| Comment number | Name and organisation | Section number | Comment  | NICE response |
| --- | --- | --- | --- | --- |
| 1 | Global Kinetics Corporation | 3.6 There is limited evidence on how much technologies can improve symptoms or health-related quality of life | The Woodrow et al. 2020 study – a large, comparative, blinded, controlled trial, published in a respected journal (impact factor >6), is one of 57 published papers on the PKG. Despite this, it is noted that the report is critical of the Woodrow et al. 2020 study. To remove any potential confusion around the benefits and outcomes shown in the study, some important clarifications are detailed below.The report specifically challenges the frequency of PKG use with the statement:“clinical experts pointed out that the PKG was used every 5 weeks in the Woodrow et al. study, which would not be realistic in the NHS…”.It should be emphasised that the Woodrow paper demonstrated the PKG arm had better outcomes when compared to the control arm – with both study arms having the same 5-week frequency of follow-up. The 5-week follow-up was a design constraint of the protocol but show that consistent use of the PKG to augment clinical decision-making resulted in improved quality of life patient outcomes. Therefore, it is the clinical assessment made using the objective measurements during follow-up which results in the benefit, not the frequency of the visit. The study demonstrated that there was a statistically significant difference and clinically significant improvement in the PKG arm vs the control arm. The findings of this study show that when the objective measurements of the PKG are utilised in treating towards a target range with consistent therapeutic adjustments (e.g., medication adjustments) as indicated by trained clinicians then uncontrolled PD symptoms improve as measured by standard PD assessments (e.g., MDS-UPDRS). The purpose of the technology is to provide clinical insight that might otherwise be missed, with subsequent action taken by the clinician based on the individual data of the patient (e.g., change in medication); that action continues until the patient is optimised/controlled. The speed at which this management is done, directly correlates to how quickly the patient moves towards a controlled state, thereby reducing the risk of a costly adverse event. This point is also echoed in section 3.5 Clinical effectiveness “a potential benefit of the technologies is that they may more accurately evaluate symptoms than patient recall or clinical opinion, so a reference standard based on this could underestimate technology performance”. Furthermore, section 2.2 of the Diagnostic Consultation document states “more frequent follow ups may be needed to optimise dosage or for people who need more advanced treatments”. Additionally, NICE carried out a medical information briefing (MIB) on the PKG, published 4th May 2021. None of the other devices included in this DAP assessment have completed a MIB. The MIB confirmed that the PKG evidence was compelling and provides validated measures of PD symptoms including bradykinesia, dyskinesia, tremor immobility and fluctuation. It was on the basis of the MIB review that the NICE team believed the PKG should progress to the Diagnostic Assessment Programme (DAP). Global Kinetics’ pushback to the comment that Woodrow et al is unrealistic in an NHS setting, is that the study does have relevance to the NHS – it met its primary endpoint, demonstrating PKG as a device proven to bring value to patients, clinicians, and carers alike.  | Thank you for your comment which the committee considered.The EAG commented that the results of a trial where assessments are performed every five weeks cannot be assumed to apply if assessments were only every six or twelve months, particularly as a longer interval would give less opportunity to modify levodopa doses. The EAG noted that if PKG assessments were only every six months then there would presumably be a consequent delay in controlling a patient’s condition, with less certainty that adverse events could be prevented. As noted in the consultation comment, clinical experts stated PKG use every 5 weeks, as in the Woodrow et al. study, would not be realistic in the NHS (see section 3.6 of the diagnostics guidance document). The committee agreed that the Woodrow trial did not reflect the likely frequency of use of the device in the NHS. Therefore, while considering the data reported in Woodrow et al. in its decision-making (as described in section 3.6 of the diagnostics guidance document), the committee concluded there is limited evidence on how much the technologies can improve symptoms or health-related quality of life, and further data is needed for all technologies on this (see section 3.15 of the diagnostics guidance document). . |
| 2 | Parkinson’s UK (web comment) | 1.3 “The largest amount of evidence is for PKG, but its generalisability to the NHS is not certain because in the main trial more check ups were done, both for people who did and did not have the device, than they would in the NHS. The device was also used more frequently than would be expected in NHS care.” | The trial (Woodrow et al (2020). ‘A blinded, controlled trial of objective measurement in Parkinson's disease.’ NPJ Parkinsons Dis 2020;6:35.) referred to here tested an arm using the Personal Kinetigraph (PKG) and another arm not using PKG. There was an improvement of 8.5 points on the MDS-UPDRS scale for those using the PKG compared with those who did not. Appointments were more frequent (every 5 weeks) than standard practice, as there was only a limited time to conduct the trial. Given the PKG device provides objective monitoring of symptoms, it is likely to show a more significant impact in current practice, where NICE recommends 6 or 12 months between regular appointments and where monitoring of symptoms happens less frequently. We are also aware that the device is currently being used by over 30 hospitals in the NHS, indicating generalisability for use in the NHS. We recommend that the greater frequency of appointments in this trial is not regarded as a barrier to generalisability for use in the NHS more widely. | Thank you for your comment which the committee considered.The EAG highlighted that this is a mis-reading of the Woodrow paper. According to EAG analysis the improvement in UPDRS-Total score for PKG compared to standard care was at most 4.2 points. The EAG did not agree that it is “likely to show a more significant impact” if used every 6 to 12 months, since there was no evidence to demonstrate the effectiveness of PKG when used routinely every 6 to 12 months.The committee agreed that the Woodrow trial did not reflect the likely frequency of use of the device in the NHS or current standard of care. It discussed that there was no evidence reflecting device use in this context and decided not to change the DGD as a result. |

| Comment number | Name and organisation | Section number | Comment  | NICE response |
| --- | --- | --- | --- | --- |
| 3 | PD Neurotechnology Limited | 2.15 | The price of PDMonitor is subject to use. An outright purchase is at 12,000 GBP, while a yearly subscription is at 350 GBP per month, with purchase of the device being free of charge. Depending on the context a combination of the above scenarios could apply, while discounts are also possible, based on volume. As an example, for a 2 month follow up of a patient a price quoted to an NHS hospital has been 500 GBP. All price references as per above entail unlimited number of monitoring sessions within the said time horizon.  | Thank you for your comment which the committee considered. The EAG used the costs based on company response to the NICE request for information (£12,000), as no information on an alternative yearly subscription model was provided. Section 2.15 in the DGD has been updated to reflect the alternative pricing model described in the consultation comment “At consultation on the draft guidance the company added that an alternative pricing model is available: a yearly subscription is at £350 per month, with purchase of the device being free of charge and possible discounts available based on volume. The length of subscription required for this pricing model was not provided.” |
| 4 | Parkinson’s UK (web comment) | The diagnostics tests. The comparator - 2.22 | When using ‘standard care’ as the comparator to assess cost-effectiveness it will be important to distinguish when ‘standard care’ refers to a nurse-led service and when it refers to a consultant-led service. An issue raised earlier in the consultation process.The Economic Advisory Group (EAG) model uses NHS England 2019/2020 National Cost Collection tariffs for a Specialist Parkinson's nurse with a face-to-face consultation cost of £81 and £56 remote to represent the cost of ‘standard care’. In response to comments on the Diagnostic Assessment Report section B issue 4, the reason given for the use of the specialist nurse cost over the cost of a consultant neurologist outpatient appointment (£187 face to face, £105, remote consultation) was that survey data (Gumber A, Ramaswamy B, Ibbotson R, Ismail M, Thongchundee O, Harrop D, et al. Economic, social and financial cost of Parkinson's on individuals, carers and their families in the UK. Project report. Sheffield: Centre for Health and Social Care Research, Sheffield Hallam University; 2017.) showed people with Parkinson's as more likely to see a Parkinson's nurse than a neurologist. However, this is based on data provided by only 610 people with Parkinson's, and, therefore, is unlikely to truly represent the wider population of people with Parkinson’s. This data showed that consultations with a Parkinson's Nurse represented 10% of total consultations, and for neurologists, 6.24%, a difference of less than four percent. For the model to only consider the cost of specialist nurse care to represent the 'Standard of Care' cost appears flawed when measuring the cost-effectiveness of the remote monitoring devices being assessed.We recommend that the report states that when commissioners assess the cost-effectiveness of the remote devices used in the NHS, they consider the cost implications for use by a nurse-led or consultant-led service. We further recommend that the EAG model be reviewed and amended to consider the scenario of the devices being used in a consultant-led service and in a nurse-led service. | Thank you for your comment which the committee considered. The EAG previously provided a response to this point in the appendix of its response to the stakeholder comments (issue 4 from Global Kinetics PTY). The EAG conducted an additional scenario analysis where the model used the cost of consultant neurologist outpatient appointment (£187 face to face, £105, remote consultation) instead of a nurse-led service (£81.41 face to face, £56.41, remote consultation). Both scenarios (nurse-led service and a consultant-led service) were available to committee for decision-making. The committee noted that results were similar in both scenarios. |

| Comment number | Name and organisation | Section number | Comment  | NICE response |
| --- | --- | --- | --- | --- |
| 5 | Global Kinetics Corporation | 1. Recommendations | All wearable devices operate on unique algorithms and have undergone different validation studies to demonstrate efficacy. In its current form, the draft recommendations fail to recognise the difference in clinical data available for the individual devices. Because each device included in the assessment undergoes its own validation studies, collecting ongoing evidence, efficacy data, post-market surveillance data, etc., these results are not transferable between devices, and the evidence cannot be treated in a generic fashion.Given the complete absence of information directly comparing the outcomes of one device with another, it is a justifiable concern that generalising PKG with other devices described in the NICE recommendation is not evidence-based.Outlined below are several issues regarding the decision to recommend all devices equally, along with supporting evidence justifying the position to uniquely recognise PKG based on its clinical data:* PKG has completed 57 studies; a wealth of evidence – especially when compared to the other devices. The studies represent a massive scientific and financial commitment over the last 15 years by the company and we request that the Committee give greater weight to this evidence base within the recommendations.
* The EAG’s states “that there is too little evidence for KinesiaU or PDMMonitor to draw any conclusions as to their clinical value”3 and “The evidence was limited in extent and often low quality. For all devices **except PKG** there was little to no evidence on the clinical impact of the technology”3.

The draft recommendation in its current form, however, gives insufficient weight to these statements and lists these devices together with PKG – a device with substantial positive validation and clinical utility evidence. Further, regarding including these other devices interchangeably with PKG – there is the question of legality from a medical device regulatory perspective. The EAG’s own documents recognise there is only sufficient clinical evidence to make a recommendation for the PKG. Both UK and EU MD regulations forbid clinical generalisation of devices, other than for those devices which are defined as being legally equivalent, as defined by UK and EU legislation. The current EU MDR explains legal equivalence as a medical device that can claim biological (e.g., materials and sub-characteristics), technical (e.g., design, use, performance, and sub-characteristics) and clinical equivalence (e.g., clinical conditions, population, site in the body, sub-characteristics); in claiming such, there is increased scrutiny by Notified Bodies and Designating Authorities2,4,5,6.The information above, and references below, evidence why the draft recommendation is potentially insufficient from a clinical viewpoint and is incompatible with existing medical device legislation from a regulatory standpoint4,5,6. An accurate and legally compliant recommendation would recognise PKG as having significantly more data regarding the device mechanism, and that its algorithms have been thoroughly validated and have demonstrated clinical benefit.The recommendation should clearly separate PKG from the other devices reviewed – as none of the other devices are, nor claim to be, legally equivalent to the PKG. A recent MHRA Consultation document outlines the importance of this too: “After careful consideration of consultation responses, the government intends to introduce requirements on entire equivalence on a biological, technical and clinical basis (please note that we have amended the wording from “physical” basis in the consultation document to “technical” basis in order to align with the recognised international terminology). **This approach would take us beyond the equivalence requirements in the EU MDR**”1 1. (Consultation on the future regulation of medical devices in the United Kingdom, MHRA, 26th June 2022; <https://www.gov.uk/government/consultations/consultation-on-the-future-regulation-of-medical-devices-in-the-united-kingdom/outcome/chapter-7-clinical-investigation-and-performance-studies>
2. MDCG 2020-05, Clinical Evaluation – Equivalence, A guide for manufacturers and Notified Bodies, April 2020 <https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2020_5_guidance_clinical_evaluation_equivalence_en_0.pdf#:~:text=The%20MDR%20requires%20that%20biological,with%20similar%20release%20characteristics%20of>
3. DAP61 EAG’s Assessment Group Report, Devices for remote continuous monitoring of people with Parkinson’s disease, 2nd Aug 2022, Pg 11, Conclusion and Page 3&4 Limitations
4. CLINICAL EVALUATION: MEDDEV 2.7/1 revision 4, A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES UNDER DIRECTIVES 93/42/EEC and 90/385/EE, Guidelines on Medical Devices, June 2016
5. UK MDR 2002

MDR Regulation (EU) 2017/745 | Thank you for your comment which the committee considered.The committee considered the EAG’s report at the first meeting when deciding on the draft recommendations. While the EAG’s comments and conclusions are taken into account by committee, it is the committee who decide the recommendations for the guidance.All devices included in the guidance have a CE or UKCA mark, and the devices are individually described in the opening sections of the guidance (see section 2.6 onwards).The diagnostics consultation document did not state that data from 1 device could be used to show performance of another. The committee noted the EAG’s comment that it should not be assumed that any clinical benefits observed for 1 technology would also be found with the other technologies, and that no identified studies compared performance of 1 technology to another. The committee also noted that the technologies differed in how sensors are worn and the algorithms that they use. Further text has been added to section 3.15 of the diagnostics guidance document to reflect this. The committee concluded that there is limited evidence for all technologies assessed in terms of how much they improve symptoms or health-related quality of life (see section 3.6 in the diagnostics consultation document), and that further data is needed for all technologies on this. Further text has been added to section 3.15 in the diagnostics guidance document to highlight this point. As described in responses to consultation comments above, the committee considered data from of the Woodrow et al. study in its decision-making.The committee noted in the first meeting for this topic that the PKG had the most evidence of the technologies considered (see section 3.15 of the diagnostics consultation document, and in the section on ‘Why the committee made these recommendations’). The committee noted that a lot of identified data, including for the PKG, was on test accuracy. It had concern about how suitable accuracy estimates are to assess the performance of these technologies (see section 3.5 of the diagnostics consultation document) and considered that it is uncertain how much remote monitoring devices would change decisions about care in the NHS (see section 3.8 of the diagnostics consultation document).  |
| 6 | Global Kinetics Corporation | 4. Evidence generation recommendations | The PKG is currently in use clinically in 33 NHS hospitals and community-based services; over 12,000 NHS patients have utilised the PKG since 2015 – and this alone speaks to the success of the PKG. From a post-market studies perspective, there have been >7 clinical posters and 5 publications on NHS patients. Additionally, there was an EU/UK experts consensus publication in 2018. GKC agrees with NICE that further data collection is required. GKC will continue to gain evidence through hospital evaluations, audits and clinical trials and is committed to obtaining and publishing meaningful real-world data. GKC will continue to actively adhere to the Post Market Surveillance (PMS) and Post Market Clinical Follow-up (PMCF) requirements, as defined in the EU MDR legislation for a Class iia medical device. We are aware such requirements will apparently be mirrored by the UK, as stated in a recent MHRA consultation document: “…it remains the government’s intention to proceed with the proposal to amend the UK medical devices regulations to clarify and strengthen the requirement for manufacturers to implement a post-market surveillance system, in respect of all medical devices they have placed on the UK market”1. 1. (Consultation on the future regulation of medical devices in the United Kingdom, MHRA, 26th June 2022; <https://www.gov.uk/government/consultations/consultation-on-the-future-regulation-of-medical-devices-in-the-united-kingdom/outcome/chapter-7-clinical-investigation-and-performance-studies>
 | Thank you for your comment which the committee considered. |
| 7 | Global Kinetics Corporation | 3.1 People with Parkinson’s disease could benefit from remote monitoring technologies | Patient and carer comments in the NICE DAP 61 only refer to their experience of wearing the PKG. This is again borne out in comments made by the patients and carers in part 1 of the committee meeting. It is inaccurate to state that all the patient feedback relates to all of the devices. As discussed, the strategy of grouping medical devices together which are not legally equivalent is contrary to current legislation – and, as such, should be reassessed. Some devices have specific algorithms that must be validated; some devices have completely different modes of action or positioning on a patient, etc. Therefore, patients will ultimately have very different experiences, and output from the devices will consequently be very different. The regulations are there to protect patients and every device must produce its own clinical data for it to be assessed and made available to patients. It is fair for GKC to assume that where a difference exists in the quality and amount of clinical data between the PKG (substantial amounts of high quality data) and the other devices, that this should be accurately reflected in the NICE recommendation. E.g., for consistency – if NICE expects patient feedback on each device, devices that make that data available vs those that don’t should be dealt with entirely differently, not grouped together. In this case, there is no substantiating evidence to support the patients’ comments on any of the wearables apart from the PKG. | Thank you for your comment which the committee considered. The committee considered that all devices assessed have the potential to have benefits for people with Parkinson’s disease and their carers, as described in section 3.1 of the diagnostics consultation document. The difference in the number of sensors and how they are worn for the different technologies was described in the diagnostics consultation document (from section 2.6). The committee noted that the devices differ in how they work and where sensors are attached, so some may be more suited to some people than others, for example people with missing limbs or with restricted movement (see section 3.1 of the diagnostics consultation document).Section 3.1 of the final guidance document has been amended to note that “The EAG identified 8 papers that reported patient or carer opinions on PKG, 2 papers on STAT-ON, 1 on Kinesia 360 and 1 on KinesiaU.” |
| 8 | Great Lakes NeuroTechnologies | 1 | We appreciate the recommendation that further evidence should be generated and we look forward to working with the NHS and healthcare providers in the UK on such a project.  | Thank you for your comment which the committee considered. |

| Comment number | Name and organisation | Section number | Comment  | NICE/EAG considerations |
| --- | --- | --- | --- | --- |
| 9 | PD Neurotechnology Limited | General | There is likely evidence to be published or to be submitted for publishing until January 2023. What is the cutoff point for new evidence to be taken into account? What about after January 2023? | Thank you for your comment which the committee considered. Please make NICE aware of new and relevant evidence as it becomes available. New evidence can be submitted to the diagnostics assessment programme at diagostics@nice.org.uk |
| 10 | Parkinson’s UK (web comment) | Committee-discussion. People with Parkinson's disease could benefit from remote monitoring technologies 3.1. “It recognised that offering face to face appointments is still essential, and that remote assessment would not replace this entirely, but could offer more flexible options for care for some people.” | We believe it needs to be made clear that remote monitoring is not intended to replace face-to-face appointments but to complement face-to-face appointments by providing objective monitoring of symptoms to improve decision-making and outcomes for people with Parkinson's. We recommend the wording is amended here to give more clarity that remote monitoring is to complement and not replace face-to-face appointments. | Thank you for your comment which the committee considered.The committee decided to change the text in section 3.1 to further emphasize this point “Experts commented that use of the technology should be considered complementary to face-to-face appointments.” |