosology, emphasizing coding and clinical classification systems. A study published in the British Journal of General Practice analyzed the use of SNOMED-CT codes for Long COVID in primary care in England, highlighting disparities in coding practices among general practitioners.[41] The National Center for Advancing Translational Sciences (NCATS) studied Long COVID coding using the ICD-10-CM U09.9 code, providing insights into characterizing the condition through existing coding frameworks.[42] The article by Deer et al. discussed earlier (Fig. 2) explores the application of the HPO to standardize descriptions of Long COVID's clinical manifestations. Similarly, the NIH RECOVER study identifies Long COVID subtypes using phenotypic data modeled from electronic health records,[43] leveraging the HPO to assess phenotypic similarity among patients.

Online Bibliographic Resources

Several online bibliographic services on Long COVID exist: The **Haute Autorité de Santé (HAS)** (France) publishes epidemiological data and pathophysiological mechanisms related to prolonged COVID-19 symptoms.[44] However, the documents are presented as downloadable XLS files, targeting researchers and epidemiologists rather than clinicians. The **LitCovid Database**, maintained by the U.S. National Library of Medicine, compiles scientific articles on COVID-19, including a dedicated Long COVID section. [45] It is regularly updated and offers topic-based searches. The ComPaRe Long COVID study by Assistance Publique - Hôpitaux de Paris (AP-HP) provides information and publications but is not a continuously evolving bibliography.[46] The Long Covid France patient association maintains a bibliographic database of a similar type, initially in the form of a Google Sheet file, and later as a Zotero file, though with less specific categorizations.[47] The clinical bibliography outlined here appears to be distinctive, as it is directly connected to clinical care and systematically categorized.

Limitations and Future Directions

It could be argued that this bibliographic effort represents a personal selection, established by a single author with occasional input from peers. However, precisely because the author is a clinician, other clinicians may find value in it and, potentially, suggest new entries.

Some citations require verification to correct errors or refine their classification. Improved management of references spanning multiple ICPC or Q-Code categories would enhance its utility. While not exhaustive, this bibliography serves as a starting point for researchers seeking to deepen their work on Long COVID.

Conclusion

A bibliography is an indispensable tool for managing the complexity of real-world challenges. It is as essential as the travel journals of Humboldt or Darwin,[17] contributing to understanding the complexity of life and its response to the SARS-CoV-2 attack, a virus that can turn us into an astronomer of thought by following in the footsteps of Olivier Sacks.[48]

The resources organized in this bibliography are freely accessible and provide a robust foundation for scientific exploration of Long COVID.

Abbreviations

3CGP: Core Content Classification in General Practice
HPO: Human Phenotype Ontology
ICD-11: International Classification of Diseases, 11th Revision
ICPC: International Classification of Primary Care
ICPC-2: International Classification of Primary Care, Second Revision
ICPC-3: International Classification of Primary Care, Third Revision
LCPO: Long COVID Phenotype Ontology
MD: Doctor of Medicine
MedDRA: Medical Dictionary for Regulatory Activities
NCATS: National Center for Advancing Translational Sciences
PET: Positron Emission Tomography
Q-Codes: Qualitative Codes used in medical classification systems
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
SNOMED-CT: Systematized Nomenclature of Medicine - Clinical Terms
WONCA: World Organization of Family Doctors
X (formerly Twitter): Social media platform used for information dissemination

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