

## INTRODUCTION

Parkinson's disease (PD) is the fastest growing neurodegenerative disorder globally (Dorsey et al. 2018); its prevalence and incidence are predicted to almost double by 2065 in the UK. In keeping with other non-malignant conditions, the care of people with PD at the end of life is challenging, due to the complex symptoms faced and the fluctuating progression of the disease. Extending palliative care to those with long term neurological conditions has been a priority over the last two decades, both in the UK and internationally. The UK National Service Framework for Long-term Neurological Conditions, published in 2005 (GOV.UK 2005), included a requirement for comprehensive and individualised end of life care, a sentiment echoed by the National Institute for Health and Clinical Excellence Parkinson's disease guidelines (NICE 2017). More widely, the European Association of Palliative Care Taskforce collaborated with the European Academy of Neurology to develop an evidence-base consensus for palliative care for patients with progressive neurological disease, promoting early integration of palliative care services and palliative care training for neurologists (Oliver 2015).

Whilst there has been an increase in research into improving the provision of palliative care services for patients with PD, this has mainly focussed on the development of tools to assess palliative symptom burden and advance care planning. Furthermore, death certification data has enabled us to know *what* patients die of, and *where* they die, rather than *how* they die. As a result, the quality of life in the last weeks and days, as well as the management of terminal complications, is poorly understood.

## AIMS

To systematically review and synthesise the current literature concerning the terminal period in Parkinson's disease, including the symptoms in the dying phase and the management of such symptoms.

## METHODS

### Search strategy and selection of articles

Following an initial scoping search of the literature, inclusion and exclusion criteria were clarified and search strategies developed.

Terminal care was broadly defined to include care in the last weeks and days of life. Studies concerning palliative care or advance care plans without specifying the terminal phase were excluded. We restricted our search to only idiopathic PD, excluding those with Parkinson-plus syndromes, given that the illness trajectories are vastly different amongst the Parkinsonian syndromes.

Qualitative, quantitative and mixed-methods studies reporting new empirical data were included. This mixed methods approach was utilised in order to expand the range of enquiry and also to facilitate convergence and correspondence of results from different methods. Publications were restricted to peer-reviewed journals. Studies were not restricted by country, but only articles that were published in English were included. Conference abstracts were included. The protocol was registered on PROSPERO (ID CRD42020221320).

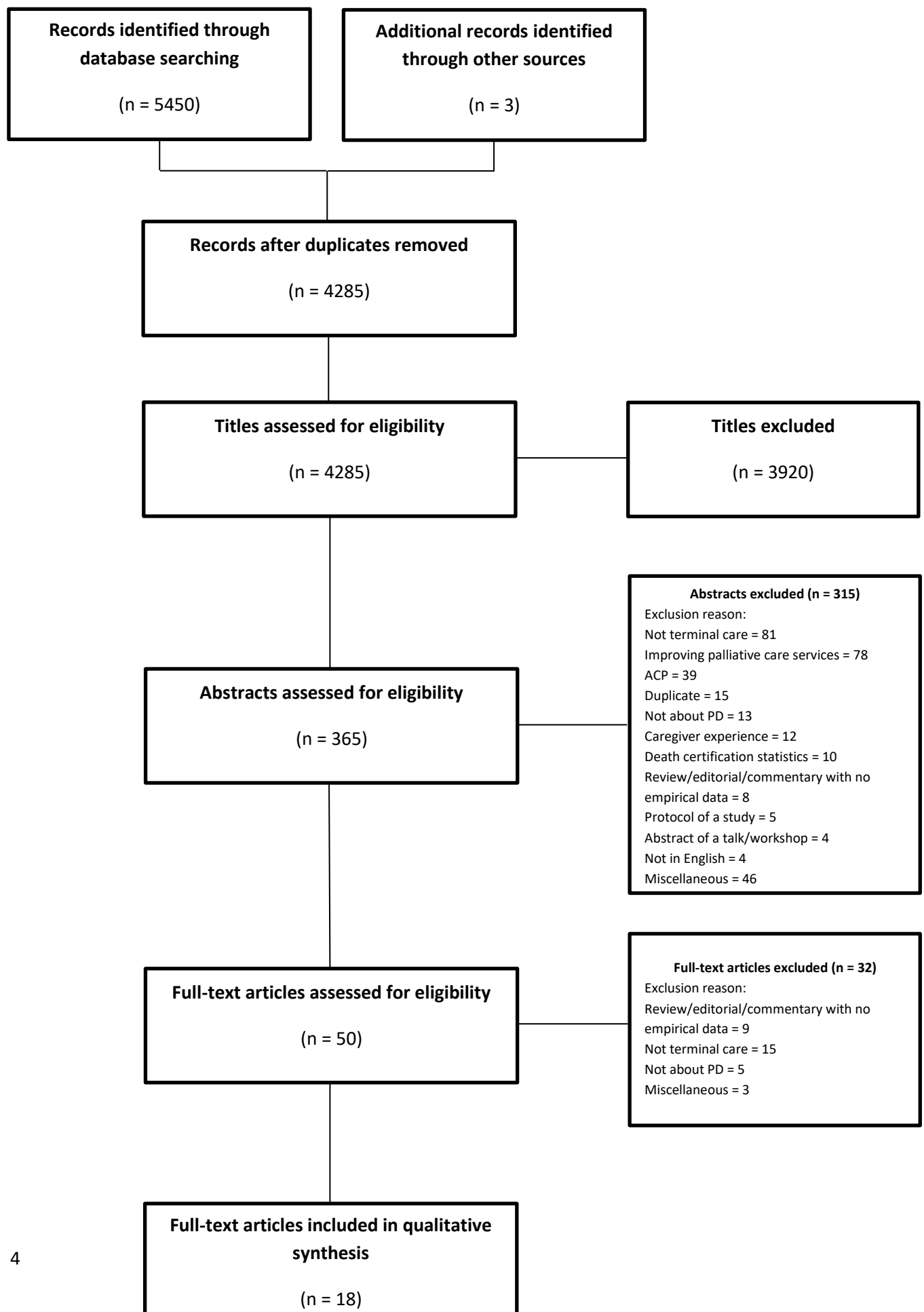
Searches were undertaken for papers published between 1990 and 2020 in five databases (Medline and Embase via OVID; CINAHL and psycINFO via ebscoHOST and Web of Science). The grey literature was searched via OpenGREY; searching of relevant dissertations and theses was via ProQuest Dissertations and Theses Global. The searches took place on 15th October 2020. Reference and citation searching of the included papers was also performed. **Table 1** shows the Medline search strategy.

**Table 1: Medline search strategy**

("Parkinson's disease" OR "Parkinson disease" OR parkinsonism\$ OR Parkinsonian).af.
AND
(palliative or palliation OR "hospice care" OR "end-of-life" OR "end of life" OR EOLC OR "terminal care" OR dying or bereave\$).af.

Search results were downloaded into EndNote X8 and duplicates removed. Titles, shortlisted abstracts and shortlisted full-text articles were screened independently by AR and ST with uncertainty or disagreements resolved by discussion. **Figure 1** presents the PRISMA diagram.

**Figure 1: PRISMA Diagram**



## **Data extraction and analysis**

Author AR extracted data into a review-specific data extraction form which recorded characteristics of each study (author, country, study design) and key findings that answered the review aims. For quantitative articles, findings regarding the input of palliative care services, terminal symptoms and prescribed medications were extracted. For qualitative studies, relevant information in the results and discussion were extracted for thematic analysis.

We utilised a ‘three synthesis’ approach whereby two initial syntheses were undertaken, one each for quantitative and qualitative studies (Tashakkori A 2010). Quantitative data was synthesised using a narrative synthesis approach, given that the studies were descriptive numerical studies and not appropriate for meta-analysis. Qualitative data was analysed thematically, using the approach as detailed by Braun and Clarke (Braun 2006): data was coded inductively using NVivo version 12, with codes grouped into themes.

In the integration phase, findings from the quantitative synthesis were mapped onto the themes from the thematic analysis of qualitative data to produce the final results.

## **Quality assessment**

AR and ST independently evaluated each paper in terms of its strength, quality and contribution towards answering the review question using Gough’s ‘Weight of Evidence (WoE)’ framework (Gough 2007); disagreements as to the overall assessment of each paper were resolved by discussion.

## **RESULTS**

### **Included papers**

A summary of the 18 included papers is presented in **Table 2**.

**Table 2: Included papers**

First Author and Institution	Title	Source	Type of Study	Main Points	Gough Weighting
<b>Quantitative Studies</b>					
<b>Auffret</b>  Université de Rennes, France	Modes of death of hospitalised patients with Parkinson's disease: a 12 year retrospective analysis	<i>Neurology</i> 2019;92(15 Suppl1):P2.6-051  (abstract)	Retrospective analysis of patient notes  132 patients with PD who died at the University Hospital of Rennes between 1 <sup>st</sup> January 2006 and 31 <sup>st</sup> January 2018.	Antiparkinsonian treatments were suspended/stopped prematurely in 42% cases.  Alternative routes of administration were considered in less than 10 cases.  Palliative care consults were requested in only 15.1% cases.  End of life treatment consisted of morphine, midazolam and/or scopolamine.	Medium
<b>Bradburn</b>  Royal Berkshire NHS Foundation Trust, UK	Improving end of life Care in Parkinson's disease	<i>Journal Of Parkinson's Disease</i> 2013;1:193-194  (abstract)	Retrospective analysis of patient notes  88 patients with PD who died at the Royal Berkshire NHS Foundation Trust between 1 <sup>st</sup> January 2010 and 31 <sup>st</sup> December 2012.	Antiparkinsonian treatments were discontinued in 24% of patients.  Haloperidol was prescribed in 24% of patients; metoclopramide in 9%.  44% of patients were started on a formal end of life care pathway.	Medium
<b>Butt</b>  Reading, UK	Use of Syringe Driver in End of Life Care in Parkinson's Disease	<i>Movement Disorders</i> 2019;34(Suppl 2):S280  (abstract)	Retrospective analysis of patient notes  38 patients with PD who died at a hospital in Reading between 1 <sup>st</sup> January 2017 and 31 <sup>st</sup> December 2017.	65.8% were commenced on a syringe driver at the end of life. Combinations included morphine (n = 9), morphine + midazolam (n = 7), morphine + midazolam + hyoscine (n = 8) and morphine and haloperidol (n = 1).  23.7% did not require palliative medications at the end of life.  73% of patients were reviewed by the hospital palliative care team. 65% were started on a formal end of life care	Medium

				<p>pathway.</p> <p>There was overall good awareness of medication to avoid (e.g. metoclopramide and haloperidol).</p>	
<p><b>Chen</b></p> <p>JFK Medical Center Palm Beach, US</p>	<p>Safe Use of Subcutaneous Diphenhydramine in the Inpatient Hospice Unit</p>	<p><i>American Journal of Hospice &amp; Palliative Medicine</i> 2017;34(10): 954-7</p>	<p>Retrospective analysis of patient notes</p> <p>109 terminally ill patients, including 1 with Parkinson's disease, who received at least one subcutaneous injection of diphenhydramine.</p>	<p>Diphenhydramine was used for the PD patient as they were not able to take oral levodopa/carbidopa.</p> <p>No adverse reactions were reported.</p>	<p>Low</p>
<p><b>Goy 2007</b></p> <p>Health Services Research and Development Portland Veterans Affairs Medical Center; and Department of Psychiatry, Oregon Health &amp; Science University, Portland, Oregon, US</p>	<p>Parkinson Disease at the End of Life: Caregiver Perspectives</p>	<p><i>Neurology</i> 2007;69(6):11-2</p>	<p>Interview</p> <p>47 caregivers of patients with PD who died 6-53 months before the interview.</p>	<p>Only 30% of those dying with/of PD received pain medication in the last month of life.</p> <p>Pain was prevalent and undertreated in this population, especially in those who did not receive hospice or skilled nursing care.</p>	<p>Medium</p>
<p><b>Goy 2008</b></p> <p>As above</p>	<p>Neurologic Disease at the End of Life: Caregiver Descriptions of Parkinson Disease and Amyotrophic Lateral Sclerosis</p>	<p><i>Journal of Palliative Medicine</i> 2008;11(4):548- 54</p>	<p>Interview</p> <p>52 caregivers of patients with PDRD and 50 caregivers of patients with ALS.</p>	<p>27% of PDRD patients with moderate/worse pain received no pain medication in the last month of life.</p> <p>Confusion was more frequent and severe during the last weeks of life in those with PDRD compared to those with ALS.</p> <p>Difficulty eating was the most common and severe physical symptom in both PDRD and ALS patients.</p>	<p>Medium</p>

				Social isolation is a problem at the end of life for PDRD patients.	
<b>Ibrahim</b> Southmead Hospital, North Bristol NHS Foundation Trust, UK	Evaluating the Acute Use of Rotigotine Patch for Dopaminergic Replacement in An Inpatient Population	<i>Age and Ageing</i> 2019;49(Suppl 1)  (abstract)	Retrospective analysis of patient notes  33 PD patients, 13 of whom were EoL.	The correct dosage of rotigotine was prescribed in 39% of patients.  69% of patients who were prescribed rotigotine for EoL had evidence of terminal agitation.	Medium
<b>Mole</b> Exeter, UK	End of life care in Parkinson's Disease	<i>Movement Disorders</i> 2017;32(Suppl 2):869  (abstract)	Retrospective analysis of patient notes  30 PD patients that died in hospital between 2013 and 2015.	23% received contraindicated medications, and a further 20% had contraindicated medications prescribed but did not receive them.  Dopaminergic medication was stopped prematurely in 33% of patients. Alternative routes were considered in 90% of patients.  The specialist PD team was involved in 77% of cases.	Medium
<b>Qualitative Studies</b>					
<b>Dewhurst</b> Northumbria Healthcare NHS Trust, UK	The pragmatic use of apomorphine at the end of life	<i>Palliative Medicine</i> 2009; 23(8):777-9	Case study  1 patient (73M) with PD.	Subcutaneous apomorphine achieved relief of symptoms (including terminal agitation) at a dose of 2mg administered 6 hourly.	Medium
<b>Feve</b> Leopold Bellan Hospital Paris, France	End of Life in Parkinson's Disease	<i>Parkinsonism and Related Disorders</i> 2009;15(Supplement 2):S62  (abstract)	Retrospective analysis of medical and nurse reports  12 patients with PD and 2 patients with PDRD dying in the hospital's Parkinson's Unit.	Pain was less common compared to confusion at the end of life.	Low
<b>Gonzalez</b> Hospice of Palm Beach County, Florida, US	Diphenhydramine may be useful as a palliative treatment for patients dying with Parkinson's disease and tremors: a case report and discussion	<i>American Journal of Hospice and Palliative Medicine</i> 2009;26(6):474-5	Case study  1 patient (95F) with PD, dying of heart failure.	The patient was unable to take her oral levodopa/carbidopa and developed severe tremors. Diphenhydramine (25mg subcutaneously every 6 hours) helped alleviate tremors.	Medium



<b>Hindmarsh</b>  City Hospitals Sunderland NHS Foundation Trust, UK	The combination of levomepromazine (methotrimeprazine) and rotigotine enables the safe and effective management of refractory nausea and vomiting in a patient with idiopathic Parkinson's disease	<i>Palliative Medicine</i> 2019;33(1):109-13	Case study  1 patient (64F) with early stage PD	The authors hypothesise that the combination of rotigotine and levomepromazine may be a safe and effective therapeutic option for the management of refractory nausea and vomiting in terminal patients with Parkinson's disease.	Medium
<b>Lee</b>  NHS South of Tyne and Wear Community Health Services, UK	End-of-Life Care Guidance for Parkinson's Disease	<i>British Journal of Neuroscience Nursing</i> 2011;7(3):565	Summary of guidelines generated from consensus opinion of experts.	There are a number of issues at the end of life, including diagnosing dying, excluding reversible causes, withdrawing medications and symptom control (of pain, nausea, secretions, agitation, breathlessness).	Low
<b>Lennaerts</b>  Department of Neurology, Radboud University Medical Centre, The Netherlands	Palliative care for persons with Parkinson's disease: a qualitative study on the experiences of health care professionals	<i>BMC Palliative Care</i> 2019;18(1):53	Interview of 10 and focus group of 29 healthcare professionals who had treated someone with PD in the last two years who had subsequently died.	Healthcare professionals expressed concerns of titrating dopaminergic medication. Issues as to whether leave feeding tubes in place were also expressed.	Low
<b>Perez</b>  Institut Municipal d'Investigació Mèdica Barcelona, Spain	The use of subcutaneous Scopolamine as a Palliative Treatment in Parkinson's Disease	<i>Palliative Medicine</i> 2011; 25(1):92-3	Case report  1 patient (68F) with PD, dying of gastric cancer.	Subcutaneous scopolamine was used successfully to control tremors in a dying patient who was unable to take her oral PD medication and for whom subcutaneous apomorphine and transdermal rotigotine had been unsuccessful.	Low
<b>Sankary</b>  Center for Bioethics Cleveland Clinic, US	Deep Brain Stimulation at End of Life: Clinical and Ethical Considerations	<i>Journal of Palliative Medicine</i> 2020;23(4):582-5	Case report and discussion  1 patient (77M) with PD	There are a number of considerations regarding discontinuing DBS machines at the end of life. Off trials may be helpful to evaluate the ongoing benefit of DBS compared to other comfort measures.	Low
<b>Selge</b>  Department Of Neurology, Ludwig-	Rectal Administration of Baclofen at the End of Life	<i>Journal of Pain and Symptom Management</i> 2018;56(5):e1-e3	2 cases studies, of which 1 is of a patient (76M) dying of PD	Rectal administration of baclofen was successful at relieving rigidity.	Low

Maximilians University, Germany					
<b>Wilcox</b>  Leeds General Infirmary, UK	Extending Palliative Care to Patients with Parkinson's disease	<i>British Journal of Hospital Medicine</i> 2010;71(1):26-30	Review of literature and case study (64F with PD, dying of metastatic breast cancer)	Midazolam and glycopyrronium were used in a syringe driver to relieve distress of being unable to swallow secretions.  Trihexyphenidyl was used to alleviate tremors.	Low

### Abbreviations

ALS = amyotrophic lateral sclerosis

DBS = deep brain stimulation

EoL = end of life

PD = Parkinson's disease

PDRD = Parkinson's disease and related disorders

As anticipated, there is a paucity of literature on the terminal phase of PD. We found seven retrospective studies of patient records at the end of life (Auffret et al. 2019; Bradburn et al. 2013; Butt et al. 2019; Chen et al. 2017; Feve et al. 2009; Ibrahim et al. 2019; Mole 2017), six of which contained mostly quantitative data. All but one of these retrospective studies was a conference abstract with no corresponding published manuscript.

Seven case studies (Dewhurst et al. 2009; Gonzalez 2009; Hindmarsh et al. 2019; Perez et al. 2011; Sankary et al. 2020; Selge et al. 2018; Wilcox 2010) characterised the use of specific medications for patients dying of or with PD. Two papers (Goy et al. 2008; Goy et al. 2007) interviewed bereaved caregivers of Parkinson's patients; a further two papers (Lee 2011; Lennaerts et al. 2019) detailed the experiences of healthcare professionals caring for patients at the end of life.

Gough's 'Weight of Evidence' framework assessed 10 studies as medium and 8 as low WoE.

### **Use of palliative care services**

Not all patients dying with or of PD received input from palliative care services at the end of life.

Retrospective studies of patient records show a variation in the number of patients receiving palliative care involvement, with 15% of patients receiving specialist input in a hospital in France (Auffret et al. 2019) to 73% (Butt et al. 2019) and 77% (Mole 2017) in the UK. 'Formal' end of life pathways, such as the Liverpool Care Pathway (LCP, phased out from 2013), were commenced for 44% (Bradburn et al. 2013) and 65% (Butt et al. 2019) of UK patients. Clinicians reported difficulty diagnosing dying in this cohort of patients (Lee 2011), with patients being started and then subsequently taken off the LCP if their condition improved.

### **Management of the terminal phase**

A number of papers acknowledge that the terminal phase is poorly characterised for PD patients (Butt et al. 2019; Goy et al. 2007; Lennaerts et al. 2019). Consequently, the lack of evidence for therapeutic interventions was perceived to be a barrier to high quality care.

## **Motor symptoms**

### *Dopaminergic medication*

Healthcare professionals highlighted a particular challenge of titrating dopaminergic medication at the end of life, given the need to balance the therapeutic benefits of alleviating motor symptoms versus the side effects of dopaminergic drugs (Lee 2011; Lennaerts et al. 2019). If dopaminergic treatment were to be altered, healthcare professionals recommended that this be done on an individual basis (Lee 2011).

The case studies describe a variety of triggers for consideration of parenteral routes of dopaminergic medication, including intractable nausea and vomiting (Dewhurst et al. 2009; Hindmarsh et al. 2019; Perez et al. 2011; Wilcox 2010), low Glasgow Coma Scale (Gonzalez 2009), tremors (Perez et al. 2011) and dysphagia (Dewhurst et al. 2009).

Retrospective patient records show that while antiparkinsonian medications were prematurely stopped in, on average, a third of patients (24% (Bradburn et al. 2013), 33% (Mole 2017), 42% (Auffret et al. 2019)), administration via non-oral routes was considered in a varying percentage of patients: 7.5% in a hospital in France (Auffret et al. 2019) compared to 90% in a hospital in the UK (Mole 2017). Dosing of parenteral alternatives can also be challenging; one paper concluded that dosing of rotigotine patches was correct in only 39% of a cohort of PD patients at the end of life despite the availability of dosing calculators such as OPTIMAL (Ibrahim et al. 2019).

Only one case report explored the use of deep brain stimulation (DBS) devices at the end of life, recommending that towards the end of life batteries should be replaced in such devices if a supervised 'off trial' had proven that the motor symptoms had worsened when the device had been switched off (Sankary et al. 2020).

### *Terminal complications*

The case studies report successful pharmacological management for specific motor complications, including subcutaneous apomorphine (Dewhurst et al. 2009) and rectal baclofen (Selge et al. 2018) for terminal rigidity and subcutaneous diphenhydramine (Chen et al. 2008; Gonzalez 2009), subcutaneous scopolamine (Perez et al. 2011) and trihexyphenidyl (Wilcox 2010) for severe tremors.

## **Non-motor symptoms**

### *Pain*

Pain was rated as being both frequent and severe in terminal PD (Goy et al. 2008; Goy et al. 2007) , although less prevalent compared to confusion and breathing difficulties (Feve et al. 2009). Continuous subcutaneous morphine was the common choice for analgesia at the end of life (Auffret et al. 2019; Butt et al. 2019; Selge et al. 2018).

### *Nausea and vomiting*

The management of nausea and vomiting can prove to be difficult in PD given the need to avoid D2 antagonists which can precipitate extrapyramidal side effects. Retrospective patient notes demonstrate that these recommendations are not always followed, with a proportion of patients receiving contraindicated anti-emetics at the end of life (9% (Bradburn et al. 2013) and 23% (Mole 2017)). Domperidone is a common pharmacological option for nausea (Dewhurst et al. 2009; Wilcox 2010). One case study recommended the use of levomepromazine with rotigotine patches (Hindmarsh et al. 2019).

### *Psychological, emotional and social symptoms*

Confusion at the end of life is a particular issue, comparably more so in Parkinson's patients compared to those with motor neurone disease (Goy et al. 2008), and more common than pain (Feve et al. 2009). Distress in the dying phase can have physical causes, such as terminal rigidity (Dewhurst et al. 2009), or existential causes, such as feeling like a burden or fearing death (Goy et al.

2008). Subcutaneous midazolam is the most common pharmacological management for anxiety and agitation (Auffret et al. 2019; Butt et al. 2019; Perez et al. 2011; Selge et al. 2018; Wilcox 2010). In the retrospective studies, haloperidol was prescribed for agitation in 3% (Butt et al. 2019) and 24% (Bradburn et al. 2013) of patients, against consensus for treatment and recommendation of guidelines.

Social isolation was perceived by carers to be high for patients with PD, with fewer visits in the last month of life and fewer relatives present at the time of death compared to those with motor neurone disease (Goy et al. 2008).

## **DISCUSSION**

### **Summary of findings**

#### *Use of palliative care services*

The retrospective studies of patient records provide a limited understanding of what the current standards of care are for patients with PD at the end of life, and prudent extrapolation is necessary given that they are all single centre studies with a low number of participants. Nonetheless, as far as we are able to determine from these studies, it appears that a proportion of patients with PD does not receive formal palliative care input.

Despite the small numbers of studies and patients, these findings are in keeping with what is known about managing PD at the end of life. There is a marked difficulty in prognostication: the prolonged course of the disorder (Glover and Kluger 2019) and the unpredictable disease trajectory (Campbell et al. 2010) make anticipating and preparing for terminal events problematic. Equally, there are few reliable indicators or 'red flags' that signal the terminal phase (Richfield et al. 2013), meaning that referrals to palliative care services may be delayed or missed entirely. In the retrospective studies, no analysis is provided as to whether palliative care input differed depending on whether the patient

was dying *with* or *of* their PD. It would be interesting in future studies to differentiate if patients with PD were more likely to receive specialist palliative care input if they were admitted due to a more commonly 'palliated' condition, e.g. malignancy.

All but two papers (Goy et al. 2008; Goy et al. 2007) concern patients dying in a hospital. The experience of GPs and community nursing teams looking after PD patients in homes or nursing/residential facilities is almost non-existent, and thus the particular struggles that primary and community care clinicians face cannot be enacted upon. Further studies are needed to determine where expertise from specialist palliative or PD colleagues may be needed to improve care.

### *Management of terminal symptoms*

Despite some papers suggesting that no formal guidelines for management of PD patients at the end of life exist, the UK has published guidelines in the Palliative Care Formulary (PCF 2020). Anecdotally, we know that they are not widely known by non-specialist practitioners who may see the patient initially.

### *Motor symptoms*

The motor symptoms in the terminal phase are poorly characterised. The case studies report that tremor and rigidity are common terminal motor complications, but there is no current data on the prevalence or severity of specific motor symptoms from larger cohort studies.

There is a general consensus to continue dopaminergic medication in the terminal phase (Richfield et al. 2013) particularly if the patient is dying with and not of PD (PCF 2020). Abrupt discontinuation of levodopa derivatives, which was documented in some of the retrospective studies, is regarded as poor practice given that it is associated with worsening of motor function, pain and, very rarely, Parkinson hyperpyrexia syndrome (Glover and Kluger 2019). Equally, if dopamine agonists are not tapered slowly, this can precipitate Dopamine Agonist Withdrawal Syndrome (DAWS), characterised

by anxiety and panic attacks (Richfield et al. 2013). DBS devices should also be continued in the dying phase (Katz et al. 2018; Sankary et al. 2020). If dopaminergic medication is to be reduced it should always be done on an individual basis and under the supervision of a movement disorder specialist (PCF 2020); practical guides for doing so – such as how often to assess dopaminergic response and how to taper doses – currently do not exist. Such guidelines would be particularly useful for the generalist clinician where there is limited access to specialist Parkinson's services.

The case studies demonstrate that there is good awareness of consideration of parenteral routes if oral dopaminergic medication cannot be continued. The case studies describe multiple options, many of which (scopolamine, diphenhydramine, baclofen) are off-label indications and not included in national formularies. In contrast, the UK Palliative Care Formulary advises the use of subcutaneous apomorphine, transdermal rotigotine and subcutaneous midazolam at the end of life (PCF 2020). However, as described in one case study (Perez et al. 2011), if these recommended options fail, there is uncertainty about what medication to try next. Further studies for successful management of motor complications is needed to provide a robust evidence base for alternative pharmacological options.

### *Non-motor symptoms*

It is recommended that symptoms at the end of life are 'deconstructed' in order to determine if there are potentially more treatable causes of pain or delirium, for example intercurrent infections or constipation (Glover and Kluger 2019; Richfield et al. 2013). Pain at the end of life in PD is multifactorial, with central pain, dystonic pain and neuropathic pain being common aetiologies (Campbell et al. 2010), which should prompt careful evaluation to guide appropriate treatment (PCF 2020). No paper discusses the prevalence of different aetiologies of pain in patients with PD at the end of life, or considers appropriate non-pharmacological management.



Studies show good awareness for avoiding D2 antagonists in the management of nausea and delirium. Nonetheless, there is evidence that these medications still get prescribed. It may be that anticipatory medication ‘bundles’, that are particularly common on electronic prescribing systems, and which will often include medication contraindicated in PD, contributes to these prescribing errors. PD specific anticipatory medication care-sets should be developed to prevent such events occurring, as promoted by one paper in the study (Bradburn et al. 2013).

Only one paper explored the existential and spiritual dimensions of the terminal phase of PD patients, highlighting that patients with PD feel high levels of isolation (Goy et al. 2008). More studies are needed to determine whether such findings are more widely universal and to develop appropriate interventions to mitigate loneliness in the last weeks and days of life.

### *Study limitations*

We aimed to include all papers that characterised ‘terminal symptoms’, which we had defined as the last weeks and days of life. Practically, this was difficult to achieve, as some papers did not specify the time period over which patients were dying.

The majority of the retrospective studies of patient records were conference abstracts with no corresponding manuscript; they therefore offer limited data as they are not full text papers. These studies had low numbers of patients and, in conjunction with the single patient case studies, mean that our data is from a very small sample of PD patients and therefore may not be representative.

## **CONCLUSIONS AND DIRECTIONS FOR FUTURE RESEARCH**

This systematic review highlights that there is still little published evidence on the prevalence and severity of symptoms in the terminal phase for patients with PD. The limited papers obtained from the review highlight that clinicians face uncertainty when managing the dying phase, and adherence to recommended practice could and should be improved. Further studies to capture the experience

of patients, carers and healthcare professionals in both hospital and community settings is needed to establish the current landscape of care and to direct efforts in developing clinical guidelines to help generalists care for this population of patients. Quality standards for care at the end of life need to be generated to facilitate evaluation of services and overall improve patient experience.

## KEYWORDS

Palliative care

Parkinson's disease

Terminal care

Movement disorders

Advance care planning

## KEYPOINTS

What was already known?

- Extending palliative care to those with PD has been a priority over the last two decades

What are the new findings?

- There remains limited evidence on the prevalence and severity of symptoms in the terminal phase

What is their significance?

- Further studies of patients in hospital and community settings is needed to improve terminal care

## REFLECTIVE QUESTIONS

1. Dopaminergic medication in the advanced stages of Parkinson's disease can be less effective.

How would you meaningfully assess a patient's response to dopaminergic medication?

2. If quality standards were to be developed to evaluate and audit end of life care for patients with Parkinson's disease, what would you include?

3. How can advance care planning be used to prepare patients and their families for the end of life?

How often should these plans be reviewed?

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