

# Content and impact of pharmacy services for patients with Parkinson's disease

## A systematic review and meta-analysis

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### Abstract

**Background:** Medicines optimisation is important for the management of Parkinson's disease (PD). As many patients with PD have other long-term conditions, treatment is complex and risk of adverse events for these patients is high.

**Objective:** To explore the role of pharmacists and impact of pharmacy interventions for PD patients.

**Methods:** We comprehensively searched PubMed, Embase, the Cochrane Library and Chinese databases Sinomed, China National Knowledge Infrastructure to identify studies reporting pharmacist interventions and pharmacy services for PD patients using a predefined search strategy. The search period was from inception to March 2019. We also manually searched the reference list of included studies and ClinicalTrials.gov. We conducted meta-analyses to synthesize the evidence quantitatively.

**Results:** A total of 1607 studies were identified by applying the search criteria. After screening, 19 cross-sectional and case-controlled studies with 1458 PD patients from 9 countries were included. Pharmacist interventions for PD patients most commonly related to adverse drug reactions (ADRs) (13 studies), adherence assessment (12 studies), medication review (12 studies), identification of drug interactions (11 studies), monitoring response to medication therapy (11 studies), identification of inappropriate medication (11 studies), and patient education (10 studies). Most pharmacy services were provided in outpatient settings (13 studies). Reported impact measures included adherence (8 studies), quality of life (7 studies), and identification of drug-related problems (6 studies) such as ADRs (393 times out of 1760 times, 22.33%, 6 studies), inappropriate drug choice (349 times, 19.83%, 6 studies), inappropriate dosage (335 times, 19.03%, 6 studies), inappropriate drug use (257 times, 14.60%, 3 studies) and drug-drug interactions (146 times, 8.3%, 4 studies). Pooled results from 3 studies indicated no statistically significant impact of pharmacy services on all subscales of PD Questionnaire-39.

**Conclusion:** ADRs were the most widely reported drug-related problems for PD patients; pharmacy services may have a role to play in medication adherence but were not found to impact on quality of life.

**Abbreviations:** ADRs = adverse drug reactions, CIs = confidence intervals, DRPs = drug-related problems, MD = mean difference, PD = Parkinson's disease, PDQ = Parkinson's disease questionnaire, QoL = quality of life, RCTs = randomized controlled trials.

**Keywords:** drug-related problems, medication adherence, parkinson's disease, pharmaceutical service, quality of life

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## 1. Introduction

Parkinson's disease (PD) is a common neurodegenerative disease, characterized by progressive degeneration of dopaminergic neurons and pathological changes in the formation of Lewy bodies, and decreased dopamine transmitters in the striatum.<sup>[1]</sup> The estimated incidence of PD is 10 to 18 per 100,000 person-years globally<sup>[1]</sup> and 250 persons per 100,000 in the UK.<sup>[2]</sup> Epidemiological studies indicate that the prevalence of PD in the Chinese population aged 65 and over is 1.7%, and that this is rising as the population is aging, in common with global estimates of large increases in PD prevalence.<sup>[3]</sup> As a consequence, the treatment and management of PD patients represent a growing financial burden due to the high medication costs, hospitalization and productivity loss associated with the progression of PD.<sup>[1]</sup>

Choice of medication for PD patients is complicated, and is dependent on age of disease onset and stage of disease development.<sup>[4]</sup> Moreover, because PD patients often have a variety of comorbidities and require multiple therapeutic drugs, and are therefore likely to experience polypharmacy, PD patients are at an increased risk of drug interactions.<sup>[5]</sup> In addition, as the course of disease progresses, the likelihood of adverse events such as hypotension and hallucinations increases, which further complicates treatment decisions.<sup>[6]</sup> As a consequence, pharmacists can play an important role in improving medicines optimisation for PD patients, ensuring the safe and rational use of medication.

Pharmacists have a role in assessing patients' previous medication history, drug allergy history, adverse events, and drug interactions, especially for multiple drugs and low safety index drugs. Martin et al conducted a cluster randomized trial on the effectiveness of a pharmacist-led educational intervention for older adults, and found greater discontinuation of prescriptions for inappropriate medication after 6 months compared with usual care.<sup>[7]</sup> Meanwhile, from an economic perspective, pharmacists' participation in drug treatment management can reduce drug-related problems (DRPs) and by preventing medication errors and other associated costs pharmacists' contributions to patient care are cost effective.<sup>[8]</sup>

Pharmacy services for PD patients are also becoming popular. Such services include pharmacists participating in outpatient clinics, reviewing patients' previous medicines, providing drug information, patient education, evaluating medication adherence, and monitoring drug treatment effects.<sup>[9]</sup> The results of a number of pharmacy service evaluations have shown that patients' adherence and quality of life (QoL) improved following pharmacist intervention.<sup>[10,11]</sup> However, a theory or logic model for how pharmacist interventions and pharmacy services produce these outcomes for PD patients and the likely causal mechanisms through which pharmacist interventions and pharmacy services work, and the influence of context on mechanisms and outcomes, have not been established. The first step in addressing this gap is to undertake a systematic review to identify what is already known about pharmacist interventions and pharmacy services for PD patients and the methods that have been used to evaluate them. In this study, we investigate the role of pharmacists and impact of pharmacy interventions for PD patients as a precursor to devising a logic model useful for informing future design and evaluation of a complex intervention for PD patients.

## 2. Materials and methods

### 2.1. Search strategy

We searched PubMed, Embase, the Cochrane Library, and 2 Chinese databases including Sinomed and China National Knowledge Infrastructure from inception to March 26th, 2019 to identify studies reporting findings related to pharmacy service for PD. The search terms included the following keywords

“Parkinson's disease”, “pharmacist”, “pharmaceutical care”, “pharmaceutical service”, “medication therapy management” and “drug-related problems” (Appendix 1, Available at: <http://links.lww.com/MD/E417>). We also manually searched the reference list of the included studies. We limited the language of articles to English and Chinese only, but had no limits on the type of pharmacy service or on the country in which the service was provided. We also manually searched the reference list of the included studies and ClinicalTrials.gov as a supplementary source for relevant literature. Experts in this field of study were consulted for advice regarding the search strategy. The systematic review with meta-analysis was registered on PROSPERO (No. CRD 42018107614). However, because it is a systematic review and meta-analysis it is exempt from requiring ethical approval, as the study involves analysis of previously published, anonymized data.

### 2.2. Study selection and outcome measures

The investigators worked in pairs (TTL and QYT; TTL and ZMY) to manually screen the references of all retrieved records for potentially relevant studies, beginning with title and abstract screening in the first stage, and full-text screening in the second. In the title and abstract screening stage, studies appearing to meet the inclusion criteria, or with insufficient information to make a clear judgment, were included in the full-text screening process. We obtained full texts of all these studies for the full-text screening. We included studies if they reported on pharmacy services for PD patients where either a description of the content or outcomes of a pharmacy service was given. Studies using randomized controlled trials or observational designs were included. All disagreements about study selection were resolved through discussion amongst the team.

Primary outcomes extracted for inclusion in the review were contents of pharmacy services and evidence of impact of the pharmacy service on patients. Secondary outcomes extracted included types and methods for measuring impact and outcomes of pharmacy service.

### 2.3. Data extraction and quality assessment

Data extraction was performed by the same 2 pairs (TTL and QYT; TTL and ZMY) using a pre-designed data collection tool. The following information was extracted from included studies: first author, publication year, country, patient source, number of patients, age, gender, duration of PD, number of medications/PD medications per patient, content and outcomes of pharmacy services.

We assessed the risk of bias of randomized controlled trials included in this study using the Cochrane collaboration tool, and used the ROBINS-I tool for other study designs.<sup>[12]</sup> The ROBINS-I tool for assessing risk of bias considers bias due to confounding, classification of participants, classification of intervention,

missing data, outcome measurements, and selective outcome reporting. The categories for risk of bias judgements are “low risk”, “moderate risk”, “serious risk” and “critical risk” of bias. The assessment was independently performed by TTL and QYT, and any discrepancies were resolved through discussion with ZMY.

### 2.4. Statistical analysis

We explored treatment effect through meta-analysis in an intention to treat manner (following the allocation of participants in studies). We pooled results of the same types of studies evaluating similar interventions in similar participants. We calculated the mean difference (MD) with 95% confidence intervals (CIs) for continuous outcomes and risk ratio for categorical outcomes. We performed meta-analyses with RevMan 5.3 software using the random-effect model. Statistical heterogeneity was assessed with the Mantel-Haenszel chi-square test and quantified with the  $I^2$  test ( $P$ -value of heterogeneity was .10). Sensitivity analysis was conducted by changing the random-

effect methods to fixed-effect methods to pool the trials in terms of heterogeneity of findings. Finally, publication bias was examined by funnel plot if the number of included studies was over 10.

## 3. Results

### 3.1. Study selection

The initial search identified 1605 relevant records, with a further 2 additional records identified through other sources (consultation with PD experts). Of these, 1529 were excluded after duplicates were removed and title/abstract screening, leaving 78 papers eligible for full-text review. Of these 19 studies met the inclusion criteria<sup>[9-11,13-28]</sup> involving 1458 PD patients. Figure 1 provides details of the reasons for excluding studies from this review. The 2 included studies Schröder 2012 and Schröder 2011 included the same group of PD patients, thus the number of included PD patients were calculated once and similar information of the 2 studies were merged in Tables 1 and 3 and Table 5.

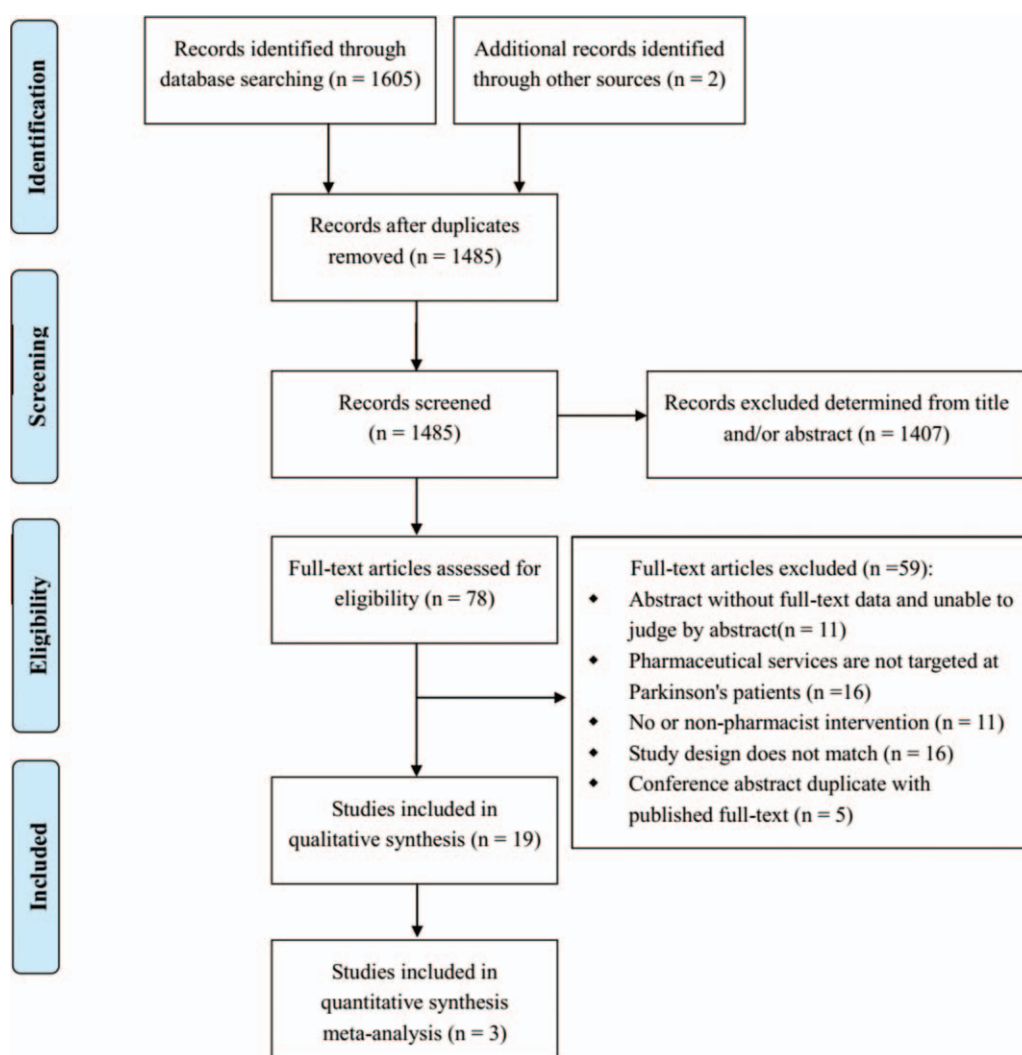


Figure 1. Flow diagram for literature search and study selection.

**Table 1**  
**Characteristics of included studies.**

Study (First author, publication year)	Country	Patient source	No. of patients	Age (mean, yr)	Male (%)	Duration of PD (mean, year)	No. of medications per patient (median)	No. of PD medications per patient (median)
Chemello 2014 <sup>[13]</sup>	Brazil	Patients with an appointment in a pharmacy training unit of the university	57	71.4	54.4	6.44	4.7	2.3 (mean)
Foppa 2016 <sup>[10]</sup>	Brazil	Patients registered in a community pharmacy	70	69.4	64.3	NR	NR	NR
Henrichsmann 2016 <sup>[23]</sup>	Germany	Deutsche Parkinson Vereinigung e.V.	90	73.0 (median)	56.7	11.0 (median)	NR	NR
Mah 2016 <sup>[19]</sup>	Canada	A geriatrics Parkinson's Clinic	86	79.0	NR	NR	11	NR
Martin 2018 <sup>[26]</sup>	US	Pharmacist-led neurology clinic within a Veterans Affairs Medical Center	21	NR	NR	NR	NR	NR
Mynors 2007 <sup>[14]</sup>	UK	Volunteers from the Parkinson's disease Society	145	69.9	55.2	5.0 (median)	NR	NR
Poon 2012 <sup>[9]</sup>	US	A Veterans Affairs outpatient clinic	131	69.0	96.0	9.1 (mean)	10	2
Schröder 2012 <sup>[15]</sup> / Schröder 2011 <sup>[16]</sup>	Germany	Outpatients	100 versus 61 (intervention versus comparison)	71.3 versus 71.4	52.0 versus 60.7	8.4 versus 9.0	NR	NR
Shueb 2012 <sup>[11]</sup>	Malta	Outpatient neurology clinic	35	74.0 (mean)	54.0	6.0 (median)	NR	NR
Stefan 2018 <sup>[17]</sup>	US	Outpatient neurology clinic	10	70.0 (mean)	100	NR	NR	NR
Stuijt 2018 <sup>[8]</sup>	Netherlands	Outpatient neurology clinic	23	66.8	61.0	10.3	8.2	3.0
Suansanae 2014 <sup>[22]</sup>	Thailand	Outpatient dispensing unit	20	NR	NR	NR	NR	NR
Verbeek 2016 <sup>[20]</sup>	Netherlands	NR	66	71.5	NR	NR	8.1	NR
Wijma-Vos 2015 <sup>[21]</sup>	Netherlands	Groningen Parkinson's short Stay ward	22	NR	NR	NR	NR	NR
Wong 2018 <sup>[27]</sup>	UK	Pharmacist led clinic	61	NR	NR	NR	NR	NR
Yi 2018 <sup>[25]</sup>	China	An outpatient neurology clinic and inpatient specialist consultations	255	Outpatients: <65 (n=65, 25.8%), ≥65 (n=187, 74.2%); Inpatients: ≥80 (n=3, 100.0%)	44.7	NR	Outpatients: 0~2 (n=144, 57.1%), 3~4 (n=103, 40.9%), ≥5 (n=5, 2%) Inpatients: 5~10 (n=1, 33.3%), 11~15 (n=1, 33.3%), ≥1 (n=1, 33.3%)	NR
Zhang 2018 <sup>[24]</sup>	China	An outpatient neurology clinic	97	38-84 (range)	49.48	NR	NR	NR
Zhang 2019 <sup>[28]</sup>	China	Hangzhou linan district people's hospital	108	65	46.7	NR	NR	NR

No. = number, NR=no reported, SD = standard difference.

**Table 2**  
Quality of included studies with the risk of bias in non-randomised studies of interventions tool.

Study (First author, publication year)	Pre-intervention		At intervention	Post-intervention				Overall bias
	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	
Chemello 2014 <sup>[13]</sup>	Low	Low	Low	No information	No information	Moderate	Critical	Critical
Foppa 2016 <sup>[10]</sup>	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Henrichsmann 2016 <sup>[23]</sup>	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Martin 2018 <sup>[26]</sup>	Critical	Critical	Low	Moderate	Low	Low	Low	Critical
Mynors 2007 <sup>[14]</sup>	Low	Low	Low	Serious	Serious	Moderate	Low	Serious
Poon 2012 <sup>[9]</sup>	Low	Low	Serious	Low	Low	Serious	Moderate	Serious
Schröder 2011 <sup>[16]</sup>	Serious	Low	Low	Low	Low	Moderate	Low	Serious
Schröder 2012 <sup>[15]</sup>	Serious	Low	Low	Moderate	Low	Moderate	Low	Moderate
Shueb 2012 <sup>[11]</sup>	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Stefan 2018 <sup>[17]</sup>	Low	Low	Moderate	Low	Low	Moderate	Moderate	Moderate
Stuijt 2018 <sup>[18]</sup>	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Yi 2018 <sup>[25]</sup>	Critical	Critical	Low	Critical	Low	Low	Low	Critical
Zhang 2018 <sup>[24]</sup>	Low	Low	Low	Moderate	Moderate	Low	Low	Moderate
Zhang 2019 <sup>[28]</sup>	Moderate	Low	Low	Low	Critical	Low	Low	Moderate

**3.2. Study characteristics and quality assessment**

The 19 included studies were from 9 countries: three were conducted in the Netherlands,<sup>[15,16,23]</sup> Germany,<sup>[15,16,23]</sup> the United States,<sup>[9,17,26]</sup> China,<sup>[24,25,28]</sup> 2 were in Brazil<sup>[10,13]</sup> and in the UK.<sup>[14,27]</sup> Others were conducted in Canada, Malta and Thailand. The number of patients enrolled in a study ranged from 10 to 255, with patients aged, on average, over 65; the proportion of male patients ranged from 44.7% to 100%; duration of diagnosis of PD ranged from 5 to 11 years. Number of medicines per-patient ranged from 4 to over 15 and number of PD medicines ranged from 2 to 3 (see Table 1 for further details).

Follow-up time varied as follows: Chemello 2014: 1 month,<sup>[13]</sup> Foppa 2016: 6 months,<sup>[10]</sup> Henrichsmann 2016: 4 months,<sup>[23]</sup> Mynors 2007: 6 months,<sup>[14]</sup> Schröder 2012: 8 months,<sup>[15]</sup> Shueb 2012: 2 months,<sup>[11]</sup> Stuijt 2018: 10 weeks, 14 weeks, 26 weeks,<sup>[18]</sup> Zhang 2018: 1 month,<sup>[24]</sup> Zhang 2019: 6 months<sup>[28]</sup>; all other studies included did not provide details of follow-up time.

Applying the ROBINS-I tool to the 19 studies that used a cross-sectional studies or case-control design, 8 studies were categorised as moderate risk,<sup>[10-11,15,17-18,23-24,26]</sup> 3 were of serious risk,<sup>[9,14,16]</sup> and 3 were of critical risk of bias<sup>[13,25,26]</sup> (Table 2). Due to different risk of bias of the 2 included studies Schröder 2012 and Schröder 2011, the evaluation results were showed separately. We were unable to assess the risk of bias of 5 conference abstracts because of limited information provided.

**3.3. Contents of pharmacy services**

Content of the pharmacy services evaluated included helping with identifying, resolving or preventing adverse drug reactions (ADRs) (13 studies),<sup>[9-10,13-16,18-19,22-23,25-27]</sup> adherence assessment (12 studies),<sup>[9-11,13-14,17-18,22-24,27-28]</sup> medication review (12 studies),<sup>[9-11,13-18,20,23,27]</sup> identification of inappropriate medication (11 studies),<sup>[9-10,13-16,18,21-23,25]</sup> monitoring response to medication therapy (11 studies),<sup>[9-10,13-17,19,21-23]</sup> identification of drug interaction (11 studies),<sup>[9-10,13-16,18,21-23,25]</sup> patient education (10 studies),<sup>[9-11,14,17-18,22-25]</sup> provision of drug information (8 studies),<sup>[9-10,13-16,23,25]</sup> unit dose

packaging (1 study)<sup>[18]</sup> and Parkinson KinetiGraph Alarm (1 study)<sup>[18]</sup> (Table 3).

**3.4. Setting of pharmacy services**

Most pharmacy services were provided in outpatient clinic (13 studies),<sup>[9,11,15-19,22-27]</sup> although some were located in both outpatient and inpatient settings<sup>[25]</sup> (see Table 1).

**3.5. Reported outcome measures of pharmacy services**

**3.5.1. Drug-related problems.** The studies included in this review used a number of different measures to determine outcomes or impact of the pharmacy services being investigated. The most widely reported outcomes were DRPs with times of drug-related problems per participant ranging from 1.58 to 3.66; of these, the most frequently occurring were ADRs (393 out of 1760 times, 22.33%, 6 studies),<sup>[10,14,16,23,25-26]</sup> inappropriate drug choice (349 times, 19.83%, 6 studies),<sup>[10,14,16,23,25-26]</sup> inappropriate dosage (335 times, 19.03%, 6 studies),<sup>[10,14,16,23,25-26]</sup> inappropriate drug use (257 times, 14.60%, 3 studies)<sup>[10,14,16]</sup> and drug-drug interactions (146 times, 8.3%, 4 studies)<sup>[14,16,23,25]</sup> (Table 4). The included studies only reported DRPs found by pharmacists during the evaluation period and hence no DRPs that occurred before this were included for comparison to establish change or difference in number of DRPs following introduction of a service; furthermore, no studies involved a control group for comparison of number and type of DRPs, preventing comparison between intervention and non-intervention groups that would allow for measurement of intervention effect.

**3.5.2. Medication adherence and QoL.** In addition to DRPs and pharmacist interventions, a number of studies used patient-reported outcome measures of medication adherence (8 studies)<sup>[10-11,13-14,18,23-24,28]</sup> and QoL (7 studies).<sup>[10-11,13-15,18,20]</sup> Six case-control studies of the 8 studies showed that pharmacy services improved patient adherence comparing with baseline data.<sup>[10-11,18,23-24,28]</sup> One study showed no statistically significant difference in adherence.<sup>[14]</sup> One study only reported the percentage of non-adherent patients.<sup>[13]</sup> However, due to



**Table 3**  
Content of pharmacy services for Parkinson’s disease patients of included studies.

Study (First author, publication year)	UDP	PKG Alarm	MR	Identification of drug interactions	Identification of inappropriate medication	Help with processing ADR	Monitoring response to medication therapy	Patient education	Provision of drug information	Adherence assessment
Chemello 2014 <sup>[13]</sup>	×	×	✓	✓	✓	✓	✓	×	✓	✓
Foppa 2016 <sup>[10]</sup>	×	×	✓	✓	✓	✓	✓	✓	✓	✓
Henrichsmann 2016 <sup>[23]</sup>	×	×	✓	✓	✓	✓	✓	✓	✓	✓
Mah 2016 <sup>[19]</sup>	×	×	×	×	×	✓	✓	×	×	×
Martin 2018 <sup>[26]</sup>	×	×	×	×	✓	✓	×	×	×	×
Mynors 2007 <sup>[14]</sup>	×	×	✓	✓	✓	✓	✓	✓	✓	✓
Poon 2012 <sup>[9]</sup>	×	×	✓	✓	✓	✓	✓	✓	✓	✓
Schröder 2012 <sup>[15]</sup> / Schröder 2011 <sup>[16]</sup>	×	×	✓	✓	✓	✓	✓	×	✓	×
Shueb 2012 <sup>[11]</sup>	×	×	✓	×	×	×	×	✓	×	✓
Stefan 2018 <sup>[17]</sup>	×	×	✓	×	✓	×	✓	✓	×	✓
Stuijt 2018 <sup>[18]</sup>	✓	✓	✓	✓	✓	✓	×	✓	×	✓
Suansanae 2014 <sup>[22]</sup>	×	×	×	✓	✓	✓	✓	✓	×	✓
Verbeek 2016 <sup>[20]</sup>	×	×	✓	×	×	×	×	×	×	×
Wijma-Vos 2015 <sup>[21]</sup>	×	×	×	✓	✓	×	✓	×	×	×
Wong 2018 <sup>[27]</sup>	×	×	✓	×	×	✓	×	×	×	✓
Yi 2018 <sup>[25]</sup>	×	×	×	✓	✓	✓	×	✓	✓	×
Zhang 2018 <sup>[24]</sup>	×	×	×	×	×	×	×	✓	×	✓
Zhang 2019 <sup>[28]</sup>	×	×	×	×	×	×	×	×	×	✓

× = not included, ✓ = included, ADR=adverse drug reaction, MR=medication review, PKG Alarm=Parkinson Kineti Graph Alarm, UDP=unit dose packaging.

inconsistency in adherence scales and methods for reporting adherence used by different studies, it was not possible to undertake a meta-analysis of medication adherence.

QoL was evaluated using either the PD questionnaire (PDQ)-8 or the PDQ-39. Two of the 7 studies showed no statistically significant difference in QoL after the intervention. One study only reported patients’ baseline QoL, 1 study reported results of the PDQ-8 scale, and 3 studies provided evidence of some subscales of PDQ-39 improving, although results were inconsistent when findings of different studies were compared. The pooled PDQ-39 data of 3 studies <sup>[10,14,20]</sup> indicated no statistically significant change in the mobility subscale (MD = 2.67, 95% CI -2.40 to 7.74), activities of daily living subscale (MD = 2.08, 95% CI -2.56 to 6.72), emotional well-being subscale (MD = -1.10, 95% CI -8.86 to 6.67), stigma subscale (MD = 0.19, 95% CI -4.62 to 4.99), social support subscale (MD = 2.39, 95% CI -2.79 to 7.56), cognition subscale (MD = 1.21, 95% CI -3.11 to 5.53), communication subscale (MD = 0.60, 95% CI -4.08 to 5.27) and bodily pain subscale (MD = 3.09, 95% CI -1.85 to 8.03) (see Fig. 2 for details). However, further

analysis of PDQ-8 data could not be undertaken due to only 1 study presenting relevant data.<sup>[18]</sup>

Eleven studies<sup>[9–10,23,14–18,21,25–26]</sup> reported impact in relation to the number of pharmacist interventions made – with the number of interventions recorded ranging from 49 to 474 and frequency of interventions per patient ranging from 0.5 to 7.2. Improved results in PDQ-39 and adherence were shown in patients receiving more interventions; for example, improvements in QoL and adherence were reported by Foppa 2016 and Stuijt 2018 where an average of 5.8 and 7.2 interventions were made per patient, respectively (Table 5).

**3.5.3. Other outcome measures.** Change in motor/ non-motor symptoms<sup>[10,18,23]</sup> and surveys capturing beliefs about medicines<sup>[18]</sup> were also used to establish impact, with considerable variation in results reported. One study indicated that clinic providers and patients were satisfied with pharmacist’s services (4.79 points using a 5-point Likert scale).<sup>[9]</sup> Four studies reported findings related to medication therapy management service for PD patients<sup>[10,17,23,25]</sup> (Table 5).

**Table 4**  
Drug-related problems in included studies.

Studies	Participants (n, %)	Type and times of drug-related problems						Times of drug-related problems per participant
		Adverse drug reaction (times, %)	Inappropriate drug choice (times, %)	Inappropriate dosage (times, %)	Inappropriate drug use (times, %)	Drug-drug interactions (times, %)	Other problems (times, %)	
Mynors 2007	145 (20.89)	71 (13.37)	127 (23.92)	60 (11.30)	149 (28.06)	6 (1.13)	118 (22.22)	3.66
Schröder 2011	113 (16.28)	44 (13.29)	41 (12.39)	52 (15.71)	65 (19.64)	31 (9.37)	98 (29.61)	2.93
Henrichsmann 2016	90 (12.97)	138 (41.95)	73 (22.19)	18 (5.47)	0 (0.00)	95 (28.88)	5 (1.52)	3.66
Foppa 2016	70 (10.09)	36 (31.03)	18 (15.52)	19 (16.38)	43 (37.07)	0 (0.00)	0 (0.00)	1.66
Martin 2018	21 (3.03)	5 (10.20)	13 (26.53)	17 (34.69)	0 (0.00)	0 (0.00)	14 (28.57)	2.33
Yi 2018	255 (36.74)	99 (24.50)	77 (19.06)	169 (41.83)	0 (0.00)	14 (3.47)	45 (11.14)	1.58

Inappropriate drug use included poor understanding of medicine or treatment, poor understanding of condition and compliance problems.

**Table 5**  
**Outcomes of pharmacy services for Parkinson's disease patients of included studies.**

Study (First author, publication year)	Quality of life (mean ±SD) (baseline versus follow up)	Medication adherence	Pharmaceutical interventions (n)	Pharmaceutical interventions per patient (n)	Symptom relief (motor/nonmotor symptoms)	Medication benefit
Chemello 2014 <sup>[13]</sup>	PDQ-39 (baseline global score): 39.2 ± 19.3	Moriski- Green-Levine:42% non-adherent	NR	NR	NR	NR
Foppa 2016 <sup>[10]</sup>	PDQ-39: emotional well-being: 39.12 ± 26.54 versus 36.89 ± 27.56, <i>P</i> = .012	Decline from 37 to 10 non-adherent patients ( <i>p</i> < 0.001).	404	5.8	On/off state not vary; all the nonmotor symptoms relieved	NR
Henrichsmann 2016 <sup>[23]</sup>	NR	9.9% of the patients had a low adherence score	95	1.1	UPDRS and MDS-UPDRS improved by a median of 1–2 point, <i>P</i> < .05	NR
Mah 2016 <sup>[19]</sup>	NR	NR	NR	NR	NR	NR
Martin 2018 <sup>[26]</sup>	NR	NR	49	2.3	NR	NR
Mynors 2007 <sup>[14]</sup>	PDQ-39: emotional well-being 35.45 ± 22.81 versus 28.94 ± 25.63, <i>P</i> = -.28; stigma 30.05 ± 26.31 versus 28.94 ± 25.36, <i>P</i> = -.04; cognitions 40.63 ± 23.80 versus 39.95 ± 25.13, <i>P</i> = -.03	MARS scores:23.17 ± 2.02 versus 23.16 ± 2.15	443	3.1	NR	NR
Poon 2012 <sup>[9]</sup>	NR	NR	69	0.5	NR	NR
Schröder 2012 <sup>[15]</sup> / Schröder 2011 <sup>[16]</sup>	Pharmacy group similar to comparison group	NR	474	4.7	NR	NR
Shueb 2012 <sup>[11]</sup>	PDQ-39: mobility 49.3 versus 45.9, <i>P</i> = .038; ADL 57.1 versus 51.9, <i>P</i> = .006; social support 42 versus 29.9, <i>P</i> = .01	A statistically significant improvement ( <i>P</i> = .00)	NR	NR	NR	NR
Stefan 2018 <sup>[17]</sup>	NR	NR	49	4.9	NR	NR
Stuijt 2018 <sup>[18]</sup>	PDQ-8 scores: 20.9 ± 3.5 versus 19.2 ± 5.3 (UDP + PKG alarm + MR versus UDP + PKG alarm), <i>P</i> = .01	MARS score: 47.9% (±29.6) versus 59.1% (±27.8), <i>P</i> = .049	165	7.2	Motor symptom:54% (±30) versus 68% (±27); No significant effects on NMS	BMQ:55.3% (±32.3) versus 68.6% (±29.4) <i>P</i> = .035
Suansanae 2014 <sup>[22]</sup>	NR	NR	NR	NR	NR	NR
Verbeek 2016 <sup>[20]</sup>	PDQ-39: control versus intervention (baseline, SE): 31.1 (3.1) versus 31.0 (4.0); change from baseline after 6 months (SE): 0.8 (1.8) versus 6.0 (3.1)	NR	NR	NR	NR	NR
Wijma-Vos 2015 <sup>[21]</sup>	NR	NR	51	2.3	NR	NR
Wong 2018 <sup>[27]</sup>	NR	NR	NR	NR	NR	NR
Yi 2018 <sup>[25]</sup>	NR	NR	404	1.6	NR	NR
Zhang 2018 <sup>[24]</sup>	NR	Morisky:1.88 ± 1.00 versus 0.75 ± 0.91	NR	NR	NR	NR
Zhang 2019 <sup>[28]</sup>	NR	Morisky: intervention: good and moderate adherence from n = 42 to n = 56, bad from n = 21 to n = 7 versus control: from n = 36 to n = 32 and from n = 9 to n = 13	NR	NR	NR	NR

ADL = activities of daily living, BMQ = beliefs about medicines questionnaire, DRPs = drug-related problems, MARS = medication adherence response scale, MDS-UPDRS = movement disorder society unified Parkinson's disease rating scale, NMS = nonmotor symptoms, NR = not reported, PDQ-8 = Parkinson's disease questionnaire with 8 domains, SE = standard error, UPDRS = unified Parkinson's disease rating scale.

**3.6. Sensitivity analysis and publication bias**

The *I*<sup>2</sup> of pooled results of emotional well-being subscale of PDQ-39 was 68% indicating heterogeneity among pooled studies (Fig. 2). As a result, we conducted a sensitivity analysis by changing the random-effect methods to fixed-effect methods to pool the trials and the results remained unchanged. Due to a

limited number of included studies used to provide data related to the pooled outcome, we could not assess risk of publication bias.

**4. Discussion**

We conducted a systematic review to identify the role of pharmacists and impact of pharmacy interventions for PD

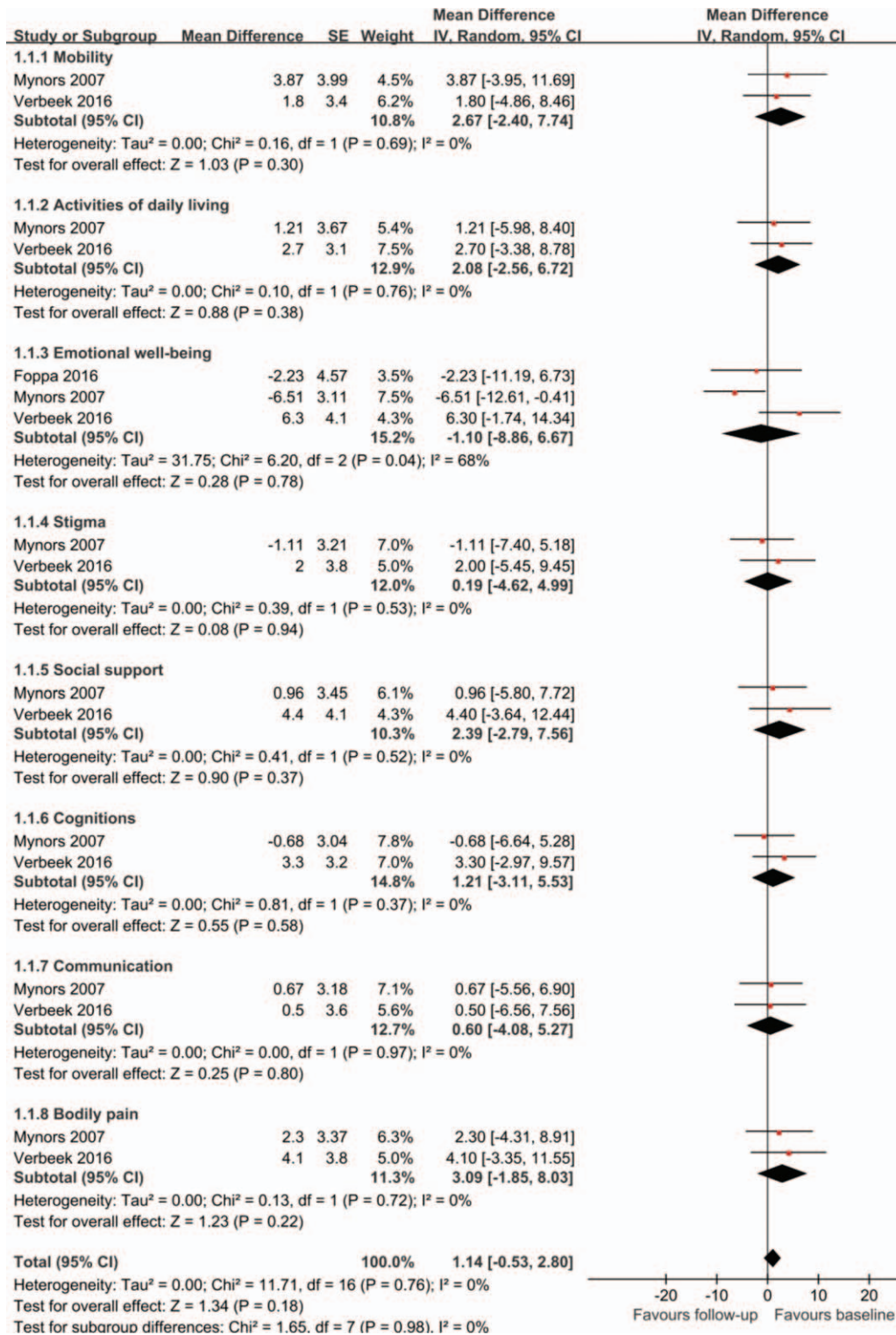


Figure 2. Changes of PDQ-39 from baseline. PDQ-39=Parkinson's disease questionnaire with 39 domains.

patients with a view to using the evidence produced by this review to design a complex intervention following the guidance produced by the Medical Research Council.<sup>[29]</sup> Findings from this review indicate that most pharmacy services for PD include help with identifying, resolving or preventing ADRs, adherence assessment, medication review, identification of drug inter-

actions, monitoring response to medication therapy, identification of inappropriate medication, and patient education. This review has also found that the most widely reported DRPs of PD patients were ADRs and that pharmacy services may have an impact on medication adherence but not on self-reported QoL.



To the best of our knowledge, this study is the first systematic review to analyse pharmacist services for PD patients. We included studies from all over the world to ensure the comprehensiveness of the systematic review and the relevance of results. In addition, we sought to identify the setting of pharmacy services and the impact of these services to begin to describe the contexts in which pharmacists are most likely to have an influence on patient outcomes and the likely mechanisms through which the work of pharmacists and pharmacy services work and produce patient-reported outcomes. Yet while the results of this review provide valuable evidence that pharmacy services are effective and has identified validated measures used by studies to investigate the outcomes and impact of these services, it is apparent from the findings of this review that although hospitals around the world are developing pharmacy services for patients, most of these pharmacy services have not designed using a theoretical framework or logic model to inform the development and evaluation of such complex interventions.

Our study has some limitations. First, the number of studies included limited further analysis, such as comparison between treatments and services designed for PD patients at country level, comparison between services provided in different (hospital, outpatient) settings or analysis to identify differences occurring as a result of frequency and/or duration of an intervention. Moreover, only the PDQ-39 data from 3 studies could be combined due to different outcome measures used by studies included in this review, limiting sample size used in the analysis and may explain our finding that pharmacy services overall have no impact on QoL, despite some previously published studies<sup>[10,11]</sup> indicating improvement in QoL following the implementation of pharmacy services for PD patients. Furthermore, only English-language and Chinese-language studies were included, although studies were conducted in many different countries and health systems. We tried to include conference abstracts in databases searching, but we failed to find those reporting findings in sufficient detail to be included in the review. Fourth, only cross-sectional studies and case-control studies with moderate to critical risk of bias were found, which limited comparability of the studies and the quality of evidence.

Although PD guidelines for pharmacists were published by the Parkinson Society Canada in 2014,<sup>[30]</sup> there is still no consensus regarding best practice or a gold standard for providing pharmacy services for PD patients. Our review provides evidence to inform this, and further provides a synthesis of the types of pharmacist interventions and outcome measures that have been used previously in evaluations of pharmacy services for PD patients. What is currently missing, is a process evaluation or theory-based evaluation supported by an underpinning theory of how a pharmacy service works that has clearly defined mechanisms of impact linking the content of the service to outcomes through a process of change. Having established what has been previously been successfully implemented our findings can be used to design an evidence-based pharmacy service intervention that can be tested with a large samples and long follow-up time, using patient-reported and pharmacist interventions as outcome measures. Such an approach has previously been successful in developing and evaluating complex healthcare interventions in geriatrics<sup>[31]</sup> and nursing,<sup>[32]</sup> and is needed for PD patients

## 5. Conclusion

This review provides evidence that the most frequently reported DRPs of PD patients were ADRs and that pharmacy services may have an impact on medication adherence but not QoL. However, evidence is limited due to study limitations and poor generalizability. As a result, there are unanswered questions related to the mechanisms or process of change producing reported impact and outcomes of pharmacy services for PD patients.

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## Author contributions

All the authors contributed extensively to the work presented in this paper. ZMY led the study design and model selection. ZMY, TTL and QYT conducted the literature review, designed and data analysis. YZ, SW and SDZ reviewed data analysis. All authors jointly contributed to result in interpretations and manuscript writing. All authors read and approved the final manuscript.

## References

- [1] Kalia LV, Lang AE. Parkinson's disease. *Lancet* 2015;386:896–912.
- [2] Rogers G, Davies D, Pink J, et al. Parkinson's disease: summary of updated NICE guidance. *BMJ* 2017;358:j1951.
- [3] McLean G, Hindle JV, Guthrie B3, et al. Co-morbidity and polypharmacy in Parkinson's disease: insights from a large Scottish primary care database. *BMC Neurol* 2017;17:126.
- [4] Fox SH, Katzenschlager R, Lim SY, et al. Movement disorder society evidence-based medicine committee. International Parkinson and movement disorder society evidence-based medicine review: update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord* 2018;33:1248–66.
- [5] Vrdoljak D, Borovac JA. Medication in the elderly - considerations and therapy prescription guidelines. *Acta Med Acad* 2015;44:159–68.
- [6] Mantri S, Fullard M, Gray SL, et al. Patterns of dementia treatment and frank prescribing errors in older adults with Parkinson's disease. *JAMA Neurol* 2019;76:41–9.
- [7] Martin P, Tamblyn R, Benedetti A, et al. Effect of a pharmacist-led educational intervention on inappropriate medication prescriptions in older adults: the D-PRESCRIBE randomized clinical trial. *JAMA* 2018;320:1889–98.
- [8] Avery AJ, Rodgers S, Cantrill JA, et al. A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis. *Lancet* 2012;379:1310–9.
- [9] Poon LH, Lee AJ, Chiao TB, et al. Pharmacist's role in a Parkinson's disease and movement disorders clinic. *Am J Health Syst Pharm* 2012;69:518–20.
- [10] Foppa AA, Chemello C, Vargas-Pelaez CM, et al. Medication therapy management service for patients with Parkinson's Disease: a before-and-after study. *Neurol Ther* 2016;5:85–99.
- [11] Shueb AS. Pharmacist intervention in the management of Parkinson's disease: evaluating the pharmacist's intervention at a movement disorders outpatient clinic. *Eur Geriatr Med* 2012;5:S127.
- [12] Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
- [13] Chemello C, Souza DF, Patricio ES, et al. Pharmaceutical care as a strategy to improve the safety and effectiveness of patients' pharmacotherapy at a pharmacy school: a practical proposal. *Brazilian J Pharm Sci* 2014;50:185–93.

- [14] Mynors G, Jenkinson C, MacNeill V, et al. A pilot evaluation of specialist community pharmacy services for patients with Parkinson's disease. *Pharm J* 2007;278:709–12.
- [15] Schröder S, Martu P, Odin P, et al. Impact of community pharmaceutical care on patient health and quality of drug treatment in Parkinson's disease. *Int J Clin Pharm* 2012;34:746–56.
- [16] Schröder S, Martu P, Odin P, et al. Drug-related problems in Parkinson's disease: the role of community pharmacists in primary care. *Int J Clin Pharm* 2011;33:674–82.
- [17] Stefan TC, Elharar N, Garcia G. Implementation and evaluation of Parkinson's disease management in an outpatient clinical pharmacist-run neurology telephone clinic. *Ment Health Clin* 2018;8:159–62.
- [18] Stuijt C, Karapinar-Carkit F, van den Bemt B, et al. Effect of pharmacist-led interventions on (non)motor symptoms, medication-related problems, and quality of life in Parkinson's disease patients: a pilot study. *Clin Neuropharmacol* 2018;41:14–9.
- [19] Mah G, Lee J, Lin M, et al. Impact of telephone intervention service provided at a community-based geriatrics clinic for Parkinson's: an observational study. *J Parkinsons Dis* 2016;6:155.
- [20] Verbeek A, Oonk N, Munster E, et al. The effect of a structured medication review on quality of life in patients with Parkinson's disease. An interim analysis. *Mov Disord* 2016;31(suppl 2):S170–1.
- [21] Wijma-Vos L. Contribution of a pharmacist to the multidisciplinary consultation on Parkinson's short-stay ward. *Mov Disord* 2015;30(suppl 1):S136–7.
- [22] Suansanae T, Wongpraprutdee P, Duangdee M, et al. Drug-related problems in patients with Parkinson's disease identified by pharmacists at the outpatient pharmacy unit. *Mov Disord* 2014;29:S19–20.
- [23] Henrichsmann M, Hempel G. Impact of medication therapy management in patients with Parkinson's disease. *Int J Clin Pharm* 2016;38:54–60.
- [24] Zhang C, Luo W, Han JY. Application of clinical model which consisted of clinician and clinical pharmacists in compliance of patients with Parkinson's disease. *Chinese J Clin Pharm* 2018;27:43–6.
- [25] Yi ZM, Ni XF, Li TT, et al. Practice and experience of pharmaceutical service in medication therapy management for Parkinson's disease. *Clin Med J* 2018;16:61–4.
- [26] Martin AW, Heberle AP, Knight JM. Interventions associated with implementation of a pharmacist-led neurology pharmacotherapy clinic in an ambulatory care setting. *J Am Coll Clin Pharm* 2018;1:1–7.
- [27] Wong E. Exploring the role of a prescribing pharmacist in the management of Parkinson's disease. *Movement Disorders* 2018;33 (supplement 2):S403.
- [28] Zhang C, Han JY, Bao HR, et al. Effect of new model of pharmaceutical service on patient compliance in "Parkinson's Disease Patient Association". *Chin J Mod Appl Pharm* 2019;36:349–52.
- [29] Developing and evaluating complex interventions Following considerable development in the field since 2006, MRC and NIHR have jointly commissioned an update of this guidance to be published in 2019. Available at: [www.mrc.ac.uk/complexinterventionsguidance](http://www.mrc.ac.uk/complexinterventionsguidance). Accessed 29th May 2019.
- [30] Patel T, Chang F. Parkinson Society Canada Parkinson's disease guidelines for pharmacists. *Can Pharm J (Ott)* 2014;147:161–70.
- [31] Faes MC, Reelick MF, Esselink RA, et al. Developing and evaluating complex healthcare interventions in geriatrics: the use of the medical research council framework exemplified on a complex fall prevention intervention. *J Am Geriatr Soc* 2010;58:2212–21.
- [32] Pinto S, Caldeira S, Martins J. The use of the Medical Research Council framework in the study of complex interventions in nursing: a literature review. *Nurse Res* 2018;May 15. doi: 10.7748/nr.2018.e1530. [Epub ahead of print].