

# **Establishing a Long COVID Registry for Wales**

December 2021

## Executive Summary

Since the emergence of COVID-19, the Bevan Commission, in its capacity as the leading think tank for Health and Care in Wales, has provided advice and support to the Minister and Welsh Government. This includes publications such as the COVID-19 Evidence Series, Beyond the Curve and Doing Things Differently series. More recently, the Bevan Commission has been asked to make recommendations to Welsh Government on how Wales should set about establishing a voluntary Long COVID Registry. This report provides an overview of the findings, including insight from the exploratory desktop research, the Advisory Board and wider stakeholder consultation.

## Summary of Findings and Recommendations

The following summarises the findings and recommendations from the exploratory desktop research, Advisory Board meetings and patient representative input.

- The Advisory Board and patient representatives confirmed the importance of a Long COVID Registry to address unanswered questions, improve the management of Long COVID and the experience of patients.
- There are currently a range of organisations, databases, apps and systems within Wales that contribute to and/or support Long COVID. These include Health and Care Research Wales (HCRW), Digital Health and Care Wales (DHCW), Public Health Wales (PHW), the Office of National Statistics (ONS), the Secure Anonymised Information Linkage (SAIL) database and HealthWise Wales (HWW).
- Digital infrastructure and data linkage are key to the success of a registry. In particular, connecting current systems and databases to link primary care and hospital records, coronavirus and antibody testing data, vaccination records and death registrations.
- Greater clarity and coordination is needed across agencies and organisations to realise the full potential of a future Long COVID Registry in Wales.
- A Long COVID Registry should be interventional and have a dual purpose for both research and service improvement to enable a greater understanding of the patient experience as it evolves.
- A Long COVID Registry offers many advantages prospectively and retrospectively for research and service improvement. These include long-term monitoring, a consistent and coordinated database, treatment stratification and prudent use of resources across services, databases and stakeholders.
- Other key issues considered included: the adoption of Prudent Healthcare to support service improvement, equitable access, data and information protocols, inconsistency in coding particularly in primary care and the need for knowledge transfer and collaboration.
- A potential framework has been developed to understand how to set about establishing a Long COVID Registry. Key steps identify the purpose, operational requirements, inclusion criteria, data and ethics, communication and intervention strategy, and key outcomes.
- The most feasible configuration for a Long COVID Registry was confirmed through an option appraisal exercise. This includes the consolidation of existing databases, recruitment of self-referred population and a communication strategy.
- DHCW has been identified as the most suitable body to lead a proposed Long COVID Registry, with SAIL, HWW, ONS and PHW as key collaborators.

## The Bevan Commission

The Bevan Commission is a group of international experts to help ensure that Wales can draw on best practices from across the world, while remaining true to the principles of the NHS as established by Aneurin Bevan. The Commission is not a formal part of the NHS in Wales and acts as an impartial advisory group to the Minister for Health and Social Sciences.

## Long COVID Registry Advisory Board

The programme will be supported through the Bevan Commission Team, an external Advisory Board and patient representatives. There will also be supporting stakeholders involved through the Bevan Commission networks and based on the desktop research carried out as part of this work.

Baroness Ilora Finlay of Llandaff – ***Chair of Advisory Group***

Mr Daniel Ayoubkhani – ONS Statistician

Mr Iain Bell – National Director for Public Health Knowledge and Research

Sir John Bell – Regius Chair of Medicine Oxford University

Mr Tom Brufatto – All-Party Parliamentary Group on Coronavirus Secretariat

Professor Tom Connor – Professor of Genomics at Cardiff University and Bioinformatics Lead PHW

Dr Tracey Cooper – Chief Executive Public Health Wales

Ruth Crowder – Chief Allied Health Professions Advisor

Dr Sunill Dolwani – Consultant Gastroenterologist Cardiff and Vale UHB and HealthWise Wales

Professor Adrian Edwards – Professor of General Practice Cardiff University and Director of Wales COVID Evidence Centre

Professor Andrew Freedman – Consultant in Infectious Diseases, Cardiff University Head of Department (Medicine) and UHW

Professor Christopher Griffiths – Foundation Professor of Dermatology, University of Manchester

Katy Hossack – Welsh Government Head of Shielding and Long COVID

Mr Gareth John – Head of Information Development and Delivery DHCW

Professor Chris Jones – Welsh Government Deputy Medical Chief Officer and Professor of Health Services Swansea University

Professor Keir Lewis – Professor of Respiratory Medicine and Respiratory Lead, Hywel Dda

Professor Ronan Lyons – Professor of Public Health and Co-Director SAIL Databank, Swansea University

Professor Ewan Macdonald OBE – Commissioner and Occupational Physician

Rachael Powell – Deputy Director of Information DHCW

Professor Calum Semple – Professor of Child Health and Outbreak Medicine, Consultant Respiratory Paediatrician and DHSC Government Advisor

Professor Sally Singh – Head of Cardiac Rehabilitation Leicester Hospitals/Your COVID Recovery App

Helen Thomas – CEO Digital Health and Care Wales

Professor Kieran Walshe – Director of Health and Care Research Wales

Dr Heather Payne – Consultant Paediatrician and Senior Medical Officer Welsh Government

Rachel Powell - DHCW Deputy Director of Information

## **Patient Representatives**

Five patient representatives

## **Bevan Commission Team**

Mrs Helen Howson – Director

Dr Rupa Chilvers – Deputy Director

Dr Fern Davies – Senior Research Officer

## **Abbreviations**

AI – Artificial Intelligence

AMS – Academy of Medical Sciences

COPI – Control of Patient Information

CIS – Coronavirus Infection Survey

CPI – Confidential Patient Information

DHCW – Digital Health and Care Wales

DHEW – Digital Health Ecosystem Wales

DSPP – Digital Services for Patients and Public

GDPR – General Data Protection Regulation

HWW – Healthwise Wales

NEET – Not in Education, Employment or Training

NICE – National Institute for Health and Care Excellence

PHW – Public Health Wales

PII – Personally Identifiable Information

SAIL – Secure Anonymised Information Linkage

ONS – Office of National Statistics

UK – United Kingdom

WHO – World Health Organization

## Contents

1. Introduction
2. Long COVID
  - 2.1 Defining Long COVID
  - 2.2 Long COVID symptoms and systems
  - 2.3 Long COVID prevalence
3. Long COVID Registry
  - 3.1 The UK and international context for setting up voluntary Long COVID Registries
  - 3.2 Role and format of a Registry
  - 3.3 Overview of the current evidence on Long COVID
4. Findings
  - 4.1 What are the purposes of a Welsh Long COVID Registry?
  - 4.2 Why establish a Welsh Long COVID Registry?
  - 4.3 How do we set about establishing a Welsh Long COVID Registry?
  - 4.4: Co-production with patients
5. Option Appraisal
  - 5.1 Welsh Long COVID Registry options
  - 5.2 Evaluation of Welsh Long COVID Registry options
6. Option 3 – Consolidate existing databases and recruit a self-referred population with a communication strategy
  - 6.1 Consolidation of existing databases and access to data
  - 6.2 Recruitment of self-referred population
  - 6.3 Communication strategy
  - 6.4 Technology and apps
  - 6.5 Patient consent
7. Potential Long COVID Registry Framework
8. Other Issues Considered
9. Conclusions and Recommendations
10. Annexes
11. References

## Tables

Table 1: COVID-19 Definitions

Table 2: WHO Post COVID-19 Clinical Case Definition

Table 3: Wales Long COVID Registry Options

Table 4: Wales Long COVID Registry Option Appraisal

# 1. Introduction

The Bevan Commission, the leading independent think tank for health and care in Wales, has been asked by the Minister for Health and Social Services, Eluned Morgan, to make recommendations on *'how we should set about establishing a voluntary registry for Long COVID in Wales so that we can undertake long term monitoring of this condition and provide support and opportunities for volunteers to participate in trials if new treatments are forthcoming'*. The main objectives of this work are as follows.

Exploratory desktop research objectives:

- To understand the UK and international context for setting up voluntary Long COVID registries
- To understand the role and format of a registry
- To provide an overview of the current evidence on Long COVID

Overall objectives of the Long COVID Registry work:

- To understand the purpose of a Welsh Long COVID Registry
- To understand why a Welsh Long COVID Registry should be established
- To understand how to set about establishing a Welsh Long COVID Registry

The Bevan Commission will undertake this work by completing the following activities:

## **Exploratory desktop research**

- Exploratory research to understand the United Kingdom (UK) and international context for setting up voluntary long COVID registries

## **Formation of an Advisory Board/Expert Panel**

- The formation of an Advisory Group consisting of an 'expert panel' drawing from internationally renowned experts in the field and key partners in Wales

## **Monthly meetings of the Advisory Board**

- Four meetings of the Advisory Group to collate information and to consider the three main objectives of the work (see above)

## **Wider stakeholder engagement**

- Wider stakeholder engagement to bring in the most recent experiences of Long COVID through patient representatives and a workforce perspective

This report aims to provide an overview of the exploratory desktop research, key findings, option appraisal and recommendations from the Advisory Board and wider stakeholders. It also provides key concluding points and recommendations for consideration.

## 2. Long COVID

### 2.1 Defining Long COVID

Coronavirus disease 2019 (COVID-19) has had a profound impact on the lives and health of people around the globe<sup>i</sup>. As of the 7<sup>th</sup> December 2021, more than 264 million confirmed cases of COVID-19 have been recorded worldwide and more than 5.24 million deaths have been reported by the World Health Organization (WHO)<sup>ii</sup>. Recent evidence has shown that a range of persistent symptoms can remain long after the acute SARS-CoV-2 infection, commonly referred to as Long COVID<sup>i</sup>. The diversity in presentation and severity of symptoms makes Long COVID difficult to define, but current clinical definitions developed by the National Institute for Health and Care Excellence (NICE) broadly identify it as signs and symptoms that develop after acute COVID-19 infection, that cannot be explained by an alternative diagnosis. This definition includes ongoing symptomatic COVID-19 from 4-12 weeks and post-COVID-19 syndrome lasting longer than 12 weeks<sup>iv</sup>.

**Table 1: COVID-19 Definitions (NICE, 2021)**

|  |
|--|
| <b>Acute COVID-19</b> is defined as signs and symptoms of infection for up to the first 4 weeks.   |
| <b>Ongoing symptomatic COVID-19</b> is defined as signs and symptoms of infection from 4-12 weeks.   |
| <b>Post-COVID-19 syndrome</b> is defined as signs and symptoms of infection consistent with COVID-19 lasting longer than 12 weeks.                         |
| <b>Long COVID</b> is defined as signs and symptoms persisting after the first 4 weeks, so encompasses both ongoing symptomatic and post COVID-19 syndrome. |

The World Health Organization (WHO) have recently published a clinical case definition of post COVID-19 condition that includes 12 domains. It was developed through a Delphi consensus study and is available for use in all settings<sup>iii</sup>. The definition of post COVID-19 condition is identified below, although a separate definition may be applicable for children.

**Table 2: WHO Post COVID-19 Clinical Case Definition**

| <b>WHO – Post COVID-19 Clinical Case Definition</b>   |
|---|
| <i>Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others* and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time. A separate definition may be applicable for children<sup>iii</sup>.</i> |
| <i>Notes: there is no minimum number of symptoms required for diagnosis; though symptoms involving different organ systems and clusters have been described.</i>  |

### 2.2 Long COVID Symptoms and Systems

Long COVID can affect those with very mild acute disease to those with the most severe forms<sup>i</sup>. Symptoms are known to range between mild and disabling and can involve multiple organs and

systems (see Annex 1, 2 and 3). These include, but are not limited to, respiratory, cardiovascular, neurological, gastrointestinal, musculoskeletal, psychological and dermatological systems<sup>iv</sup>. The symptoms of Long COVID are variable and wide-ranging, with differing manifestations. Some of the most commonly reported symptoms include malaise, fatigue, dyspnoea, cardiac abnormalities, cognitive impairment, headaches, concentration problems, sleep disturbances, nausea, joint and muscle pains, depression and anxiety, loss of taste and/or smell and skin rashes<sup>1</sup>. However, the long-term consequences of infection are still largely unknown.

### 2.3 Long COVID Prevalence

The long-term symptoms of COVID-19 could have a devastating impact on public health<sup>v</sup>, with a substantial proportion of people with symptomatic COVID-19 going on to have persistent symptoms for 12 weeks or longer<sup>viii</sup>. Estimates of the number of people affected by Long COVID vary, but on the 2<sup>nd</sup> December 2021, the Office of National Statistics (ONS) identified that there were 1.2 million (1.9%) people living in private households in the UK who were experiencing self-reported Long COVID symptoms<sup>vi</sup>. Of people with self-reported Long COVID, 71% first had (or suspected they had) COVID-19 at least 12 weeks previously and 36% first had (or suspected they had) COVID-19 at least one-year previously<sup>vi</sup>.

The same data identified that symptoms adversely affect the day-to-day activities of 775,000 people (64% of those with self-reported Long COVID) and as a proportion of the UK population, prevalence of self-reported Long COVID was greatest in people aged 35 to 69 years, females, people living in the most deprived areas, those working in health or social care, and those with another activity-limiting health condition or disability<sup>vi</sup>.

Whilst the prevalence of Long COVID remains highly uncertain<sup>1</sup>, modelling suggests that a third peak of COVID-19 infections over the summer of 2021 will put pressure on the health service and lead to higher levels of Long COVID<sup>vii</sup>. Managing the long-term sequelae of SARS-CoV-2 infection in the population will therefore remain a major challenge for health and care services in the next stage of the pandemic. Despite not knowing the extent of the resultant public health burden<sup>viii</sup>, it is undeniable that Long COVID will have long-term population health and socio-economic implications.

## 3. Long COVID Registry

### 3.1 UK and International Context for Setting up Voluntary Long COVID Registries

Exploratory desktop research was conducted and replicated by two researchers and confirmation was sought from the expert panel to establish the UK and international context for voluntary Long COVID registries. Whilst there are registry-based studies on long COVID<sup>ix</sup> and registries that have been

---

<sup>1</sup> For a comprehensive summary of studies that have explored the persisting symptoms post COVID-19 infection, please refer to *'Long covid – mechanisms, risk factors, and management'*<sup>i</sup> and for a review of long COVID research in Wales, the Wales COVID Evidence Centre – *'Summary of Active and Prospective Long-COVID Research in Wales Report'*<sup>xviii</sup>.



updated to record Long COVID information<sup>x</sup>, it is evident from this work that there are no known voluntary registries specifically for Long COVID that have been launched in the UK to date.

Evidence was found to suggest that a Scottish Long COVID Registry was in development, but correspondence with Scottish Government representatives confirmed that at present, there are no plans for a registry to go ahead. The NHS England Long COVID plan for 2021/2022<sup>xi</sup> also identified the development of Long COVID patient registry by July 2021, but this is specifically for patients attending the Post-COVID Assessment Clinics and there is no clear indication that this has been launched.

Information from the US to date indicates that legislation has been introduced in New York<sup>xii</sup> to establish a COVID-19 Health Registry to monitor the long-term effects of COVID and RTI International published advice to suggest that a longitudinal registry of COVID-positive patients would be a solution to target prevention efforts and provide care to patients<sup>xiii</sup>. However, again there is no indication that a registry has been launched.

## **3.2 Definition, Role and Format of a Registry**

### **3.2.1 Definition**

There are numerous types of registries that can serve many roles, but medical registries more broadly can be defined as “a database of identifiable persons containing a clearly defined set of health and demographic data collected for a specific public health purpose”<sup>xiv</sup>. A Welsh Long COVID Registry specifically could also be identified as a voluntary patient or disease registry. A patient registry can be defined as “an organised system that collects data and information on a group of patients defined by a particular disease, condition of exposure, and that serves a predetermined scientific, clinical and/or public health (policy) purpose”<sup>xv</sup>, whereby a disease or condition registry uses “the state of a particular disease or condition as the inclusion criteria”<sup>xvi</sup>.

Discussions to date suggest that a voluntary patient registry would be suitable to collect data and information from Long COVID sufferers and to enable a greater understanding of the patient experience as it evolves. The inclusion of control groups has been identified as a key area for consideration and is included in the proposed registry framework.

### **3.2.2 Purposes**

A patient registry can have multiple roles including scientific, clinical and to inform health policy<sup>xvi</sup>, observational or interventional, or to provide statistical analysis. However, typically the purpose of a patient registry is to serve as a tool to:

- Observe the course of a disease
- To understand variations in treatment and outcomes
- To examine factors that influence prognosis and quality of life
- To describe care patterns
- To assess effectiveness to monitor safety and harm
- To measure quality of care<sup>xvi</sup>
- To gain an understanding of the patient experience
- To provide intervention

Discussions to date have suggested that a Long COVID Registry in Wales should have two prime functions, research and service improvement to the benefit of the patient. This is discussed in further detail in Section 4.1.

### 3.2.3 Format

The format of a registry will largely depend on the intended purpose (form follows function), with many registries developed to serve more than one purpose. When planning a registry there are a number of important factors that will need to be considered to ensure that the registry is formatted in the most appropriate way, taking into account local conditions and existing infrastructures. The following provides a number of important factors that will need to be considered in order to help guide and inform a framework for Wales.

1. Purpose and scope of the registry
2. Determine if the registry is an appropriate means to achieve the purpose
3. Identify key stakeholders
4. Assess the feasibility of a registry
5. Establish a registry team
6. Determine governance processes
7. Identify and define the data sets, including patient outcomes and target population
8. Develop a project plan and appropriate protocols<sup>xvi</sup>

### 3.3 Overview of the current evidence on Long COVID

The exploratory desktop research has identified several key organisations whose main function is to review the evidence on Long COVID in Wales and wider afield. The following provides an overview of the key reviews, research studies and technical papers that are used alongside other evidence to inform the work.

#### 1. Health and Care Research Wales - Wales COVID Evidence Centre

Welsh Government has established the COVID-19 Evidence Centre, a 24-month investment of £3m to provide a Welsh-specific programme of research, evidence synthesis and knowledge mobilisation to meet priorities and urgent needs arising from COVID-19. The presentation and management of Long COVID is a priority of the COVID-19 Evidence Centre and a review of Long COVID research studies across the UK has been conducted. The summary of Long COVID Research in Wales report is linked below and was presented during the second 'Long COVID Advisory Board' meeting. See Annex 4 for the full list of research projects.

[Wales COVID-19 Evidence Centre | Health Care Research Wales \(healthandcareresearchwales.org\) Summary long COVID Research Wales eng Nov 2021.pdf \(healthandcareresearchwales.org\)](https://healthandcareresearchwales.org/Summary-long-COVID-Research-Wales-eng-Nov-2021.pdf)

#### 2. National Institute for Health Research (NIHR)

The National Institute for Health Research has awarded £19.6 million to fund 19 new research studies to help diagnose and treat Long COVID (see Annex 5). Specifically, this is to examine the causes of Long COVID, trial drugs, and investigate symptoms. Studies will also evaluate health services and explore ways that patients can monitor the condition to optimise their recovery and return to work.

[News: £19.6 million awarded to new research studies to help diagnose and treat long COVID | NIHR](#)

The NIHR themed reviews (last published March 2021) provide a dynamic review of the evidence around Long COVID.

### **3. National Core Studies Programme – Health Data Research UK**

The National Core Studies Programme is enabling the UK to use health data and research to inform both the near and long-term responses to COVID-19, as well as accelerating progress to establish a world-leading health data and research infrastructure for the future. There are six programmes: Epidemiology and Surveillance, Clinical Trials Infrastructure, Transmission Environment, Immunity, Longitudinal Health and Wellbeing, and Data and Connectivity.

<https://www.hdrk.ac.uk/covid-19/covid-19-national-core-studies/>

### **4. The Post-Hospitalisation COVID-19 Study (PHOSP COVID)**

Wales is taking part in the UK study called ‘The Post-Hospitalisation COVID-19 Study (PHOSP COVID)’ funded by the NIHR and MRC UK Research and Innovation in order to assess the long-term effects of COVID-19 on patient health and recovery in 10,000 participants across the UK.

[PHOSP](#)

### **5. UK Coronavirus Infection Survey (CIS)**

The Coronavirus Infection Survey (CIS) is the largest regular survey of coronavirus (COVID-19) infections and antibodies, providing information to help the UK’s response to the pandemic. It provides a monthly estimate of the number of people experiencing self-classified Long COVID in Wales. It is being delivered in partnership with the University of Oxford, University of Manchester, Public Health England and Wellcome Trust. The study is jointly led by the ONS and the Department for Health and Social Care (DHSC) working with the University of Oxford and Lighthouse laboratory to collect and test samples.

[COVID-19 Infection Survey - Office for National Statistics](#)

### **6. The ‘Inspiratory Muscle Training (IMT) post COVID-19 recovery study**

The ‘Inspiratory Muscle Training (IMT) post COVID-19 recovery study has been set up by Swansea University to address patient recovery from the impact of COVID-19 such as shortness of breath and fatigue.

### **7. Long COVID Technical Advisory Group**

The Technical Advisory Group published a paper in February 2021 which sets out what we know about Long COVID and what we still need to understand.

[Technical Advisory Group: Long-COVID | GOV.WALES](#)

### **8. Long COVID – Mechanisms, Risk Factors, and Management**

Researchers from the faculty of Medicine in Imperial College London and Cardiff University completed a review summarising studies researching the long-term effects of COVID-19 in hospitalized and non-hospitalized patients and described persistent symptoms that they endure.

[Long covid-mechanisms, risk factors, and management - PubMed \(nih.gov\)](#)

#### **9. Recommendations for the recognition, diagnosis, and management of long COVID: a Delphi study**

A Delphi study was conducted with a panel of primary and secondary care doctors in order to provide a rapid expert guide for GPs and long COVID clinical services. Recommendations were generated relating to the investigation and management of long COVID.

[Recommendations for the recognition, diagnosis, and management of long COVID: a Delphi study | British Journal of General Practice \(bjgp.org\)](#)

#### **10. Quality Principles for a Long-COVID Service**

The study sought to document Long COVID patients' lived experience, including accessing and receiving healthcare and ideas for improving services. The paper suggests quality principles for a Long COVID service. For example, ensuring access to care, reducing the burden of illness, taking clinical responsibility and providing continuity of care, multidisciplinary rehabilitation, evidence-based investigation and management, and further development of the knowledge base and clinical services.

[Persistent symptoms after Covid-19: qualitative study of 114 "long Covid" patients and draft quality principles for services | BMC Health Services Research | Full Text \(biomedcentral.com\)](#)

## **4. Findings**

### **4.1 What are the purposes of a Welsh Long COVID Registry?**

Understanding the purpose of a registry is essential before feasibility is established. Initial discussions with the Advisory Board therefore focused on the purpose of a Welsh Long COVID Registry and identified the following key points.

- Dual purpose with a focus on research and service improvement
- Focus on both longitudinal and comparative research
- Focus on service development, delivery and evaluation
- Answer questions which sufferers, clinicians and policymakers ask
- Inform NHS and wider sector planning responses
- An opportunity to identify people eligible for research interventions, including new drugs as they become available
- An opportunity for Welsh patients to enter (as yet unspecified) studies testing interventions to improve patient outcomes
- Understand and influence the patient experience in a positive way
- Demonstration of Wales' commitment to addressing an issue of considerable concern

## 4.2 Why establish a Welsh Long COVID Registry?

The following information was derived from the initial meetings of the Wales Long COVID Registry advisory board and publications from key organisations such as PHW, NICE, WHO and the Academy of Medical Sciences (AMS). It outlines the key reasons why a Welsh Long COVID Registry should be established.

*“I think it would be difficult to assume that there would be no longer-term neurological sequelae and, as a result, some kind of cohort mechanism to capture and monitor these people over time might prove to be immensely valuable”*

Sir John Bell

- **Long term monitoring** - an opportunity for long term monitoring and mapping of the disease to understand the prevalence, range, aetiology, severity, duration and sequelae of Long COVID
- **Building a database** – the opportunity to build a database over time that could be used for varying purposes including research and service improvement to improve the patient experience
- **Understanding the effects of variants and waves** – it has potential to look at the effects of various waves and variants of Long COVID, including wave one patients who lacked access to COVID-19 testing
- **Service development and improvement for patients** - an opportunity for service development configurations and health outcomes to have equal priority to research for the benefit of the patient
- **Treatment stratification and provision** – it provides an opportunity to stratify different treatments and provision of treatment options for sufferers in a prudent manner
- **Support for healthcare professionals** – there is an opportunity to support healthcare professionals in primary and secondary care, particularly GPs if fast track voluntary information is available
- **Collaboration with third sector and community access** - linkages with third sector and access to communities through initiatives such as voluntary patient groups
- **Patient care and promotion of rehabilitation and occupational support** - to support patient care, rehabilitation and returning to work with the infrastructure to support this
- **Collaboration with current services, databases and stakeholders** – utilisation of and collaboration with current services, databases and stakeholders to avoid duplication of effort and promote data efficiency (see Annex 6)
- **Formulation of an exemplar voluntary registry framework** - for Public Health Wales and other diseases

*“A specific attempt to capture a population of these individuals and follow them over time, perhaps thinking about interventions that they might find helpful, would be of considerable benefit”*

Sir John Bell

### 4.3 How do we set about establishing a Welsh Long COVID Registry?

A key focus of the meetings of the advisory board was to understand how to set about establishing a Welsh Long COVID Registry. The following summarises the key findings of these discussions with the expert panel and patient representatives:

#### How do we get there?

- Understand the context of a Long COVID Registry
- Explore organisations and systems that provide support for Long COVID
- Map existing data sets and linkages
- Clarify existing roles and responsibilities
- Potential opportunities for Long COVID Registry
- Defined purpose of the registry
- Identify lead co-ordinator, collaborators and resources
- Clarify the inclusion criteria
- Agree on data flows and linkages required for the registry
- Consideration of consent, ethics and data security
- Finalise option appraisal and potential registry framework
- Interventions and feedback for patients and key stakeholders
- Clearly defined registry outcomes

### 4.4 Co-production with Patients

In total five patient representatives were involved with the Long COVID Registry Advisory Board. The following outlines the experiences and perspectives from the patient representatives:

#### 4.4.1 Patient Experience of Long COVID

*“So many people do feel really abandoned”*

Patient Representative

- **Patients feel disempowered and betrayed** - patients felt betrayed and not listened to, the general lack of control and very little support, services and options designed to help and support Long COVID patients (outside of being an inpatient) was considered disempowering and exhausting. Patients described feeling lost and like a burden.
- **Daily impact of Long COVID** - it is incredibly difficult to communicate the impact of Long COVID on the lives of patients and the scale of the problems which people are experiencing. These need to be addressed.
- **Challenges of Long COVID** – challenges include the struggle to get through each day, occupational concerns, caring for family and dependents, navigating the healthcare system and barriers to being heard.
- **Difficulty accessing care** – patients found it difficult to access healthcare professionals, appropriate investigations and baseline tests to properly assess for Long COVID.

- **Complexity of Long COVID** - the complexity of this illness needs to be captured. The symptoms, signs and findings of Long COVID are wide-ranging and unpredictable. This has implications for the complexity of treatment and support.
- **Unknown long-term implications** - the future risks and complications of Long COVID (e.g. cardiac, neurological and respiratory) are unknown and patients feel as though there is nowhere to seek answers. Undiagnosed damage to organs and the neurotropic nature of Long COVID creates concerns for the future.
- **Definitional limitations** - the recent WHO post-COVID condition clinical case definition<sup>iii</sup> is limited according to patients. Other diseases such as diabetes and pulmonary embolism can co-exist, it does not mean that the original diagnoses of Long COVID no longer exists. The word 'persisting' within the NICE Long COVID definition is also queried. It is not a simple continuation of COVID-19, but often a second illness that often starts after a period of time.
- **Trialling of common treatments and simple safe medicines** - options should be provided to look at and observe common treatments. For example, anti-coagulates and low-risk interventions such as the use of inhalers to treat the symptoms of Long COVID.

#### 4.4.2 Patient Perspectives on a Long COVID Registry

*“There are people out there who are genuinely suffering and struggling, not understanding what is going on with them, and they would be only too pleased to participate in a registry”*

Patient Representative

- **Importance of a registry** - there are a lot of unanswered research questions in relation to Long COVID. Patients urged the importance of developing a working and comprehensive registry to identify these areas and to provide answers. It will help to measure the scale of the task, determine resources needed and provide a cohort of people willing to engage in treatment and management interventions.
- **A need to go beyond existing datasets** - the registry cannot rely only on existing datasets as they will not identify all Long COVID patients. Many patients have had disjointed care, sought private care and some have given up seeking help.
- **NHS collaboration** - if the purpose of the registry is research and service provision it needs to be in collaboration with the NHS. This will allow integration with services and access to the necessary expertise to enact positive change in the management and treatment of Long COVID.
- **Accurate GP coding** is critical for a Long COVID registry.
- **Pattern recognition and the combination of symptoms** – the pattern and combination of symptoms that define Long COVID is important and something that the registry should address.
- **Self-referral** – the potential for self-referral into a registry was deemed essential by patients for equity of access and to include the population of people suffering from Long COVID symptoms without a diagnostic test.
- **Working with patient groups** – co-production with patient groups such as LongCovidWales, the Long Covid Doctors' groups and connections thereafter to reach those not technologically

able was identified as an essential mechanism for self-referral and for the development of a comprehensive registry.

- **Avoiding duplication of data** – patients are often recruited to multiple apps and databases. There will need to be a robust means of merging datasets if records and entries are recorded from different apps and databases to avoid duplication of data.
- **Limitations of apps** - many Long COVID patients stopped using the ZOE app. Navigation of the app and correct input of data was perceived to be complex, particularly when feeling unwell.
- **Limitations of focusing on pathology** - patients on Long COVID rehabilitation programmes may have had diagnostic tests but cannot pinpoint a pathology. If looking at interventions exclusively for people with a particular pathology, it may exclude a significant proportion of individuals who would otherwise warrant an intervention of some sort.

## 5.0 Option Appraisal

Through the expert advice of the Advisory Board and real-life experiences of patient representatives, the following options were identified in order to inform decision making and contribute key recommendations to understand the feasibility of setting up a Long COVID Registry in Wales.

### 5.1 Welsh Long COVID Registry Options

**Table 3: Wales Long COVID Registry Options**

|                 |  |
|-----------------|--|
| <b>Option 1</b> | Do nothing and carry on as we are  |
| <b>Option 2</b> | Consolidate existing databases (DHCW/SAIL/HWW/ONS/PHW) using existing architecture   |
| <b>Option 3</b> | Consolidate existing databases (DHCW/SAIL/HWW/ONS/PHW) and recruitment of self-referred population with a communication strategy for the benefit of patients |
| <b>Option 4</b> | New programme and primary data collection (funding required)   |

### 5.2 Evaluation of Welsh Long COVID Registry Options

The four options proposed have been analysed according to the scale presented in Annex 7. This included eight criteria deemed as essential for a Long COVID Registry in Wales: cost, interoperability, service improvement, research, feasibility, patient-focused, sustainability and certainty of funding, and flexibility. The option appraisal was validated by the expert panel and patient representatives. The following table provides an overview of the pros and cons of each of the options. Further details can be found in Annex 8.



**Table 4: Wales Long COVID Registry Option Appraisal Summary**

| <b>Options</b>  | <b>Pros</b>  | <b>Cons</b>   |
|---|--|---|
| <b>Option 1 – Do nothing</b>  | <ul style="list-style-type: none"> <li>✓ Low cost</li> <li>✓ High feasibility</li> <li>✓ Average research capabilities</li> </ul>  | <ul style="list-style-type: none"> <li>X Low interoperability with other databases</li> <li>X Not focused on service improvement</li> <li>X Does not address patient needs currently</li> <li>X Not sustainable</li> <li>X No flexibility to respond to changing needs</li> </ul>   |
| <b>Option 2 – Consolidate existing databases</b>  | <ul style="list-style-type: none"> <li>✓ Moderately low cost</li> <li>✓ High feasibility</li> <li>✓ Good research capabilities</li> <li>✓ Average in terms of financial sustainability</li> </ul>  | <ul style="list-style-type: none"> <li>X Low patient focus</li> <li>X Lack of certainty over funding due to yearly funding cycles</li> <li>X Low flexibility to respond to changing needs</li> <li>X Use of existing databases will exclude many people suffering with Long COVID</li> <li>X Outstanding ethical and data considerations</li> </ul> |
| <b>Option 3 – Consolidate existing databases and recruit self-referred population with communication strategy</b> | <ul style="list-style-type: none"> <li>✓ High interoperability between databases</li> <li>✓ Strong focus on service improvement</li> <li>✓ Strong focus on research</li> <li>✓ Very flexible to respond to changing needs</li> </ul>                                     | <ul style="list-style-type: none"> <li>X Average cost due to recruitment of self-referred participants and communication strategy</li> <li>X Average feasibility and sustainability due to the potential cost and uncertainty of funding for key databases</li> <li>X Outstanding ethical and data considerations</li> </ul>                        |
| <b>Option 4 – New programme and primary data collection</b>   | <ul style="list-style-type: none"> <li>✓ High interoperability would be built in as a requirement</li> <li>✓ High focus on research and service improvement would be integrated</li> <li>✓ Flexibility built into this programme to respond to changing needs</li> </ul> | <ul style="list-style-type: none"> <li>X Very high development and implementation cost</li> <li>X Low feasibility due to the high cost and current strain on resources</li> <li>X Low sustainability and certainty of funding</li> </ul>  |

## **6.0 Option 3 - Consolidate existing databases and recruit self-referred population with a communication strategy**

The option appraisal indicates that Option 3 is the most feasible route to establish a Long COVID Registry in Wales. The option appraisal was confirmed and validated by the expert panel and patient representatives during the final official meeting on November 16<sup>th</sup>, 2021 (see Annex 9). The information below provides further detailed information to support the Option 3 proposal.

## 6.1 Consolidation of Existing Databases and Access to Data

Access to data and information is core to any registry, both retrospectively and prospectively, as is the ability to utilise data to inform research, service improvement and patient care. The consolidation of existing databases held within different organisations would allow a unified approach to access data to inform a Long COVID Registry.

Digital infrastructure and linkage are key to the success of a registry. The first stage of Option 3 is therefore the consolidation of existing databases and resources with data related to Long COVID. This is following recognition from the Advisory Board that there is a current disconnect and need for enhanced coordination of digital resources, databases and systems that support Long COVID in Wales. In order to inform a Long COVID Registry, several key collaborators have been identified. However, it is important to note that funding for SAIL, HWW and the ONS is confirmed annually and therefore sustainability of funding is a major outstanding consideration.

The following outlines further details on what each of the different organisations can contribute to a Long COVID Registry.

### DHCW

Digital Health and Care Wales (DHCW) is the national organisation building and designing digital services for health and care in Wales. They have a leading role in delivering the national programmes needed for modern technology-enabled healthcare and through the Digital Services for Patients and Public (DPSS) are developing an NHS Wales app. This app is described as a “one-stop” shop for health and care and will allow anyone with a smartphone or tablet to manage their health and have access to important information. DHCW are already a Trusted Third Party (TTP) that inform SAIL datasets through reliable record matching. Due to the embeddedness of DHCW within the NHS, the consequent sustainability of funding and existing collaborations with current datasets, it is recommended that they would be suitably placed as the coordinating body for a Long COVID Registry in Wales. This would provide greater clarity and coordination across agencies.

[About us - Digital Health and Care Wales \(nhs.wales\)](https://www.nhs.uk/about-us/)

[Digital Services for Patients and Public - Digital Health and Care Wales \(nhs.wales\)](https://www.nhs.uk/digital-services-for-patients-and-public/)

### SAIL

The SAIL databank has 10 years of experience as a leader in the field of data linkage. They have access to billions of anonymised person-based records combined with a complete data linkage and analysis toolset that helps researchers answer important questions for the benefit of society. For example, to improve health, wellbeing and services. They are ISO certified and adhere to strict compliance and legal requirements surrounding the use of person-based data. SAIL has access to positive PCR test data for Covid-19 as aligned with DHCW, PHW and HWW. However, they are primarily funded for the storing of datasets, therefore any requirements for the analysis or mining of data in relation to the Long COVID Registry will require additional investment.

## [SAIL Databank - The Secure Anonymised Information Linkage Databank](#)

### **HWW**

Healthwise Wales' core business as a research database and platform, is in recruitment to studies from the population of Wales through generic core modules and bespoke questionnaires. They have significant experience of recruiting from the Welsh Population to research studies and linking this prospectively collected data via SAIL through health record linkage. This is on the SeRP portal as a trusted research environment. They have ethics approval and therefore invite participants (approximately 42,000 at present) to consent to their record linkage and to be re-contacted for future studies of interest. Importantly, they also have the ability to advertise or action registrations and data collection via mobile technology, including web applications. HWW have experience of effective recruitment to COVID-19 studies, although this is for the purpose of research and not service improvement. As with all of the databases, the funding for this platform is low in sustainability due to the unpredictability of the yearly funding cycle. However, due to existing partnerships and well-established operational processes with SAIL and DHCW, it would be logical and cost-effective to utilise the HWW platform to inform the Long COVID registry.

[Home - HealthWise Wales \(gov.wales\)](#)

### **ONS**

The Office of National Statistics (ONS) collects, analyses and disseminates statistics about the UK's economy, society and population. They are currently responsible for collecting data for the COVID-19 Infection Survey as one of the largest data collections outside of the Census, although this can only be used for statistical analysis and research and not operational purposes such as service delivery and improvement. The COVID-19 Infection Survey data is already available and random sampling means that data is approximately representative of the population. Those without prior COVID-19 infection are also included, which allows for a control group to be selected for analysis. Additionally, participants are regularly tested, allowing for most infections (including those who were asymptomatic at the acute phase) to be picked up after study enrolment. However, the data is only collected for a small sample of the population and the COVID-19 Infection Survey comprises of approximately 20,000 participants in Wales, of whom only 1.4% would currently describe themselves as having Long COVID. Additionally, the COVID-19 Infection Survey is only funded until the end of the financial year, with the future of surveillance studies for COVID-19 unclear.

[Home - Office for National Statistics \(ons.gov.uk\)](#)

### **PHW**

PHW is the national public health agency in Wales that exists to protect and improve health and wellbeing and reduce health inequalities for people in Wales. They report to the Minister for Health and Social Service and have seven strategic priorities to 2030, including to 'protect the public from infection and environmental threats to health'. PHW have access to COVID-19 data that could be of

benefit to a Long COVID Registry and as the national public health agency of Wales should be considered as a key collaborator.

[Home - Public Health Wales \(nhs.wales\)](https://nhs.uk)

## 6.2 Recruitment of Self-Referred Population

Expert and patient feedback identified the importance of going beyond existing datasets for a Long COVID Registry (see Section 4.4). Whilst the inclusion and coordination of these datasets is extremely important for the registry, they do not identify all Long COVID patients. For example, to date, large scale studies and databases rely on the recruitment of patients whilst attending or being discharged from hospital or attending their GP. In order to adjust for recruitment bias, promote equity of access for the Long COVID Registry and overcome issues related to Personally Identifiable Information (PII), Option 3 included the recruitment of a self-referred population of Long COVID sufferers.

The concept is to recruit large numbers of the population who self-identify as having Long COVID to create a hybrid system with existing databases. Potential registry users could be approached through a public health campaign, current healthcare systems, platforms such as HWW, apps, patient groups, social media, employers and social enterprises in order to embed a larger number of recruited individuals with Long COVID symptoms and necessary controls. These users could be embedded within a total population electronic cohort using the ConCOV (controlling COVID through data linkage) platform using the SAIL databank. This would capture traditionally hard to reach, vulnerable groups and achieve a more representative estimate of population burden and need.

## 6.3 Communication Strategy

The communication and marketing strategy is an integral aspect of Option 3. This will allow the registry to contribute to service improvement. The purpose of this function is to:

|    |  |
|----|--|
| 1. | Engage with long COVID patients to ensure their views and experiences are properly addressed |
| 2. | Identify and highlight how to access local and national services for care and treatment      |
| 3. | Provide rapid feedback to patients, clinicians and policymakers                              |
| 4. | Market UK trials and recruit patients into interventions to improve outcomes                 |

## 6.4 Technology and Apps

The optimisation of technology and use of a large-scale electronic collection device will be essential for a Long COVID Registry. Digital Services for Patients and Public (DPSS) have been identified as a suitable team to inform this work for a Long COVID Registry as developers of the NHS Wales App. Apps, reporting devices and artificial intelligence could also be utilised for data retrieval and to capture lost information for the self-reported population referred to above. The possibility to use existing apps such as the ZOE app and Scienap to import large numbers of people to the Long COVID Registry should be explored. SAIL has successfully imported links on large numbers of people through the ZOE

app, but matching rates were approximately 50% due to limited fields. Feedback from patient representatives also suggest that patient engagement and perceived value with the ZOE app is restricted (see Section 4.4). Scienap is currently used within the Hywel Dda Health Board in order to deliver the CHAI app, there is a possibility that this could be expanded for the purposes identified above, or a new app developed by DSPP for the Long COVID Registry, aligned with the NHS Wales App. However, there would need to be robust measures in place to merge and avoid duplication of data. Digital literacy and IT availability would also need to be considered for accessibility to the registry.

## 6.5 Patient Consent

Accessing and using patient information for a variety of uses is subject to strict governance, confidentiality and accountability regulations.

The Health Service Control of Patient Information (COPI) Regulations 2002 allows the processing of Confidential Patient Information (CPI) for specific purposes. Regulation 3 provides for the processing of CPI in relation to communicable diseases and other threats to public health and in particular allows the Secretary of State to require organisations to process CPI for purposes related to communicable diseases. The COPI notices cover a range of purposes related to diagnosing, managing, and controlling the spread of communicable diseases. For COVID-19 purposes this could include but is not limited to:

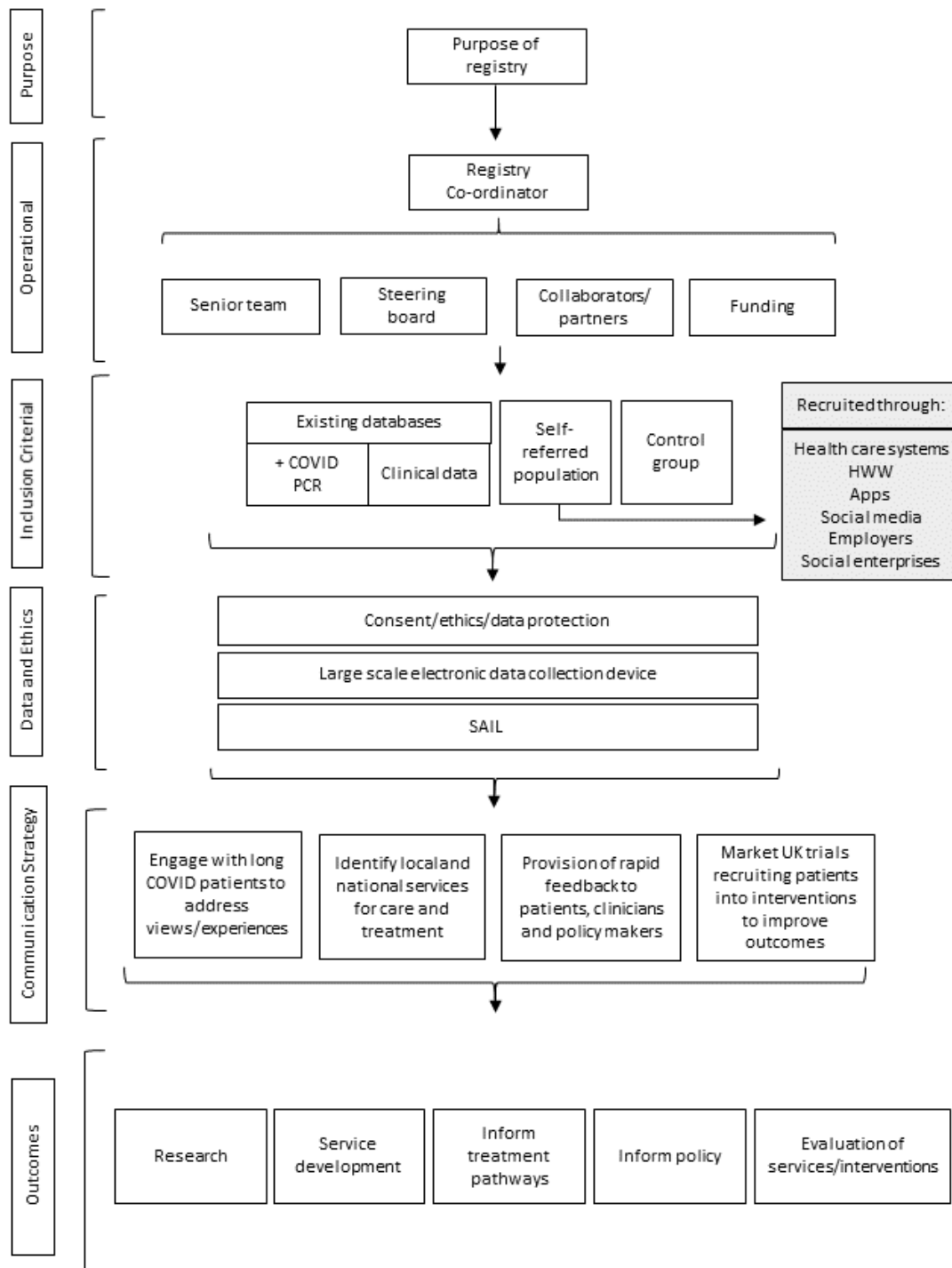
- Understanding COVID-19 and risks to public health, trends in COVID-19 and such risks, and controlling and preventing the spread of COVID-19 and such risks
- Identifying and understanding information about patients or potential patients with or at risk of COVID-19
- Delivering services to patients, clinicians, the health services
- Research and planning in relation to COVID-19

The notice covers confidential patient information. This means any data, regardless of its identifiability, which is being used for the purposes set out above is covered. It will all be treated in line with the principles of the General Data Protection Regulation (GDPR) - fairly, lawfully and securely. COPI notices have now been extended until the end of March 2022 to help give healthcare organisations and local authorities the confidence to share the data needed to respond to COVID-19.

The information outlined above provides a time-limited opportunity for a Long COVID Registry, unless the notice is extended beyond March 2022. However, within this timeframe it would be possible to identify, contact and gain consent from identified individuals to enter them into a Long COVID Registry and longitudinal study. This consent would continue beyond the COPI relaxation for COVID-19 and would resolve potential issues with PII and the retrospective identification of individuals who have had Long COVID. Beyond the COPI relaxation for COVID-19, a prospective recruitment methodology would be required.

## 7.0 Potential Long COVID Registry Framework

The following provides a potential framework of how a Long COVID Registry could be established in Wales. The diagram and table of supplementary information below is informed by the Advisory Board.



| <b>Potential Long COVID Registry Framework</b> |  |
|--|--|
| <b>Purpose</b>                                 | <ul style="list-style-type: none"> <li>- Dual purpose of research and service improvement.</li> <li>- Most registries are observational, but for a dual-purpose and interventional registry, the ability to be dynamic and respond to changing needs is essential.</li> <li>- Collaboration with the NHS is required to achieve the above.</li> <li>- See Annex 10 for potential strategic priorities of the registry.</li> </ul>  |
| <b>Operational</b>                             | <ul style="list-style-type: none"> <li>- DHCW to coordinate registry.</li> <li>- Recruitment of senior team and steering board.</li> <li>- Key collaborators and partners include the NHS, SAIL, HWW, ONS, PHW and HCRW.</li> <li>- Identification of funding is essential.</li> </ul>   |
| <b>Inclusion criteria</b>                      | <ul style="list-style-type: none"> <li>- COVID positive test results, GP referral, clinical diagnosis and data including serology, T-cells and antibodies.</li> <li>- Self-referred population and controls as outlined in Option 3 to address recruitment bias and promote equity of access. A public health campaign is suggested to assist with recruitment to the registry.</li> <li>- Paediatric cases should be captured.</li> <li>- Accurate GP coding is essential.</li> </ul>   |
| <b>Data and ethics</b>                         | <ul style="list-style-type: none"> <li>- Data to be processed by DSPP, DHCW and SAIL through a large-scale electronic data collection device such as the NHS Wales App.</li> <li>- Data analysis should be prospective and retrospective, and the use of AI considered.</li> <li>- Consent, ethics and data protection to be considered in detail upon registry confirmation.</li> <li>- The use of personally identifiable information for COVID-19 can be utilised until March 2022 under the relaxation of the Control of Patient Information Regulations 2002 and Long COVID sufferers identified and consent sought for longitudinal contact.</li> <li>- Data can be extracted from GP practices according to SNOWMED-CT codes.</li> <li>- Equality impact statement required.</li> <li>- See Annex 11 for proposed data steps for anonymised data.</li> <li>- See reference <sup>xvii</sup> for minimum data set of a COVID-19 registry system.</li> </ul> |
| <b>Communication strategy</b>                  | <p>Communication strategy is required for an interventional registry to:</p> <ol style="list-style-type: none"> <li>1. Engage with patients to address their views and experiences</li> <li>2. Determine the most effective treatment and support and identify appropriate local and national services for care.</li> <li>3. Provide rapid feedback to patients, clinicians and policymakers. AI should be utilised for data analysis and rapid feedback, the Life Sciences Hub and DHEW are potential collaborators.</li> <li>4. Market UK trials that are recruiting patients into interventions (see <sup>xviii</sup> for WCEC summary of Long COVID Research in Wales).</li> </ol>   |
| <b>Outcomes</b>                                | <p>Key outcomes include:</p> <ol style="list-style-type: none"> <li>1. Research</li> <li>2. Service improvement</li> <li>3. Informing treatment pathways by understanding the diverse symptomatology of Long COVID</li> <li>4. Evaluation of services and interventions</li> <li>5. Inform policy</li> </ol>   |

## 8.0 Other Issues Considered

### 1. Resourcing and service improvement

- Understanding resource challenges and minimal operational and resource requirements. The concept of Prudent Healthcare<sup>xix</sup> needs to be adopted, and prudent principles adhered to in order to derive the best value from a Long COVID Registry.
- The implications of signposting to services that vary across Wales and already have long waiting lists. Apps, technological support, third sector and utilisation of patient groups such as LongCovidWales have been identified to provide additional support.

### 2. Equitable access for patients to be entered on a Long COVID Registry

- Inequality in accessing the registry and healthcare services and adjustment for recruitment bias. The recommendation of a self-referred population for the Long COVID Registry recognises the need to support those who do not have a positive PCR test.
- The NHS App in development by DHCW and DSPP will not be available to children, if this app is used for the purposes of a Long COVID Registry this would need to be considered.
- The targeting and inclusion of vulnerable groups such as Black, Asian, minority ethnic and socio-economically deprived groups. An equality impact statement is required and the Long COVID Registry should maximise existing data sets in order to analyse according to all aspects of equality and social disparity. This should be addressed by a method using population-focused databases, to include:
  - All ages
  - Preschool children and parents
  - School-age children under 16
  - 16-17 year olds (in school, college, training or NEET)
  - 18-24 year olds
  - Working age 25-50
  - 60+
  - 70+
  - Pregnancy and maternity
  - Disabled including learning disabilities
  - Mentally ill
  - Digitally excluded especially those on benefits and living in poverty
  - Black and ethnic minority people
  - Refugees and asylum seekers
  - Prison populations
  - Faith groups
  - LGBTQI+ communities

### 3. Data and ethics

- Retrospective identification and contact of Long COVID patients through PCR+ COVID-19 test results and clinical diagnosis is not permitted due to issues concerning personally identifiable information.



- Relaxation of the Control of Patient Information Regulations 2002 for COVID-19 would allow identification and contact of Long COVID sufferers until March 2022. A prospective methodology would be required beyond this point for entry into a Long COVID Registry in Wales.

#### 4. Inconsistency in coding of Long COVID

- Inconsistency in coding of Long COVID and improving the quality of data is an important issue. Addressing the consistency and application of coding Long COVID in primary care specifically, is a key recommendation from the Advisory Board.
- Aggregate data has been extracted per GP practice in relation to post-COVID-19 syndrome (disorder) and ongoing symptomatic disease caused by severe acute respiratory syndrome coronavirus 2 (disorder). GP system suppliers have created local codes to link the SNOWMED-CT codes to aid GP practice data entry.
- The above considerations would allow data to become part of the national data resource and engage in longitudinal analysis of the long-term sequelae and consequences of Long COVID.

#### 5. UK relevance

- The need for networks and links outside of Wales to ensure that the registry has relevance at a UK level. Long COVID patients have already enrolled on UK wide studies and these links will be important for control data.
- The Advisory Board advocates the need for knowledge transfer and collaboration to share developments across borders and wider afield.

## 9.0 Conclusions and Recommendations

### 9.1 Conclusions

The findings of this work indicate that there are no known Long COVID registries that have been launched within the UK. Links are being maintained with other UK countries to identify any developments.

The Advisory Board and patient representatives unanimously agreed that there is a need for a Long COVID Registry in Wales, which should have a dual purpose to address research and service improvement.

The utilisation of technology, data linkage and coordination across multiple organisations and sources will be key to success for the registry and enable a greater understanding of the patient experience as it evolves.

The Advisory Board recommends the consolidation of existing databases, recruitment of self-referred population and development of a communication strategy as the optimal model for a registry. A potential framework has been developed to provide further details on how to set up a Long COVID Registry in Wales.

It is proposed that Digital Health and Care Wales would be the most suitable coordinating body to progress this work.

## 9.2 Recommendations

- **Long COVID Registry for Wales** – the establishment of a Long COVID registry is recommended in order to address unanswered questions and inform research, service improvement and patient care.
- **Dual Purpose Registry** – a Long COVID registry should be interventional with a dual purpose of research and service improvement.
- **Proposed Model** – the option appraisal exercise identified Option 3 as the most feasible. This includes the consolidation of existing databases, recruitment of self-referred population and communication strategy.
- **Recommended Lead Agency** – it is recommended that Digital Health and Care Wales, as the principal digital agency for Wales, should lead and co-ordinate the proposed Long COVID Registry. This will ensure effective coordination, integration and sustainability within the national infrastructure.
- **Key collaborators** – SAIL, HWW, ONS, PHW, DSPP and DHEW have been identified as key collaborators to support the establishment of a Long COVID Registry in Wales.
- **Retrospective patient consent** – urgent action is needed (before March 2022) to gain consent from Long COVID patients within the amended timeframe for COVID-19 (Control of Patient Information Regulations 2002). A prospective methodology is required beyond this point.
- **Working with patient groups** – collaboration with patient groups such as LongCovidWales and the Long Covid Doctors' groups will be important in the co-production and development of a Long COVID Registry for Wales.
- **Quality of coding** – improvements are needed in the quality of coding for Long COVID, specifically in primary care. This is important to ensure effective integration as part of the national resource to track Long COVID, particularly as a neurotropic virus.

## 10.0 Annexes

### Annex 1: Long COVID Symptoms<sup>iv</sup>

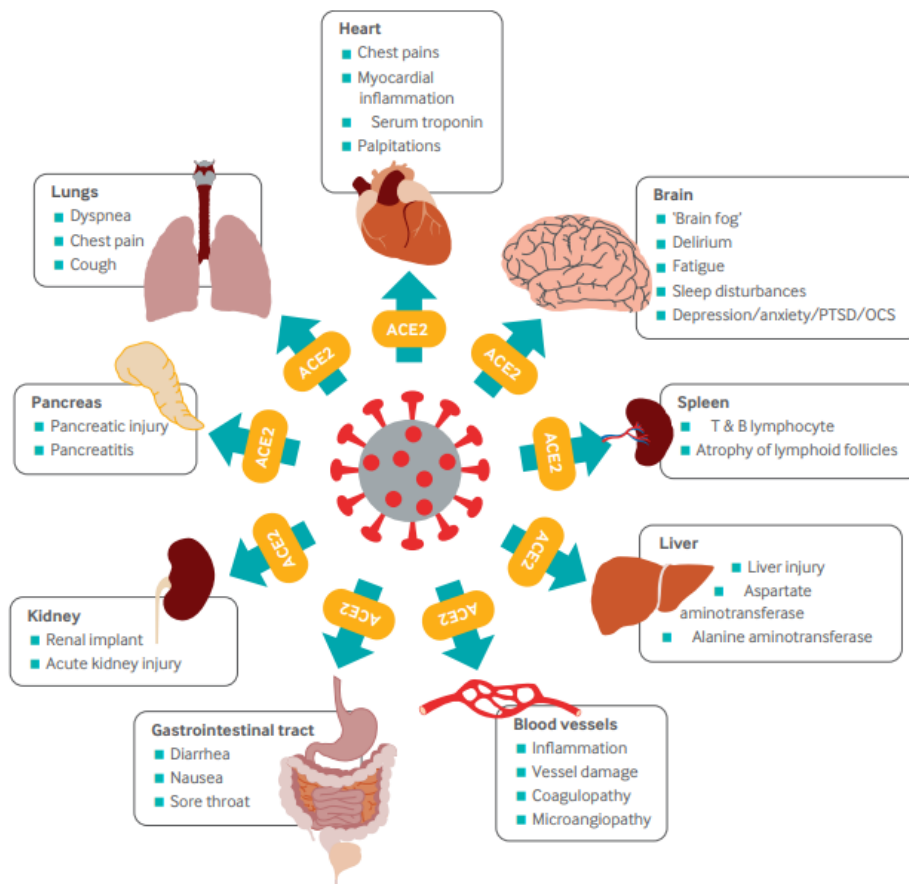
| <b>Systems</b>       | <b>Symptoms</b>   |
|----------------------|---|
| General              | Fatigue<br>Fever<br>Pain  |
| Respiratory          | Breathlessness<br>Cough   |
| Cardiovascular       | Chest tightness<br>Chest pains<br>Palpitations  |
| Neurological         | Cognitive impairment such as loss of concentration and memory loss<br>Headache<br>Sleep disturbances<br>Peripheral neuropathy including paraesthesia and numbness |
| Gastrointestinal     | Abdominal pain<br>Nausea<br>Diarrhoea<br>Anorexia and reduced appetite (in older people)  |
| Musculoskeletal      | Joint and muscle pains  |
| Psychological        | Depression and anxiety  |
| Ear, nose and throat | Tinnitus<br>Earache<br>Sore throat<br>Loss of taste and/or smell  |
| Dermatological       | Pernio, papulosquamous rashes, livedo reticularis   |

### Annex 2: Multi-organ complications of Long COVID<sup>i</sup>

| <b>Organ</b> | <b>Symptoms</b>   |
|--------------|---|
| Heart        | Chest pains<br>Myocardial inflammation<br>Serum troponin<br>Palpitations              |
| Lungs        | Dyspnoea<br>Cough   |
| Brain        | Brain fog<br>Delirium<br>Fatigue<br>Sleep disturbances<br>Depression/anxiety/PTSD/OCS |
| Spleen       | T&B lymphocyte<br>Atrophy of lymphoid follicles                                       |
| Pancreas     | Pancreatic injury   |

|                        |  |
|------------------------|--|
|                        | Pancreatitis   |
| Liver                  | Liver injury<br>Aspartate aminotransferase<br>Alanine aminotransferase |
| Kidney                 | Renal implant<br>Acute kidney injury                                   |
| Blood vessels          | Inflammation<br>Vessel damage<br>Coagulopathy<br>Microangiopathy       |
| Gastrointestinal tract | Diarrhoea<br>Nausea<br>Sore throat                                     |
| Skin                   | Rashes   |

Annex 3: Diagram of multi-Organ Complications of Long COVID<sup>i</sup>



\*Skin is an additional multi-organ complication to the diagram above.

**Annex 4: Active and Prospective Long COVID research studies in Wales** Error! Bookmark not defined.

|   |  |
|---|--|
| <b>PHOSP-COVID</b><br>(currently active)          | Post-hospitalisation COVID-19 study: a national consortium to understand and improve long-term health outcomes (PHOSP-COVID)<br><a href="https://www.phosp.org">https://www.phosp.org</a>  |
| <b>HEAL-COVID</b><br>(currently active)           | HElping Alleviate the Longer-term consequences of COVID-19 (HEAL-COVID): a national platform trial <a href="https://www.heal-covid.net/">https://www.heal-covid.net/</a>   |
| <b>REGAIN</b><br>(currently active)               | Rehabilitation Exercise and psycholoGical support After covid-19 InfectioN (REGAIN): a multi-centre randomised controlled trial<br><a href="https://warwick.ac.uk/fac/sci/med/research/ctu/trials/regain/">https://warwick.ac.uk/fac/sci/med/research/ctu/trials/regain/</a>   |
| (currently active)                                | Understanding Experiences of Long COVID in Families<br><a href="https://www.phc.ox.ac.uk/research/health-experiences/understanding-experiences-of-Long-covid-in-families">https://www.phc.ox.ac.uk/research/health-experiences/understanding-experiences-of-Long-covid-in-families</a>   |
| <b>LOCOMOTION</b><br>(prospective)                | LONg COvid Multidisciplinary Consortium: Optimising Treatments and servlces acrOss the NHS (LOCOMOTION)<br><a href="https://medicinehealth.leeds.ac.uk/dir-record/research-projects/1394/long-covid-multidisciplinary-consortium-optimising-treatments-and-services-across-the-nhs-locomotion">https://medicinehealth.leeds.ac.uk/dir-record/research-projects/1394/long-covid-multidisciplinary-consortium-optimising-treatments-and-services-across-the-nhs-locomotion</a> |
| <b>LISTEN</b><br>(prospective)                    | Long Covid Personalised Self-managementT support- co-design and Evaluation (LISTEN) <a href="https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/listen">https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/listen</a>  |
| (prospective)                                     | The immunologic and virologic determinants of Long-COVID   |
| <b>EXPLAIN</b><br>(prospective)                   | HypErpolarised Xenon magnetic resonance PuLmonary imAging in patieNts with Long COVID (EXPLAIN)  |
| <b>CICERO</b><br>(prospective)                    | Cognitive Impairment in long COVID: PhEnotyping and RehabilitatiOn (CICERO)  |
| <b>STIMULATE-ICP</b><br>(set up under discussion) | Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways (STIMULATE-ICP)   |

**Annex 5: NIHR Funded Long COVID Projects**

| Reference    | Project Title   |
|--------------|---|
| COV-LT-0040  | REACT Long COVID (REACT-LC)   |
| COV-LT-0009  | Characterisation, determinants, mechanisms and consequences of the long-term effects of COVID-19: providing the evidence base for health care services  |
| COV-LT-0022  | Non-hospitalised Children and young people (CYP) with Long Covid (The CLoCK Study)  |
| COV-LT-0013  | Therapies for Long COVID in non-hospitalised individuals: From symptoms, patient-reported outcomes and immunology to targeted therapies (The TLC Study) |
| COV-LT2-0022 | Percutaneous Auricular Nerve Stimulation for Treating Post-COVID Fatigue (PAuSing-Post-COVID-Fatigue)   |

|              |   |
|--------------|---|
| COV-LT2-0027 | Immune analysis of Long COVID to inform rational choices in diagnostic testing and therapeutics   |
| COV-LT2-0041 | The immunologic and virologic determinants of long COVID  |
| COV-LT2-0004 | Development of a robust T cell assay to retrospectively diagnose SARS-CoV-2 infection and T cell cytokine release assay as diagnostic and monitoring assay in Long COVID patients |
| COV-LT2-0073 | Quality-of-life in patients with long COVID: harnessing the scale of big data to quantify the health and economic costs   |
| COV-LT2-0006 | Impact of COVID-19 vaccination on preventing long COVID: a population-based cohort study using linked NHS data  |
| COV-LT2-0072 | Long COVID Core Outcome Set (LC-COS) project  |
| COV-LT2-0005 | Understanding and using family experiences of managing long Covid to support self-care and timely access to services  |
| COV-LT2-0043 | STIMULATE-ICP (Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways)                            |
| COV-LT2-0016 | LOng Covid Multidisciplinary consortium: Optimising Treatments and services across the NHS (LOCOMOTION)   |
| COV-LT2-0014 | Cognitive Impairment in Long COVID: PhEnotyping and Rehabilitation (CICERO)   |
| COV-LT2-0009 | Long Covid Personalised Self-management support co-design and Evaluation (LISTEN)   |
| COV-LT2-0010 | Using Activity Tracking and Just-In-Time Messaging to Improve Adaptive Pacing: A Pragmatic Randomised Control Trial   |
| COV-LT2-0049 | HypErolarised Xenon Magnetic Resonance PuLmonary Imaging in PATleNts with Long-COVID (EXPLAIN)  |
| COV-LT2-0059 | ReDIRECT: Remote Diet Intervention to REduce long Covid symptoms Trial  |

## Annex 6: Databases, Organisations and Applications to Inform a Long COVID Registry in Wales

|  |   |  |
|--|---|--|
| SAIL   | Anonymised person-based data for research to improve health, wellbeing and services   | <a href="#">SAIL Databank - The Secure Anonymised Information Linkage Databank</a>   |
| ONS  | The ONS collect, analyse and disseminate public health data for UK official statistics.   | <a href="#">Home - Office for National Statistics (ons.gov.uk)</a>   |
| HWW  | Health Wise Wales (HWW) is a data collection platform and register of 40,000+ participants that are ready to take part in research studies.   | <a href="#">Home - HealthWise Wales (gov.wales)</a>  |
| PHW  | Public Health Wales is the national public health agency in Wales.  | <a href="#">Home - Public Health Wales (nhs.wales)</a>   |
| DHCW   | Digital Health and Care Wales are the new Special Authority created to take forward digital transformation for better health and care in Wales. They host the National Data Resource (NDR) programme as a component of the Digital Architecture Review.   | <a href="#">Home - Digital Health and Care Wales (nhs.wales)</a><br><br><a href="#">NDR - Digital Health and Care Wales (nhs.wales)</a>                              |
| The European Observatory on Health Systems and Policies            | The European Health Observatory on Health Systems and Policies works in partnership with researchers, research centres, governments and international organisations to comprehensively describe and analyse health systems and the changes they undergo and it engages directly with policy-makers.   | <a href="#">Home (who.int)</a>   |
| CHAI Community – Long COVID tracker and ‘Download my Data’ service | CHAI Community is an electronic care system for community use developed from secondary care (care plans and risk assessments).<br><br>Welsh developers of CHAI have added a Long Covid symptom tracker that is co-designed with Keir Lewis (COVID Lead at Llanelli) in collaboration with HDUHB. It provides access to reported symptoms for GPs and helps to signpost towards self-help, community support, NHS support. | <a href="#">For Healthcare Providers – CHAI LongCovidTracker</a>   |
| COVID Recovery App Wales   | The COVID recovery app is bilingual and was developed by the NHS Wales respiratory health group (led by Dr Fiona Jenkins) on behalf of the Welsh Government. It is designed to offer a bespoke tool and personal coach to help with COVID recovery.   | <a href="#">Recovery app launched in Wales to help support people with long COVID   GOV.WALES</a><br><br><a href="#">COVID Recovery on the App Store (apple.com)</a> |
| ZOE COVID Symptom Study  | The ZOE COVID Symptom Study is a not for profit initiative launched in March 2020 to support COVID-19 research. It was launched by health science company ZOE with scientific analysis provided by King’s College London.   | <a href="#">About this Research (joinzoe.com)</a>  |

## Annex 7: Option Appraisal Scale

| <b>Criteria</b>     | <b>Scale (1-5)</b>   |
|---------------------|--|
| Cost                | Cost of the option from high cost (1) to low cost (5)  |
| Interoperability    | Ability for databases to work together and share information from low interoperability (1) to high interoperability (5)    |
| Service Improvement | Focus on service improvement from minimal focus on service improvement (1) to high focus on service improvement (5).       |
| Research            | Focus on research from minimal focus on research (1) to high focus on research (5).  |
| Feasibility         | Feasibility of the option based on complexity and time to implementation from low feasibility (1) to high feasibility (5). |
| Patient focused     | Focus on the Long COVID patient from minimal focus (1) to high focus (5).  |
| Sustainability      | Sustainable infrastructure of funding sources from low sustainability (1) to highly sustainable (5).                       |
| Flexibility         | The ability to flex and response to needs as and when they emerge from low flexibility (1) to high flexibility (5).        |



## Annex 8: Option Appraisal Table

The four options proposed above have been analysed and scored according to the scale presented in Annex 7. Each option has been given a score between 1 and 5 according to eight criteria deemed as essential for a Long COVID Registry in Wales. One is the lowest score and five is the highest score. The option with the highest total is appraised as the most feasible. The option appraisal was validated by the expert panel and patient representatives.

| No.      | Options   | Cost | Interoperability | Service Improvement | Research | Feasibility | Patient Focused | Sustainability/<br>Certainty of Funding | Flexibility | Total |
|----------|---|------|------------------|---------------------|----------|-------------|-----------------|---|-------------|-------|
| Option 1 | Do nothing and carry on as we are   | 5    | 1                | 1                   | 3        | 5           | 1               | 1                                       | 1           | 18    |
| Option 2 | Consolidate existing databases using existing architecture                                      | 4    | 3                | 2                   | 4        | 4           | 2               | 3                                       | 2           | 24    |
| Option 3 | Consolidate existing databases and recruit self-referred population with communication strategy | 3    | 4                | 4                   | 4        | 3           | 5               | 3                                       | 3           | 29    |
| Option 4 | New programme and primary data collection   | 1    | 4                | 5                   | 5        | 1           | 5               | 2                                       | 4           | 27    |

(Please refer to Annex 7 for the Option Appraisal scale)

## Annex 9: Advisory Board Meetings

|                                     |  |
|-------------------------------------|--|
| <b>Preliminary Informal Meeting</b> | July 20 <sup>th</sup> 2021 9:00-10:00am      |
| <b>Meeting 1</b>                    | August 17 <sup>th</sup> 2021 9:00-10:00am    |
| <b>Sub-group Meeting</b>            | September 9 <sup>th</sup> 2021 9:00-10:00am  |
| <b>Meeting 2</b>                    | September 21 <sup>st</sup> 2021 9:00-10:00am |
| <b>Meeting 3</b>                    | October 18 <sup>th</sup> 2021 10:00-11:00am  |
| <b>Meeting 4</b>                    | November 16 <sup>th</sup> 2021 09:00-10:00   |

## Annex 10: Key Strategic Priorities

The Advisory Board outlined a number of key strategic priorities for the registry to address, as identified below:

| <b>Strategic Priorities of the Registry</b> |   |
|---|---|
| Priority 1                                  | Whether there is reversible pathology in the current population and what can be changed and improved in the current population.                                     |
| Priority 2                                  | Long term planning for the needs of people who have Long COVID.   |
| Priority 3                                  | Effective use of resources and a prudent approach. For instance, money spent on therapies that are not proven to do good or might do harm if not properly assessed. |
| Priority 4                                  | A fourth consideration to add to the list above is communication and setting realistic expectations for the population.   |

## Annex 11: Proposed Data Steps for Anonymised Data

- a. Periodic data extracts of personal identifying details are sent to Digital Health Wales (DHCW) (this file contains no symptom history - just ID). The associated app record ID will be included with the personal ID information. Public and legitimate interest would be the legal basis for sharing this information with DHCW.
- b. Symptom history is sent to SAIL with the associated record app IDs. No personally identifying information is sent. There is no processing of personal information as defined by GDPR for this operation because it has been anonymised.
- c. DHCW will send SAIL a key that will enable SAIL to match the app records with other records that they hold about the individuals. At no time will SAIL ever receive the personal identifying details. This process is publicly available on SAIL's website.
- d. The CHAI app, ZOE app, LongCOVIDTracker and others would require some change in design and function in order to efficiently capture the appropriate list of symptoms, their importance, how they change over time and their social and economic impact. It is suggested that DSPP are involved in this process to align with the NHS Wales App.

## 11.0 References

---

- <sup>i</sup> Crook, H., Raza, S., Nowell, J., Young, M., & Edison, P. (2021). Long covid – mechanisms, risk factors, and management. *BMJ*. DOI:10.1136/8.n1648
- <sup>ii</sup> World Health Organization. (2021). *Weekly operational update on COVID-19—7 December 2021*. WHO. [Weekly operational update on COVID-19 - 7 December 2021 \(who.int\)](#).
- <sup>iii</sup> World Health Organization. (2021). *A clinical case definition of post COVID-19 condition by a Delphi consensus*. WHO. [A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021 \(who.int\)](#)
- <sup>iv</sup> NICE. (2021). *How do I manage someone with the long term effects of COVID-19?* NICE. [Scenario: Managing long-term effects | Management | Coronavirus - COVID 19 | CKS | NICE](#)
- <sup>v</sup> Ladds, E., Rushforth, A., Wieringa, S, et al. (2020). Persistent symptoms after Covid-19: qualitative study of 114 “long Covid” patients and draft quality principles for services. *BMC Health Serv Res*. 20, 1144. <https://doi.org/10.1186/s12913-020-06001-y>
- <sup>vi</sup> ONS. (2021). *Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 2 December 2021*. ONS. [Prevalence of ongoing symptoms following coronavirus \(COVID-19\) infection in the UK - Office for National Statistics \(ons.gov.uk\)](#)
- <sup>vii</sup> Academy of Medical Sciences. (2021). *COVID-19: Preparing for the future. Looking ahead to winter 2021/2022 and beyond*. Academy of Medical Sciences. [ams-preparing-for-winter.pdf \(publishing.service.gov.uk\)](#)
- <sup>viii</sup> Whitaker, M., Elliott, J., Chadeau-Hyam, M., Riley, S., Darzi, A., Cooke, G., Ward, H., & Elliott, P. (2021). Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508,707 people. *BMJ*. <https://doi.org/10.1101/2021.06.28.21259452>
- <sup>ix</sup> McMahon, D., Gallman, A., Hruza, G., Rosenbach, M., Lipoff, J., Desai, S., et al. (2021). Long COVID in the skin: a registry analysis of COVID-19 dermatological duration. *Lancet Infectious Diseases*, 21(3), 313-314. [https://doi.org/10.1016/S1473-3099\(20\)30986-5](https://doi.org/10.1016/S1473-3099(20)30986-5)
- <sup>x</sup> EULAR. (2021). *EULAR COVID-19 Registry*. [EULAR | EULAR COVID 19 Registry](#)
- <sup>xi</sup> NHS England. (2021). *Long COVID: the NHS plan for 2021/2022*. NHS England. [Report template - NHSI website \(england.nhs.uk\)](#)
- <sup>xii</sup> The New York State Senate. (2021). *Senator Hoylman Announces Legislation to Establish COVID-19 Health Registry to Monitor “Long COVID”*. [Senator Hoylman Announces Legislation to Establish COVID-19 Health Registry to Monitor “Long COVID” | NY State Senate \(nysenate.gov\)](#)
- <sup>xiii</sup> Whitehead, N., & MacDonald, P. (2020). A COVID-19 Survivor Registry May Ameliorate Future Outbreaks. RTI International. [COVID-19 Survivor Registry | RTI](#)
- <sup>xiv</sup> Solomon, D., Henry, R., Hogan, J., Van Amburg, G., Taylor, J. (1991). Evaluation and implementation of public health registries. *Public Health Rep*, 106, 142-150.
- <sup>xv</sup> ENCePP. (2021). *ENCEPP Guide on Methodological Standards in Pharmacoepidemiology*. [ENCEPP Home Page](#)
- <sup>xvi</sup> Gliklich, R., Dreyer, N., Leavy M. (Eds.). (2014). *Registries for Evaluating Patient Outcomes: A User’s Guide*. NCIB. [Registries for Evaluating Patient Outcomes - NCBI Bookshelf \(nih.gov\)](#)
- <sup>xvii</sup> Zarei et al. (2021). *A Study to design minimum data set of COVID 19 registry system*. [A study to design minimum data set of COVID-19 registry system | BMC Infectious Diseases | Full Text \(biomedcentral.com\)](#)
- <sup>xviii</sup> WCEC. (2021). *Summary of Active and Prospective Long-COVID Research in Wales Report 000017 – November 2021*. [Summary long COVID Research Wales eng Nov 2021 \(1\).pdf](#)
- <sup>xix</sup> Bevan Commission. (2015). *Prudent Health Principles*. [Prudent Health Principles \(bevancommission.org\)](#)