National Institute for Health and Care Excellence

Parkinson's Disease (update)
Scope Consultation Table
5th August - 10th September 2014

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	AbbVie	1	4.3.1 e)	AbbVie considers that it is essential that Duodopa is included within the scope of this Parkinson's Disease Clinical Guidelines update. UK Movement Disorder Specialists regard Duodopa as an important option in the treatment of advanced Parkinson's and clear guidance on its appropriate use will greatly benefit appropriately selected patients. Duodopa can be transformative in the lives of patients and carers. Also for many patients, such as those over the age of 70 who may not be considered for deep brain stimulation, Duodopa may be one of the only treatments available. Guidance on which patients are eligible for treatment with Duodopa, and are considered appropriate for this treatment, would give much needed support to clinicians working in this area. It should be noted that several prospective clinical trials using Duodopa have recently been published adding greatly to the evidence base available in relation to this treatment.	We thank you for your comment. We can confirm that Duodopa will now be considered in the scope of this guideline.
SH	AbbVie	2	4.3.2 e)	Evidence shows that Parkinson's can have a substantial effect not only on the quality of life of those with the condition but also on those who care for them (1). AbbVie considers that the scope of this clinical guidance update should be expanded to explore how carers' needs are assessed and how these needs are subsequently met. It is evident that there is a high degree of regional variation in the level of support for carers. It is generally accepted that the presence of a PD Specialist Nurse can be crucial to the provision of carer support, however, once again regional variation in the availability of this key member of the Parkinson's care team is significant.	We thank you for your comment. Carer experience and the impact of different aspects of Parkinson's disease upon carers will be covered as an outcome of interest in many of the review questions. Parkinson's disease nurse specialist intervention was not highlighted as an area where there was new evidence and therefore this has not been included within the update of this guideline.
SH	AbbVie	3	4.3.2 f)	Inclusion of palliative care guidance is essential within the scope of the PD clinical guidance update as it necessary to address the huge challenge faced by patients, carers and clinical at this stage of the	We thank you for your comment. This has been taken this into consideration and a review of palliative care needs in people with

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				disease. Providing palliative care can help maintain patients' independence and improve their quality of life at every stage of the Parkinson's pathway. It is important to consider that the provision of palliative care should not necessary be restricted to the end of life; guidance on the particular aspect of timing of palliative care services is sorely needed. In the current guidelines there is a lack of detail for clinicians around when to discuss end of life care with patients and on specific issues such as when to either increase or decrease medication. Feedback from Movement Disorder Specialists suggests that on reflection they do not perhaps discuss advanced care planning early enough. The updated guidelines should also provide advice on how people with Parkinson's Disease are given the opportunity to discuss end of life issues and to plan in advance for how their care is managed at the later stages of the disease. We understand from discussions at the stakeholder scoping meeting that a more general NICE clinical guideline on palliative care is due to be published soon. Patients with Parkinson's – particularly those in the later stages – have specific needs that are unlikely to be met within this more general clinical guidance. An example is the issue of whether to maintain dopaminergic care even in the last days of life. This is a specific issue that has been raised by clinicians with experience of the difficulties in this clinical situation.	Parkinson's disease will be included within the guideline update.
SH	AbbVie	4	General	There is currently a lack of guidance available on when patients with Parkinson's should be referred to neurological specialist centres to be considered for an advanced treatment; namely Duodopa infusion, subcutaneous apomorphine infusion or deep brain stimulation. There is no consensus on the timing of referral, or on the appropriate patients that should be referred for consideration of these treatments. As these treatments are often	We thank you for your comment. We can confirm that the efficacy and referral criteria for Duodopa will now be considered in the scope of this guideline.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				only available at a specialist neurological centre (funding for deep brain stimulation and Duodopa initiation is only available at specialist centres; although the location of the initiation of apomorphine infusion can vary depending on region), timely referral is crucial to ensure that the opportunity to use these therapies is not lost. As the clinicians at specialist centres are best placed to make this decision with the patient and carers, delay in referral can have a significant impact on the benefit that can be derived from these treatments. Clinicians have also reported to us that inappropriate patient referrals for consideration of an advanced treatment can overburden busy specialist neurological centre clinics. It is our belief that clearer guidance on which patients to refer and when would allow a more rational use of the limited resources available.	
SH	AbbVie	5	General	AbbVie considers that guidance is needed on what constitutes a PD specialist. We believe that without a definition of what a PD specialists' qualifications, level of clinical experience and specific PD expertise and perhaps even location (i.e neurological specialist centre vs district general hospital) is, this definition is likely to be a cause for confusion. It is noted that in the current Scottish SIGN guidelines on Parkinson's (2) the characteristics of 'specialist' is defined with the guidelines stating that "patients with suspected Parkinson's disease should be referred untreated to a hospital clinician with sufficient expertise in movement disorders to make the diagnosis."	We thank you for your comment. The guideline development group will take this into account and will define what they believe to be a Parkinson's disease specialist.
SH	AbbVie	6	General	1 Parkinson's UK, National Parkinson's Audit Summary 2011, 2011 2 Scottish Intercollegiate Guidelines Network, Diagnosis and pharmacological management of Parkinson's disease A national clinical guideline, January 2010, (Page 11)	We thank you for your comment
SH	AGILE – Chartered Physiotherapists working with	1	3.1.0	We would suggest that the title of this section "Epidemiology" is widened as the section contains neuropathology, clinical features etc which is more than epidemiology alone.	We thank you for your comment. We have amended the title to Background to be consistent with the headings used in other NICE scope documents.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	older people				
SH	AGILE – Chartered Physiotherapists working with older people	2	3.1.0 a	Sentence is rather shorthand in nature – consider expanding to , " …condition … in which the death of dopamine-containing cells of the SN in the brain plays a key role."	We thank you for your comment. We feel the current sentence is more easily read so we have not amended this section of the scope.
SH	AGILE – Chartered Physiotherapists working with older people	3	3.1.0 e	The statement after …..*as a primary movement disorder; however, other symptoms may be prominent, such as depression, [add cognitive impairment] and dementia*. Cognitive impairment should be added as it affects people sooner and with more early impact than dementia.	We thank you for your comment. We have taken this into account and amended the scope accordingly.
SH	AGILE – Chartered Physiotherapists working with older people	4	3.2.0 Current practice - d and e	Current practice. The word '*may*' be considered, ought to be changed to '*should*' be considered in both statements if people are to have a real choice.	We thank you for your comment. The wording has not been amended as the word 'may' reflects that this is a description of typical practice at present rather than a section on recommended care.
SH	AGILE – Chartered Physiotherapists working with older people	5	4.2.0 Setting - a	Setting: A lot of exercise is run through local Exercise Referral Schemes through City Councils, or classes specifically run by the Parkinson's UK Branches, not the NHS. The Guideline would be restrictive if it did not permit for such provision out with the NHS. Also, should consider the place of social care if a main outcome is to be Resources and costs (4.4.c)	We thank you for your comment. The use of exercise therapy and local Exercise Referral Schemes have not been prioritised for review in this guideline. The physical therapies to be covered include occupational therapy and physiotherapy, as newly published evidence was available on these topics.
SH	AGILE – Chartered Physiotherapists working with older people	6	4.3.0 Management	Areas not in the original guideline that will be included in the update. Should consider Social Care (there is a Sheffield Hallam University research report available, and the health economists are currently looking into the potential cost saving of earlier social care interventions as opposed to management of crisis. As mentioned above, it will help with the 4.4.c Main outcome on 'Resources and costs'.	We thank you for your comment. Social care costs will be covered within health economic modelling where possible and appropriate.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	AGILE – Chartered Physiotherapists working with older people	7	4.3.1 b	AGILE welcomes the inclusion of non-pharmacological management, especially physiotherapy. However we would like to accentuate (following reading the workshop notes) that the Alexander Technique is rarely provided as a key intervention within NHS settings.	We thank you for your comment.
SH	AGILE – Chartered Physiotherapists working with older people	8	4.4.0 Main outcomes	e) Disease severity – are we talking of the old UPDRS, or the updated Movement Disorder Society one which has input directly from people with Parkinson's? e) & f) Both these outcomes measure progression / severity predominantly based on physical manifestation, some of which can be ameliorated by medications in the first few years, so not accurate reflection of the progression of the condition if someone is managing well as a consequence on drug therapy.	We thank you for your comment. We have added examples of the types of outcome measures we will be covering to section 4.4. These will be pooled and combined where appropriate and we will rely on guideline development group advice as to the applicability of the individual measures to answer each individual review question in terms of version of the measures and the point in the care pathway the review question is placed.
SH	AGILE – Chartered Physiotherapists working with older people	9	4.3.2 f) Issues not covered - and 4.5.7 a) Review questions, Palliative care	First section states Palliative care will not be updated, but second section raises a question about advance directions and palliative care plans.	We thank you for your comment. This has been taken this into consideration and a review of palliative care needs in people with Parkinson's disease will be included within the guideline update.
SH	AGILE – Chartered Physiotherapists working with older people	10	4.5.8 a	AGILE welcomes the inclusion of this section	We thank you for your comment.
SH	Boston Scientific Ltd	1	4.5.5	Given recent studies demonstrating positive outcomes from the use of Deep Brain Stimulation earlier in Parkinson's disease patients (cf. EARLYSTIM), we welcome NICE's inclusion of a review question to assess the benefits of using Deep Brain Stimulation therapy at	We thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				earlier stages of the disease	
SH	Boston Scientific Ltd	2	4.3.1 - 4.5.5	We welcome the addition of pedunculopontine nucleus stimulation as an additional stimulation option in the treatment of PD patients with Deep Brain Stimulation	We thank you for your comment.
SH	Boston Scientific Ltd	3	4.5.5	We would be interested in NICE's view as to whether the relative benefits of different types of pulse generators for the administration of Deep Brain Stimulation therapy (e.g., rechargeable vs. non-rechargeable devices, constant-current vs. voltage-driven devices, single source vs. multiple-source devices) should also be included as part of the guidance review	We thank you for your comment. The review question on deep brain stimulation will reflect the available evidence. The guideline development group will take the different methods of delivery into account when they deliberate on the evidence available to them.
SH	Britannia Pharmaceuticals	1	General	Thank you for the opportunity to comment on the draft scope. Our key comments relate to the pharmacological management of Parkinson's disease (PD) and the need to distinguish between apomorphine intermittent injections and the continuous infusion with regards to their effectiveness at different stages of the patient pathway. The current clinical guideline does not capture the roles of the two formulations in clinical practice and whilst we welcome the review of the guideline and the fact that the scope lists both formulations we would request that during development of the guideline specific consideration is given to the place of the two treatments at different stages of the patient pathway. While both formulations are intended for use in patients with PD who are experiencing motor fluctuations despite optimised oral PD medications the two formulations have different positions in the treatment pathway: • apomorphine intermittent injections provide a rapid and reliable response and can be used in patients experiencing only a few predictable or unpredictable 'on/off' episodes, so is suitable for patients early in the disease pathway • continuous infusion is intended for use in patients later in the disease pathway who are developing into more complex Parkinson's.	We thank you for your comment. We have revised out review questions to reflect the different apomorphine administration methods.
SH	Britannia	2	3.1.0	In order to fully describe the disease additional text is required to	We thank you for your comment. The full

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Pharmaceuticals			highlight the issues associated with the development of motor fluctuations (referred to as 'on-off' episodes) where they change from a relatively well-controlled parkinsonian state ('on') to having marked symptoms of tremor, bradykinesia and rigidity('off') in a matter of seconds or minutes. This is an important characteristic of PD with 'off' periods occurring at the end of the oral anti-Parkinson's disease medication dosing interval and/or at unpredictable times. A prevalent and significant 'off' period for patients is first thing in the morning (early morning 'offs') when they require rapid and reliable treatment to move them to an 'on' state before they can start their daily life. The significant role and prevalence of gastroparesis through all stages of Parkinson's has important implications for the reliability of treatment given by the oral route of administration, something which non-oral medications can help address.	guideline will contain more information about the disease itself than the scope. The guideline development group will take this into account when drafting the guideline.
SH	Britannia Pharmaceuticals	3	3.2.0 e	We recommend that the list of non-motor symptoms is expanded to include dystonic pain and urgency, along with sleep disturbance and depression. These four constitute the most significant non-motor symptoms reported to affect the quality of life of patients with Parkinson's.	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the field of sleep disorders has been found, and thus sleep disorders will be covered within the present scope with review questions for both hypersomnolence and nocturnal akinesia.
SH	Britannia Pharmaceuticals	4	4.3.1 a	We agree with the list of medicines included in section 4.3.1 and are pleased to see that the different formulations of apomorphine (intermittent injections and continuous infusion) are listed. Both have an important role in the management of patients with	We thank you for your comment. We can confirm that both continuous infusion and intermittent injection of apomorphine will be considered.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Parkinson's disease (PD). While both are intended for use by PD patients experiencing motor fluctuations despite optimised oral PD medication: • Apomorphine intermittent injection is an adjunct to oral therapy for those patients experiencing only a few predictable or unpredictable 'off' episodes per day and who do not require a continuous infusion – so is suitable for patients early in the treatment pathway. It provides a rapid and reliable 'on' state. This is particularly important in relation to early morning 'offs' and allows a patient to can quickly start their day. • Apomorphine continuous infusion is suitable for PD patients later in the disease pathway (irrespective of their age or disease duration) who are experiencing frequent motor fluctuations and require continuous access to treatment. We would like to highlight that, as raised at the scoping workshop and documented in the workshop notes, there is significant new evidence for the intermittent use of apomorphine intermittent injection (Penject) which was not available at the time in the original guideline was developed. Britannia would welcome the opportunity to highlight this information further in response to a call for evidence.	
SH	Britannia Pharmaceuticals	5	4.3.1 a	We would recommend that as discussed and recommended at the scoping workshop pain is added to the list of factors to be considered under 'pharmacological treatment of non motor symptoms' with a specific focus on the types of pain characteristic of PD (e.g dystonic pain). Pain is a major issue for patients with PD and a review of the most effective treatment will be important to clinicians and patients.	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the field of sleep disorders has been found, and thus sleep disorders will be covered within the present scope with review questions for both

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					hypersomnolence and nocturnal akinesia. Pain has not been prioritised due to the lack of available conclusive clinical evidence on pain management in Parkinson's disease (PD). Recognition of pain as a primary feature of PD will be brought forward from the current PD guideline (NICE clinical guideline 35), and we will cross-refer to the recent neuropathic pain guideline (CG173), which we feel is relevant to the pain experienced by those with Parkinson's disease
SH	Britannia Pharmaceuticals	6	4.5.1	We agree with the review question: *'What is the comparative effectiveness of pharmacological interventions (monoamine oxidase B inhibitors, dopamine agonists, catechol-O-methyl transferase inhibitors amantidine, apomorphine) as adjuvants to levodopa?'* but request that in order to highlight the two different formulations of apomorphine and ensure these are evaluated separately the question is re-worded as follows: '*What is the comparative effectiveness of pharmacological interventions (monoamine oxidase B inhibitors, dopamine agonists, catechol-O-methyl transferase inhibitors amantidine <u>and</u> apomorphine [<u>intermittent injections and continuous infusion</u>]) as adjuvants to levodopa?* It will be important to also differentiate where in the treatment pathway each formulation is of most value. As stated above in comments 1 and 3 apomorphine intermittent injections can be used early in the treatment pathway in patients experiencing only a few predictable or unpredictable 'on/off' episodes while continuous infusion is intended for use in patients later in the disease pathway who are developing more complex PD and experiencing frequent	We thank you for your comment. We have taken this into account and amended accordingly.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				motor fluctuations.	
SH	Britannia Pharmaceuticals	7	4.5.1	Due to the importance of managing motor fluctuations to both the patient and clinician we recommend that the following review question is added to the current list: 'What is the comparative efficacy of pharmacological interventions for managing motor fluctuations in particular 'off' periods'?'	We thank you for your comment. We propose to examine motor fluctuations during 'off' periods within the context of the overall efficacy of pharmacological interventions to treat motor features of Parkinson's disease.
SH	Britannia Pharmaceuticals	8	4.5.2	Further to our comment on section 4.3.1 and the inclusion of pain as a non-motor symptom we request that the following review question is added to the current list: 'What is the comparative effectiveness of pharmacological interventions for pain characteristic of PD?'	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the field of sleep disorders has been found, and thus sleep disorders will be covered within the present scope with review questions for both hypersomnolence and nocturnal akinesia. Pain has not been prioritised due to the lack of available conclusive clinical evidence on pain management in Parkinson's disease (PD). Recognition of pain as a primary feature of PD will be brought forward from the current PD guideline (NICE clinical guideline 35), and we will cross refer to the recent neuropathic pain guideline (CG173), which we feel is relevant to those with Parkinson's disease.
SH	Britannia Pharmaceuticals	9	4.5.6	In order to ensure to fully address the issue of impulse control disorder as an adverse effect of dopaminergic treatment we would recommend that the following review question is added:	We thank you for your comment. While we recognise that the incidence of impulse control disorder (ICD) varies according to different

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				'How do the different dopaminergic treatments vary in relation to the incidence of impulse control disorder as an adverse event?' The incidence of impulse control disorders varies between current dopaminergic treatments and it will be important to review this within the development of the clinical guideline.	dopaminergic treatment, we have decided not to examine the different dopaminergic drug contributions to the development of ICD's, and instead focus on different management strategies for ICD. We may be able to cover evidence on different dopaminergic treatments in relation to the risk of development of ICD should we find evidence for this as part of the review question on the patient information relation to ICD's and the guideline development group are supportive of this approach.
SH	British Association for Counselling and Psychotherapy	1	General	The British Association for Counselling and Psychotherapy (BACP) welcomes the opportunity to comment on the National Institute for Health and Care Excellence's (NICE) 'Parkinson's disease update scope consultation'.	We thank you for your comment.
SH	British Association for Counselling and Psychotherapy	2	3.1.0 e	BACP welcomes NICE's recognition of depression as a symptom of Parkinson's Disease. This is reflective of research such as Chaudhuri et al., (2006), who suggests that depression is an additional non-motor symptom. BACP would recommend that the guideline addresses this symptomatic relationship.	We thank you for your comment. We have decided not to examine depression explicitly in this guideline update as it has been recognised that there is a paucity of clinically conclusive data, and CG91 has been considered relevant and appropriate to cross-refer to in this guideline. We will, however, bring forward the standing recommendations from the previous guideline in relation to depression in Parkinson's disease.
SH	British Association for Counselling and Psychotherapy	3	4.3.2 j	The scope states interventions and management of co-morbidities will not be included as part of the scope unless treatment differs from that in people without Parkinson's disease. BACP would suggest that the co-morbid relationship between Parkinson's Disease and depression is recognised in the guidance. This relationship has been highlighted in research such as Veazey et al (2005). Psychological therapies are an effective intervention for those with Parkinson's Disease who have depression. Research completed by	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Dobkin et al (2011) highlighted that those with Parkinson's who had received Cognitive Behavioural Therapy (CBT) had a greater reduction in depression than those in the clinical monitoring group. It should also be recognised that people with physical conditions recover more quickly and are better able to manage their disabilities and symptoms if they have good mental health and wellbeing (Ardino & Knapp, 2013), and therefore treating co-morbid depression in those with Parkinson's will lead to better clinical outcomes for the Parkinson's, not just the depression. Dobkin et al (2011) also demonstrated that CBT had a positive outcome on Parkinson's disease symptom ratings. Psychological therapies given to those with Parkinson's disease also differ from normal treatment – the Dobkin et al (2011) study modified CBT to meet the unique needs of the Parkinson's disease population. Similarly Cole and Vaughan stated, 'the therapist would need to facilitate the process of guided discovery more conscientiously than would be necessary with a cognitively unimpaired individual' (2005, 273). Referral to the NICE clinical guidance on depression for co-morbid depression would not therefore be sufficient, and so its treatment using psychological therapies should be included separately in the Parkinson's Disease guideline. **Bibliography** Ardino, V., Knapp, M (2013) Counselling and psychotherapy: is there an economic case for psychological interventions? Lutterworth: BACP Dobkin, R. D., Allen, L. A., & Menza, M. (2007). Cognitive-behavioral therapy for depression in Parkinson's disease: A pilot study. Movement disorders, 22(7), 946-952. Chaudhuri, K., Healy, D. G., & Schapira, A. H. (2006). Non-motor	field of sleep disorders has been found, and thus sleep disorders will be covered within the present scope with review questions for both hypersomnolence and nocturnal akinesia. We have made the decision not to examine depression explicitly in this guideline update as it has been recognised that there is a paucity of clinically conclusive data, and Depression in adults with a chronic physical health problem (NICE clinical guideline 91) has been considered relevant and appropriate to cross-refer to in this guideline. We will, however, bring forward the standing recommendations from the previous guideline in relation to depression in Parkinson's disease.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				symptoms of Parkinson's disease: diagnosis and management. The Lancet Neurology, 5(3), 235-245 Cole, K., & Vaughan, F. L. (2005). The feasibility of using cognitive behaviour therapy for depression associated with Parkinson's disease: A literature review. Parkinsonism & related disorders, 11(5), 269-276. Veazey, C., Aki, S. O. E., Cook, K. F., Lai, E. C., & Kunik, M. E. (2005). Prevalence and treatment of depression in Parkinson's disease. The Journal of neuropsychiatry and clinical neurosciences, 17(3), 310-323.	
SH	British Association of Prosthetists and Orthotists (BAPO)	1	General	BAPO acknowledges that some people with a diagnosis of Parkinson's may require orthoses to manage aspects of the condition such as weakness, gait problems, progressive deformity and head positioning. Treatment may include ankle foot orthoses, therapeutic footwear or cervical orthoses. Whilst there is limited evidence in the literature for use of orthoses in this group, presentation to orthotic clinics is common and referral should be considered by members of the MDT. BAPO believes that assessment and provision of appropriate orthoses can lead to improvements in function and QOL although further research is required to substantiate this.	We thank you for your comment. Foot orthoses may be considered by the guideline development group as part of the review questions on physiotherapy and occupational therapy.
SH	British Association of Prosthetists and Orthotists (BAPO)	2	3.2.0 d) & 4.3.1 b)	Consider including 'orthotics' as an assessment/treatment option alongside physiotherapy and occupational therapy.	We thank you for your comment. The guideline development group will consider this as part of the review questions on physiotherapy and occupational therapy if they think this is appropriate.
SH	British Geriatrics Society Movement Disorders Section	1	4.3.2	We wondered why palliative care (in this section) will not be updated by an evidenced review as more evidence has emerged on this since the previous NICE Clinical Guideline 35 in 2006	We thank you for your comment. This has been taken this into consideration and a review of palliative care needs in people with Parkinson's disease will be included within the guideline update.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	British Geriatrics Society Movement Disorders Section	2	4.5.7	This states there will be a review for the needs of people with Parkinson's disease for advance directives and palliative care plans throughout the course of their disease and we would support this. However, it does not include management at the end of life. We note that in section 5.2, Guidance in Development, there is a guideline under development for care of the dying adult. It would be helpful to know whether this includes a specific section on Parkinson's disease. If not, we feel it would be appropriate to include this in the current guidelines review. In the Parkinson's disease stakeholder workshop notes in section 4.3.2 h (palliative care) this issue was raised, including the specific question "When to either increase medication or begin to withdraw treatment". As social and legal frameworks have changed, eg Liverpool Care Pathway no longer used, we feel that this is a very important area to address.	We thank you for your comment. This has been taken this into consideration and a review of palliative care needs in people with Parkinson's disease will be included within the guideline update.
SH	College of Occupational Therapists	1	General – with reference to the original NICE PD guideline R75 (section 9.4, p.128, NICE, 2006).	Falls recommendations need to be reviewed and updated within the Scope and next NICE Parkinson's disease (PD) guideline. The main causes and management of falls in people with PD are NOT the same as falls in the general population. The cost of treating people with PD who fall and sustain a fracture is higher than in the general population, as people with PD tend to stay considerably longer in hospital and to recover much slower. (See recent years data in Parkinson's UK NHS PD patient Audits – for health economics analysis.) Postural instability (resulting in falls and 'near-misses') is a cardinal motor symptom of PD. Other common PD specific triggers are; postural hypotension, dyskinesia, poor balance, retarded saving reactions, falls out of bed, a shuffling gait, and also occur when an individual is turning to face another direction, experiencing start hesitation, freezing, festination (walking disorders), or being distracted. Further to this, some people with PD fall due to visio-spatial distortions (problems with the perception of space). Occupational Therapists need advice / signposting within the NICE PD guideline to the evidence based approaches and interventions	We thank you for your comment. Falls as the focus of a specific review question within this guideline has not been prioritised for update as we feel that it is an area better examined as an outcome of interest within our physical intervention review questions for both physiotherapy and occupational therapy.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				already demonstrated to be most suited to people with PD. Occupational therapists, when appropriately informed, can deliver PD specific interventions to reduce the risk of falls, and to ensure help can be called without delay if a fall occurs. The (UK) Occupational Therapy best practice guidelines for people with Parkinson's covers topics including; mobility, walking, transfers on/off toilets/chairs and beds (Aragon and Kings, COT, 2010, p.p. 33 – 38. This guidance is due to be updated in 2015). Cueing strategy training, home adaptations (e.g. handrails and other environmental modifications) are specifically used by occupational therapists to address the paradoxical nature of PD and thus improve safety, increase self-management abilities and use of coping skills. Improving management of freezing of gait etc, can also reduce fear of falling (Nieuwboer et al 2007). References; Aragon A, Kings J (2010) *Occupational therapy for people with Parkinson's: Best practice guidelines*. London: College of Occupational Therapists in partnership with Parkinson's UK. Nieuwboer A, Kwakkel G, Rochester L, Jones D, van Wegen E, Willems A, Chavret F, Hetherington V, Baker K, Lim I (2007) Cueing training in the home improves gait related mobility in Parkinson's disease: the RESCUE trial. *Journal of Neurology, Neurosurgery and Psychiatry, 78,* 134-140.	
SH	College of Occupational Therapists	2	General – with reference to the original NICE PD guideline R75 (section 9.4,	Physiotherapists in the current NHS often hold PD specific Falls clinics/groups involving individual or group exercise and movement training specifically for people with PD. This happens as the needs of people with PD cannot be met in the general Falls clinics/groups, suited to people who fall without PD. Exercise programmes involving balance exercises, and Tai Chi, which also challenges balance, show small but encouraging trends towards reducing falls in people with PD. Significant reductions in falls were seen in the Tai Chi intervention (Li et al 2012) and a balance exercise programme (Smania et al 2010).	We thank you for your comment. Falls as the focus of a specific review question within this guideline has not been prioritised for update as we feel that it is an area better examined as an outcome of interest within our physical intervention review questions for both physiotherapy and occupational therapy. Falls will be examined as an outcome of interest for the intervention questions of physiotherapy and occupational therapy, and where evidence is available. Non-pharmacological

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			p.128, NICE, 2006).	References: Li F, Harmer P, Fitzgerald K, Eckstrom E, Stock R, Galver J, Maddalozzo G, Batya S (2012) Tai Chi and Postural Stability in patients with Parkinson's disease. *New England Journal of Medicine, 366 (6),* 511-519. Smania N, Corato E, Tinazzi M, Stanznai C, Fiaschi A, Girardi P, Gandolfi M (2010) Effect of balance training on postural instability in patients with idiopathic Parkinson's disease. *Neurorehabilitaion and Neural Repair, 24 (9),* 826- 834.	management of falls has not been prioritised for an evidence review within this update as we do not believe there to be sufficient high quality existing evidence to warrant an extensive review in this area.
SH	College of Occupational Therapists	3	General – with reference to the original NICE PD guideline R75 (section 9.4, p.128, NICE, 2006).	Other related evidence on falls in people with PD can be found in the sources listed below. Allen N, Canning C, Sherrington C, Lord S, Latt M, Close J, O'Rourke S, Murray S, Fung V (2010) The effects of an exercise program on Fall Risk Factors in people with Parkinson's disease: A Randomized controlled trial. *Movement Disorders, 25 (9),* 1217-1225. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan L, Fitton C (2007) A randomised controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry, 78,* 678-684. Goodwin V, Richards S, Henley W, Ewings P, Taylor A, Campbell J (2011) An exercise intervention to prevent falls in people with Parkinson's disease: a pragmatic randomised controlled trial. *Journal of Neurology, Neurosurgery and Psychiatry, 82(11)*, 1232–1238. Protas E, Mitchell K, Williams A, Quresby H, Caroline K, Lai E (2005) Gait and step training to reduce falls in Parkinson's disease.	We thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				NeuroRehabilitation, 20, 183-190.	
SH	Department of Health	1	General	Thank you for the opportunity to comment on the draft scope for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	We thank you for your comment.
SH	Medtronic Ltd	1	4.4.0	Under the section, 'Main outcomes', Health-related quality of life was removed as a measurement for PD since the publication of the first draft of the Scope. The most commonly used tool for the assessment of disease-specific quality of life is the PDQ-39 (Parkinson's Disease Questionnaire). This tool has substantial evidence to suggest that it is reliable, valid, and feasible and was chosen as the primary outcome in several Key DBS RCTs (Schüpbach 2007 & 2013, Williams 2010, Deuschl 2006). We request that this be re-included in the Main outcomes section of the guidelines. In addition, for measurement of disease severity, we propose that the H&Y scale be considered.	We thank you for your comment. The most appropriate tool to assess Parkinson's disease (PD) health related quality of life (HRQOL) will be decided upon by the guideline development group (GDG). This may include reviewing evidence from the P PDQ-39 where available alongside other such measures. The outcomes listed are provided as examples of the types of outcome measures that may be considered by the guideline development group. Each outcome measure will be assessed by the guideline group when deciding upon the most appropriate and relevant measures to include within a given review.
SH	Medtronic Ltd	2	4.5.5 (a)	We welcome the addition of the review question on referral criteria for DBS. However, we believe it is of central importance that these referral criteria be framed more specifically than in the 2006 NICE guidelines. We believe the term "medically refractory" (as per the 2006 guidelines) to be overly restrictive and it denies a proportion of PD patients who would benefit from DBS from receiving the therapy. Level 1 clinical evidence has consistently shown large treatment effects of DBS can be achieved in a range of patient-relevant outcomes, even at early stages of disease progression, when motor complications and/or other medication side effects have just started to occur. The inclusion criteria of the EARLYSTIM RCT (Schüpbach et al: NEJM 2013) give an indication of what referral criteria for early referral could be:	We thank you for your comment. The guideline development group will consider the positioning of deep brain stimulation in the care pathway as part of the review question on deep brain stimulation.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				- Parkinson's Disease for at least 4 years - Presence of bothersome disease related symptoms and/or side effects for at least 4 years (e.g. motor fluctuations, dyskinesia, persisting tremor) - Clear motor improvement with dopaminergic medication or presence of medically refractory tremor - Absence of medical conditions precluding surgery - Absence of ongoing severe, medically-resistant neuropsychiatric diseases (e.g. severe depression) A Clinical advisory board involving 3 practicing NHS Movement Disorder Specialists and 1 Neurosurgeon convened by Medtronic on 26th Aug 2014 outlined that the following PD patients are considered as part of their current clinical practice for DBS and therefore we would request that NICE include their consideration as referral criteria for DBS : 1. PD patients with Motor Complications (Dyskinesia and motor fluctuations) 2. PD patients with levodopa-refractory tremor 3. PD patients with intolerable side effects from dopamine agonists (DA) and/or levodopa In these patients, DBS should be considered if: - They are levodopa-responsive (groups 1 +3) or have levodopa-refractory tremor - their disease-related symptoms (motor complications, intolerable side effects, persisting tremor) are significant and have an impact on their quality of life." - There are no clinical or surgical exclusion criteria (such as dementia) - resistant neuropsychiatric diseases (e.g. severe depression)	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Medtronic Ltd	3	4.5.5 (b)	It is unclear from the document whether "early" and "late" in this review question refers to the definition of "early" and "late" in the current 2006 guidelines. The terms do not seem to be used the same way (i.e. Early in the scoping document refers to DBS being considered in patients with motor complications, whereas late in the 2006 guidelines refer to patients currently on levodopa with presence of motor complications). We suggest that these be clarified and clear, unambiguous definitions be provided in the guidelines. A solid level 1 evidence base exists suggesting DBS should not be at the end of the treatment algorithm and that patients benefit as soon as motor complications have started to occur. The EARLYSTIM trial (Schüpbach 2013) is the most recent piece of evidence for this. In spite of this evidence and recommendation with the 2006 guidance, it is often the case that that the clinical community's consider DBS as an intervention after pharmaceuticals have failed to elicit sufficient patient benefit. We therefore request that wording in the guideline be made clinically more specific in order that DBS be considered as a treatment option within the pathway according to patient symptoms not solely prior interventions, in line with the advice provided by the our clinical advisors and the those appointed to the development group. Clearly all decisions regarding intervention should be discussed within the Multi-disciplinary team and in conjunction with the patient. The incremental quality of life benefit of DBS & BMT vs BMT alone in the EARLYSTIM RCT, was as high as the benefit observed in the RCTs in more advanced patients (e.g. Deuschl 2006, Williams 2010) PD Patients in the EARLYSTIM trial are on average about 7yrs	We thank you for your comment. The guideline development group will consider whether 'early' and 'late' are used now as they were in previous guidelines and will use the updated glossary definition to reflect current use of these terms

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				younger than in the Deuschl 2006 RCT of advanced patients, so while the benefit is not increased in the early patients, patients may benefit longer from therapy in terms of quality of life and maintaining a higher-level of ADL and social functioning. Schuepbach WM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. 2013;368(7):610-622.	
SH	Medtronic Ltd	4	4.5.5 (c)	The evidence for DBS is mainly in STN and GPI (see list of RCTs below) PPN Stimulation while experimental might be useful in certain patient groups, similarly, thalamic stimulation can be an option in tremor-dominant PD. There are no RCTs on these different DBS targets, as patient numbers are small, and evidence is mainly from case series. However, they do hold an important place in clinical practice and it is important to include them in the scope of the guideline update. RCTs Studying DBS Therapy in Patients with Parkinson's Disease (PD) • Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. N Engl J Med. 2006;355(9):896-908. • Follett KA, Weaver FM , Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. N Engl J Med. 2010;362(22):2077-2091. • Odekerken VJ, van Laar T, Staal MJ, et al. Subthalamic nucleus versus globus pallidus bilateral stimulation for advanced Parkinson's disease (NSTAPS study): a randomized clinical trial. Lancet Neurology. 2013;12(1):37-44. • Okun MS, Gallo BV, Mandybur G, et al. Subthalamic deep brain stimulation with a constant current device in Parkinson's disease: an open label randomized clinical trial. Lancet Neurology. 2012;	We thank you for your comment. We propose to examine different surgical targets within the surgical review questions, however we cannot comment at this stage whether we will examine comparative effectiveness of different surgical targets. This will be decided with the guideline development group.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				11(2):140-149. • Schuepbach WM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. 2013;368(7):610-622. • Weaver FM , Follett K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson's disease: a randomized controlled trial. JAMA. 2009;301(1):63-73. • Williams A, Gill S, Varma T, et al. Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomized, open-label trial. Lancet Neurology. 2010;9(6):581-591.	
SH	Medtronic Ltd	5	4.3.1 a	Apomorphine: We request that the positioning of apomorphine be clarified in the clinical guideline, and that the review questions in the Scope be also specific towards this point to include a question on patient eligibility for apomorphine. It appears from the review question that apomorphine be considered as an adjuvant to levodopa as part of a "BMT regimen". However, the clinical advisory panel consulted on this topic suggested that this may be misleading: DBS is generally considered after diminishing effectiveness of BMT, but potential DBS patients should not have to try apomorphine injections first. There are valid clinical and patient related reasons that would exclude apomorphine in a patient with motor complications (e.g. DA side effects, hallucinations, sedative effect, persistent tremor, needle phobia) and this should be made specific in the guidelines. DBS has strong clinical evidence in both advanced and less advanced PD patients, so DBS should not be considered after apomorphine failure only.	We thank you for your comment. The guideline development group will consider the positioning off apomorphine during the later stages of disease as part if one of the proposed review questions. We would also like to note that one of the proposed review questions will examine the referral criteria for deep brain stimulation (DBS) and whether there may be greater benefit in earlier compared to later referral for DBS.
SH	Medtronic Ltd	6	General	We request an update of the patient pathway for it to be more specific than it currently is in terms of where in the pathway DBS therapy would be considered. These pathways are widely used in	We thank you for your comment. The Parkinson's disease pathway will be updated by the NICE pathway team according to the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				practice so it makes sense that a guideline update should be followed by an update of the pathway.	evidence base and recommendations made within the current update.
SH	Multiple System Atrophy Trust	1	4.3.2 (c)	The Trust believes that depression management and information on anti-depressants should be considered within Scope and also cross referenced for more information to the Depression Guideline. It is an important issue for MSA patients as well as PD patients.	We have made the decision not to examine depression explicitly in this guideline update as it has been recognised that there is a paucity of clinically conclusive data, and Depression in adults with a chronic physical health problem (NICE clinical guideline 91) has been considered relevant and appropriate to cross-refer to in this guideline. We will, however, bring forward the standing recommendations from the previous guideline in relation to depression in Parkinson's disease.
SH	Multiple System Atrophy Trust	2	4.3.2 (i)	The Trust believes dementia management should be considered within Scope and that cross referencing to a Dementia Guideline is not enough: new Norwegian study indicates that eight year following PD diagnosis, 80% of PD patients will have dementia.	We thank you for your comment. The pharmacological management of dementia associated with Parkinson's disease is included within the scope and the guideline development group will consider this during development.
SH	Multiple System Atrophy Trust	3	4.5.1 (c)	The Trust believes Duodopa should be included in the update because equal numbers of PD patients will be put on Duodopa as will try deep brain stimulation and it is likely to become more widely utilised in the lifetime of the updated guideline.	We thank you for your comment. We can confirm that Duodopa will now be considered in the scope of this guideline
SH	Multiple System Atrophy Trust	4	4.5.2	The Trust believes this area needs to be clarified and key autonomic problems should be identified - one solution is unlikely to address all autonomic problems. It is a particular issue in MSA; not infrequently, PD patients may be re-diagnosed with MSA during their disease course, support by the presence of significant dysautonomia.	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the field of sleep disorders has been found, and thus sleep disorders will be covered within the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					present scope with review questions for both hypersomnolence and nocturnal akinesia. We propose to cover autonomic disturbances including thermoregulation andorthostatic hypotension within this guideline. Saliva management will also be covered. We would also like to note that we will be examining only populations in which a Parkinson's disease diagnosis is confirmed. We will not be covering differential diagnosis, and therefore, any differential diagnoses such as multiple system atrophy (MSA).
SH	Multiple System Atrophy Trust	5	4.5.4	The Trust believes the Scope should consider recommending therapist involvement focused on severe PD groups as this may be beneficial in severe PD and atypical parkinsonism. The Trust believes it is important that the Scope makes clear reference to the fact that symptoms of parkinsonism may be because of other causes such as MSA which is often re-diagnosed after an initial diagnosis of PD.	We thank you for your comment. We have decided not to cover atypical or non-Parkinson's disease Parkinsonism within the scope of the guideline update, as the population of interest for this guideline has been defined as only those with a confirmed diagnosis of Parkinson's disease Differential diagnosis will not be covered in this update and we will therefore not be able to examine other differential diagnoses, such as multiple system atrophy (MSA).
SH	Multiple System Atrophy Trust	6	4.5.7	The Trust believes the Scope should update the current Guideline section on palliative care as it is out-of-date. The Liverpool Care Pathway no longer exists, the role of palliative care is broadening and there should be awareness of the opportunity to do advance care planning critical for MSA patients as well as PD patients. The Trust would like to see specific reference to the needs of MSA patients within this area, including the proactive consideration of symptom management and early referral to palliative care.	We thank you for your comment. This has been taken this into consideration and a review of palliative care needs in people with Parkinson's disease will be included within the guideline update.
SH	Multiple System	7	4.5.8	Given people with MSA have often first been given a diagnosis of	We thank you for your comment. We have

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Atrophy Trust			PD, the Trust believes it is important the Scope includes reference to where people can find out about MSA, should their diagnosis be changed (of significance to healthcare teams too). It may be that inclusion in the information given to PD patients while their diagnosis remains as PD would be inappropriate, but consideration should be given as to how a re-diagnosis would be managed by healthcare professionals and communicated to patients, their families and carers and the level and type of information/signposting which would be required. The Trust would be happy to be consulted on this.	decided not to update the section from the previous guideline on diagnosis of Parkinson's disease as there was no new evidence that would lead to a change in the existing recommendations. Therefore, we will be unable to review or discuss differential diagnoses within this guideline update. All reviews and recommendations about diagnosis will be brought forward from the previous guideline into the present guideline update.
SH	NHS England	1	General	Please consider organisation of services in the scope since this is vital to good efficient and effective PD services. Knitting the services together with provision and access to appropriate multidisciplinary team is vital. This should include neurology elderly care therapists specialist nurse psychiatry dementia services supported by GP and social care. Failure to do this results in a fragmented service with delays and poor patient experience and care. It is difficult to prove this though Blas Bloem in Holland has tried but it is obviously likely to be more effective. Appropriate processes make major differences to care.	We thank you for your comment. Service organisation has not been prioritised for update within this guideline update.
SH	Non Motor Parkinson's Study Group (affiliated with European Parkinson's Disease Association and International Parkinson's and Movement Disorders Society)	1	3.1.0	It is somewhat surprising that only depression is included. A wide body of published studies suggest sleep problems (up to 99%) and pain (45-65%) of cases are equally if not more important non motor symptoms in PD (Chaudhuri and Schapira , Lancet Neurology 2006). Non motor symptoms also occur equally and sometimes dominantly in early and untreated phase of PD and statement suggests that non motor symptoms are typically seen in advanced PD only. This is misleading given non motor symptoms are one of the key determinants of quality of life in PD of patient and caregiver. Mollenhauer B et al. *Neurology* 2013;**81**:1–9. Khoo et al. *Neurology* 2013;**80**:276-281.	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the field of sleep disorders has been found, and thus sleep disorders will be covered within the present scope with review questions for both hypersomnolence and nocturnal akinesia. We thank you for your comment. We would like to note that We have made the decision not to

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					examine depression explicitly in this guideline update as it has been recognised that there is a paucity of clinically conclusive data, and Depression in adults with a chronic physical health problem (NICE clinical guideline 91) has been considered relevant and appropriate to cross-refer to in this guideline. We will, however, bring forward the standing recommendations from the previous guideline in relation to depression in Parkinson's disease. We would also like to note that those non-motor symptoms where we believe there to be a significant amount of new evidence, such as the management of autonomic disturbances, psychosis, sleep disturbances, and dementia, have all been prioritised for review as it has been recognised that there is extensive new research within these areas that may lead to a change in existing recommendations.
SH	Non Motor Parkinson's Study Group (affiliated with European Parkinson's Disease Association and International Parkinson's and Movement Disorders Society)	2	4.3.1 (a)	Updates on management should also include pain. Pain has emerged as one of the dominant non motor issues in PD, sometimes preceding development of motor PD. By the time the guidelines are updated the first international randomised placebo controlled trial addressing pain as a primary outcome variable will be reported and published. Other studies are also under way. https://clinicaltrials.gov/ct2/show/NCT01439100?term=OXN2504&rank=1	Error! Reference source not found.
SH	Non Motor Parkinson's	3	4.4.0 (f)	Re non motor outcomes the committee may consider also the original PDSS, which is patient completed and validated worldwide.	We thank you for your comment. The guideline development group will take this into

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Study Group (affiliated with European Parkinson's Disease Association and International Parkinson's and Movement Disorders Society)			(so one option may be to include PDSS and PDSS 2)	consideration when developing the evidence review protocols. We would like to note that the outcome measures currently listed in section 4.4 provide only examples of the types of outcome measures that will be considered for each relevant review. Each outcome measure, such as the Parkinson's disease sleep scale (PDSS), will be separately assessed by the guideline group as to the applicability and effectiveness for each review. .
SH	Parkinson's Disease Nurse Specialist Association	1	3.1.0 b	Clarification on gathering of data to inform epidemiology, ie. sources	We thank you for your comment. References for all epidemiology information will be provided in the guideline.
SH	Parkinson's Disease Nurse Specialist Association	2	4.2.0	Concern re care homes and equity of service access/ treatments	We thank you for your comment. The guideline development group will take this into consideration; however we will only examine NHS-provided care, as stipulated within the scope inclusion criteria. We are unable to examine equity of service access within this guideline update.
SH	Parkinson's Disease Nurse Specialist Association	3	4.3.1 d	Use of Transdermal patch and calculation for use specifically when person is nil by mouth	We thank you for your comment. We would like to note that transdermal patches will be considered within the scope of this guideline, as listed in section 4.3.1.
SH	Parkinson's Disease Nurse Specialist Association	4	4.5.6	Use of individual care plans with rational for adjustment of dopamine agonist shared with relevant parties	We thank you for your comment. The guideline development group will take into account the use of individual care plans when drafting guideline recommendations.
SH	Parkinson's Disease Nurse Specialist Association	5	4.4.0 d	ACE-R no longer in use it is now called ACE111, having removed any element of MMSE	We thank you for your comment. We have taken this into account and amended accordingly.
SH	Parkinson's Disease Nurse	6	4.5.5	Potential for earlier DBS not at expense of those in later stage who might be eligible and possibly benefit	We thank you for your comment. Deep brain stimulation is included within the scope of the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Specialist Association				guideline.
SH	Parkinson's Disease Nurse Specialist Association	7	4.3.2 d	Concern update +should include latest evidence re value and benefit of access to PDNS especially in view of number of posts under threat.	We thank you for your comment. Unfortunately, an update on Parkinson's Disease Nurse Specialists (PDSN) has not been considered as a priority for this guideline update. The previous recommendations about access to PDNS for all Parkinson's disease patients will be brought forward into the present guideline update.
SH	Parkinson's UK	1	General	Parkinson's UK strongly endorses NICE's commitment to ensuring that 'no areas from the original guideline will be removed'. We therefore urge that NICE honours this commitment.	We thank you for your comment.
SH	Parkinson's UK	2	General	Currently there is no mention of stress or anxiety in the NICE clinical guideline. Parkinson's UK strongly believes that an updated version of the guideline must include reference to these issues and their impact on a person's conditions. Research has demonstrated that there is a link between anxiety and the exacerbation of Parkinson's symptoms. (1) For example, the disabling motor symptoms such as tremor, rigidity, bradykinesia, and postural instability, which often occur intermittently, have been shown to increase when the person with Parkinson's is concentrating or feeling anxious. (2) Similarly, numerous studies have noted the relationship between stress and symptom intensity. (3,4) To ensure the effective treatment and management of people with Parkinson's, these factors and their impact on someone with Parkinson's must be highlighted within the updated clinical guideline.	We thank you for your comment. The guideline development group will take these factors which affect patients and carers into account as they develop guideline recommendations. We would also like to note that we will cross refer to the NICE clinical guidelines on generalised anxiety disorder (CG113), and depression in chronic physical health conditions (CG91).
SH	Parkinson's UK	3	General	Parkinson's UK has grave concerns that mild cognitive impairment is not currently addressed by the NICE clinical guideline. The link between Parkinson's and dementia is clearly established and has been recognised in the clinical guideline (although needs updating, as has been referred to above), yet there is no mention of mild cognitive impairment.	We thank you for your comment. Cognitive impairment will be taken into account as an adverse outcome of interest where appropriate. If the guideline development group feel it is appropriate, we will seek to clarify the relationship between mild cognitive

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				As with dementia, cognitive impairment poses particular challenges when treating someone with Parkinson's. Decision-making capacity can render patients vulnerable in a way that requires ethical considerations by clinicians regarding medical decision making, research participation, and public safety – particularly relating to issues around driving. (5) This oversight is particularly concerning as research indicates that patients with Parkinson's and mild cognitive impairment have a higher risk of developing dementia than cognitively intact Parkinson's patients. (6) This suggests that mild cognitive impairment in Parkinson's is an early indicator of dementia. Therefore, it is essential that clinicians are aware of this link so they can make informed decisions about future treatments as early as possible in a person's care. As a means of comparison, cognitive impairment is mentioned on no less than on 9 occasions in the Scottish Intercollegiate Guidelines Network (SIGN) guideline on Parkinson's. (7) It is referred to in both its relationship with depression and dementia. As such Parkinson's UK strongly believes that mild cognitive impairment and its link to dementia must be referred to in the updated NICE clinical guideline.	impairment and dementia in the Parkinson's disease-associated dementia evidence review, however mild cognitive impairment as a potential pre-curser to dementia will not be covered within this guideline update. We have prioritised the treatment of dementia associated with Parkinson's disease for this guideline, rather than any factors that may lead to the development of dementia
SH	Parkinson's UK	4	General	Parkinson's is inherently variable day to day. (8) However, in current NICE guidelines fluctuations are only referred to in the context of treating a patient with a dopamine agonist. It should be remembered that fluctuations are part of everyday life for people with Parkinson's and have an impact on numerous other aspects of the conditions such as anxiety, stress, depression and medicines adherence. Fluctuations affect both motor and non-motor aspects of Parkinson's. (9) Motor-fluctuations are often unpredictable and add significantly to the lack of control that some people feel they have in their day-to-day lives. Patients susceptible to motor fluctuations and who find the experience distressing report "testing" their motor function or "scanning" for signs of an impending off-period that would require a dose of medication. Such focus on, and attempt to	We thank you for your comment. The guideline development group will take this these factors which affect patients and carers into account as they develop guideline recommendations.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				control, an often unpredictable event typically serves to maintain state anxiety rather than reduce it. Motor fluctuations can therefore exacerbate anxiety. Non-motor symptoms can impact on fatigue, depression and sleep disturbance. They are unpredictable and complex. As is the case with cognitive impairment, the SIGN guideline makes much greater referral to fluctuations and the impact of this on people with Parkinson's. (10) One of many examples reads '*Emphasis should be placed on assessing whether mood disturbance is linked to fluctuations in motor symptoms*'. Owing to the impact of fluctuations on numerous aspects of a person's condition, Parkinson's UK strongly believes that updated NICE Guidelines should be brought into line with the SIGN Guideline on Parkinson's by making much greater reference to fluctuations.	
SH	Parkinson's UK	5	4.3.2 (c)	Parkinson's UK urges NICE to include 'Depression in Parkinson's disease' as one of the areas from the original guideline that will be updated. Major depressive disorder is common among patients with Parkinson's. Research indicates that prevalence of depression may range from 8% in community-based patients to more than 20% in outpatient or inpatient settings, while depressive symptoms are even more common. (11) Depression in Parkinson's is associated with a variety of poor outcomes for both patients and their families. Besides personal suffering, depression is related to greater disability, faster progression of physical symptoms, reduced cognitive performance, less ability to care for oneself, poorer adherence to treatment, poorer quality of life and increased distress in carers. (12) Depression is also associated with increased mortality in Parkinson's patients and is the most important risk factor for suicide, especially after neurosurgical treatment of Parkinson's. Therefore, recognising and treating depression in the context of Parkinson's is vital to reduce disability and improve prognosis. (13)falls	We have made the decision not to examine depression explicitly in this guideline update as it has been recognised that there is a paucity of clinically conclusive data, and Depression in adults with a chronic physical health problem (NICE clinical guideline 91) has been considered relevant and appropriate to cross-refer to in this guideline. We will, however, bring forward the standing recommendations from the previous guideline in relation to depression in Parkinson's disease.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Furthermore, as the references for this section demonstrate (which represent a small proportion of what has been published post-2006), there has been much new research published on this area since the last NICE Clinical Guideline on Parkinson's C35 was published in 2006. Owing to this and considering how important this issue is in the treatment and management of someone's condition, Parkinson's UK feel this must be incorporated as an area the guideline update will address.	
SH	Parkinson's UK	6	4.3.2 (d)	Parkinson's UK would like to see the area of 'specialist nurse interventions' included one of the areas from the original guideline that will be updated. Parkinson's nurses are specialist practitioners whose essential skills include clinical leadership, case management, education and evaluation of care. This may be in hospitals, clinics, health centres, the person's own home or care home, and might be on a routine or emergency basis. They liaise with professional and voluntary organisations, as appropriate, to provide a comprehensive Parkinson's service ensuring ongoing, joined-up care. Parkinson's nurses are ideally placed to provide education not only to patients, their families and carers, but also to a range of health and social care professionals, who may only come across a small number of people affected by Parkinson's. This will ensure everyone involved properly understands the condition and people with Parkinson's are supported in self management. Therefore, these nurses are an essential part of a person's multi-disciplinary team, starkly highlighted by the fact that on average a Parkinson's nurse can save the NHS each year: (14) • £43,812 in avoided consultant appointments • £80,000 in unplanned admissions to hospital • £147,021 in days spent in hospital Parkinson's UK does not recommend a full review of this section of the guideline, only a strengthening of the wording used in relation to the role of the specialist nurse. The existing guideline repeatedly states that certain services, for example providing a reliable source	We thank you for your comment. The guideline development group recognises the unequivocally important role that specialist nurses play within the care of people with Parkinson's disease; however we have decided not to update this area within the present guideline. Parkinson's disease nurse specialist intervention was not highlighted as an area where there was significant new evidence that would lead to a change in the current recommendations, and therefore this has not been included within the update of this guideline. We propose to bring forward the previous recommendations which recommend that patients be given access to PD specialist nurse care. .

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				of information about clinical and social matters of concern to people with Parkinson's and their carers and providing an accessible point of contact with specialist services '*could*' be done through nurse specialists. However, in light of the essential role played by nurses and the anecdotal evidence we have to suggest that the wording in the current guideline means that these functions are sometimes not ascribed to nurse specialists, Parkinson's UK would like to see this wording strengthened. We believe this should state that NICE *'strongly recommends'* that a nurse specialist carries out these roles or that a nurse specialist *'should'* perform these functions.	
SH	Parkinson's UK	7	4.3.2 (e)	Parkinson's UK strongly believes that the carers and family members aspect in this part of the clinical guideline must be reviewed and strengthened as part of the update to reflect the NHS constitution. The NHS constitution makes a number of pledges regarding the involvement of carers and family members in a person's care and also explicitly spells out the rights of carers and family members as valued partners in the a patient's multi-disciplinary team. It is the view of Parkinson's UK that more needs to be included in the updated guideline to reflect this. Carers and family members of those with Parkinson's are very often the experts in their loved-ones condition regarding symptoms, fluctuations, medicines timing and many other aspects, but they feel their information and opinions are being ignored by health and social care professionals. Carers often provide the bulk of personal care and are an important source of continuity, as well as a resource with knowledge of the person's needs, wishes, values and preferences. We receive regular feedback that the carers and family members of people with Parkinson's are often not informed of incidents that have happened to someone with Parkinson's in a clinical setting. Additionally, we also know that people with Parkinson's often don't get their medication on time when in hospital (15) and also that carers and families are not listened to when they first raise	We thank you for your comment. The main section on communication with people with Parkinson's disease (PD) and their carers has not been prioritised for update although the existing recommendations in NICE clinical guideline 35 will be brought forward. We have included the impact of PD upon the carer as an outcome of primary interest in many of our review questions.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				concerns. People with Parkinson's often experience mild memory loss, mild cognitive impairments and Lewy body dementia as part of their condition. In fact, up to 80% of people who have lived with Parkinson's 10 years or more may develop dementia.(16) As such many of our members have shared experiences where carers only discover an incident has happened in hospital (such as a fall or a urinary tract infection) long after it has taken place. This can often be because, although the person with Parkinson's may have been informed, they have not remembered to pass on this information. This incomplete picture has led to inappropriate care being administered and even re-admission into hospital. Therefore, it is essential carers and families must be given full recognition of their importance as part of a person's multi-disciplinary team. The wife of a person with Parkinson's told us the following: *"One of the most important things to improve any complaints procedure… is to listen to the people at the sharp end - the carers or family – which currently nobody does. The carers, families and patient themselves are the expert, they know much more about a person's condition than any specialist in the world."* Therefore, Parkinson's UK asks that the section relating to '*Communication with people with Parkinson's disease and their carers*' is included as part of the update of the NICE clinical guideline on Parkinson's.	
SH	Parkinson's UK	8	General	1 Dissanayaka et al, The clinical spectrum of anxiety in Parkinson's disease, 2014. 2 Hanna and Cronin-Golomb, Impact of Anxiety on Quality of Life in Parkinson's Disease, 2011. 3 Backer, The symptom experience of people with Parkinson's disease, 2006. 4 Hemmerle et al, Stress exacerbates experimental Parkinson's	We thank you for highlighting these references.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				disease, 2014. 5 Emre et al, Cognitive Impairment and Dementia in Parkinson's Disease: Practical Issues and Management, 2014. 6 Janvin et al, Subtypes of Mild Cognitive Impairment in Parkinson's Disease: Progression to Dementia, 2006 7 Scottish Intercollegiate Guidelines Network (SIGN), Diagnosis and pharmacological management of Parkinson's disease, 2010. 8 Grittiths et all, Automated Assessment of Bradykinesia and Dyskinesia in Parkinson's Disease, 2012. 9 Storch et al, Nonmotor fluctuations in Parkinson disease: Severity and correlation with motor complications, 2013. 10 SIGN, Diagnosis and pharmacological management of Parkinson's disease, 2010. 11 Skapinakis et al, Efficacy and acceptability of selective serotonin reuptake inhibitors for the treatment of depression in Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials, 2010. 12 Rocha e al, Antidepressants for depression in Parkinson's disease: systematic review and meta-analysis, 2013. 13 Skapinakis et al, Efficacy and acceptability of selective serotonin reuptake inhibitors for the treatment of depression in Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials, 2010 14 Parkinson's UK, Parkinson's nurses – affordable, local, accessible and expert care: A guide for commissioners in England, 2011	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				15 A 2014 YouGov survey completed by 3,630 people who have either been diagnosed with the condition or are family members or carers of a person with Parkinson's, found that 60 per cent reported that they had not always been able to get their Parkinson's medication on time while in hospital. 16 Perez F et al (2012) Risk of dementia in an elderly population of Parkinson's disease patients: A 15-year population-based study. Alzheimer's & Dementia; 8:463-469.	
SH	Royal College of General Practitioners	1	General	The update seems relevant and appropriate	We thank you for your comment.
SH	Royal College of Nursing	1	4.2.0	We feel it would be useful to be assured that this covers care home settings.	We thank you for your comment. The guideline development group will take care homes into consideration as they look at the evidence reviews conducted as part of the update.
SH	Royal College of Nursing	2	General	There is no mention of consideration of interventions that would improve sexual functioning/management of expressions of sexuality.	We thank you for your comment. Sexual functioning has not been prioritised for consideration within this guideline update as preliminary searches in this area revealed a paucity of relevant high quality clinically conclusive literature.
SH	Royal College of Speech and Language Therapists	1	4.3.1 (Areas from the original guideline that will be updated: Speech and language therapy b	In the previous guideline swallowing difficulties were not included in the main guideline and were not subjected to a full literature review or critical appraisal by the GDG. It is hoped that swallowing and saliva management should now be included under Speech and language therapy especially as 'nutritional support' is to be added to the guideline under 4.3.1.f.	We thank you for your comment. We propose to examine swallowing as an outcome of interest in the speech and language therapy review question. The guideline will also cover pharmacological management of salivary function.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			& f)		
SH	Royal College of Speech and Language Therapists	2	4.5.2 (Pharmacological management of non-motor symptoms)	There are also non pharmacological interventions which could be included here such as the swallow saliva buzzer	We thank you for your comment. We will be including reviews on the non-pharmacological physiotherapy and occupational therapy interventions for swallowing in the guideline.
SH	Royal College of Speech and Language Therapists	3	4.5.4 c	'What is the effectiveness of speech and language therapy compared with usual care?' – Can this question be worded like the medical pharmalogical questions i.e. *'What is the comparative effectiveness of different SLT treatment approaches for communication difficulties in Parkinson's?'* **And then** *What is the comparative effectiveness of different SLT treatment approaches for swallowing difficulties in Parkinson's?*	We thank you for your comment. We assure the RCSLT that both swallowing and communication will be examined within the context of speech and language therapy intervention. We propose to leave the review question as it stands. Review questions in the scope are draft until these are checked and agreed with the guideline development group. Should the guideline development group, feel that two separate sub questions for swallowing and communication are important, rather than one question which would examine swallowing and communication as primary outcomes of interest, we will amend our review protocol.
SH	St Jude Medical	1	4.5.5 (a)	A) AAN recommendation (April 2006) a. Level B evidence that preoperative response to levodopa should be considered as a factor of predictive outcome of DBS of the STN b. Younger age and short (less than 16 years) duration = greater improvement c. Level C evidence suggests younger patients with shorter disease duration do better than older patients with STN DBS	We thank you for this reference.
SH	St Jude Medical	2	4.5.5	A) Blue Cross & Blue Shield Association 2011	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			(a)	a. GPi and STN DBS advocated after a good response to levodopa; have a minimal 30 point score on the motor part of UPDRS after withdrawal of medication for a minimum 12 hours and residual motor complications not controlled by pharmacological therapy	
SH	St Jude Medical	3	4.5.5 (a)	A) Medicare (August 16th 2010) covers DBS for PD a. Thalamic VIM DBS is approved for idiopathic PD which is the tremor-dominant form; marked disabling tremor of 3-4 on the Fahn-Tolosa-Marin Clinical Tremor Rating Scale (or equivalent) in the intended treatment limb causing significant limitation in daily activities despite optimal medication and willingness & ability to cooperate with all aspects of the treatment	We thank you for this reference.
SH	St Jude Medical	4	4.5.5 (a)	a. STN & GPi DBS is covered if all the following criteria are met a. Diagnosis of PD based upon minimum 2 cardinal symptoms b. Advanced idiopathic PD determined by Hoehn & Yahr stage or UPDRS part III motor subscale and c. Levodopa responsive with clear "On" periods and d. Persistent disabling Parkinson's symptoms or drug side-effects (e.g. dyskinesias, motor fluctuations or disabling "Off" periods) despite optimal medical therapy and Willingness and ability to cooperate during a conscious operative procedure, as well as during post-surgical evaluations, adjustments of medications and stimulator settings	We thank you for this reference.
SH	St Jude Medical	5	4.5.5 (a)	A) UK PD Surg Study: 366 patients enrolled between Nov 2000 to Dec 2006 (183 randomised DBS vs. 183 BMT). Patient eligibility included: a. Diagnosis of PD by the Brain Bank Criteria	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				b. Advanced PD not controlled by current medical therapy and for whom alternative medical therapy (e.g. apomorphine, a second oral agonist or further adjustments of levodopa preparations might be considered c. PD patients with less advanced disease (e.g. onset of motor complications) for which medical options are available but for whom early surgery is also considered to be an option d. Able to cope with surgical intervention & unlikely to require surgery within one year of entry e. Not demented as determined by DRS-II f. Provided written informed consent Patients were randomised by the "uncertainty principle" that is, if the clinical team was substantially uncertain which treatment (DBS or BMT) a patient should be offered at the current time, then the patient would be eligible to be randomised. This allowed a more heterogeneous population to receive surgery whilst allowing the clinical team to choose the optimal timing of intervention based upon stage of disease or level of disability of the patient.	
SH	St Jude Medical	6	4.5.5 (a)	A) National Standards for the Designation of Centres for Deep Brain Stimulation (prepared by the SWSCG & NWSCG). Stated that surgery may be considered in people who have responded poorly to drugs, who have severe side effects from medication or who have severe fluctuations in response to drugs. All patients for DBS should be discussed by the multi-disciplinary team (MDT) which should include, as a minimum, a movement disorder subspecialist neurologist, a neurosurgeon experienced in DBS and a psychologist. The MDT should believe that the patient would gain significant benefit from DBS i.e. regaining lost functions and/or an improvement in independence.	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				a. All patients should have an established diagnosis of idiopathic Parkinson's disease b. Have no evidence of significant cognitive decline c. Good general health and considered to have a reasonable life expectancy d. Have failed to respond adequately to, or be unable to tolerate appropriate medical therapy e. Have had a trial of levodopa to exclude levodopa responsive dystonia f. Have symptoms severe enough to significantly compromise quality of life and activities of daily living g. Disability due to motor fluctuations and/or dyskinesia h. Severe depression and significant cognitive impairment are contraindications	
SH	St Jude Medical	7	4.5.5 (a)	B) Technology Assessment Number 57 (Diagnosis and Treatment of PD: A Systematic Review of the Literature – AHRQ Publication No. 03-E040 June 2003). In 1999 saw the development of a broader set of perioperative evaluations, the Core Assessment Program for Surgical Interventional Therapies in Parkinson's disease (CAPSIT-PD). The CAPSIT-PD committee advised that patients considered for surgery should: a. Patients should have a disease duration of at least 5 years prior to surgery b. "Levodopa responsiveness" was replaced by "dopaminergic responsiveness" which included dopamine agonists c. Expert opinion agreed that surgery should only be considered in PD patients who are responsive to medical therapy but are suffering intolerable side-effects from PD	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				medications	
SH	St Jude Medical	8	4.5.5 (a)	A) University of California San Francisco Guidelines for Referring Neurologists for DBS a. Clear diagnosis of idiopathic PD b. Intact cognitive function (mini-mental status test greater or equal to 26 is ideal; less than 24 an absolute contraindication) c. Clear evidence of motor improvement with levodopa with good motor function in the best on-medication state. Screening test of UPDRS part III, performed 12 hours off medication and repeated following a suprathreshold levodopa dose with a minimum 30% improvement in score. The patient should be ambulatory in the best on-state. d. Patients who fluctuate between good motor function when "on" and poor function when "off" are generally good surgical candidates e. Lack of comorbidity – serious cardiac disease, uncontrolled hypertension or any other chronic systemic illness f. Realistic expectations g. Patient age – DBS benefits tend to decline with advancing age. Patients over 75 years of age are informed that benefits are likely to be modest h. Screening MRI should reveal no severe vascular disease, atrophy or signs of atypical parkinsonism i. Patients should have an "off" medication UPDRS-III score of greater than 25. Ideal timing of surgical intervention is when the patient is beginning to lose the ability to perform meaningful activities especially if the patient may be forced to retire from work through	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				disability j. Willingness and ability to be seen for follow-up visits	
SH	St Jude Medical	9	4.5.5 (a)	A) The National Collaborating Centre for Chronic Conditions publication on Parkinson's Disease published by The Royal College of Physicians (2006) a. Patients with motor complications refractory to best medical treatment b. Biologically fit with no clinically significant active comorbidity c. Levodopa responsive d. No clinically significant active mental health problems e.g. depression or dementia	We thank you for this reference.
SH	St Jude Medical	10	4.5.5 (a)	A) Australian DBS Referral Guidelines Working Group (J Clin Neurosci 2009 Aug; 16(8):1001-8) a. Levodopa responsive b. Motor fluctuations and/or dyskinesias not adequately controlled with optimised medical therapy c. Medication-refractory tremor d. Intolerance to medical therapy e. Early referral recommended as soon as optimised medical therapy fails to offer satisfactory motor control f. Thalamic DBS recommended for patients with disabling medication-resistant tremor who have minimal rigidity or bradykinesia. They should not have significant cognitive impairment, mood or behavioural disturbances	We thank you for this reference.
SH	St Jude Medical	11	4.5.5	A) NHS Commissioning Board: Clinical Commissioning Policy:	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			(a)	Deep Brain Stimulation (DBS) in Movement Disorders. April 2013 Reference: NHSCB/D03/P/b a. An established diagnosis of Parkinson's disease as assessed by the UK Parkinson's Disease Society Brain Bank Criteria b. Fitness to undergo DBS surgery with no contraindications for surgery c. Be considered to have a life expectancy of 5 or more years d. Motor complications severe enough to significantly compromise function & quality of life as supported by PDQ39 & Unified Parkinson's Disease Rating Scale (UPDRS) Part II scores (on/off fluctuations; levodopa induced dyskinesias or medication resistant functionally impairing tremor e. If the indication is on/off fluctuations and or Levodopa induced dyskinesias a. Assessment will indicate the patient is spending more than 30% of a 24 hour period in either disabling "off" state or with disabling dyskinesias supported by detailed clinical history, UPDRS Part IV scores and will be despite optimisation of best medical therapy b. A levodopa response of greater than or equal to a 40% improvement in UPDRS Part III motor scale sub-scores following a practically defined period off medication f. If the indication is medication resistant functionally impairing tremor a. Detailed assessment demonstrates tremor to be sufficiently severe to significantly impair activities of daily living to a degree that impairs quality of life as supported by PDQ39, UPDRS II scores and a clinical	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				tremor rating scale (Fahn Tolosa Marin (FTM) tremor rating scale) b. All options for best medical therapy will have been considered, tried or exhausted by a movement disorder consultant neurologist working with a functional neurosurgery team c. Patient is free from clinically significant cognitive impairment measured by DRS 2 (score of 6 or below). No evidence of clinical dementia	
SH	St Jude Medical	12	4.5.5 (a)	A) Identifying Candidates for Deep Brain Stimulation for Parkinson's Disease. Joohi Jimenez-Shahed Practical Neurology November / December 2012 a. Generally accepted criteria a. Idiopathic Parkinson's disease b. Robust response to levodopa c. Complications of medical therapy (e.g. motor fluctuations or dyskinesias) d. Lack of significant psychiatric and/or mood symptoms e. No dementia f. Age under 70 b. Less common criteria a. Disabling tremor refractory to medical therapy b. Individual risk/benefit analysis and subjective considerations (e.g. quality of life)	We thank you for this reference.
SH	St Jude Medical	13	4.5.5 (a)	A) Referring Patients for Deep Brain Stimulation. Maya Katz et al. Arch Neurol 2011;68(8):1027-1032 (Mount Sinai Medical Centre) a. Diagnosis of medically refractory idiopathic PD	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				b. Symptoms substantially interfere with the patient's quality of life & functionality c. Intact cognition d. The absence of an untreated or disabling psychiatric illness e. Realistic expectations f. The ability & willingness to participate in regular follow-up visits g. Absence of comorbidities that are contraindications to DBS h. Symptom duration for 5 years or longer i. Documented positive response to levodopa therapy j. History of on-off fluctuations k. Marked disability in the off-medication state l. Severe dyskinesias or tremor	
SH	St Jude Medical	14	4.5.5 (a)	A) Deep Brain Stimulation for Patients with Parkinson's Disease. Swedish Neurosciences Institute September 2009 a. Clear diagnosis of Parkinson's disease b. Robust response to levodopa c. Cannot tolerate high doses of medication d. Severe dyskinesias e. Middle stage of PD disease (5-15 years) with good function in "on" state f. Realistic expectations & good social support system g. Younger patients respond better in general but no age cut-off No severe cognitive impairments	We thank you for this reference.
SH	St Jude Medical	15	4.5.5 (a)	A) Deep Brain Stimulation for Parkinson's Disease – A Review. Christopher R Honey and Manish Ranjan US	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Neurology; 2012;8(1):12-9 a. STN stimulation is indicated in patients with severe motor fluctuations (e.g. bradykinetic-rigid to moving well to peak-dose dyskinesia to moving well to bradykinetic-rigid) b. Levodopa responsive symptoms (e.g. "off" freezing, tremor, rigidity or balance improve with medications)	
SH	St Jude Medical	16	4.5.5 (a)	A) National Parkinson Foundation 2009 a. PD Symptoms for at least 5 years b. Levodopa induced on / off motor fluctuations with or without dyskinesia c. Continued good response to levodopa d. Exhausted all medication combinations whilst under the care of a neurologist specializing in movement disorders e. Has PD symptoms that interfere with daily activities Realistic expectations	We thank you for this reference.
SH	St Jude Medical	17	4.5.5 (b)	A) Cost-Effectiveness of Deep Brain Stimulation in Patients With Parkinson's Disease Judith Dams et al, Movement Disorders 2013;28(6):763-771 a. Incremental cost-utility ratio for DBS at an early stage of PD was calculated at approximately €3400 per QALY over a lifetime horizon which increased to approximately €6700 per QALY for patients aged 60 years b. In older patients, DBS accounted for approximately €14,300 per QALY gained c. Therefore scenario analysis indicates that early intervention of DBS could result in more cost-	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				effectiveness	
SH	St Jude Medical	18	4.5.5 (b)	B) Espay AJ et al, Mov Disord 2010;25:1456-1463 a. Compared effectiveness in QALYs of STN DBS in patients with early PD (off time 10-20%) versus delayed stage (off time greater than 40%) b. Early STN DBS was preferred with a quality-adjusted life expectancy of 22.3 QALYs a gain of 2.5 QALYs over those with delayed surgery (19.8 QALYs) c. Early DBS provided 2.5. additional QALYs compared with late DBS for a patient population aged 45 years over a lifelong time horizon concluding DBS may convey great quality of life expectancy	We thank you for this reference.
SH	St Jude Medical	19	4.5.5 (b)	C) Zhang PP et al, Morbidity and mortality of deep brain stimulation surgery patients greater or equal age 70: A single centre review. Poster 537 Movement Disorders, Vol 27, Suppl. 1, 2012	We thank you for this reference.
SH	St Jude Medical	20	4.5.5 (b)	D) Kleiner-Fisman G et al, Movement Disorders Vol. 21, Suppl. 14, 2006 ppS290-S304 a. Performed a summary & meta-analysis of long-term DBS outcomes and commented that milder PD disease (lower baseline UPDRS III medication "off" scores) patient outcome was superior to those with higher baseline "off" scores b. 35 consecutive patients age ≥70 underwent 39 implantations of which 30 patients had PD. Mean age 75.5 years (range 70-86) with 8 patients greater than 80 years old. c. 14 patients (40%) experienced medical / surgical complications within the first 30 days of DBS (2	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				mortality, 2 asymptomatic cerebrovascular events, 3 significant falls leading to fractures or cerebral oedema, 3 altered mental status & several serious medical morbidity (DVT, mi, hypertension, hyperglycemia) d. DBS can lead to significant complications in elderly patients	
SH	St Jude Medical	21	4.5.5 (b)	E) Schuepbach WM et al, N Engl J Med 2013; 368:675-676. Neurostimulation for Parkinson's disease with early motor complications a. EARLYSTIM trial randomized 251 PD patients to either DBS plus medical therapy or medical therapy alone b. Investigated the effect of DBS on QoL in PD patients with significantly shorter disease duration and a history of levodopa induced motor complications of ≤3 years. c. The DBS group reported significant improvements in QoL, motor disability, ADL's and levodopa-induced motor complications after 2 years of follow-up than the best medical therapy group alone. d. The authors suggested consideration of earlier DBS than is currently reflected by clinical practice and to potentially offer DBS to patients within the first 3 years after the onset of motor complications.	We thank you for this reference.
SH	St Jude Medical	22	4.5.5 (b)	F) Relevance of ERALYSTIM in a Tertiary Movement Disorder Centre. Letters. New Observations. Movement Disorders. DOI: 10.1002/mds.25631 (Dr. Fabienne Sprenger) a. Applied the inclusion & exclusion criteria of EARLYSTIM to all PD patients seen at the Department of Neurology at the Medical University Innsbruck between January 1st 2012 and December 31st 2012 b. 594 PD patients were seen with 2.5% meeting the	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				EARLYSTIM criteria c. Concluded that earlier DBS intervention should only be considered in very carefully selected earlier PD patients in tertiary movement disorder centres	
SH	St Jude Medical	23	4.5.5 (b)	G) Duke University Press Release; August 25th 2014 a. Data analysis of 1,757 PD patients implanted with DBS between 2000 and 2009 b. 7.5% experienced a minimum of one complication within 90 days of the implantation surgery including wound infections, bleeding, pneumonia & pulmonary embolism c. Older patients were found to be more likely to develop pneumonia compared with younger patients (however it was noted that this increased risk was common after surgery in older people) d. Concluded that older patients (including those over 75 years of age) were no more likely to experience complications than younger patients	We thank you for this reference.
SH	St Jude Medical	24	4.5.5 (c)	A) Functional asymmetry of Subthalamic nucleus revealed by gait analysis in PD patients under-going deep brain stimulation. Luca CC et al, Poster 670; Movement Disorders 2014; Vol. 29: Issue S1 a. 12 PD patients with STN-DBS were tested off medication in 4 randomly assigned conditions – bilateral ON, right ON, left ON and bilateral OFF separated by a one hour interval. b. UPDRS was blindly assessed by a movement disorder specialist with gait kinematics measured using wireless sensors attached to the patient's ankles & trunk	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				c. Bilateral STN DBS improved UPDRS motor score by 47.02%, velocity 13.38% and stride length by 14.51% greater than the other 3 assigned stimulation conditions. d. Dominant STN stimulation had a significant effect on stride length, velocity and stride time variability.	
SH	St Jude Medical	25	4.5.5 (c)	A) Twelve month prospective observational study on combined Subthalamic and nigral stimulation for resistant gait impairment. Scholten MA et al, Poster 709; Movement Disorders 2014; Vol. 29: Issue S1 a. Open-label prospective observational study of 17 patients with advanced idiopathic PD and combined STN + SNr stimulation were followed over 12 months and seen at 6 weeks, 3 months, 6 months & 12 months. b. 4 patients were treated with STN stimulation alone and were switched to STN + SNr when entering the study c. Statistical analysis was performed on 13 patients that remained on STN + SNr during the full 12 months d. Freezing of gait was assessed using the freezing of gait questionnaire (FOG-Q) & the freezing assessment course (FAC) e. Both FOG-Q & FAC were stable over time meaning STN + SNr stimulation may primarily improve resistant FOG f. Quality of life & axial motor symptoms were normally distributed with quality of life remaining constant	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	St Jude Medical	26	4.5.5 (c)	A) Do Parkinson's patients with mild cognitive impairment have different immediate and long-term outcomes after DBS? Abboud H et al, Poster 1171. Movement Disorders 2014; Vol. 29; Issue S1 a. 130 PD patients identified from a single centre between 2006 and 2011 were analysed to study the effect of mild cognitive impairment (MCI) type (none, single domain, multiple domain, cognitive domains and performance on the dementia rating scale (DRS) and depression scale (PHQ9) on immediate postoperative outcomes and long-term outcomes (6 month and 1-year postoperative UPDRS II and quality of life (EQ-5D) scales and Patient Global Impression Scale (PGIS) b. Mean age 63 years +/- 9.1; PD duration 10.7 years +/- 5.1 c. Preoperative assessment revealed 60% of patients had multiple domain MCI, 21% single domain MCI and 19% normal cognition. d. The presence and type of MCI had no significant association with immediate or long-term DBS outcomes, similarly, DRS score was non-influential e. Attention impairment predicted longer postoperative hospitalisation (P=0.0015) and showed a trend towards occurrence of postoperative confusion (P=0.089) f. There was weak evidence of association between visuospatial impairment and a worse functional score at 6 months (P=0.0652), and between language impairment and a worse QOL score at 1-year (P=0.0517) adjusting for preoperative scores g. Preoperative PHQ9 predicted worse QOL score at	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				6 months (P=0.0322) and 1-year (P=0.0116) but not after adjusting for preoperative scores h. It was concluded that the presence of MCI in itself does not seem to affect DBS outcomes however the types of impaired domains may be more detrimental. MCI patients should not be denied surgery however detailed cognitive testing can help stratify low and high-risk patients based on their pattern of cognitive dysfunction	
SH	St Jude Medical	27	4.5.5 (c)	Impact of deep brain stimulation of bilateral subthalamic nuclei on non-motor symptoms in Parkinson's disease patients. Borgohain R et al, Poster 1176. Movement Disorders 2014; Vol. 29; Issue S1	We thank you for this reference.
SH	St Jude Medical	28	4.5.5 (c)	A) Differential effects of levodopa and subthalamic nucleus deep brain stimulation on bradykinesia in Parkinson's disease. Timmermann L et al, Mov Disord 2008; Jan 30;23(2):218-27 a. Eight hypokinetic-rigid PD patients with chronic STN stimulation were compared with 14 healthy volunteers as controls for the differential effects of levodopa and STN stimulation on bradykinesia. b. UPDRS III scores were assessed by rater neurologists blinded to the stimulation parameters with a second blinded experienced rater who performed UPDRS scoring solely on videotaped sessions c. All patients were tested after at least 12-hour overnight withdrawal from PD medication in a standardized sequence – STN stimulation (OFF meds / ON stim), no stimulation (OFF med / OFF	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				stim), after 1.5x the morning dose (including dopamine agonists), and with combination of levodopa and STN stimulation (ON med / ON stim) d. Handedness was tested using the Annett's handedness test e. UPDRS scores were poor in all patients OFF med / OFF stim with a significant improvement ($P<0.05$) to a similar extent under levodopa (ON med / OFF stim) and STN DBS (OFF med / ON stim) which were not significantly different ($P>0.05$). f. However, during ON med / ON stim, UPDRS results were significantly better than with levodopa (ON med / OFF stim) or STN DBS (OFF med / ON stim) alone ($P<0.05$). This result could also be found in the akinesia-subscore g. The study demonstrated that levodopa and STN DBS have differential effects on fast diadochokinesia and finger movements in PD patients. Levodopa has a greater effect on movement amplitude of distal finger movements whereas effects of STN DBS are more pronounced on diadochokinesia h. The combination of both therapies is more effective than each therapy alone as measured by total UPDRS suggesting complementary mechanisms of action thought to be due to a reconstitution of the functionally highly relevant supplementary motor area of the cortex and the primary motor cortex i. Concluded that STN DBS improves frequency, amplitude and smoothness of diadochokinesia whereas levodopa does not. Levodopa appears to have a better effect on distal finger movements	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	St Jude Medical	29	4.5.5 (c)	A) Effects of deep brain stimulation and medication on bradykinesia and muscle activation in Parkinson's disease. Vaillancourt DE et al, Brain 2004 Mar, 127(Pt 3):491-504. Epub 2003 Dec 8 a. 9 PD DBS STN patient study to investigate movement speed along with the amplitude & temporal features of EMG activity to determine how and what extent these parameters are changed by DBS and medication b. Patients were examined in each of 4 treatment conditions – OFF treatment; STN DBS; Meds and Meds plus STN DBS. An age & gender-matched control subjects were also examined c. Medication & STN DBS both increased movement speed, increased the amplitude of the first agonist burst, increased burst duration, reduced the number of agonist bursts, reduced cocontraction, increased the size of the antagonist EMG, and reduced the centroid time of the antagonist EMG d. When medication and STN DBS were combined, only temporal measures of burst duration and the number of agonist bursts were different from medication alone e. Movement speed of neurologically intact patients was over 40% higher during both flexion and extension movements f. Conclusion that there was a link between basal ganglia function in scaling both the amplitude & temporal parameters of the input to the motor neuron pool	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	St Jude Medical	30	4.5.5 (c)	A) Subthalamic nucleus stimulation for Parkinson's disease preferentially improves akinesia of proximal arm movements compared to finger movements. Wenzelburger R et al, Mov Disord 2003; Volume 18: Issue 10 a. Consecutive series of 35 PD patients treated with bilateral STN DBS b. Impact on motor function was assessed in STN DBS and a levodopa test on the timing of the precision grip c. Improvement in UPDRS-items reflecting hand functions and the shortening of the first phases of the precision grip were more distinct in the levodopa test than in the pure STN DBS condition d. Additional akinesia items and the time for build-up of lifting force were equally improved in both conditions. e. Conclusion that routine STN DBS might not be equally effective on all aspects of fine motor functions	We thank you for this reference.
SH	St Jude Medical	31	4.5.5 (c)	A) Axial parkinsonian symptoms can be improved: the role of levodopa and bilateral subthalamic stimulation. Bejjani P et al, J Neurol Neurosurg Psychiatry 2000;68:595-600 a. 10 severe PD patients were evaluated on the efficacy of STN stimulation on total motor disability score (UPDRS part III). Sub-scores were studied separately for limb akinesia, rigidity and tremor (known to respond to levodopa) and axial signs of speech, neck rigidity, rising from a chair, posture, gait & postural stability known to respond less well to levodopa b. Patient assessments conducted prior to STN DBS	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				in the ON and OFF medication condition during a levodopa challenge test and repeated 6 months after surgery under continuous STN stimulation c. UPDRS part II (activities of daily living) were obtained from each patient questionnaire d. STN DBS and levodopa (pre-operative challenge test) improvements were statistically similar –total motor disability score (62% vs. 68%); limb signs (62% vs. 69%); axial signs (72% vs. 59%) e. Combined STN DBS & levodopa provided further improvement in total motor disability (80%) compared with pre-operative levodopa challenge test through an additional improvement in axial signs (84%) mainly for posture and postural stability. f. Axial symptoms from the ADL showed similar additional improvement when levodopa & STN DBS were combined g. Concluded that bilateral STN stimulation improves most axial features of PD and that a synergistic effect can be obtained if combined with levodopa	
SH	St Jude Medical	32	4.5.5 (c)	A) Dopa-sensitive and dopa-resistent gait parameters in Parkinson's disease. Blin O et al, J Neurol Sci 1991 May;103(1): 51-4 a. Quantitative analysis of gait performed in 20 PD patients before and 1-hour post an acute administration of levodopa to determine between levodopa-sensitive and levodopa-resistant kinematic gait parameters b. Stride length and the kinematic parameters (swing	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				velocity & peak velocity) related to the energy were levodopa-sensitive c. Temporal parameters (stride & swing duration, stride duration variability), related to rhythm, were levodopa-resistant	
SH	St Jude Medical	33	4.5.5 (c)	A) Common and unique responses to dopamine agonist therapy and deep brain stimulation in Parkinson's disease: $H_2{}^{15}O$ PET study. Bradberry TJ et al, Brain Stimul Oct 2012;5(4):605-615 a. Analysis of the different basal ganglia-thalamocortical motor circuitry affected by dopamine agonist therapy and STN DBS yet produce similar symptomatic improvements b. 9 PD patients scanned before and after injection of apomorphine & 11 PD were scanned while bilateral stimulators were off and on c. Both treatments produced common deactivations of the neocortical sensorimotor areas including the supplementary motor area (SMA), precentral gyrus (PrG) & postcentral gyrus (PoG), and in subcortical structures including the putamen & cerebellum d. Observed concomitant activations of the superior parietal lobule and the midbrain in the region of the substantia nigra / STN e. Unique effects of apomorphine & STN DBS i. STN DBS exhibited more widespread decreases in regional cerebral blood (rCBF) volume in the SMA, PrG & PoG whilst apomorphine, in contrast, activated these neocortical sensorimotor regions ii. The globus pallidus was activated by STN	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				DBS but unaffected by apomorphine iii. Apomorphine deactivated relatively wider areas of the putamen & cerebellum iv. rCBF increased with STN DBS in the posterolateral cerebellum (Crus II) but decreased by apomorphine and a similar effect was observed in the activity of the ventrolateral thalamus v. STN DBS exclusively activated the amygdala vi. Both treatments activated the hippocampus with STN DBS activating the more ventral portions vii. The inferior frontal gyrus was activated by STN DBS yet deactivated by apomorphine viii. The superior temporal gyrus was uniquely activated by apomorphine ix. STN DBS activated anterior portions of the middle temporal gyrus while deactivating posterior portions x. It was thought that STN DBS provides therapeutic benefit by increasing activity in target outputs of the structure in which the stimulating leads are implanted xi. Both treatments activated the hippocampus with STN DBS activating the more ventral portions xii. The inferior frontal gyrus was activated by STN DBS yet deactivated by apomorphine xiii. The superior temporal gyrus was uniquely activated by apomorphine xiv. STN DBS activated anterior portions of the	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				middle temporal gyrus while deactivating posterior portions xv. It was thought that STN DBS provides therapeutic benefit by increasing activity in target outputs of the structure in which the stimulating leads are implanted	
SH	St Jude Medical	34	4.5.5 (c)	A) Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. Kleiner-Fisman G et al, Mov Disord 2006 Jun;21 Suppl 14:S290-304 a. Medline & Ovid database review between 1993 and 2004 b. 37 cohorts were included in the review and 22 studies were included in the meta-analysis c. Decrease in UPDRS II & III scores post DBS in the stimulation ON / medication OFF state compared to pre-op medication OFF state were 13.35 and 27.55 respectively d. Average reduction in L-dopa equivalents following surgery was 55.9% (50%-61.8%) e. Average reduction in dyskinesia following surgery was 69.1% (62% - 76.2%) f. Average reduction in daily OFF periods was 68.2% (57.6% - 78.9%) g. Average improvement in quality of life (PDQ-39) was 34.5% +/- 15.3% h. UPDRS III improvements were higher with higher baseline UPDRS III OFF scores, increased disease duration prior to surgery & higher baseline L-dopa responsiveness i. Later studies suggested that DBS was being offered to patients with milder disease severity	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				(lower baseline UPDRS III OFF scores) j. Most common serious AE was intracranial haemorrhage in 3.9% of patients	
SH	St Jude Medical	35	4.5.5 (c)	A) In a rush to decide: Deep brain stimulation and dopamine agonist therapy in Parkinson's disease. Djamshidian A et al, J Parkinsons Dis 2014 June 24 (Epub ahead of print) a. Studied the clinical effect of L-dopa monotherapy and L-dopa in combination with a dopamine agonist in 27 PD DBS patients when performing perceptual decision making b. All PD patients treated with a dopamine agonist made faster decisions than controls and L-dopa monotherapy patients c. All patients made more errors than controls with no difference between the two groups d. Concluded that dopamine agonist therapy rather than DBS is likely responsible for the inability to slow down in high conflict situations in PD thereby emphasizing the need to reduce agonists post-DBS to prevent patients making inadvisable decisions	We thank you for this reference.
SH	St Jude Medical	36	4.5.5 (c)	A) A comparative study of the efficacy of deep brain stimulation of the subthalamic nucleus and pharmacological treatment in advanced Parkinson's disease. Bril EV et al, Zh Nevrol Psikhiatr Im S S Korsakova 2014;114(6 Vypusk 2 Nevrologiia I psikhiatriia pozhilogo vozrasta):55-61 a. 22 patients received STN DBS (mean age 53.2 years with mean disease duration 9.6 years) b. Patients were examined in OFF medication and ON medication at 3, 6, 9, 12, 24 & 36 months c. STN DBS improved UPDRS II & III scores, reduced	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				dyskinesias and motor fluctuations whilst dopaminergic therapy was reduced by approximately 54.5% d. In the control group L-dopa dose was increased by 20.5% at 36 month follow-up	
SH	St Jude Medical	37	4.5.5 (c)	A) Ten-year outcome of subthalamic stimulation in Parkinson disease: a blinded evaluation. Castrioto A et al, Arch Neurol 2011 Dec;68(12):1550-6 a. 10-year video assessments were completed by an independent rater blinded to stimulation and medication condition in 18 PD patients b. STN DBS at 10-years significantly improved the UPDRS total motor score (P=0.007) and resting and action tremor (P <0.01 an P =0.02 respectively) and bradykinesia (P= 0.01) subscores c. UPDRS II scores in the no medication and medication conditions, UPDRS IV dyskinesia and motor fluctuation scores and L-dopa equivalent daily dose were also significantly reduced compared with baseline d. Axial symptoms showed the most progressive decline	We thank you for this reference.
SH	St Jude Medical	38	4.5.5 (c)	A) Meta-analysis comparing deep brain stimulation of the globus pallidus and subthalamic nucleus to treat advanced Parkinson disease. Liu Y et al, J Neurosurg 2014 Sep;121(3):709-18 a. Database search of English-language studies published before April 2013 b. Six eligible studies of a total 563 patients c. DBS of the GPi or STN equally improved motor	We thank you for this reference.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				function measured by UPDRS III within 1-year post-surgery i. Change score for ON medication phase was 0.68 (P >0.05) (5 studies of 518 patients) ii. Change score for OFF medication phase was 1.83 (P >0.05) (5 studies of 518 patients) iii. UPDRS II scores for patients ON medication improved equally in both DBS groups (P=0.97) iv. STN DBS allowed medication dosages to be reduced more than GPi DBS v. Psychiatric symptoms (Beck Depression Inventory) showd greater improvement from baseline after GPi DBS than after STN DBS vi. Conclusion that the therapeutic efficacy of GPi & STN DBS were equivalent except STN DBS allowed greater medication reduction and GPi BS provided greater relief from psychiatric symptoms	
SH	UCB Pharma Ltd	1	4.3.1 a)	**Pharmacological management:** We would like this to be written as 'Pharmacological management of motor and non-motor symptoms' to reflect the description of the disease as defined in section 3.1 e)	We thank you for your comment. We have taken this into account and amended accordingly.
SH	UCB Pharma Ltd	2	4.3.1 a)	**Initial treatment of Parkinson's disease (monotherapy) and Drugs to be used with levodopa (as adjuvants) in the later stages of Parkinson's disease:** It is important to define Dopamine agonists separately as immediate release and modified release in the same way you have defined the preparations of Levodopa as evidence show that continuous drug delivery is an important	We thank you for your comment. The guideline development group will take the initial treatment of Parkinson's disease and adjuvants to levodopa in later stages of the disease into consideration when developing the guideline.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				differentiator of Dopamine agonist treatments	
SH	UCB Pharma Ltd	3	4.3.1 a)	**Pharmacological treatment of the following non-motor symptoms:** It is important to consider that there are other more prominent non-motor symptoms that need to be included (as referred to in section 3.1 e)) - depression, pain and GI disturbance that could be managed effectively through effective dopaminergic therapy as well as other pharmacological treatments	We thank you for your comment. Depression, pain and urgency have not been prioritised for update within the guideline as preliminary searches into these areas have revealed a paucity of new clinically conclusive evidence that would warrant extensive reviews in these areas. We will cross-refer to the neuropathic pain (CG173) and depression in chronic physical health condition (CG91) guidelines respectively. Emerging evidence within the field of sleep disorders has been found, and thus sleep disorders will be covered within the present scope with review questions for both hypersomnolence and nocturnal akinesia.
SH	UCB Pharma Ltd	4	4.3.1 a)	**Pharmacological treatment of the following non-motor symptoms**: It is important to consider that the management of non-motor symptoms can be achieved through effective dopaminergic treatment as well as other pharmacological treatments	We thank you for your comment.
SH	UCB Pharma Ltd	5	4.3.1 a)	We would like to see RLS highlighted in the scope as an area for guidance as it is present in 20-30% of people with Parkinson's and it may be appropriate to review how this can be managed	We thank you for your comment. We propose to update review questions on daytime hypersomnolence and nocturnal akinesia within this guideline, but restless leg syndrome will not be covered in the guideline update. Previous information and recommendations regarding this will be brought forward from the previous guideline into the update.
SH	UCB Pharma Ltd	6	4.3.1 g)	**Predictors of impulse control disorder as an adverse effect of dopamine treatments.** We recommend this reads 'Screening guidelines for patients to identify risk factors and predictors of impulse Control Disorders'. Assessment of prediction tools, e.g. QUIP, should be covered.	We thank you for your comment. We have decided that the current wording is a more appropriate reflection of the type of review questions that we propose to undertake in relation to impulse control disorders. We will, however, include tools such as Questionnaire for impulsive-compulsive disorders (QUIP), as outcome measures of interest within the predictors for impulse control disorder review

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					question if we find evidence for these measures.
SH	UCB Pharma Ltd	7	4.3.2 e)	**Depression in Parkinson's disease**: Depression is highlighted as a key issue for patients with Parkinson's disease in section 1.3 e) we therefore suggest that it would be useful to give recommendation on how dopaminergic treatments can benefit PD related depression a key non-motor symptom	We have made the decision not to examine depression explicitly in this guideline update as it has been recognised that there is a paucity of clinically conclusive data, and Depression in adults with a chronic physical health problem (NICE clinical guideline 91) has been considered relevant and appropriate to cross-refer to in this guideline. We will, however, bring forward the standing recommendations from the previous guideline in relation to depression in Parkinson's disease.
SH	UCB Pharma Ltd	8	4.3.2 j)	**Generic health problems for which the care for people with Parkinson's disease does not differ from that for the general population (for example, constipation).** We would suggest that constipation in PD is different and its manifestation is due to the patient's decline and contributes to a high number of non-elective admissions for patients with PD. Evidence also shows that for PD patients suffering with constipation thought should be given to the route of drug delivery avoiding the GI route of absorption.	We thank you for your comment. Constipation has not been prioritised for update within the guideline. Constipation will be assessed where appropriate as an adverse outcome within the pharmacological intervention review questions. We will also bring forward the previous information and recommendation pertaining to constipation from the previous guideline.
SH	UCB Pharma Ltd	9	4.4.0	**Main Outcomes:** Other outcome measures that should be used are as follows: QUIP/semi structured interviews and outcomes in relation to ICDs	We thank you for your comment. The GDG guideline development group will take this into consideration when developing the evidence review protocols which form the basis of the evidence reviews in the guideline. We would like to note that the outcome measures provided in the scope section 4.4. merely provide potential examples of the types of scales that may be considered by the guideline group. Each relevant outcome, such as the Questionnaire for impulsive-compulsive disorders in Parkinson's disease (QUIP), will be separately considered by the group when determining the most appropriate and effective outcome measures to include for a review

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					question.
SH	UCB Pharma Ltd	10	4.4.0 f)	**Main Outcomes non-motor symptoms:** Both PDSS1 and PDSS2 should be included	We thank you for your comment. The guideline development group will take these into consideration when developing the evidence review protocols, which form the basis of the evidence reviews in the guideline. We would like to note that the outcome measures provided in the scope section 4.4. merely provide potential examples of the types of scales that may be considered by the guideline group. Each relevant outcome, such as the PDSS, will be separately considered by the group when determining the most appropriate and effective outcome measures to include for a review question.
SH	UCB Pharma Ltd	11	4.4.0 f)	**Main Outcomes: Non-motor symptoms** :NMSS2 (non-motor symptom score 2)	We thank you for your comment. The guideline development group will take this into consideration when developing the evidence review protocols which form the basis of the evidence reviews in the guideline. We would like to note that the outcome measures provided in the scope section 4.4. merely provide potential examples of the types of scales that may be considered by the guideline group. Each relevant outcome, such as the non-motor symptom score 2, will be separately considered by the group when determining the most appropriate and effective outcome measures to include for a review question.
SH	UCB Pharma Ltd	12	4.5.1	**Pharmacological management of motor symptoms:** We would like to highlight the importance of considering the management of symptoms over the full 24 hour period including early morning and wearing off that can only be achieved through continuous dopaminergic treatment.	We thank you for your comment. The guideline development group will take this into consideration

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	UCB Pharma Ltd	13	4.5.1 a)	**What is the comparative effectiveness of levodopa, monoamine oxidase B inhibitors, dopamine agonists and anticholinergics as first-line treatment of motor symptoms**: We would like to highlight that it is important that individual therapies are considered separately not grouped into classes of treatments and formulations (extended release and immediate release formulations) when looking at comparative effectiveness. It is also important to consider the same review question but focus on 'non-motor' symptoms	We thank you for your comment. The guideline development group will take this into consideration. Where appropriate, we can confirm that we will examine both immediate and prolonged-release preparations.
SH	UCB Pharma Ltd	14	4.5.1 b)	**What is the comparative effectiveness of pharmacological interventions (monoamine oxidase B inhibitors, dopamine agonists, catechol-O-methyl transferase inhibitors amantadine, apomorphine) as adjuvants to levodopa:** We would like to highlight that it is important that individual therapies are considered separately not grouped into classes of treatments and formulations (extended release and immediate release formulations) when looking at comparative effectiveness It is also important to consider the same review question but focus on 'non-motor' symptoms	We thank you for your comment. The guideline development group will take this into consideration. We can confirm that where appropriate, we will examine both immediate and prolonged-release preparations. We would like to note that under NICE methodology, drugs are reviewed in their classes and formulations as standard, unless there is a specific reason for looking at individual drugs. This approach will be taken in the present review.
SH	UCB Pharma Ltd	15	4.5.1 c)	**What is the effectiveness of duodopa intestinal gel?** Why is duodopa intestinal gel the only treatment that will be assessed separately for effectiveness and not through comparative effectiveness?	We thank you for your comment. As duodopa is a new drug, its efficacy needs to first be established before it can be examined within the context of comparative effectiveness. The referral criteria for duodopa is different to other pharmacological interventions (i.e. it is often prescribed later in the disease course), and thus the population of interest for this drug will be different to the other adjuvant therapies, which makes it inappropriate to include within a network meta analyses.
SH	UCB Pharma Ltd	16	4.5.1	We would like to suggest that evidence of compliance and concordance of dopaminergic management is considered	We thank you for your comment. The guideline development group will take evidence for compliance and concordance of dopaminergic management into consideration, should there be evidence for this.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	UCB Pharma Ltd	17	4.5.2	**Pharmacological management of non-motor symptoms:** Our comment is that this should be defined as dopaminergic and non-dopaminergic management of non-motor symptoms to recognise the beneficial effect and primary end points of studies that have looked at the non-motor symptoms of Parkinson's Disease	We thank you for your comment. The guideline development group will take this into consideration, however we would like to note that this level of detail is usually considered by the guideline group in the early stages of protocol development, and not examined as early as the scoping stages.
SH	UCB Pharma Ltd	18	4.5.2	**We would suggest an additional review question on the management of sleep symptoms associated with Parkinson's Disease as the outcome measures for sleep have already been defined in section 4.4 f) this would read:** What is the comparative effectiveness of pharmacological interventions and dopaminergic interventions for symptoms of sleep in Parkinson's Disease?	We thank you for your comment. The guideline development group will take this into consideration. We would like to highlight that we have included review questions on both excessive daytime sleepiness (hypersomnolence), as well as nocturnal akinesia within the proposed guideline update scope.
SH	UCB Pharma Ltd	19	4.5.6 – 4.5.8	**We would suggest an additional section here that would be:** Management of PD in care settings (hospital/care home/ domiciliary settings) What are the management needs of patients: • Nurse and junior doctor training on the need for PD medication administration on time • Improved access to PD medication in hospitals, especially out-of-hours • Swallow assessment and appropriate medicine use in patients with swallowing difficulties • Ensure adequate hydration	We thank you for your comment. The issues you have suggested have not been prioritised for update within this iteration of the guideline. We would like to highlight the NICE patient experience in the NHS guideline, which also covered many of the listed aspects, such as adequate hydration and access to specialist information and medication.
SH	UK Clinical Pharmacy Association	1	General	The UKCPA have no further comments to make and we support the draft scope.	We thank you for your comment.

These organisations were approached but did not respond:

5 boroughs NHS Foundation Trust Partnership

Adults Strategy and Commissioning Unit

Aintree University Hospital NHS Foundation Trust

Airedale NHS Trust
Allocate Software PLC
Alzheimer's Society
Anglia community leisure
Apetito Ltd
Association for Continence Advice
Association for Family Therapy and Systemic Practice in the UK
Association for Palliative Medicine of Great Britain
Association of Anaesthetists of Great Britain and Ireland
Association of British Healthcare Industries
Association of British Neurologists
Association of Chartered Physiotherapists in Neurology
Association of Dance Movement Therapy UK
Association of Professional Music Therapists
Barchester Healthcare
Barts and the London NHS Trust
Bayer HealthCare
Bedfordshire and Hertfordshire Tissue Viability Nurses Forum
Belfast Health and Social Care Trust
Birmingham Clinical Trials Unit
Boehringer Ingelheim
Boots
Bradford District Care Trust
Brain and Spine Foundation
Bristol and Avon Chinese Women's Group
Bristol-Myers Squibb Pharmaceuticals Ltd
Britannia Health Products Ltd

British Association for Psychopharmacology
British Association of Art Therapists
British Association of Neuroscience Nurses
British Association of Social Workers
British Dental Association
British Dietetic Association
British Geriatrics Society-Special Interest Group in Diabetes
British Medical Association
British Medical Journal
British National Formulary
British Neuropsychiatry Association
British Nuclear Cardiology Society
British Nuclear Medicine Society
British Psychological Society
British Red Cross
British Society for Stereotectic and Functional Neurosurgery
British Society of Neuroradiologists
British Society of Rehabilitation Medicine
BUPA Foundation
Cambridge University Hospitals NHS Foundation Trust
Camden Carers Centre
Camden Link
Camden Provider Services
Capsulation PPS
Care Quality Commission
Cephalon UK Ltd
Chartered Physiotherapists in Mental Health

Chartered Physiotherapists Promoting Continence
Chartered Society of Physiotherapy
CHESs Research Centre
City University
Clarity Informatics Ltd
Cochrane Movement Disorders Group
College of Mental Health Pharmacists
Coloplast Limited
Community District Nurses Association
Co-operative Pharmacy Association
Croydon Clinical Commissioning Group
Croydon Health Services NHS Trust
Croydon University Hospital
Cumbria Partnership NHS Foundation Trust
Cumbria Partnership NHS Trust
Cure Parkinsons Trust, The
CWHHE Collaborative CCGs
Cyberonics
David Lewis Centre, The
Dementia & Neurodegenerative Diseases Research Network
Department of Health, Social Services and Public Safety - Northern Ireland
Ealing Hospital NHS Trust
East & South East England NHS Specialist Pharmacy Services
East and North Hertfordshire NHS Trust
East Kent Hospitals University NHS Foundation Trust
East Sussex County Council
Economic and Social Research Council

Eisai Ltd

Eli Lilly and Company

Empowerment Matters

Equalities National Council

Essex Centre for Neurological Sciences

Ethical Medicines Industry Group

Expert Patients Programme CIC

Faculty of Public Health

Five Boroughs Partnership NHS Trust

Four Seasons Health Care

Fremantle Hospital

GE Healthcare

Genus Pharmaceuticals Ltd

George Eliot Hospital NHS Trust

GlaxoSmithKline

Global Kinetics Corporation

Gloucestershire Hospitals NHS Foundation Trust

Gloucestershire LINk

GP update / Red Whale

Great Western Hospitals NHS Foundation Trust

Greater Manchester Neurosciences Network

Greater Manchester West Mental Health NHS Foundation Trust

Guidelines and Audit Implementation Network

Guy's and St Thomas' NHS Foundation Trust

Hampshire Partnership NHS Trust

Health & Social Care Information Centre

Health and Care Professions Council

Healthcare Improvement Scotland
Healthcare Quality Improvement Partnership
Help the Hospices
Hertfordshire Neurological Service
Hertfordshire Partnership NHS Trust
Herts Valleys Clinical Commissioning Group
Hindu Council UK
Hockley Medical Practice
HQT Diagnostics
Humber NHS Foundation Trust
Imperial College Healthcare NHS Trust
Independent Healthcare Advisory Services
Institute of Sport and Recreation Management
Integrity Care Services Ltd.
International Neuromodulation Society
James Parkinson Centre
Joint Royal Colleges Ambulance Liaison Committee
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Leeds North Clinical Commisioning Group
Leeds Teaching Hospitals NHS Trust
Lewy Body Society, The
Liverpool Community Health
Lundbeck UK
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
Medicines and Healthcare products Regulatory Agency

Medway NHS Foundation Trust

Mental Health Nurses Association

Merck Sharp & Dohme UK Ltd

Mid Staffordshire NHS Foundation Trust

Ministry of Defence (MOD)

Napp Pharmaceuticals Ltd

National Association of Primary Care

National Care Forum

National Clinical Guideline Centre

National Collaborating Centre for Cancer

National Collaborating Centre for Mental Health

National Collaborating Centre for Women's and Children's Health

National Deaf Children's Society

National Institute for Health Research Health Technology Assessment Programme

National Institute for Health Research

National Patient Safety Agency

National Public Health Service for Wales

National Tremor Foundation

Nester Healthcare Group Plc

Neuromodulation Society of the United Kingdom and Ireland

Neuromodulation Society of UK & Ireland

Newcastle, North Tyneside and Northumberland Mental Health NHS Trust

NHS Barnsley Clinical Commissioning Group

NHS Choices

NHS Connecting for Health

NHS Cornwall and Isles Of Scilly

NHS County Durham and Darlington

NHS Dudley
NHS Halton CCG
NHS Hardwick CCG
NHS Health at Work
NHS Herefordshire
NHS Leeds West CCG
NHS Luton CCG
NHS Newcastle
NHS North Somerset CCG
NHS Plus
NHS Plymouth
NHS Sheffield CCG
NHS South Cheshire CCG
NHS Wakefield CCG
NHS Warwickshire North CCG
NHS West Hampshire CCG
Norgine Limited
North and East London Commissioning Support Unit
North East London Community Services
NORTH EAST LONDON FOUNDATION TRUST
North Essex Mental Health Partnership Trust
North of England Commissioning Support
North Staffordshire Combined Healthcare NHS Trust
Northern Health and Social Care Trust
Northumberland, Tyne & Wear NHS Trust
Nottingham City Hospital
Novartis Pharmaceuticals

Nursing and Midwifery Council
Nutricia Advanced Medical Nutrition
Orion Pharma
Orphan Europe UK
Oxford Health NHS Foundation Trust
Oxfordshire Clinical Commissioning Group
Oxleas NHS Foundation Trust
Parenteral and Enteral Nutrition Group
Parkinsons Disease Information Network
Parkwood Healthcare
Pathfinders Specialist and Complex Care
Patient Assembly
Peninsula Community Health Services
PERIGON Healthcare Ltd
Peterborough and Stamford Hospitals NHS Foundation Trust
Pfizer
Pharmametrics GmbH
PHE Alcohol and Drugs, Health & Wellbeing Directorate
Pilgrims Hospices in East Kent
Primary Care Neurology Society
Primary Care Pharmacists Association
Primrose Bank Medical Centre
Profile Pharma
Progressive Supranuclear Palsy Association
Public Health England
Public Health Wales NHS Trust
Qbtech Ltd

Quality Institute for Self Management Education and Training

Queen Elizabeth Hospital King's Lynn NHS Trust

Rochdale and District Disability Action Group

Roche Products

Royal Berkshire NHS Foundation Trust

Royal College of Anaesthetists

Royal College of General Practitioners in Wales

Royal College of Midwives

Royal College of Obstetricians and Gynaecologists

Royal College of Paediatrics and Child Health

Royal College of Paediatrics and Child Health, Gastroenetrology, Hepatology and Nutrition

Royal College of Pathologists

Royal College of Physicians

Royal College of Psychiatrists

Royal College of Radiologists

Royal College of Surgeons of England

Royal Cornwall Hospitals NHS Trust

Royal National Institute of Blind People

Royal Pharmaceutical Society

Royal Society of Medicine

Royal West Sussex NHS Trust

Salford Royal NHS Foundation Trust

Sanctuary Care

Sanofi

Scottish Intercollegiate Guidelines Network

Sheffield Teaching Hospitals NHS Foundation Trust

Sherwood Forest Hospitals NHS Foundation Trust

Skills for Care
SNDRi
Social Care Institute for Excellence
Society and College of Radiographers
Society for Acute Medicine
Society for Research in Rehabilitation
Society of British Neurological Surgeons
Society of teachers of the Alexander technique
Solvay
South Eastern Health and Social Care Trust
South Gloucestershire Council
South London & Maudsley NHS Trust
South Staffordshire and Shropshire Healthcare NHS Foundation Trust
South West Yorkshire Partnership NHS Foundation Trust
Southern Health & Social Care Trust
Southport and Ormskirk Hospital NHS Trust
St Andrews Healthcare
St Josephs Hospice
St Mary's Hospital
Staffordshire and Stoke on Trent Partnership NHS Trust
Stockport Clinical Commissioning Group
Stockport Clinical Commissioning Pathfinder
Sue Ryder
Sutton and Merton Community Services
Tameside Hospital NHS Foundation Trust
Teva Pharmaceuticals Ltd
Teva UK

The Association of the British Pharmaceutical Industry
The College of Social Work
The Neurological Alliance
The Patients Association
The Princess Alexandra Hospital NHS Trust
The Relatives and Residents Association
The Rotherham NHS Foundation Trust
The Stroke Association
The Walton Centre for Neurology and Neurosurgery
The Wiltshire Trust
Torbay and Southern Devon Health and Care NHS Trus
Tourettes Action UK
Tunstall Healthcare UK Ltd
Turning Point
UK Specialised Services Public Health Network
United Kingdom Council for Psychotherapy
University College London Hospital NHS Foundation Trust
University Hospital Birmingham NHS Foundation Trust
University Hospital of North Staffordshire NHS Trust
University Hospitals Birmingham
University of York
Valeant Pharmaceuticals
Walsall Local Involvement Network
Way Ahead Care
Welsh Government
Welsh Scientific Advisory Committee
Wessex Neurological Centre

West Midlands Ambulance Service NHS Trust

Western Health and Social Care Trust

Western Sussex Hospitals NHS Trust

Westminster Local Involvement Network

Worcestershire Health and Care NHS Trust

York Hospitals NHS Foundation Trust