DIGITAL TECHNOLOGIES TO SUPPORT THE DELIVERY OF PULMONARY REHABILITATION FOR ADULTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE [GID-HTE10019]

FINAL PROTOCOL

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PROJECT TITLE

Digital technologies to support the delivery of pulmonary rehabilitation for adults with chronic obstructive pulmonary disease.

1.1 Plain English Summary

Pulmonary rehabilitation is an exercise and education programme for people with lung disease, including chronic obstructive pulmonary disease (COPD), who experience breathlessness. Evidence suggests that most people who complete a pulmonary rehabilitation programme experience increased exercise capacity and improved quality of life. However, it is currently only offered to a small minority of eligible COPD patients. Clinical experts state that limitations in workforce and service funding restrict the ability of the NHS to provide pulmonary rehabilitation to all people who may benefit.

Digital technologies to support pulmonary rehabilitation are a possible treatment option for adults with COPD. Delivering digitally supported pulmonary rehabilitation may be able to improve access, engagement and adherence to pulmonary rehabilitation programmes. These technologies may also reduce unplanned hospital admissions, reduce exacerbations, prevent deterioration of a person's condition and reduce health inequalities by reducing variations in access to and outcomes of care. However, discussions at the scoping workshop suggested that there are uncertainties about whether digital technologies to deliver pulmonary rehabilitation are as effective as existing pulmonary rehabilitation techniques, and whether the use of digital technologies will be suitable for all people with COPD.

This early value assessment (EVA) considers whether digitally supported pulmonary rehabilitation is beneficial and safe to use for adults with COPD. At present, there is limited evidence available for digitally supported pulmonary rehabilitation and this assessment will provide an initial view on whether further research and use of these technologies in the National Health Service (NHS) is justified while further evidence is generated. Based on preliminary evidence, the assessment will also take an early view on whether these technologies may represent good value for money for the NHS. Based upon the final scope, seven digital rehabilitation and self-management interventions will be compared with standard of care treatment options offered by the NHS.

1.2 Decision Problem

1.2.1 Purpose

The topic has been identified by NICE for EVA. The objective of an EVA is to identify promising technologies in health and social care where there is significant need and potentially enable early conditional access to these while informing further evidence generation. A rapid appraisal of the evidence is conducted to determine if these offer plausible value to the NHS. The evidence developed will demonstrate if the expected benefits of the technologies are realised and will be used to inform a subsequent final NICE evaluation when a decision will be made on the routine use of the technologies in the NHS.

1.2.2 The interventions

Seven digital technologies to support pulmonary rehabilitation for adults with COPD are included in the scope. They are:

- **Active+me REMOTE (Aseptika)** is a cloud-based platform that supports the hybrid delivery of pulmonary rehabilitation and remote monitoring of adults with COPD at home. The Active+ REMOTE app includes an education programme delivered in small lessons and interactive exercise videos that increase in difficulty as a person's fitness and strength improves. The technology also collects patient generated data via an add-on pulse oximeter, spirometer and smart inhaler. The technology can be accessed via a mobile phone, tablet or desktop.

- **CliniTouch (Spirit Health)** is an online platform that supports the delivery of a 6-week digital pulmonary rehabilitation programme and facilitates remote monitoring of adults with COPD and other conditions. The digital pulmonary rehabilitation programme can be accessed via a mobile phone, tablet or desktop. The programme includes exercise sessions 3 times a week and users are asked to complete questionnaires before and after each session. Users are also contacted weekly by local healthcare professionals to monitor their progress and increase the complexity of exercises.

- **Kaia Health COPD (Kaia Health)** facilitates the delivery of a personalised pulmonary rehabilitation programme. The technology includes educational modules, customisable daily training sessions and mindfulness exercises. It also facilitates communication with health coaches. The technology can be accessed via a mobile phone or tablet.

- **myCOPD (my mhealth Ltd)** is an online education, self-management, symptom reporting and pulmonary rehabilitation system. The myCOPD app includes a 6-week

pulmonary rehabilitation course consisting of an incremental exercise programme with education sessions to help promote self-management of COPD. The app also has a dashboard of self-care tools and educational resources for people with all stages of COPD. The app can be accessed via a mobile phone or tablet.

- **Rehab Guru (Rehab Guru)** is a digital exercise programme management software. Clinicians can use the technology to prescribe a personalised digital pulmonary rehabilitation programme. The technology includes exercise videos and users can share feedback with their clinician after each exercise and each session. Exercises are adjusted depending on a person's ability and goals. The technology can be accessed via a mobile phone, tablet or desktop.

- **Space for COPD (University Hospitals of Leicester NHS Trust)** is a digital self-management programme designed to help people with COPD manage their condition more effectively. The programme contains educational topics including information about medication, breathing control, exercise and nutritional advice. Users are encouraged to set goals, progress through a prescribed exercise programme and achieve weekly targets. The technology can be accessed via a mobile phone, tablet or desktop.

- **Wellinks (Wellinks)** is an online platform that supports the delivery of a digital pulmonary rehabilitation programme and facilitates remote monitoring of adults with COPD. The programme includes tailored exercises, education, and motivational support. It also collects patient generated data via an add-on pulse oximeter and spirometer. Wellinks can be accessed via a mobile phone or tablet.

1.2.3 Care pathways

At present, pulmonary rehabilitation is recommended for all people with a confirmed diagnosis of COPD.[1] Guidance suggested that pulmonary rehabilitation programmes should last at least 6 weeks and include a minimum of 2 sessions per week. Programmes are typically delivered in groups of 8 to 16 people and may be held in local hospitals or a range of venues such as community halls, health centres and leisure centres. Pulmonary rehabilitation teams include trained healthcare professionals such as physiotherapists, nurses and occupational therapists. Clinicians note that few people eligible to receive pulmonary rehabilitation receive this treatment as recommended. During Covid-19, people received pulmonary rehabilitation via video link, though this has largely stopped and there were concerns about effectiveness and reduced uptake compared to in-person pulmonary rehabilitation.

Digital technologies to support pulmonary rehabilitation may offer the opportunity for people to receive pulmonary rehabilitation in their home. In the scoping workshop, clinicians noted that there was uncertainty about where digital pulmonary rehabilitation would be used in the treatment pathway, i.e. whether this would replace the need for pulmonary rehabilitation or would be offered to people on the waiting list for pulmonary rehabilitation. Clinicians noted that people using digitally supported pulmonary rehabilitation would still need to attend in-person appointments for their initial and end assessments. Digitally supported pulmonary rehabilitation would be delivered as part of a wider respiratory pathway where people can access multiple interventions and treatment options from different parts of the pathway at the same time. Referrals may come from a broad range of sources where an accurate diagnosis of COPD has been made. This may include, but is not limited to, primary care, intermediate care, secondary care, tertiary care, occupational health, private health or self-referrals for people who have an accurate diagnosis. Patient preference and engagement should be considered when helping people make decisions about the care that they want to receive.

More details about the scope and the place of digital pulmonary rehabilitation for the purposes of this EVA can be found on the Final Scope[2] document on the NICE website.

1.2.4 Population

As per the final scope,[2] the eligible population for this appraisal is as follows:

Adults with a confirmed diagnosis of COPD who:

- Have had a recent hospitalisation because of an acute exacerbation, or whose functional baseline has greatly changed and is not following the expected recovery path

or

- Have an MRC dyspnoea score of 2 or above

or

- Have decreased exercise capacity as measured by a validated outcome measure such as the 6-minute walk test

1.2.5 Comparators

Comparators will include the following:

- Standard care face-to-face pulmonary rehabilitation, either in a clinical or home-based setting

- No treatment or waiting list

Additional comparators of interest for digital rehabilitation include:

- Hybrid of face-to-face and remote live pulmonary rehabilitation
- Non-digital non-face-to-face options for components of pulmonary rehabilitation, for example printed exercise sheets

However, within the timeline of this appraisal and in acknowledgement of the evidence currently available for digital pulmonary rehabilitation, it is unlikely that this appraisal will consider these comparators.

1.2.6 Healthcare settings

Secondary or community care

1.2.7 Outcomes to be examined

Outcomes of interest for evaluating digital technologies include:

<u>High priority</u>

- Exercise capacity measured by a validated outcome measure
- Health-related quality of life

<u>Medium priority</u>

- Other measures of respiratory function (including but not limited to the COPD assessment test [CAT] score, the MRC and the modified MRC dyspnoea score)
- Intervention completion (receiving a final assessment), adherence, rates of attrition (dropouts)
- Intervention-related adverse events
- Acute exacerbations, hospital admissions, readmissions or emergency admissions

<u>Other (where feasible)</u>

- Intervention uptake from those offered the technologies
- Daily activity
- Patient experience, technology usability and acceptability

- Healthcare professional experience

Due to resource and timeline constraints, it is likely to be necessary to prioritise the inclusion of high priority outcomes likely to be most pertinent to decision-making. Where feasible, additional outcomes will be considered. This may include outcomes not listed on the scope where these are considered by the EAG to be relevant to the decision problem. Decisions about further prioritisation of outcomes will be made on the basis of discussions with the technical team and Specialist Committee Members (SCMs).

1.2.8 Sub-groups to be examined

Where feasible, the following population subgroups will be considered:

- Level of breathlessness (MRC dyspnoea score)
- Having or not having comorbidities (including frailty)
- Living in a rural or urban setting
- Having had an exacerbation which required hospitalisation in the previous 12 months

Due to data sparsity for the subgroups and the resource and timeline constraints of an EVA, it may not be feasible to assess outcomes in all sub-groups.

1.3 Objective

The purpose of this EVA is to summarise and critically appraise existing evidence on the plausible clinical- cost-effectiveness of digital pulmonary rehabilitation for adults with COPD. A rapid review will be conducted to identify relevant evidence for the included interventions in the target population. Where feasible, a de novo economic model will also be developed to provide an early view of the potential cost-effectiveness of the included interventions. The following objectives are proposed:

1.3.1 Clinical Effectiveness

- Identify and assess evidence relating to the use and clinical effectiveness of the included technologies as it pertains to the scope
- Report on any potential safety issues
- Report the evidence gaps, highlighting what data may need to be collected to inform these gaps

- If evidence is included that is not directly related to the scope, outline the potential generalisability and limitations of the evidence. These points will also be addressed for evidence within the scope.

1.3.2 Cost-Effectiveness

- Identify and assess economic evidence relating to the use of the included digital PR technologies within the scope
- Subject to sufficient evidence, develop a conceptual economic model related to the scope, that can be used to inform future research and data collection
- Report available model inputs and evidence gaps
- Report on the technologies' costs and effects (where available), and an early assessment of whether there is a *prima facie* case for their use to be a cost-effective alternative to standard care in the NHS and no treatment (if data available).

1.4 Evidence review

A rapid review will be undertaken to identify evidence for the plausible clinical and cost-effectiveness of included technologies will be undertaken following the general principles published by the Centre for Reviews and Dissemination (CRD) at the University of York.[3] A systematic literature review (SLR) to comprehensively search for all relevant evidence for the appraisal is beyond the scope of an EVA. However, the review methods, including the literature search strategy and evidence synthesis, will be rigorous and conducted in a transparent manner, with the aim to produce a comprehensive overview of the key literature as relevant to the decision-making context.

Based on initial scoping searches, the EAG expects there to be a large body of evidence for the included technologies, and that this evidence base should be identified through our planned searches. If the evidence base identified is large, the EAG will prioritise the inclusion of evidence that is of the best quality and most pertinent to the objectives of the EVA. If technologies have little evidence in line with the scope, the EAG will consider including potentially relevant evidence, identified through the EAG's existing searches, that is broadly relevant to the decision problem but does not adhere strictly to the scope (for example in terms of the population or comparator).

At study commencement, the EAG or NICE will request that the manufacturers supply any unpublished evidence they wish to be considered and reviewed by the EAG.

1.4.1 Search strategy

Searches for clinical and cost-effectiveness evidence will be conducted in one combined search strategy, without any study type filters, to reduce screening burden. An exemplar search strategy for MEDLINE is provided in Appendix 1.

The search process will comprise the interrogation of the following main elements:

- Electronic databases, including MEDLINE (inc In-Process and PubMed-not-MEDLINE records), EMBASE and Cochrane.
- Economics sources, such as NHS EED, ScHARR HUD and CEA Registry.
- Manufacturer websites.
- The WHO International Clinical Trials Registry Platform (ICTRP) and the US National Library of Medicines registry at clinicaltrials.gov.
- MHRA field safety notices and the MAUDE database will be searched for adverse events.
- In addition, any industry submissions to NICE, as well as any relevant systematic reviews identified by the search strategy, will be scrutinised to identify additional relevant studies.
- Relevant clinical guidelines from NICE, SIGN and INAHTA, especially for economic modelling.

In addition to the above searches, a targeted search of the broader literature on people with COPD may be undertaken if necessary to identify the evidence base on HRQoL (i.e. health state utility values), resource use and costs for treatment and side-effects (UK studies only if available), and the methods available for the modelling of COPD to inform cost-effectiveness analyses. The search strategies employed will be reported, and findings from these exploratory searches will be presented in summary format, using a tabular approach and narrative text.

1.4.2 Clinical evidence to be included

This assessment will look across a range of evidence types including RCTs and real-world evidence. Systematic reviews meeting the inclusion criteria will also be identified. Studies may report either quantitative or qualitative evidence for the scoped outcomes. The following evidence types will be excluded:

- Animal models
- Pre-clinical and biological studies
- Narrative reviews, editorials, opinions
- Meeting abstracts, for studies where full-text papers are available. If studies are only available as meeting abstracts, inclusion will depend on sufficient information being available to offer meaningful critique.
- Studies not available in the English language.

1.4.3 Economic evidence to be included

Full economic evaluations, costing studies and studies reporting health related quality of life measures that inform either the design of the EAG's own analysis or provide a source of input data will be included where they meet the inclusion criteria set out for the review of clinical effectiveness (see section 1.2). Priority will be given to more recent studies and those with a UK NHS setting.

1.4.4 Study selection

The abstracts and titles of references retrieved by the searches will be screened against the inclusion criteria for relevance. Three levels of study selection will be conducted:

Step 1: Titles and abstracts of records identified in literature searches will be screened against a subset of the inclusion criteria (population, intervention, comparator)

Step 2: Full publications will be retrieved for records included at Step 1 and will be screened according to the inclusion criteria

Step 3: If the evidence base identified is large and infeasible to appraise in full within the timeline of the EVA, publications included at Step 2 will be screened and a subset of publication will be prioritised for inclusion. At least one publication will be included for each intervention, and publications will be prioritised where these are higher evidence quality and of greater relevance to the decision problem.

Independent, second review of study selection may be conducted subject to time and resource availability.

Quality assessment strategy

Formal risk of bias assessment will not be conducted. Discussion will be included in the EAG report on potential biases in key studies and how the risk of bias could affect key outcomes. The report will explicitly detail the potential sources of bias such as the main confounding factors and will comment on the generalisability of the results to clinical practice in the NHS.

1.4.5 Data extraction strategy

Data will be extracted from included studies into a bespoke database. Independent, second review of data extraction may be conducted subject to time and resource availability. Data points to be extracted include information about the study reference and design, the population and intervention characteristics, relevant outcomes and their measurement.

1.4.6 Methods of analysis / synthesis

Clinical data will be tabulated and narratively synthesised.

Methods and findings from included economic evaluations will be summarised in a tabular format and synthesised in a narrative review. Economic evaluations carried out from the perspective of the UK NHS and Personal Social Services (PSS) perspective will be presented in greater detail.

Key sources of risk of bias will be discussed. The generalisability of findings to clinical practice in the NHS will be considered.

1.5 Economic modelling

If data allows, an economic model will be constructed either by adapting an existing model or developing a new model using available evidence and following guidance on good practice in conduct and reporting of decision analytic modelling for HTA.[4-6] If data do not allow construction of a model, the EAG will describe the appropriate characteristics of the model that would be required (e.g. structure, setting, input parameters and ideal sources of data).

The structure of any model will be determined on the basis of research evidence and clinical expert advice (from specialist committee members) about:

- appropriate assumptions to make where no suitable data are identified for effectiveness for some of the interventions/comparators (for instance, per the company submissions received so far none of the intervention studies included a comparison with ‘no treatment’ and provided any costs or outcomes for the same. Therefore, comparison

with ‘no treatment’ may solely be driven based on clinical expert opinion and other assumptions based on literature where feasible)

- appropriate assumptions to make if there are data gaps in the information available to populate resource use or quality of life information per health state.

All assumptions applied in the modelling framework will be clearly stated. All data inputs and their source will be clearly identified.

Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:

- Costs of technologies, including licensing.
- Costs to set up new pathways and change service delivery. These could include:
  - Healthcare professional training
  - Hardware costs
  - Internet access costs
  - Healthcare professional grade and time for intervention delivery

The EAG notes that smaller service areas may have higher costs per user due to not needing as many licences for the technology.

Where appropriate, and if data allow, sensitivity analyses will be undertaken to explore uncertainty. These may include one-way and multi-way sensitivity analyses, use of probabilistic sensitivity analyses (PSA), and value of information analyses where modelling permits. The use of PSA involves sampling of parameter inputs from distributions that characterise uncertainty in the mean estimate of the parameter. PSA is used to characterise uncertainty in a range of parameter inputs simultaneously, to consider the combined implications of uncertainty in parameters. Value of Information analysis helps to identify where future research can be most efficiently targeted to reduce uncertainty.

Where probabilistic modelling is undertaken, results will be presented as expected costs and outcomes, with uncertainty represented using cost-effectiveness planes and/or cost-effectiveness acceptability curves/frontier (CEACs/CEAF).

1.6 Gap Analysis

Evidence gaps identified pertaining to the intermediate and final outcomes from the scope and those pertaining to the economic modelling will be summarised in tabular and narrative form. If appropriate, a 'traffic light' scheme will be used to highlight relative importance of the gap. Key areas for evidence generation will be summarised in tabular form. Narrative text will also address missing clinical evidence for other parts of the scope, such as population, setting and comparators.

1.7 Handling the company submissions

Data received from the company will be appraised and, where consistent with the decision problem, will be extracted and appraised in accordance with the procedures outlined in this protocol. Data provided (e.g. cost and resource use data) will be assessed against NICE's manual (2022[7]), reasonableness of assumptions made and appropriateness of the data used.

Any academic or commercial in confidence data taken from a company submission will be marked up as appropriate in the report.

1.8 Competing interests of authors

None.

1.9 References

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2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value Health. 2022;25(1):3-9.

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Appendix 1 Sample Search Strategy (Medline)

Ovid MEDLINE(R) ALL <1946 to July 31, 2023>

#	Searches	Results
1	exp Pulmonary Disease, Chronic Obstructive/	67012
2	(chronic adj4 obstruct* adj4 (lung* or pulmonar*) adj4 (disease* or disorder*)).ti,kw,ab.	64447
3	1 or 2	96774
4	Rehabilitation/	18690
5	exp Exercise Therapy/	63477
6	Physical Therapy Modalities/	40854
7	Exercise Movement Techniques/	872
8	(pulmonar* adj4 rehab*).ti,ab.	5115
9	or/4-8	123134
10	Digital Technology/	719
11	Mobile Applications/	11550
12	exp Internet/	97734
13	exp Cell Phone/	22449
14	exp Computers, Handheld/	13081
15	Medical Informatics Applications/	2551
16	Therapy, Computer-Assisted/	6973
17	(app or apps).ti,ab.	43223
18	(online or web or internet or digital*).ti.	138461
19	((online or web or internet or digital*) adj3 (based or application* or intervention* or program* or therap* or enabl*)).ab.	81394
20	(phone* or telephone* or smartphone* or cellphone* or smartwatch*).ti.	27106
21	((phone* or telephone* or smartphone* or cellphone* or smartwatch*) adj3 (based or application* or intervention* or program* or therap*)).ab.	16923
22	(mobile health or mhealth or m-health or ehealth or e-health or emental or e-mental).ti.	8503

23	((mobile health or mhealth or m-health or ehealth or e-health or emental or e-mental) adj3 (based or application* or intervention* or program* or therap*)).ab.	5889
24	(mobile* adj3 (based or application* or intervention* or device* or technolog*)).ti,ab.	21800
25	or/10-24	344806
26	3 and 9 and 25	123
27	("Active+me" or "Active + Me").af.	4
28	CliniTouch.af.	0
29	("Kaia COPD" or "Kaia Health COPD").af.	3
30	"myCOPD".af.	6
31	"Rehab Guru".af.	1
32	"Space for COPD".af.	17
33	"Wellinks".af.	1
34	or/26-33	146