Devices for remote continuous monitoring of people with Parkinson's disease: a systematic review and cost-effectiveness analysis

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Scientific summary

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Scientific summary

Background

Parkinson's disease (PD) is a condition that affects the brain, resulting in a progressive loss of co-ordination as well as movement problems. In the early stages of PD, the three main motor symptoms are shaking (tremor), slowness of movement (bradykinesia) and muscle stiffness (rigidity). There are around 145,500 people living with PD in the UK. The risk of developing the disease increases sharply with age.

Levodopa is the most prescribed treatment for managing the motor symptoms of PD in the early stages. However, it may be associated with significant motor complications, including response fluctuations and dyskinesias (involuntary movements). Response fluctuations are characterised by large variations in motor performance, with normal function during the 'on' period, and weakness and restricted mobility during the 'off' period. Deep brain stimulation and levodopa–carbidopa intestinal gel can be considered in people with advanced PD whose symptoms do not respond adequately to best medical therapy.

The National Institute for Health and Care Excellence (NICE) recommends that people with Parkinson's disease (PwP) should be seen by a specialist every 6–12 months initially, then more often with increasing disease complexity, although this is often difficult because of the increasingly ageing population and demands on PD services.

Remote monitoring devices are intended to be used alongside clinical judgement to assess disease severity and help manage PD symptoms and adverse effects of treatment. Results of the monitoring are analysed remotely and a summary provided to the specialist physician and/or to the patient. The data should be used to determine whether any changes in the treatment regimen are desirable, in consultation with the patient.

This assessment considers only wearable, remote monitoring devices that produce results with no input, or limited input, from the user. Five relevant devices were identified for consideration:

- Personal KinetiGraph (PKG) Movement Recording System (Global Kinetics);
- Kinesia 360 motor assessment system (Great Lakes NeuroTechnologies);
- KinesiaU motor assessment system (Great Lakes NeuroTechnologies);
- PDMonitor (PD Neurotechnology); and
- STAT-ON (Sense4Care).

Objectives

To determine the clinical and cost-effectiveness of the five included remote monitoring devices in PwP.

Methods

Systematic review

Systematic reviews were conducted following the general principles recommended in the Centre for Reviews and Dissemination (CRD) guidance and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Comprehensive searches of the literature were conducted to identify all studies relating to the use of the five remote continuous monitoring devices. MEDLINE, EMBASE, CENTRAL, ClinicalTrials.gov and

other databases and registries were searched on 1 February 2022. Two reviewers independently screened all titles and abstracts.

All clinical studies of any of the five included devices, where used in people with PD (of any severity or stage), were eligible for inclusion. The key comparator was clinical judgement of disease symptoms without the use of remote monitoring devices; however, included studies did not have to have a comparator group. Outcomes of interest included:

- association and diagnostic accuracy between outputs of remote monitoring (such as bradykinesia score, dyskinesia score) and clinical measures [such as Unified Parkinson's Disease Rating Scale (UPDRS) score or clinical judgement of symptoms];
- all impacts on clinical decision-making, such as changes in therapy and dose modification;
- all clinical outcomes, such as UPDRS or Hoehn and Yahr scores, morbidities and mortality; and
- all patient, carer or clinician opinions on the technologies.

Data reported in publications were extracted by one reviewer and independently checked by a second reviewer. Study quality was assessed using suitable tools, such as Quality Assessment of Diagnostic Accuracy Studies-2 for diagnostic accuracy studies and the Cochrane Risk-of-Bias tool for clinical trials.

Evidence was synthesised using a narrative synthesis approach. The results of data extraction were presented in structured tables and as a narrative summary. A broad thematic synthesis was used to identify key issues arising from the extracted evidence. Due to the diversity of reporting across studies, meta-analysis was not feasible for any outcomes. One clinical trial provided its individual participant data; this was re-analysed for this report.

Economic analysis

Two cost-effectiveness reviews were conducted: (1) a review of remote monitoring devices for people with PD, and (2) a review of existing decision models evaluating treatments for people with PD. The titles and abstracts of all reports identified by the bibliographic searches were screened independently by two researchers. Key findings were summarised narratively.

A de novo decision-analytic model was developed to assess the potential health gains and costs associated with implementing remote monitoring in the NHS. The base-case analysis considers only the cost-effectiveness of PKG and Kinesia 360, which are compared on a pairwise basis with current standard of care (SoC). The cost-effectiveness of other remote monitoring technologies was explored in scenario analysis. Based on company information, real-world applications of PKG and expert clinical advice, the External Assessment Group (EAG) assessed two alternative monitoring strategies: (1) one-time use: remote monitoring implemented at model baseline and as a one-time aid to clinical assessment, and (2) routine use: remote monitoring used at every follow-up assessment (i.e. over the review period at regular intervals) to routinely assist clinical judgement.

The EAG model was based on a Markov model structure, which sought to capture changes in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) domain scale scores, as an indicator of the level of symptom control associated with the use of remote continuous monitoring devices relative to SoC. These changes in MDS-UPDRS were informed by the clinical literature and were linked to health-related quality of life to assess quality-adjusted life-year (QALY) changes associated with remote monitoring. The economic analysis also captured cost differentials between SoC and alternative remote monitoring strategies considering: (1) costs associated with using each remote monitoring device, (2) changes in levodopa-equivalent medication use, (3) implementation costs and (4) follow-up consultations. The costs applied were independent of MDS-UPDRS scores modelled. Changes in levodopa-equivalent medication were, however, informed by the relevant clinical effectiveness literature so as to align with the applied treatment effects.

Clinical effectiveness results

Seventy-seven studies of clinical effectiveness were included in the systematic review. There were 57 studies of PKG. The diagnostic accuracy studies suggested that PKG has good accuracy for assessing bradykinesia, dyskinesia and tremor, but lower accuracy to detect sleep disturbance. Studies reporting changes in management found that PKG provided additional information leading to a change in the clinical management plan in 31.8–79% of patients (depending on study), most commonly an increase in treatment dose.

One non-randomised comparative trial of 162 patients provided individual participant data to the EAG. The results show that the use of PKG appears to improve UPDRS scores, particularly UPDRS III (by around 3.1 points) and UPDRS IV (by around 1.2 points). This is likely to be because PKG use is reducing time with bradykinesia (by 2.1 percentage points) dyskinesia (by 1.5 percentage points) and tremor (by 0.6 percentage points), although none of these reductions achieved statistical significance. The trial data suggested that PKG use predominately improves symptoms (particularly bradykinesia and UPDRS scores) in people who were not 'in target' and whose condition was not adequately controlled. Other trials reporting clinical outcomes were not comparative, but generally supported the evidence that PKG use improves UPDRS scores.

Patient opinion was broadly supportive of PKG use, particularly as a reminder to take medication. Patients mostly felt that PKG provided additional useful information on their symptoms (59–79% felt this), but clinicians were more equivocal; only 33–47% felt PKG provided additional information.

There were 15 included studies of the STAT-ON device. STAT-ON had high diagnostic accuracy to detect treatment 'on–off' times and bradykinesia, and high sensitivity but lower specificity to detect freezing of gait. There were no studies that presented evidence on the intermediate or clinical impact of STAT-ON.

There were three included studies for the Kinesia 360 motor assessment system. It had moderate-to-good diagnostic accuracy to detect bradykinesia, dyskinesia and tremor. Two small randomised controlled trials (RCTs, 64 patients) found some inconclusive evidence that Kinesia 360 improved UPDRS III and Parkinson's Disease Quality of Life 39 Questions scores when compared to standard management.

One small cohort study (16 patients) of KinesiaU motor assessment system was included. The EAG consider this as too small to draw any meaningful conclusions.

For PDMonitor only one conference abstract and one small case study were included. The EAG consider this as insufficient to draw any meaningful conclusions.

Cost-effectiveness results

Estimated changes in UPDRS associated with PKG show that PKG is associated with small unfavourable changes in UPDRS domains I and IV. In consideration of these highly uncertain results, the base-case analysis considered two alternative efficacy configurations for PKG: (1) an unrestricted analysis (considering all UPDRS domains), and (2) a restricted analysis (considering only UPDRS domains III and IV).

The deterministic base-case incremental cost-effectiveness ratio (ICER) for PKG using a one-time use strategy was £67,856 and £202,363 per QALY for the restricted and unrestricted analysis, respectively. Considering a routine strategy, the deterministic base-case ICER was £57,877 per QALY in the restricted analysis and £172,602 per QALY in the unrestricted analysis. The deterministic base-case ICERs for

Kinesia 360 using one-time use and routine remote monitoring strategies were £38,828 and £67,203 per QALY, respectively. Probabilistic results for PKG and Kinesia 360 aligned with the deterministic values.

Sensitivity analysis demonstrated that cost-effectiveness results were sensitive to assumptions regarding the durability of modelled treatment effects. Scenarios with low or zero waning of the treatment effect improved cost-effectiveness markedly. Results were otherwise broadly robust to a range of alternative assumptions and parameter inputs.

The EAG was not able to evaluate the cost-effectiveness of STAT-ON, KinesiaU or PDMonitor due to a lack of comparative clinical effectiveness evidence. In a cost comparison (assuming a 5-year time horizon), modelled device costs were lowest for PKG provided three devices or less were ordered per annum, followed by KinesiaU, STAT-ON, Kinesia 360 and PDMonitor.

Discussion

This assessment includes a comprehensive investigation of the diagnostic accuracy and clinical efficacy of remote monitoring devices for PD. The review used extensive database searches to identify all published evidence on the included technologies and followed rigorous recommended review methods to identify relevant publications, assess their risk of bias and undertake a narrative synthesis of the results.

The review identified a substantial literature on the diagnostic accuracy of PKG, and a smaller literature on clinical efficacy. Evidence for other remote monitoring devices was generally limited. PKG appears to accurately measure several symptoms of PD, including dyskinesia, bradykinesia, tremor and treatment-related outcomes. PKG also appears to generate clinical benefits compared with clinical management alone, with improvements in UPDRS III and IV scores. However, the available evidence was generally low quality, particularly for diagnostic accuracy. This casts some doubt on the validity of the results reported in the identified studies.

The cost-effectiveness of remote monitoring appears to be largely unfavourable with ICERs in excess of £30,000 per QALY. Cost-effectiveness results were largely robust to alternative assumptions and parameter inputs. The key drivers identified were: (1) the direction and magnitude of changes on UPDRS associated with remote monitoring strategies, (2) the persistence in changes to UPDRS (treatment waning) and (3) the number of devices requested (PKG).

Insurmountable limitations in the evidence base meant that the EAG were unable to assess the cost-effectiveness of STAT-ON, KinesiaU or PDMonitor. Comparative evidence for Kinesia 360 was also extremely limited and unlikely to be comparable with that used for PKG, thereby making comparisons problematic. This essentially limits comparisons across alternative monitoring devices to a cost-minimisation exercise, which necessarily implies strong assumptions about relative efficacy.

Conclusions

The EAG considers that the evidence for PKG shows that it could be of use in clinical practice, provided it can be made cost-effective. It provides useful information on key symptoms of PD, including bradykinesia, dyskinesia and tremor. The use of PKG leads to changes in treatment management for at least some patients, and possible improvement in symptoms.

Although there is some promising evidence for STAT-ON and Kinesia 360, the EAG considers that the evidence is currently not sufficient to be confident that these technologies will produce clinical benefits for patients. The EAG considers that there is too little evidence for KinesiaU or PDMonitor to draw any conclusions regarding their clinical value.

Almost all current evidence relates to patients receiving pharmacological therapy, mainly levodopa. The EAG notes that, at present, it is unclear whether PKG or other remote monitoring technologies offer any clinical benefit in other patients, such as those receiving advanced therapies.

Concerns about potential bias, together with the other limitations in the available evidence, means that cost-effectiveness estimates are highly uncertain. Key uncertainties relate to the magnitude and durability of treatment effects. The results of the economic analysis are largely unfavourable with ICERs in excess of thresholds typically adopted by NICE.

Suggested research priorities

The primary research priority should be to conduct further studies into the clinical impact of remote monitoring devices. This should focus on expanding the evidence base for PKG and Kinesia 360, where there is currently limited evidence on clinical effects, as well as conducting studies of STAT-ON, KinesiaU and PDMonitor, where there is currently no evidence of clinical effects.

Any future studies of comparative effectiveness should address the methodological limitations of the current evidence, as identified by this report. These would preferably be RCTs with pre-specified outcome measures. Studies should be carefully designed to consider the most applicable remote monitoring schedules and settings, as there is significant potential for variation in how remote monitoring devices could be used in practice. Specific consideration should be given to longer-term routine use of remote monitoring devices; currently all evidence pertains to short-term applications. Future studies of remote monitoring devices for PD may also consider patients with early and advanced disease. There is currently no evidence in these populations for any device.

Implementing remote monitoring may have a range of resource consequences that are currently not fully understood and may impact significantly on cost-effectiveness. This may include impacts on healthcare professionals' time and administration of the devices, as well as risks such as loss, damage or theft of devices. Where possible, future studies should seek to address these uncertainties by collecting appropriate data on resource implications.

Collecting further diagnostic accuracy evidence is considered a lower priority, but could be useful for Kinesia 360, KinesiaU and PDMonitor, where evidence is lacking. Diagnostic accuracy studies should evaluate the accuracy of these technologies for measuring bradykinesia and dyskinesia. Care should be taken to ensure the reference standard is robust and at a low risk of bias. It may be helpful for such studies to compare the technologies to PKG.

Study registration

This study is registered as PROSPERO CRD42022308597.

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