CO@H Service Evaluation Protocol
September 2021
PSTRC, IGHI, Imperial College London

Covid Oximetry at Home (CO@H)
Service Evaluation Protocol

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i. Title

Covid Oximetry at Home: Assessing the clinical effectiveness of remote oximetry as a clinical pathway for patients with Covid-19

1. Study Type

The primary study type will be a Stepped-Wedge trial accompanied by a Pre-Post Analysis.

Stepped Wedge trials are used in public health and policy analysis studies where randomised controlled trials are not possible; as is the case in evaluating CO@H. Using this method, data will be collected from sites as they roll out CO@H, capturing contextual variation. The Pre-Post Analysis will be used to assess the impact of the intervention; this will require the collection of both data preceding the intervention and, and data following the intervention.

The secondary study type, if data permits, will be observational, as we will use Pillar 2 data to assess emerging inequalities in patients' access to services and the impact this could have on their outcomes. Additionally, we will explore opportunities for conducting local analyses in London using WSIC data.

2. Purpose & Background

Purpose

The purpose of this work is derived from the UK national need to evaluate national roll out of CO@H. The purpose of this study is to quantitatively assess the clinical effectiveness of the CO@H intervention as well as variation in access and outcomes.

Background

Before the outbreak of the Covid-19 pandemic, compelling evidence already existed regarding the role of telemedicine and digital technologies in restructuring how healthcare is delivered, indicating an opportunity to expand the use of virtual pathways (1). Such evidence suggests that care delivered remotely can, in many circumstances, safely meet patients' clinical needs and personal preferences (1)(2). Specifically, remote monitoring pathways, those that rely on an initial point of contact with the health services followed by continuous symptom monitoring via phone calls, digital or app-based diaries or wearable sensors, have also demonstrated effectiveness, especially when supported by behavioural change models (3)(4). However, the clinical effectiveness, safety and economic utility of this type of monitoring is context-dependent and varies considerably across clinical conditions; therefore, more evidence is required to fully assess their impact (3).

During the Covid-19 pandemic, the UK National Health Service (NHS), and health systems across the world, rapidly adopted novel remote monitoring pathways, many relying on home pulse oximetry (5)(6)(7). The available literature behind these programmes does suggest a potential for home management of Covid to support a positive patient experience (8)(9)(10). However, while pulse oximetry and trends over time proves an effective biomarker to detect deterioration, the evidence surrounding the safety of oximetry devices, specifically low-cost pocket oximeters, is variable and more research is required to understand what oxygen saturation thresholds should indicate when a patient should seek in-person care (11)(12). Overall, the literature surrounding whether remote monitoring for Covid-19 patients is safe remains inconclusive in the literature (7)(13).

In the UK, NHS England/Improvement, the body responsible for improved delivery of NHS care, in partnership with NHS Digital and Imperial College London, set out to understand, quantitatively, whether remote monitoring via home oximetry was a safe clinical pathway to roll out nationally in advance of

future waves of Covid-19. Following the UK peak of Covid-19, in Spring and Summer 2020, three pilots of remote monitoring "virtual wards" were set up to test a system-wide approach to the early detection of Covid-19 in the community. As part of this pilot, a rapid evaluation was conducted to determine whether remote monitoring was a safe clinical pathway.

Results of this work indicated that only 5.7% of patients presented to hospital after enrolment onto the virtual ward and likelihood of presenting to hospital increased when patients were aged over 65 and/or had comorbidities. Furthermore, all-cause mortality was significantly more likely amongst this group of patients as well and for those of BAME ethnicity or those who were overweight. The variation in interventions demonstrated that all-cause mortality was also higher for those patients who initiated the virtual ward pathway after discharge from hospital. Results also reveal that many patients included had mild disease and are neither admitted nor have Covid-19 related mortality. Finally, most patients using remote monitoring were of low clinical severity on initiation and did not deteriorate during their time on the virtual ward. Specifically, the results confirmed an increased risk for those in 'at risk' groups and those with oxygen saturations <95% at onboarding. Ultimately, results supported our hypothesis that remote monitoring was a safe pathway for Covid-19 patients.

This was reported to NIRB and received review on 19 October 2020 and used to inform the national roll out for Covid Oximetry at Home (CO@H), which this study will aim to evaluate.

3. Aim & Objectives

The aim of this work is to assess the quality of remote monitoring, specifically home oximetry (CO@H), for Covid-19 patients using a mixed-methods, collaborative approach. Furthermore, the work will seek to capture and understand unwarranted variation across sites. This work will evaluate the different models of CO@H rolled out across the country and determine the clinical impact of variation.

Three objectives will support these aims:

1. To identify inequalities in access to the CO@H programme based on location, demographic and clinical traits.
2. To identify national and site-specific mortality and secondary care utilisation effects of CO@H on patients with a positive Covid test result
3. To describe variation in the patient populations, routes of onboarding and patient outcomes between sites, and to use these findings to derive near- to real-time identification of outliers.

Each of these three objectives will have a dedicated work package with discrete outputs. These work packages are further outlined in Section 5.

4. Study Summary

4.1 Setting & Participants

This evaluation will take place at a national level across England.

The CO@H intervention is due to be rolled out across all CCGs across England in accordance with a letter from NHS England/Improvement recommending the use of home oximetry as a tool for monitoring clinical deterioration of Covid or suspected Covid patients in the community. While it has been recommended to all CCGs and a Standard Operating Procedure has been issued, use of the CO@H pathway is not mandatory, and therefore will not be adopted by CCGs universally.

The patient group recommended for the CO@H pathway should meet the following criteria:

- Diagnosed with COVID-19: either clinically or positive test result and
- Symptomatic and either

- Aged 65 years or older or
- Under 65 years and clinically extremely vulnerable to COVID. (The Clinically Extremely Vulnerable to COVID list should be used as the primary guide. Clinical judgement can apply and take into account multiple additional COVID risk factors; for the most part, it is anticipated that this will already have led to inclusion on the CEV list. National criteria for inclusion on the CEV list are set and updated by the Government.)

As this definition allows for GPs and other health professionals on-boarding patients into the CO@H pathway to use clinical discretion around vulnerability, there is room for variation in terms of which patients are included.

In terms of exclusion criteria, this study will include all CO@H sites regardless of whether they have rolled out the intervention. Sites will only be excluded on the basis of inability to collect sufficient data.

4.2 Data Collection & Data Management

Data will be captured by CCG according to the SOP and a Data Collection Specification (See Appendix). Nearly all data used in this analysis will be sourced from routinely collected dataset, namely:

- GDPPR
- HES
- ECDS
- SGSS
- ONS

Non-routine data collected at onboarding/offboarding will include the following:

- NHS number
- Oxygen saturations
- Whether a patient self-discharged
- Whether a patient used a digitally-enhanced service

Given that this is a national roll out, it is likely that data collection across sites will vary, but this evaluation relies on high levels of data quality and completeness. With the exception of WSIC data, all data will be provided to the evaluation team by NHS Digital and/or NHS England/Improvement.

All data will be held by Imperial College London's Big Data and Analytical Unit (BDAU). The Big Data and Analytical Unit is a multi discipline team which collaborates with a large network of researchers across the college to ensure the maximum use, impact and dissemination of research using healthcare data. The BDAU provides the only fully certified ISO 27001:2013 research environment within Imperial College and is 100% compliant with NHS IG Toolkit Level 3 (EE133887).

4.3 Design Overview

This study will assess the clinical effectiveness of the CO@H intervention at an individual patient level as well as address variation at an organisational level. In order to achieve this, we will use a stepped-wedge approach accompanied by a pre-post analysis. Using this method, data will be collected from sites as they roll out CO@H, capturing contextual variation. The pre-post analysis will be used to assess the impact of the intervention; this will require the collection of current data, or data that precedes the intervention. In terms of a comparator for CO@H, it will be possible to analyse this intervention in the context of existing and emerging remote monitoring pathways for Covid-19 and similar conditions. If data permits, we will also use Pillar 2 data to assess emerging inequalities in patients' access to services and the impact this could have on their outcomes.

Endpoints for the evaluation will include A&E presentation, hospital admission, ICU admission, oxygen saturations at hospital presentation and mortality.

5. Study Approach

5.1 Work package 1: Identifying inequalities in access in CO@H

Objective 1:

To identify inequalities in access to the CO@H programme based on location, demographic and clinical traits.

Methods used:

- In the first work package, all patients with a positive Covid test from the date of implementation of CO@H in each site will be included.
- The probability of inclusion in Co@H conditional upon being eligible for the program based on features in GDPPR will be examined across a range of regional, demographic and clinical features.
- Binary logistic regression will be used to identify statistically significant differences in likelihood of inclusion according to these features nationally, and where possible at the level of individual sites.
- Some patients not onboarded onto CO@H may have been too unwell for onboarding, and so may not provide a suitable comparator group. A range of sensitivity analyses will be conducted to examine different assumptions relating to whether mortality or hospital presentation around the time of testing precluded enrolment, using secondary care and ONS mortality data. The ability to undertake this component will be determined by the availability of both date of test and date of result for Covid tests.
- Absence of oxygen saturations for those not onboarded precludes comparison of clinical acuity in the community.

Data requirements:

Dataset	**Inclusion**	**Time Period**
GDPPR	All patients with a positive Covid-19 test in England	Rolling from CO@H start
Covid testing data	All patients with a positive Covid-19 test in England	Rolling from CO@H start
In hospital data	All patients with a positive Covid-19 test in England	Rolling from CO@H start
ONS mortality data	All patients with a positive Covid-19 test in England	Rolling from CO@H start

Output:

- This work package will deliver ongoing regular surveillance of the occurrence of inequality in access to CO@H in relation to geographic or demographic traits.

5.2 Work Package 2: Quantifying the Impact of CO@H on Patient Outcomes and Secondary Care Utilisation

Objective 2:

To identify national and site-specific mortality and secondary care utilisation effects of CO@H on patients with a positive Covid test result

Methods used:

- This evaluation examines the effect of the CO@H programme on those individuals eligible for the programme and those not eligible for the programme. Outcome measures will include A&E presentation, hospital admission, length of stay, ICU admission and mortality with 28 days of a positive Covid-19 test.
- In order to identify confounding arising from changing base rate admission and mortality due to Covid-19 over time, we will investigate changes in admission and fatality rate over the study period.
- This evaluation requires knowledge of patients who would be eligible for CO@H prior to the initiation of the intervention, and as such can only report on those who have a positive Covid test.

- This study will use two approaches:

- Firstly, a population-level stepped wedge analysis will be undertaken. Patients eligible for the CO@H programme prior to implementation will be defined as those who are ages 65 years or more, or those who are classified based on diagnoses held in GDPPR as being 'clinically extremely vulnerable'.
- Depending on the characteristics of implementation across sites, post-implementation analysis may begin after a transition period determined according to whether sites implement from a standing start, or already have a remote monitoring programme in place. A stepped-wedge approach design will be used, accounting for different roll-out timelines across sites. The models will account for changes over time and patient-level covariates. Sensitivity analyses will be carried out to understand the sensitivity of estimates to these factors.

- Secondly, a patient-level analysis will be undertaken focussed on a smaller subset of the population who had a clinical assessment in the period around their positive Covid-19 test and who were not admitted to hospital or died within one day of assessment. These individuals are assumed to therefore have a level of clinical acuity below that of requiring hospital admission.
- For this population, coarsened exact matching will be used to derive matched enrolled and non-enrolled populations according to a range of clinical and demographic features along with the month of positive test and time from positive test to clinical assessment. We will consider using primary care consultations and / or A&E presentations as data allow. The effect of the intervention will be determined using logistic regression to compare outcomes in those enrolled vs not enrolled.
- Sensitivity analyses will compare doubly robust model specifications and covariate adjusted models.

- A start date of 1st October generally coincides with the Autumn acceleration of Covid incidence and provides approximately two months of pre-implementation data, the precise time at which may vary by site.
- Evaluation will be performed nationally and the possibility to evaluate at regional and site levels will be explored based on the volume and quantity of data.

Data requirements:

Dataset	Inclusion	Time Period
GDPPR	All patients with a positive Covid-19 test in England	Rolling from 1st October
Covid testing data	All patients with a positive Covid-19 test in England	Rolling from 1st October
In hospital data	All patients with a positive Covid-19 test in England	Rolling from 1st October
ONS mortality data	All patients with a positive Covid-19 test in England	Rolling from 1st October

Output:

Analysis quantifying the effect of CO@H on mortality and secondary care activity

5.3 Work package 3: Identifying Variation in Practice and Performance Between CO@H Sites

Objective 3:

To describe variation in the patient populations, routes of onboarding and patient outcomes between sites, and to use these findings to derive near- to real-time identification of outliers.

Methods used:

- This evaluation will begin by describing rates of uptake between sites over time, and examine variation in the characteristics of patients being onboarded and their routes of onboarding. The following five indicators will be the main outcomes of interest at each site. calculated for each site: A&E presentation, hospital admission, ICU admission, oxygen saturations at hospital presentation and mortality.
- In order to control for case-mix variation between sites, regression models (either binary or multinomial depending on the outcome variable) will be constructed using data from all sites to predict local expected values of the outcome variables. Ratios of the expected to observed outcome variables will be calculated as a means of readily identifying outlying sites to enable more detailed local evaluation as needed. Either a single predictive model, or a 'leave one site out' model for each site will be produced depending on the balance of cases between sites obtained. If data permit, we may use a mixed effects model with sites as a fixed effect to examine site-level deviation.
- This evaluation does not incorporate information from the pre-implementation period, or from patients testing positive but not onboarded onto CO@H after implementation.
- Variation in the characteristics of patients assigned to tech-enabled and non-tech-enabled pathways will be described where possible.

Data requirements:

Dataset	Inclusion	Time Period
GDPPR	All patients onboarded onto a CO@H programme.	Rolling from CO@H start
Covid testing data	All patients onboarded onto a CO@H programme	Rolling from CO@H start
Onboarding	All patients onboarded onto a CO@H programme.	Rolling from CO@H start

Offboarding	All patients onboarded onto a CO@H programme.	Rolling from CO@H start
In hospital data	All patients onboarded onto a CO@H programme.	Rolling from CO@H start
ONS mortality data	All patients onboarded onto a CO@H programme.	Rolling from CO@H start

Outputs:

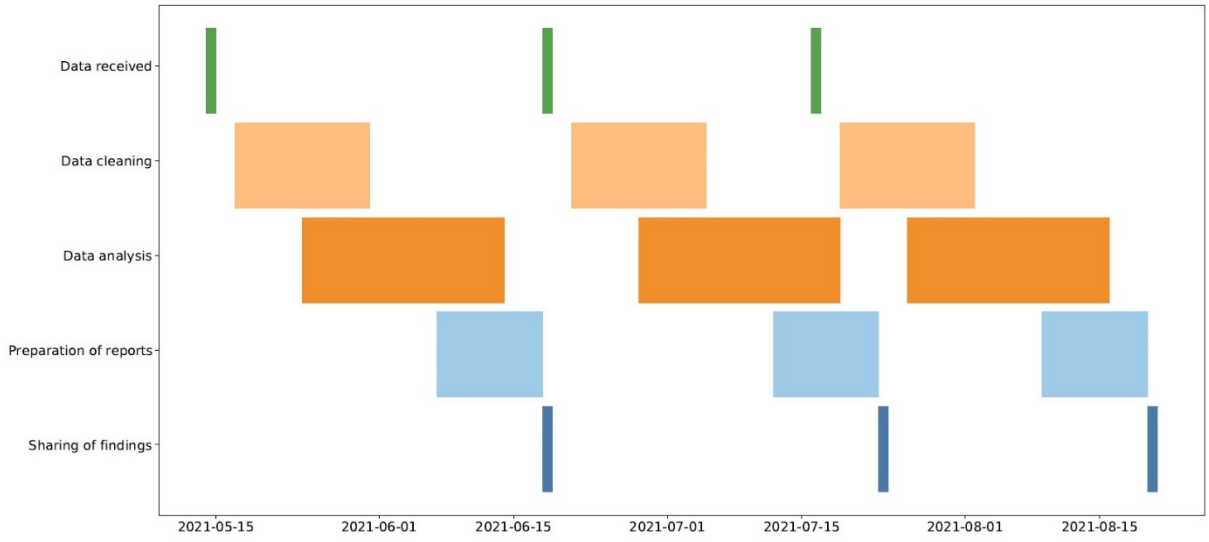
- Descriptive reports of overall uptake and characteristics of patient populations and outcomes nationally and for individual sites.
- Regularly updated measures of outlying site in terms of secondary care utilisation and mortality.
- Additionally, this package will provide insight for NHSX as to the adoption of enhanced technology pathways by providers and their availability to different patient groups.

5.4 Deliverables

The outputs described above will form four interim reports and one final report. Interim reports will be contingent upon delivery of data to the Imperial team at least 10 working days in advance of the deadline. The final report will include a more comprehensive analysis and will require data delivery 15 working days in advance of the deadline.

A preliminary timeline for reports is set out here, however, these are indicative and will change based on when NHSE/I and NHSD require are able to provide data to the evaluation team:

A Gantt chart of current project timelines based on expected data arrival dates is shown below:



6. Governance

This work has been commissioned by NHS England/Improvement; however, the contact and funding for this work will come directly from NIHR. This evaluation is subject to successful contracting with NIHR.

Given the national profile of the work, we are aware of, and work closely with, two other evaluation teams from UCL and the Implementation Analysis Unit (collaboration between the Health Foundation and NHS England/Improvement). We will work in close partnership with these evaluation partners,

adhering to clear lines of accountability for the deliverables within our respective workstreams. As a shared governance structure, we will provide transparent project management with a dedicated Project Manager on each team. We will continue to hold weekly meetings to cross-input on all work packages, avoid overlap and maximise impact. NHS England/Improvement will also be present at weekly meetings. Overall, the model will achieve fruitful collaboration, while upholding individual accountability for certain workstreams and deliverables.

Furthermore, both teams will agree on a model for interaction for receiving and responding to requests from funders. Timelines will be set out in the protocols as well as contingency plans for processing delayed or incomplete data. We would suggest fortnightly meetings with evaluation partners, funders and stakeholders to review progress and escalate concerns. Finally, we would propose that our PMO work with named CO@H site leads and any NHSE/I liaisons to the sites.

In terms of our working relationship with NHS England/Improvement and NHS Digital, our PIs and Co-Is will continue to attend weekly meetings with their team. Co-I's and researchers will work with NHSE/I and NHSD teams on a more regular basis across the duration of the CO@H evaluation.

7. Imperial Team

7.1 Leadership

Ara Darzi (PI): Academic Lead

- AD will provide high-level scientific and academic input to all work packages.
- AD will oversee all scientific outputs.

Sarah Elkin (PI): Clinical Lead

- SE will provide senior clinical leadership to all work packages and lead the strategic direction of the quantitative evaluation.
- SE will attend weekly meetings with NHSE/I and NHSD as well as weekly meetings with external evaluation partners.
- SE will be accountable for all scientific outputs and oversee their development.
- SE will make links with the larger clinical community around home oximetry.
- SE will oversee all scientific outputs.

Jonathan Clarke (Co-I): Analytics Lead

- JC will lead the development of all work packages in terms of their objectives, methods and intended outputs.
- JC will lead the analysis for all work packages and conduct portions of the analysis.
- JC will attend weekly meetings with NHSE/I and NHSD as well as larger meetings with the external evaluation partners.
- JC will brief PIs and Co-Is on analytic progress.
- JC will lead or contribute to relevant scientific outputs.

7.2 Operations

Gianluca Fontana (Co-I): Project Oversight

- GF will support the PIs in developing and executing the strategy for this evaluation.
- GF will attend weekly meetings with NHSE/I and NHSD and will maintain a working knowledge of project progress and potential risks.
- GF will contribute to relevant scientific outputs.

Kelsey Flott (Co-I): Project Manager

- KF will be responsible for the day to day management of the evaluation, including, but not limited to:

    - Attending all CO@H meetings;
    - Upholding adherence to deadlines and the professional quality of content delivered across all work packages;
    - Escalating risks and problems to Project Oversight and PIs;
    - Ensuring team collaboration and alignment;
    - Serving as the main point of contact for the work, internally and externally.
- KF will contribute to relevant scientific outputs.

Ana Luisa Neves (Co-I): Project management and evaluation support
- ALN will contribute to project management;
- ALN will contribute to and advise on all scientific outputs;
- ALN will work with the Lead Analyst to ensure that project management supports the overall objectives of the analysis team.

7.3 Analysis & Clinical Advice

Thomas Beaney (Co-I): Lead Statistician
- TB will work collaboratively with the Lead Analyst on all work packages and will attend any CO@H meetings as required.
- TB will lead or contribute to relevant scientific outputs.

Paul Aylin (Co-I): Analytics Oversight & Expert Advice
- PA will contribute to the development of analytic methods across the work packages and advise on extra analyses that could be conducted with data external to that provided by NHSD (i.e. WSIC).
- PA will meet with the Analysts as needed.
- PA will contribute to relevant scientific outputs.

Hutan Ashrafian (Co-I): Partnerships Lead
- HA will support the CO@H team in development partnerships in the larger remote monitoring academic space.
- HA will contribute to relevant scientific outputs.

Melanie Leis (Co-I): Data Management & Analytics
- ML will ensure all data management requirements are upheld and work with NHSD to process all necessary data sharing agreements.
- ML will work with the Analysts to ensure all data and analytic tools are in place within the BDAU to conduct the all work packages.
- ML will contribute to relevant scientific outputs.

Saira Ghafur (Co-I): Clinical Support
- SG will contribute clinical expertise as required by the PIs.
- SG will contribute to relevant scientific outputs.

7.4 Evaluation Team

Roberto Crespo: Analytic Support
- RC will conduct analyses for each of the work packages in close partnership with the Analysts.
- RC will contribute to relevant scientific outputs.

Ahmed Alboksmaty: Horizon Scanning & Project Support
- AA will continuously scan international and national literature (including grey literature) for new developments in home oximetry and remote monitoring for Covid patients, presenting written findings back on a weekly basis.
- AA will contribute to relevant scientific outputs.

Mahsa Mazidid: DARS support

- Mahsa will provide support related to DARS and data management.

Owen Bray: Project Management Support

- OB will support the Project Manager and Project Oversight on operations relating to the CO@H work.
- OB will contribute to relevant scientific outputs.

APPENDIX

1. CO@H SOP https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/11/C0817-sop-covid-oximetry-@home-november-2020.pdf