

Effectiveness of case management interventions in reducing common and potentially preventable complications associated with Parkinson's disease: A systematic review and meta-analysis

Angelika D. van Halteren

Radboud university medical center; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Center of Expertise for Parkinson & Movement Disorders; Nijmegen, The Netherlands

Jules M. Janssen Daalen

Radboud university medical center; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Center of Expertise for Parkinson & Movement Disorders; Nijmegen, The Netherlands

Jan H.L. Ypinga

Radboud university medical center; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Center of Expertise for Parkinson & Movement Disorders; Nijmegen, The Netherlands

Bastiaan R. Bloem

Radboud university medical center; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Center of Expertise for Parkinson & Movement Disorders; Nijmegen, The Netherlands

Marjan J. Meinders

Scientific Center for Quality of Healthcare, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen, The Netherlands

Marten Munneke

Radboud university medical center; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Center of Expertise for Parkinson & Movement Disorders; Nijmegen, The Netherlands

Sirwan K.L. Darweesh (✉ Sirwan.darweesh@radboudumc.nl)

Radboud university medical center; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Center of Expertise for Parkinson & Movement Disorders; Nijmegen, The Netherlands

Research Article

Keywords: care management, Parkinson's Disease, integrated care

Posted Date: September 23rd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-870968/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Objective

We sought to systematically examine the effectiveness of case management interventions on common and potentially preventable complications associated with Parkinson's disease, both in persons with Parkinson's disease and in persons with other chronic health conditions. We specifically focused on falls, depression, anxiety, hallucinations, urinary tract infections and swallowing impairments.

Background

There is no systematic insight in the effect of case management on common complications associated with Parkinson's disease. This is an important knowledge gap given that people living with Parkinson's have identified care coordination as one of their highest priorities. Furthermore, it remains unclear whether the putative beneficial effects of case management would vary by key patient characteristics, such as their age, gender or disease characteristics. Such insights would contribute to a shift from "one size fits all" healthcare resource allocation to personalized medicine.

Methods

Using predefined inclusion criteria, we identified studies published up till February 2021 from PubMed and Embase databases. For each study, data were extracted independently by two researchers. Narrative analysis, and when possible also meta-analysis and random-effects analyses were undertaken.

Results

23 randomized controlled trials and four non-randomized studies reported data on the effect of case management on feelings of anxiety (8 studies) or symptoms of depression (26 studies). Only one study was conducted in people with Parkinson's disease. No study were identified that reported on how case management affected falls, hallucinations, urinary tract infections or swallowing impairments. Across meta-analyses, we observed a statistically significant effect of case management on reducing anxiety (Standardized Mean Difference [SMD] = - 0.47; 95% confidence interval [CI]: -0.69, -0.32) and depression (SMD = - 0.48; CI: -0.71, -0.25). We found a large heterogeneity in effect estimates across studies, but this was not explained by patient population or intervention characteristics.

Conclusions

Among people with chronic health conditions, case management has beneficial effects on symptoms of depression and feelings of anxiety, which are two common complications of Parkinson's disease.

However, these findings were based almost exclusively on interventions in people with other diseases. Future studies should assess the utility of case management for preventing complications in people with Parkinson's disease, with a particular focus on the optimal content, frequency, and intensity of case management.

1. Introduction

Parkinson's disease (PD) is a progressive, neurodegenerative disorder affecting more than 6 million people worldwide [1, 2]. It is characterized by a combination of motor and non-motor symptoms. Given its complex nature, the treatment of PD requires continuous monitoring and ongoing interdisciplinary collaboration between health care providers of various disciplines, who ideally deliver proactive care [3]. However, current health care systems are typically designed to treat chronic diseases such as PD using a "one size fits all" approach instead of tailoring care to each patient's individual needs [4, 5]. Consequently, persons with PD often become responsible for coordinating their own care. As a result, patients receive care that is fragmented and ineffective in achieving the desired health outcomes [3, 5]. This not only increases health care costs, but also causes an unnecessary burden on patients and their carers which, in turn, negatively affects their quality of life.

To address these challenges, case management has been introduced as an approach to improve care coordination [6, 7]. Case management has been defined in different ways [6, 8], however, the common basis for each definition is that case management is a collaborative process involving one case manager or a small team that plans, coordinates and reviews the delivery of health care services to meet a patient's individual needs [9]. According to this integrated care approach, a case manager takes over the responsibility to manage the non-acute services. The interpretation of case management can vary substantially, but common core elements include the development and review of individualized care plans, organization of multidisciplinary case meetings, screening and monitoring of risk factors and symptoms, use of evidence-based guidelines, information support for involved physicians, empowerment of patients through providing education, and enhancing self-management skills [9-11].

There is emerging evidence for the promising effect of case management interventions on reducing hospital (re-)admissions and length of stay in patients with chronic illnesses other than PD, such as asthma [12, 13], diabetes [14, 15], chronic heart failure [15, 16] or chronic obstructive pulmonary diseases [17, 18]. However, the effect of case management on common complications associated with PD remains unknown. This is an important knowledge gap given that people living with PD have identified care coordination as one of their highest priorities. Furthermore, it remains unclear whether the putative beneficial effects of case management on common complications would vary by key patient characteristics, such as demographics (i.e., age or gender), disease severity or duration, or key characteristics of the intervention (e.g., the number of individual patient contact). Such insights would facilitate a wider deployment of case management to susceptible subgroups of patients, thereby contributing to a broader shift from "one size fits all"-based healthcare resource allocation to "personalized" medicine.

To close these gaps in knowledge, we conducted a systematic review and meta-analysis to examine: 1) the extent and quality of evidence for the effectiveness of case management interventions on common and potentially preventable complications associated with PD; and 2) to what extent putative effects of case management vary across patient subgroups.

2. Methods

This systematic review is guided according to the PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) [19].

2.1 Search focus

We focused our search on the following common and potentially preventable complications associated with PD [20, 21]: (1) mood disorders, including depressive symptoms and anxiety; (2) fractures or injuries caused by falls; (3) swallowing impairment; (4) urinary tract infections; and (5) neuro-psychiatric disorders, including hallucinations. Although cognitive decline is also a well-known common complication associated with PD, we did not expect any direct causal effect of case management interventions on the level of cognitive impairment and thus excluded this complication from this systematic review.

Our initial search focused exclusively on data on case management interventions in people with PD. That search yielded very few results and, therefore, we expanded our search strategy by including data on case management interventions in people with other chronic health conditions with one or more of the same five common and potentially preventable complications, in whom we hypothesized case management interventions would have similar effects as in people with PD. Specifically, we broadened the search by including data from people diagnosed with Alzheimer Disease, asthma, cancer, chronic obstructive pulmonary disease (COPD), chronic heart failure, dementia, diabetes, hypertension, multiple sclerosis or rheumatoid arthritis.

2.2 Search strategy

An initial and limited search for empirical literature was undertaken by one reviewer [ADvH] in PubMed to identify important Medical Subject Headings (MeSH) and key words describing relevant articles. Next, a systematic search for research-based literature was performed by two independent reviewers [ADvH, JMJD] using the identified MeSH terms and keywords, by which we exclusively focused on published articles referenced in PubMed and Embase online in July 2019. The following MeSH terms were used to identify studies on case management: “Case Management”, “Disease Management”, “Patient Care Management”, “Patient Care Planning” and “Patient-Centered Care” which were combined with relevant key words. The detailed search strategy for PubMed can be found in Supplemental Data I. Finally, the reference lists of included studies were screened to identify studies missed by the search. A verification search was performed in February 2021.

2.3 Selection criteria

Abstracts and titles of all obtained studies were independently, systematically examined for the selection criteria by two reviewers [ADvH, JMJD] and disagreements were resolved during consensus meetings with a third reviewer [SKLD]. Search limits were applied to include only articles in English and those articles published in a peer-review journal. We included in this systematic review studies that (1) used an observational (prospective and retrospective) or interventional study design; (2) included results on the association of a case management intervention with at least one of the five common and potentially preventable complications; (3) included populations who were diagnosed with one of the selected chronic diseases [aged \geq 18 years]; and (4) described the case management intervention clearly and contained at least three core elements; (5) defined a clear control group, usually receiving usual care; and (6) reported at the least measures of the distribution of age and gender for the intervention and control group, as potential confounders (Table 1). We excluded studies involving participants living in residential nursing homes, as those participants receive 24-hour care and were thus not comparable to other populations receiving case management. Also excluded were studies that described only study protocols or conference abstracts.

2.4 Data extraction and analysis

The quality of the articles was evaluated by two authors (JMJD and ADvH) using the Cochrane risk of bias tool for randomized controlled trials (RCTs) [22] and the ROBINS-I tool for nonrandomized studies [23]. Two review authors [ADvH, JMJD] independently screened and evaluated the studies. The following data were extracted from each study: author, publication year, trial design, country, aim of the study, study design, distribution of participant characteristics (sex, age and diagnosis of disease), characteristics of case management intervention (table 1), characteristics of care received by the control group, follow-up duration, study outcomes, and primary outcome results (mean, confidence intervals, standard deviation, standard error, interquartile range). Where possible, standard deviations (SD) were calculated from standard errors (SE). In case no SD or SE was reported, authors were contacted and asked to provide additional data. For five articles we did not receive additional data [24-28], so these articles could not be included in the meta-analysis and/or random-effects regression analysis. We calculated standardized effect sizes for the main results of each study. Heterogeneity was assessed using the I^2 statistics. We used funnel plot visualization and Egger's test for funnel plot asymmetry to assess whether there was evidence for small study effects.

We conducted meta-analyses using restricted maximum likelihood (REML) and DerSimonian-Laird estimator in a random-effects model, because of significant heterogeneity between estimates across studies. In addition, predefined random-effects regression analyses were performed to identify effect modifiers of the effects of case management interventions, if sufficient studies were available within a complication category (e.g. depressive symptoms, anxiety). In fact, two studies were excluded for this analysis on depression, as the necessary data for regression analysis was not available [29, 30]. We

included the following study population characteristics as potential effect modifiers: mean age, percentage of female participants, disease group (neurodegenerative vs internal medicine diseases). We also included the number of case management components (out of nine components, which outlined in Table 1) as a potential effect modifier. Due to restrictions in the number of potential effect modifiers we were not able to include individual components in the random-effects regression analyses for feelings of anxiety. Instead, we included the number of included case management components as potential effect modifier. Multicollinearity of covariates – the modifying effect of covariates on each other - was assessed using variance inflating factors (VIF). We considered associations with $p < 0.05$ to be statistically significant across meta-analyses and meta-regression analyses. Analyses were conducted in R [31], using packages metafor [32] and ggplot2 for visualization [33].

3. Results

3.1 Study selection

The combined PubMed and Embase searches yielded 4765 unique records. After abstract review, 57 full-text articles were assessed for eligibility, of which 23 fulfilled our selection criteria. The other 34 were excluded for the following reasons: 25 studies did not provide relevant data on the topic under study; four studies were not identified as case management interventions; two studies dealt with a different health population; two studies did not include original data; and one study presented the same cohort. Two further studies [29, 34] were identified through cross-reference checking and two study [27, 35] was added through verification search, bringing the total to 27 included studies. Figure 1 provides an overview of the search and study selection process.

3.2 Study characteristics

Tables 2 describes the characteristics of the included studies. Of the 27 studies included, 23 [24-26, 28-30, 34-50] were RCTs and four were non-randomized intervention studies [27, 51-53]. The studies were published between 2002 and 2020 and evaluated case management interventions in various countries. The majority of studies evaluated case management interventions among patients with a single health condition [24-30, 36-39, 41-43, 45, 46, 48-53] whereas five studies [34, 35, 40, 44, 47] included patients with two or more different chronic diseases, such as heart failure and/or asthma or COPD. Only one of the included studies was conducted among people with PD. Taken together, the studies included 3752 participants ascribed to case management interventions. Mean age ranged from 57 years to 80 years, with an average age across all studies of 65 years, with 51% being female among the 25 studies [24-29, 34-53] reporting gender. 3682 participants were ascribed to the usual care group. Mean age ranged from 51 years to 78 years with an average age across all studies of 51 years, and also here with 51% being women.

3.3 Risk of bias and quality assessment

Of the four non-randomized intervention studies, three were rated as carrying a high risk of bias and one as a moderate risk. Of the RCTs, only eight studies [24, 29, 34, 35, 37, 38, 40, 49] were judged to be of a good methodological quality and at low risk of carrying bias. The remaining 15 studies were of low or moderate quality with a high or unknown risk of bias among several domains. However, most RCTs were rated as having a high or unknown risk on the domains of blinding of participants and blinding of outcome assessment, which is less applicable to this kind of intervention. Details on the quality assessment are presented in Supplemental Data II.

3.4 Components of case management intervention

Across the 27 included studies, there was substantial heterogeneity across the content and duration of the various case management interventions. Table 3 displays the different strategies used in each study. Common components of case management among the 27 studies (i.e., applied in at least ... studies) were (1) regular telephone contacts combined with in-person visits; (2) monitoring of signs, symptoms and risk factors; (3) ensuring therapy adherence; and (4) providing educational support on disease management and treatment, or trainings on self-management skills. However, the content and structure of these components varied highly among these studies. For instance, the purpose of in-person home visits ranged from developing and discussing a therapeutic plan with the patient in one study [41], to monitoring changes in signs and symptoms as well as reviewing patient's safety in their own home environment in another study [37]. The location of in-person visits also varied from the patient's home to a clinical setting. Most studies were conducted through a combination of in-person and telephone contacts, with only seven studies [25, 27, 38, 42, 45, 46, 52] reporting an intervention that was exclusively conducted through telephone contact.

Providing assistance for social and financial support, organization of multidisciplinary case meetings, medication review and the development of individualized care plans were more commonly reported case management interventions. In only four studies, case management interventions also included the support of informal carers [25, 26, 35, 36]. And of these, only one study included a regular assessment of the carer's physical health and provision of education on carer's coping skills, in addition to educating carers on disease management [36].

Furthermore, several studies incorporated the use of technological support systems which not only supported the implementation of case management strategies, but also offered new possibilities. For instance, a web-based service facilitated communication between the patient and the care team, to schedule patient contacts and to keep track of progress and current disease treatment [36]. In a different study, a web-based collaborative intervention facilitated peer-to-peer support for patients with cancer through a chat room connecting all enrolled participants to each other [30].

Of the 27 studies, 23 [25-28, 30, 34-45, 48-53] reported that case management interventions were delivered by a nurse case manager or a team consisting of a nurse case manager and other health care specialists. In one study [29] the case manager was a depression clinical specialist without further clarification of the background of the specialist and in another one [24] two research coordinators fulfilled

the role as care managers. In the other two studies the background of the case manager was not specified any further [46, 47]. Length of follow-up ranged from one and a half month to 24 months, with 18 studies reporting a 12-month or even longer follow-up period (Table 2).

3.5 Overview of outcome measurements

Results of the narrative data synthesis are summarized and presented in Table 2. Nearly all included studies evaluated the effectiveness of case management interventions on depressive symptoms, whereas anxiety was addressed in only eight studies [25, 28, 41, 43, 46-48, 51]. None of the included studies reported on falls, urinary tract infections, swallowing impairment or hallucinations.

3.5.1 Effect of case management on anxiety

Eight studies (n = 1239 participants) reported outcomes on symptoms of anxiety [25, 28, 41, 43, 46-48, 51]. The most commonly used scale was the Hospital Anxiety and Depression Scale (HADS) [25, 28, 41, 43, 46, 48], followed by 7-item Generalized Anxiety Disorder [47], and State Trait Anxiety Index (STAI) [51]. Six studies reported sufficient data and were included in a random effects meta-analysis, the results of which revealed a significant effect of case management interventions in decreasing anxiety (Standardized Mean Difference [SMD]= - 0.47; 95% confidence interval [CI]: -0.69, -0.324 with moderate heterogeneity ($I^2 = 51.9\%$) (Figure 2).

Variance inflating factor (VIF) analysis showed no evidence of multicollinearity (all VIFs <5). A tendency of lower SMD was found for studies with a higher percentage females [standardized regression coefficient $\beta=0.01$, p value=0.05]. No significant effect was found for mean age of intervention group [$\beta=0.02$, p=0.13] and number of components were [$\beta=0.13$, p=0.21].

3.5.2 Effect of case management on depressive symptoms

With the exception of one study [51], all studies (n=7314 participants) reported depressive symptoms measurements using a total of six depression scales, including the 9-item Patient Health Questionnaire (PHQ-9) [24, 26, 29, 37, 38, 40, 44, 45, 47, 50, 52, 53], the Hospital Anxiety/Depression Scale (HADS) [25, 28, 41, 43, 46, 48], the Center for Epidemiologic Studies Depression scale (CES-D) [30, 35, 39, 40], 20-item Symptom Checklist (SCL-20) [28, 34, 42, 50], the Cornell Scale for depression [36] and Taiwanese Depression Questionnaire [27].

Twenty studies reported sufficient data and were included in the meta-analysis (Figure 3). Two studies [40, 50] reported two different depression outcomes (CES-D/SCL-20 PHQ-9), but for analytical reasons only one (PHQ-9) was included in the meta-analysis. A random-effects meta-analysis revealed a significant effect of case management intervention on depression (SMD= - 0.48; CI: -0.71, -0.25), but heterogeneity was high ($I^2 = 92.3\%$). A funnel plot and Egger's test of funnel plot asymmetry (p = 0.57) showed no evidence for publication bias.

Variance inflating factor (VIF) analysis showed no evidence of multicollinearity (all VIFs<5). There were no significant population or disease characteristics: neurodegenerative diseases (reference: internal medicine diseases) [$\beta=0.20$, $p = 0.80$], mean age of intervention group [$\beta= -0.01$, $p = 0.76$] and percentage of females assigned to case management intervention [$\beta=-0.01$, $p = 0.43$]. Moreover, no significant effect was found for any of the individual case management components: development and review of individualized care plans [$\beta= -0.60$, $p = 0.21$]; in-person contact with the case manager [$\beta=-0.09$, $p=0.89$]; medication review [$\beta= 0.39$, $p = 0.47$]; provision of education on disease management and treatment [$\beta=-0.08$, $p = 0.91$]; self-management support [$\beta=-0.24$, $p = 0.70$]; support and training for healthcare providers [$\beta=0.05$, $p = 0.92$]; therapy adherence [$\beta=0.73$, $p = 0.92$] and use of evidence-based guidelines [$\beta=0.27$, $p = 0.52$].

4. Discussion

This systematic review and meta-analysis shows that case management is more effective than usual care at reducing depressive symptoms and anxiety, two common and potentially preventable complications associated with PD. This effect persisted for less complex case management interventions (whereby complexity was based on the number of included elements), across countries, for different chronic diseases and given the nearly equal representation of female and male participants, also across both genders. In line with our hypotheses, we found no evidence for effect modification by case management intervention, study population characteristics, or duration of follow-up. Of note, we did not identify any studies reporting on falls, hallucinations, swallowing impairment and urinary tract infections, so the effect of case management on those complications remains unclear. Also, only one of the included interventions was conducted in people with PD [37], which is a crucial remaining gap that should be addressed by future studies. The randomized study reported that a PD nurse-led care management intervention among veterans led to better adherence to quality-of-care indicators and the screening instrument showed significant improvement among the intervention group compared to usual care [37]. In this trial, the PD nurses used four strategies to specify PD problems of each veteran and to develop an action plan: (1) a telephone-administered assessment to identify 28 problem areas; (2) evidence-based care protocols and if not available, use of expert consensus on care management; (3) patient portal for communication purposes; and (4) documentation templates to provide care that is patient-centered and coordinated. However, this study is limited by geographical and time factors. Our study extends the findings of previous studies indicating a beneficial effect of case management on patients' clinical health outcomes and functioning in everyday life [7, 54, 55]. While previous research on case management has focused on its effects on reducing hospital (re-)admissions, length of stay and costs, little research has been done regarding its potential to reduce complications. Our systematic review addresses this gap in knowledge. The findings of this systematic review favor case management interventions over usual care and suggest that even less complex case management interventions have a beneficial effect on non-motor features that can also be encountered in PD. Case management reduces feelings of anxiety and depressive symptoms, which are both complications that can have an immense impact on the quality of life in patients with PD [56, 57]. Several indirect working mechanisms may have contributed to the

beneficial effect on depressive symptoms and anxiety (Figure 4), which can both have an immense impact on the quality of life and even mortality in patients with PD [56-58]. First, patients across studies received personalized management of their chronic health condition, including individually tailored health information and problem-solving strategies provided by a case manager. Second, the availability of one main contact person for newly arising issues and the ensuing establishment of a personal relationship between patients and case managers may have further helped to reduce feelings of anxiety and depressive symptoms. Notably, previous research on improving PD care revealed that having a single point of access was rated as the top priority by people with PD [4]. Third, having little information about the rate of disease progression and treatment options is known to enhance feelings of anxiety in patients. Patient education eventually allows for more shared decision-making and thereby treatment that is better tailored to a patient's individual needs and their coping behavior which, in turn, might alleviate anxiety. Several methodological considerations need to be considered. First, heterogeneity across studies was high and effect estimates varied substantially between studies, which might have affected the results of our meta-regression, leading to inability to identify any covariates of our effect estimates. Furthermore, since only two studies [39, 48] followed patients for longer than two years, the long-term effectiveness of case management interventions remains largely unclear. Second, only a few of the included studies were of good methodological quality. In particular, limited blinding of outcome assessment, insufficient details on specification of efficacy of specific case management elements and the lack of participant selection limited our ability to more accurately assess case management impact. In addition, as a systematic search strategy cannot screen full-text articles, the risk remains that relevant articles are not captured by the used search strategy. Eggers et al. [59], for instance, conducted a RCT with a nurse case-manager led intervention with patients with PD and reported on the effectiveness of CM on reducing hospitalization caused by falls. As these findings have not been reported in the abstract of the study, this study was not captured through our search strategy. Our data showed that beneficial effects of case management interventions on anxiety were somewhat more distinct in studies with a higher percentage of men and in studies with a relatively old population, although both observations were not statistically significant. No similar trends were observed for the effects of case management interventions on depressive symptoms. This systematic review identified the need for further research into the most effective case management interventions and components, on the optimal intensity and frequency of the individual case management strategies, and on their interaction with patient characteristics. Once this knowledge becomes available, case management interventions can be implemented that are better tailored to individual needs and as such presumably more effective. Moreover, this systematic review revealed that case management implementation is more common among certain chronic diseases than in others; the commonest ones were diabetes and heart failure, while only one included study concerned patients with PD. It follows that prospective research is now warranted to (1) improve the current evidence base for case management effects on anxiety and depression in persons living with PD, and (2) to provide additional insights regarding its effectiveness on other common PD complications.

Declarations

Financial Disclosure/Conflict of Interest concerning the research related to the manuscript

The Radboudumc Center of Expertise for Parkinson & Movement Disorder was supported by a center of excellence grant of the Parkinson's Foundation.

Prof. Bastiaan Bloem currently serves as Editor in Chief for the *Journal of Parkinson's disease*, serves on the editorial board of *Practical Neurology* and *Digital Biomarkers*, has received honoraria from serving on the scientific advisory board for Abbvie, Biogen and UCB, has received fees for speaking at conferences from AbbVie, Zambon, Roche, GE Healthcare and Bial, and has received research support from the Netherlands Organization for Scientific Research, the Michael J Fox Foundation, UCB, Abbvie, the Stichting Parkinson Fonds, the Hersenstichting Nederland, the Parkinson's Foundation, Verily Life Sciences, Horizon 2020, the Topsector Life Sciences and Health, the Gatsby Foundation and the Parkinson Vereniging.

Dr. Sirwan Darweesh was supported in part by a Parkinson's Foundation- Postdoctoral Fellowship (PF-FBS-2026).

Angelika van Halteren, Jules Janssen Daalen, Jan Ypinga, Marjan Meinders and Marten Munneke have no financial disclosures or potential conflicts of interest to report.

Funding sources of study

This research is part of the PRIME project, which was funded by the Gatsby Foundation [GAT3676] as well as by the Ministry of Economic Affairs by means of the PPP Allowance made available by the Top Sector Life Sciences & Health to stimulate public-private partnerships. The Center of Expertise for Parkinson & Movement Disorders was supported by a center of excellence grant by the Parkinson Foundation.

Acknowledgement

We are grateful to Dr. Louise Rose, Dr. Shinyi Wu and Dr. Haomiao Jin for providing additional data used in the analysis.

References

1. Dorsey, E. R. *et al.* The Emerging Evidence of the Parkinson Pandemic. *J Parkinsons Dis*, **8** (s1), 3–8 (2018).
2. Collaborators, G. B. D. M. N. D. Global, regional, and national burden of motor neuron diseases 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*, **17** (12), 1083–1097 (2018).
3. van der Eijk, M. *et al.* Moving towards patient-centered healthcare for patients with Parkinson's disease. *Parkinsonism Relat Disord*, **17** (5), 360–364 (2011).

4. Vlaanderen, F. P. *et al.* The Voice of the Parkinson Customer. *J Parkinsons Dis*, **9** (1), 197–201 (2019).
5. Bloem, B. R. *et al.* *Integrated and patient-centred management of Parkinson's disease: a network model for reshaping chronic neurological care.* *Lancet Neurol*, 2020 (in press).
6. Lukersmith, S., Millington, M. & Salvador-Carulla, L. *What is Case Management? A Scoping and Mapping Review.* *International Journal of Integrated Care*, 2016. **16**.
7. Joo, J. Y. & Huber, D. L. An integrative review of nurse-led community-based case management effectiveness. *Int Nurs Rev*, **61** (1), 14–24 (2014).
8. Lee, D. T. *et al.* Case management: a review of the definitions and practices. *J Adv Nurs*, **27** (5), 933–939 (1998).
9. Hudon, C. *et al.* *Key factors of case management interventions for frequent users of healthcare services: a thematic analysis review.* *Bmj Open*, 2017. **7**(10).
10. Reilly, S., Hughes, J. & Challis, D. *Case management for long-term conditions: implementation and processes* 30p. 125–155(Ageing & Society, 2010).
11. Hallberg, I. R. & Kristensson, J. Preventive home care of frail older people: a review of recent case management studies. *J Clin Nurs*, **13** (6B), 112–120 (2004).
12. Chongmelaxme, B. *et al.* The Effects of Telemedicine on Asthma Control and Patients' Quality of Life in Adults: A Systematic Review and Meta-analysis. *J Allergy Clin Immunol Pract*, **7** (1), 199–21611 (2019).
13. Burke, H. *et al.* *A multidisciplinary team case management approach reduces the burden of frequent asthma admissions.* *ERJ Open Res*, 2016. **2**(3).
14. De La Rosa, M., Pitts, S. & Chen, P. H. *An interprofessional collaboration of care to improve clinical outcomes for patients with diabetes.* *J Interprof Care*, 2019: p.1–3.
15. McCants, K. M. *et al.* The Impact of Case Management on Reducing Readmission for Patients Diagnosed With Heart Failure and Diabetes. *Prof Case Manag*, **24** (4), 177–193 (2019).
16. Huntley, A. L. *et al.* Does case management for patients with heart failure based in the community reduce unplanned hospital admissions? A systematic review and meta-analysis. *BMJ Open*, **6** (5), 010933 (2016).
17. van Eeden, A. E. *et al.* Effectiveness of case management in the prevention of COPD re-admissions: a pilot study. *BMC Res Notes*, **10** (1), 621 (2017).
18. Alshabanat, A. *et al.* Impact of a COPD comprehensive case management program on hospital length of stay and readmission rates. *Int J Chron Obstruct Pulmon Dis*, **12**, 961–971 (2017).
19. Moher, D. *et al.* Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*, **6** (7), 1000097 (2009).
20. Low, V. *et al.* Measuring the burden and mortality of hospitalisation in Parkinson's disease: A cross-sectional analysis of the English Hospital Episodes Statistics database 2009–2013. *Parkinsonism Relat Disord*, **21** (5), 449–454 (2015).

21. Tension, E. *et al. Proactive and Integrated Management and Empowerment in Parkinson's Disease: designing a new model of care* (Parkinson's Disease, 2020). (in press).
22. Cumpston, M. *et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions*. Cochrane Database of Systematic Reviews, 2019(10).
23. Sterne, J. A. *et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ, 355*, 4919 (2016).
24. Bogner, H. R. *et al. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. Ann Fam Med, 10* (1), 15–22 (2012).
25. Egan, E. *et al. A randomized control trial of nursing-based case management for patients with chronic obstructive pulmonary disease. Lippincotts Case Manag, 7* (5), 170–179 (2002).
26. Kalter-Leibovici, O. *et al. Disease management in the treatment of patients with chronic heart failure who have universal access to health care: a randomized controlled trial. BMC Med, 15* (1), 90 (2017).
27. Lu, M. C. *et al. The effectiveness of nurse-led case management for patients with rheumatoid arthritis in Taiwan. Int J Clin Pract, 74* (2), 13443 (2020).
28. Tsuchihashi-Makaya, M. *et al. Home-based disease management program to improve psychological status in patients with heart failure in Japan. Circ J, 77* (4), 926–933 (2013).
29. Ell, K. *et al. Randomized controlled trial of collaborative care management of depression among low-income patients with cancer. J Clin Oncol, 26* (27), 4488–4496 (2008).
30. Steel, J. L. *et al. Web-based collaborative care intervention to manage cancer-related symptoms in the palliative care setting., 122* (8), 1270–1282 (2016).
31. Team, R. C. *A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria. URL <https://www.R-project.org/>. 2017.*
32. Viechtbauer, W. Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software, 36* (3), 1–48 (2010).
33. Wickham, H. ggplot2: Elegant Graphics for Data Analysis. *Ggplot2: Elegant Graphics for Data Analysis 2009*: p. 1-212.
34. Katon, W. J. *et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med, 363* (27), 2611–2620 (2010).
35. Miklavcic, J. J. *et al. Effectiveness of a community program for older adults with type 2 diabetes and multimorbidity: a pragmatic randomized controlled trial. BMC Geriatr, 20* (1), 174 (2020).
36. Callahan, C. M. *et al. Effectiveness of collaborative care for older adults with Alzheimer disease in primary care: a randomized controlled trial., 295* (18), 2148–2157 (2006).
37. Chen, Y. *et al. Effectiveness of a multidisciplinary disease management program on outcomes in patients with heart failure in China: A randomized controlled single center study. Heart and Lung: Journal of Acute and Critical Care, 2018. 47*(1): p. 24–31.

38. Connor, K. I. *et al.* Randomized trial of care management to improve Parkinson disease care quality. *Neurology*, **92** (16), 1831–1842 (2019).
39. Gabbay, R. A. *et al.* Diabetes nurse case management and motivational interviewing for change (DYNAMIC): results of a 2-year randomized controlled pragmatic trial. *J Diabetes*, **5** (3), 349–357 (2013).
40. Gellis, Z. D. *et al.* Outcomes of a telehealth intervention for homebound older adults with heart or chronic respiratory failure: a randomized controlled trial., **52** (4), 541–552 (2012).
41. Hernandez, C. *et al.* *Effectiveness of community-based integrated care in frail COPD patients: A randomised controlled trial.* npj Primary Care Respiratory Medicine, 2015. **25** (no pagination)(15022).
42. Kroenke, K. *et al.* Effect of telecare management on pain and depression in patients with cancer: a randomized trial., **304** (2), 163–171 (2010).
43. Mertz, B. G. *et al.* The effects of individually tailored nurse navigation for patients with newly diagnosed breast cancer: a randomized pilot study. *Acta Oncol*, **56** (12), 1682–1689 (2017).
44. Morgan, M. A. J. *et al.* *The TrueBlue model of collaborative care using practice nurses as case managers for depression alongside diabetes or heart disease: A randomised trial.* BMJ Open, 2013. **3** (1) (no pagination)(e002171).
45. Riegel, B. *et al.* Randomized controlled trial of telephone case management in Hispanics of Mexican origin with heart failure. *J Card Fail*, **12** (3), 211–219 (2006).
46. Rose, L. *et al.* *Program of integrated care for patients with chronic obstructive pulmonary disease and multiple comorbidities (pic COPD+): A randomized controlled trial.* American Journal of Respiratory and Critical Care Medicine. Conference: American Thoracic Society International Conference, ATS, 2017. **195**(no pagination).
47. Stoop, C. H. *et al.* Effectiveness of a stepped care intervention for anxiety and depression in people with diabetes, asthma or COPD in primary care: A randomized controlled trial. *J Affect Disord*, **184**, 269–276 (2015).
48. Titova, E. *et al.* Does an Integrated Care Intervention for COPD Patients Have Long-Term Effects on Quality of Life and Patient Activation? A Prospective, Open, Controlled Single-Center Intervention Study. *PLoS One*, **12** (1), 0167887 (2017).
49. Williams, J. W. Jr *et al.* The effectiveness of depression care management on diabetes-related outcomes in older patients. *Annals of Internal Medicine*, **140** (12), 1015–1024 (2004).
50. Wu, S. *et al.* Comparative Effectiveness of a Technology-Facilitated Depression Care Management Model in Safety-Net Primary Care Patients With Type 2 Diabetes: 6-Month Outcomes of a Large Clinical Trial. *Journal of medical Internet research*, **20** (4), 147 (2018).
51. Avci, I. A. *et al.* *Evaluation of the Efficacy of the Three-Component Health Care Management Program HEWCOT in Colorectal Cancer Patients Receiving Chemotherapy.* J Cancer Educ, 2019.
52. Crowley, M. J. *et al.* Practical Telemedicine for Veterans with Persistently Poor Diabetes Control: A Randomized Pilot Trial. *Telemed J E Health*, **22** (5), 376–384 (2016).

53. Johnson, J. A. *et al.* Collaborative care versus screening and follow-up for patients with diabetes and depressive symptoms: results of a primary care-based comparative effectiveness trial., **37** (12), 3220–3226 (2014).
54. Baker, J. M., Grant, R. W. & Gopalan, A. A systematic review of care management interventions targeting multimorbidity and high care utilization. *BMC Health Serv Res*, **18** (1), 65 (2018).
55. Vandiver, T. *et al.* Community-Based Home Health Programs and Chronic Disease: Synthesis of the Literature. *Prof Case Manag*, **23** (1), 25–31 (2018).
56. Horn, S. & Hurtig, H. The Many Faces of Parkinson's Disease. *Cerebrum* 2019. **2019**.
57. Lee, H. M. & Koh, S. B. Many Faces of Parkinson's Disease: Non-Motor Symptoms of Parkinson's Disease. *J Mov Disord*, **8** (2), 92–97 (2015).
58. Timmer, M. H. M. *et al.* What a neurologist should know about depression in Parkinson's disease. *Pract Neurol*, **17** (5), 359–368 (2017).
59. Eggers, C. *et al.* Patient-centered integrated healthcare improves quality of life in Parkinson's disease patients: a randomized controlled trial. *Journal of Neurology*, **265** (4), 764–773 (2018).

Tables

Due to technical limitations, Tables 1, 2 and 3 are only available as a download in the Supplemental Files section.

Figures

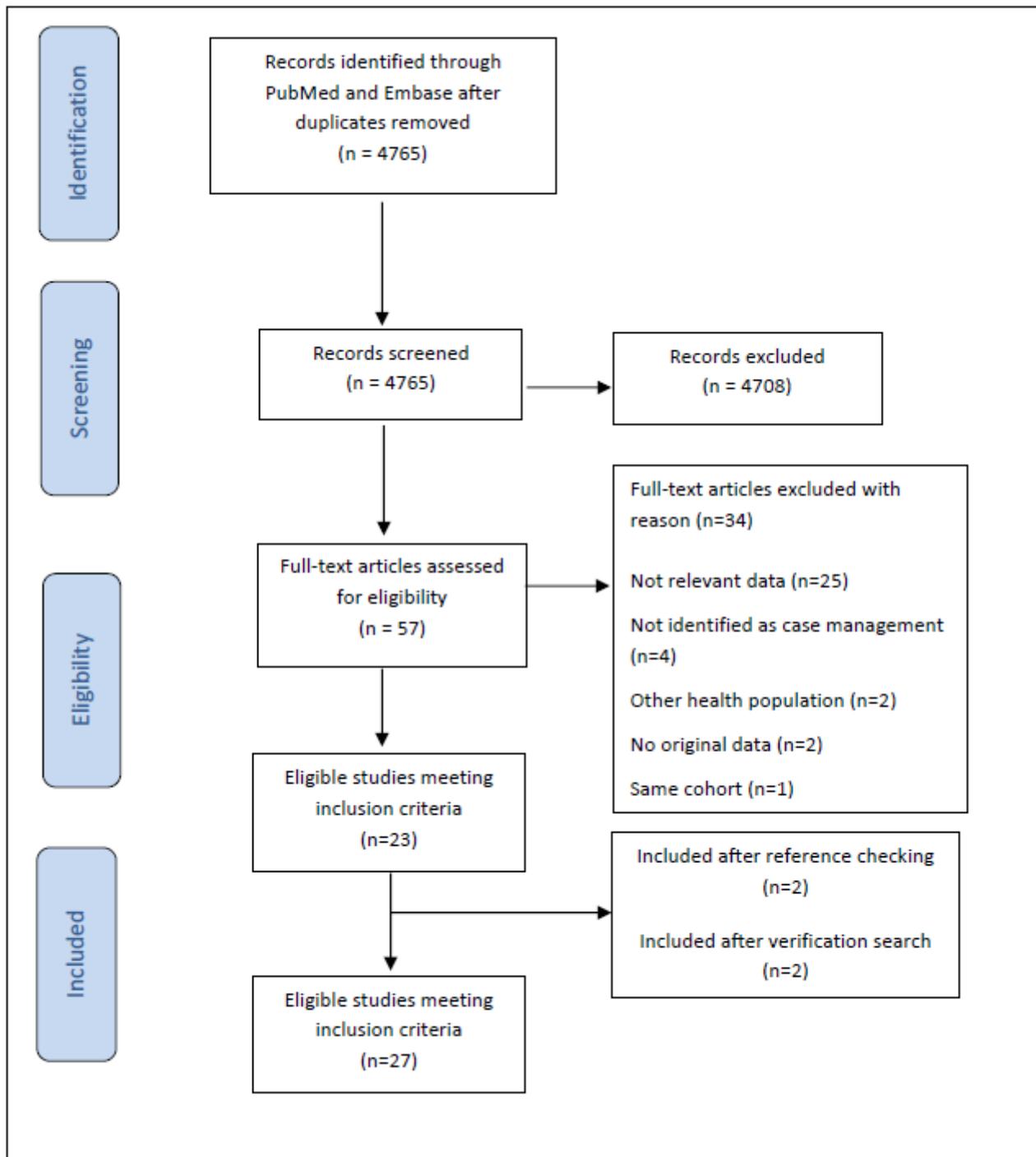


Figure 1

Study flow diagram

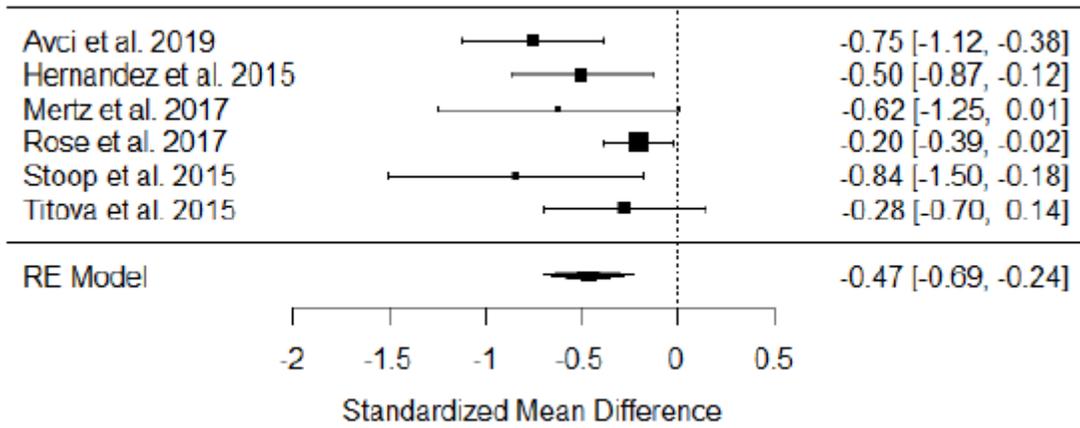


Figure 2

Forest plot on the effect of case management interventions on feelings of anxiety (random-effects model)

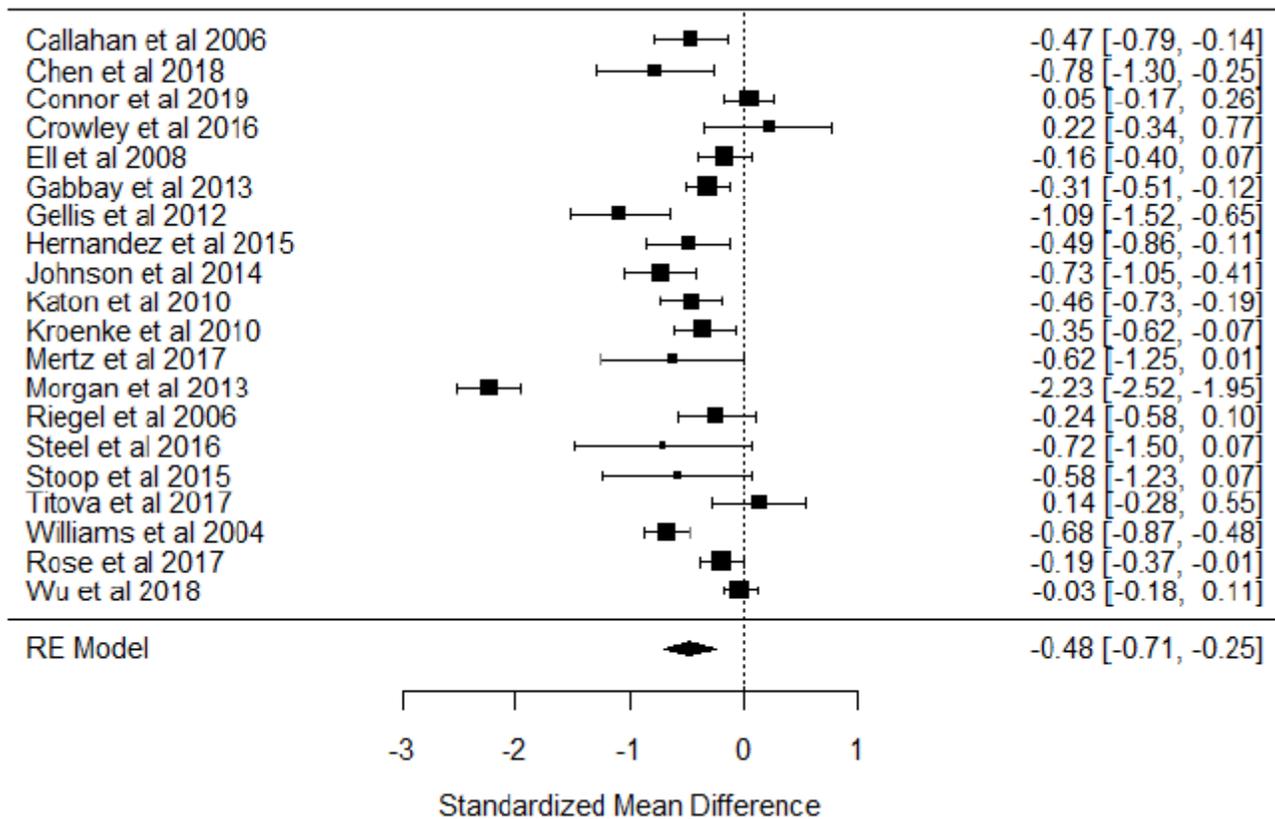


Figure 3

Forest plot on the effect of case management interventions on depressive symptoms (random-effects model)

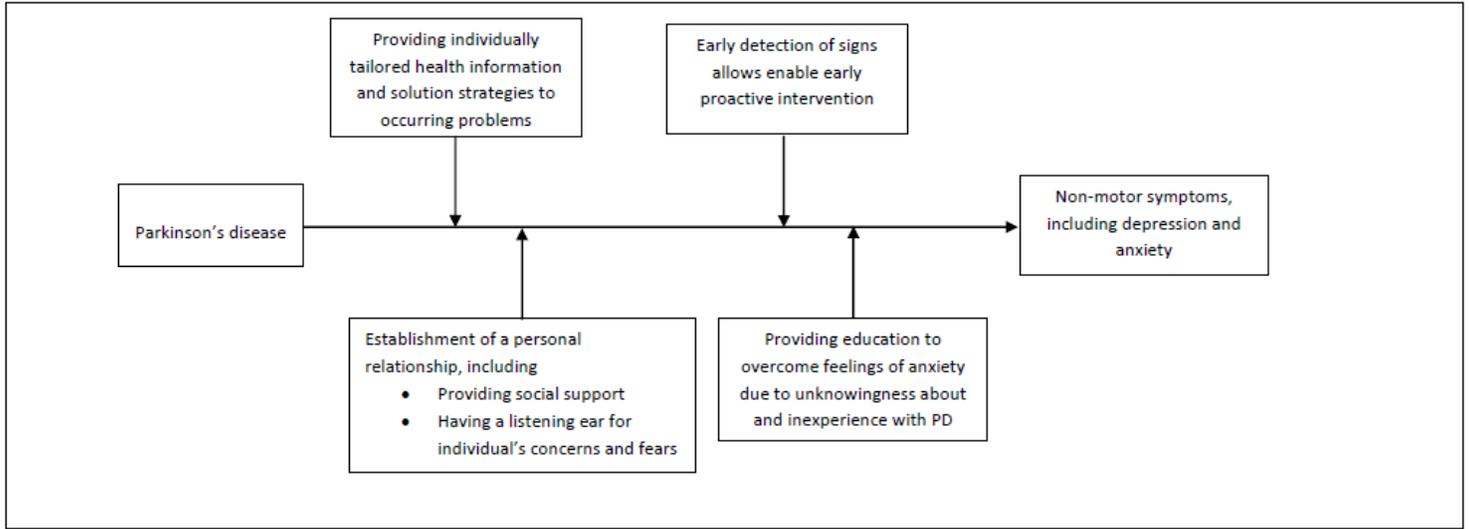


Figure 4

Mediators of the effect of case management on reduction of depressive symptoms and feelings of anxiety: hypothetical framework informed by this meta-analysis

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Tables.pdf](#)
- [Supplementaldata.pdf](#)