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Looking beyond the forest: using harvest plots, gap analysis and expert consultations to assess effectiveness, engage stakeholders and inform policy

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Abstract

We describe a combination of methods for assessing the effectiveness of complex interventions, especially where substantial heterogeneity with regard to the population, intervention, comparison, outcomes and study design of interest is expected. We applied these methods in a recent systematic review of the effectiveness of reinforced home-based palliative care (rHBPC) interventions, which included home-based care with an additional and explicit component of lay caregiver support. We first summarized the identified evidence, deemed inappropriate for statistical pooling, graphically by creating harvest plots. Though very useful as a tool for summary and presentation of overall effectiveness, such graphical summary approaches may obscure relevant differences between studies. Thus, we then employed a gap analysis and conducted expert consultations to look beyond the aggregate level at how the identified evidence of effectiveness may be explained. The goal of these supplemental methods was to step outside of the conventional systematic review and explore this heterogeneity from a broader perspective, based on the experience of palliative care researchers and practitioners. The gap analysis and expert consultations provided valuable input into possible underlying explanations in the evidence, which could be helpful in the further adaptation and testing of existing rHBPC interventions or the development and evaluation of new ones. We feel that such a combination of methods could prove accessible, understandable and useful in informing decisions, and could thus help increase the relevance of systematic reviews to the decision-making process.

Keywords

Systematic review; Complex interventions; Evidence synthesis; Harvest plot; Expert consultation

Evidence synthesis in the absence of meta-analysis: need for methods development

The challenges associated with conducting systematic reviews of complex interventions have been well-documented; a potentially broad research question that requires intricate, multidisciplinary searches may lead to the collection of very heterogeneous evidence, with a potentially wide range of methodological characteristics, included populations, interventions, comparisons, outcomes and results (Burford et al., 2013). A range of novel meta-analytical and other statistical methods exist to address and assess such heterogeneity (Petticrew et al., 2013; Pigott and Shepperd, 2013), but a critical decision for the reviewer is nevertheless whether the identified evidence is sufficiently homogenous to be statistically combined in a meta-analysis (Higgins and Green, 2011). In systematic reviews of complex interventions, the a priori expectation of substantial heterogeneity among studies often leads reviewers to forgo a meta-analysis, deciding instead for a narrative synthesis. A narrative synthesis of effectiveness evidence on its own, however, may prove lengthy and inaccessible to the end-user (Thomson and Thomas, 2013), and in fact may leave the decision-maker to make further sense of the evidence on his or her own. Thus evidence in this form may not be ideal for informing decision-makers (Sweet and Moynihan, 2007; Pettman et al., 2011).

In contrast, a clear, accessible summary is particularly important to decision-makers, and non-meta-analytical graphical summary methods have been shown to be an informative and comprehensible mode of presenting results of systematic reviews. The forest plot without a pooled effect estimate, for example, provides an overview of the effects for all studies assessing a given outcome, and is likely already familiar to various stakeholders (Higgins and Green, 2011; Valentine and Thompson, 2012). Other graphical methods, like the harvest plot (Ogilvie et al., 2008; Nehring et al., 2015; Turley et al., 2013), the effect direction plot (Thomson and Thomas, 2013) and the bubble plot (Erasmus et al., 2017; Totten et al., 2016) can summarize large bodies of information, usually facilitating the arrangement of various intervention types, outcomes and other aspects in a single structure. The albatross plot is more statistical in nature, and attempts to illustrate the relationship between the p-value, the effect size and the size of the assessed population (Harrison et al., 2017; Hunter et al., 2017). Each method is unique in its presentation of results from primary studies, but all aim to summarize and present intervention effects across studies in an accessible and user-friendly manner. The lack of a meta-analysis, nevertheless, means that most systematic reviews employing a graphical summary method will fail to provide the precise quantitative answer that decision-makers may desire, and may lead to further questions about included studies and how aspects of these studies may influence intervention effectiveness. Thus a way to extract more detailed information from the underlying systematic review, which facilitates a better understanding of included participants, interventions, outcomes, context, or other aspects, could be a valuable complement to graphical summary methods, and could thus help increase the relevance of systematic reviews to the decision-making process.

As part of the recently completed European Union-funded INTEGRATE-HTA project (Gerhardus, 2016), we developed concepts and methods for the comprehensive, integrated assessment of complex interventions. These concepts and methods were then applied in a demonstration health technology assessment (HTA) on reinforced home-based palliative care

(rHBPC), which refers to home palliative care with an additional component of lay caregiver support (Brereton et al., 2016). We chose to assess rHBPC within INTEGRATE-HTA because, based on the current literature on complexity of health interventions and health systems, it can be considered highly complex: there are multiple interacting components, a unit of care composed of the patients and their lay caregivers, as well as multiple service providers and other stakeholders at various levels, a range of physical, psychological and spiritual outcomes, and the need for a degree of tailoring (Craig et al., 2008). Additionally, the interactions between the intervention, context, setting and implementation likely influence effectiveness (Pfadenhauer et al., 2017), and these various aspects may change in adaptive ways over time (Petticrew et al., 2013; Plsek and Greenhalgh, 2001). The methods applied in the effectiveness assessment of rHBPC are presented in this paper.

In the following section, we will briefly describe the scope of the systematic review of effectiveness, including the population, intervention, comparison, outcomes and study designs of interest. In the subsequent section, we will describe the combination of methods applied for summarizing, presenting and further exploring the evidence included in this review, which included creating harvest plots and a subsequent gap analysis and expert consultations. In the final sections, we will present the results from this combined approach to evidence synthesis and interpretation, and briefly discuss the strengths and limitations of the applied methods.

Scope and overview of methods of Systematic Review of rHBPC

Following a Cochrane review that showed mixed results regarding the effectiveness of identified interventions (Gomes et al., 2013), we aimed to update the evidence base and assess the effectiveness of rHBPC interventions across a range of health outcomes in adult patients and their lay caregivers. The review scope is summarized in Box 1.

Box 1: Clinical and methodological scope of systematic review

Population: We included all adults (≥ 18 years) with any life-limiting condition receiving rHBPC. We included all lay caregivers, as the lay caregiving role may be taken on by any number of individuals, and is by no means limited to family (NICE, 2004).

Intervention: rHBPC encompasses a wide range of services. For the purpose of this review, we included any intervention which allowed patients to receive care primarily at home, and which additionally employed an explicit component focusing on supporting the lay caregiver. This additional support included any psycho-educational intervention aimed at providing assistance to lay caregivers (e.g. individual or group counselling, education, advice or respite services which alleviate burden).

Comparison: We included any comparator, as during protocol development it became clear that services offered to patients and caregivers as part of usual care were very heterogeneous.

Outcomes: Patient outcomes included pain, symptom control, quality of life (QoL), psychological health, death at home, hospitalization, response (e.g. coping, preparedness, mastery) and satisfaction with care. Lay caregiver outcomes included QoL, psychological health, response, and satisfaction with care.

Study designs: we included studies applying any of the following designs.

- Patient or cluster randomized controlled trials (RCTs)
- Patient or cluster non-randomized controlled trials (nRCTs)
- Controlled before-after studies (CBAs) with at least two intervention and two control sites (EPOC, 2014).
- Interrupted time series (ITS) studies with at least three data points both before and after a clearly defined intervention (EPOC, 2014).

We searched for and selected studies, and appraised the quality of included studies in line with Gomes et al. (Gomes et al., 2013) and guidance published by Cochrane (Higgins and Green, 2011). A more detailed description of the scope and methods can be found in the review protocol, available online (Burns et al., 2014b).

Evidence synthesis and beyond: Harvest plots, gap-analysis and expert consultations

At the evidence synthesis stage, we diverged from the methods applied in the original review by Gomes et al (Gomes et al., 2013), where a narrative synthesis and a limited number of meta-analyses were performed. Based on the expected clinical and methodological heterogeneity of studies, we decided a priori to forgo meta-analysis and to present findings graphically through harvest plots. We arranged studies on a matrix in columns according to direction of effect – favors control, no difference or favors intervention, and in rows according to the outcome category. Additionally, information regarding study design – represented by the height of the bar, and where no statistical analysis was performed – indicated with a dotted border, was portrayed. The color of the bar designates whether that study was originally included in Gomes et al. (Gomes et al., 2013) (white) or newly identified through our review update (black).

We recognized that while harvest plots are a good means of providing an overview of the evidence of effectiveness, decision makers tend to be interested in more detailed and concrete information regarding the various populations, interventions and outcomes. Systematic review authors increasingly engage content experts, both at the planning and execution stage, in the hopes to increase the relevance and utility of review results (Burns et al., 2014a; Higgins and Green, 2011; von Philipsborn et al., 2016; Woertman et al., 2013). Thus in an attempt to engage with experts in palliative care practice, we subsequently conducted a gap analysis and expert consultations in order to further explore the review results. “Gap analysis” is a catchall term used to describe a range of methods applied in many scenarios (Al-Momani, 2016; Bidulescu et al., 2017; Zeng et al., 2016). In this study, gap analysis refers to the process by which the entire review team, with expertise in palliative care, effectiveness and cost-effectiveness research and evidence synthesis, sought to examine the main findings related to rHBPC effectiveness in an open and iterative discussion. Gaps could, for example, be open questions or inconsistencies around study methods, included populations, interventions, comparisons or outcomes, as well as about the effects observed in the included studies. These identified gaps, which we refer to as “emerging aspects”, were

used as a flexible structure for the one-on-one consultations with palliative care practitioners and researchers, as explained below, and for summarizing the insights obtained.

Following the gap analysis, four palliative care professionals, including researchers and practitioners with knowledge and experience in palliative care from England, Germany and the Netherlands, were consulted individually via telephone or Skype. These individuals were purposively selected from a group of experts that had previously expressed interest in contributing to INTEGRATE-HTA. Each expert was provided the opportunity to study the review protocol and the harvest plots, and was asked to discuss methodological or palliative care-related issues relevant to the emerging aspects arising from the gap analysis. For example, if a certain type of intervention seemed to be comparatively effective, the experts would discuss, based on their knowledge and experiences, why this particular intervention may be observed as effective. As well as discussing the emerging aspects, experts were invited to contribute other relevant questions, comments or topics. Each consultation was audiotaped to ensure fidelity. We reviewed consultation findings descriptively using the emerging aspects to structure the findings. As an author team, we then aimed to further distill the insights into potential implications for research and practice.

Results

The results of the study selection process can be seen in Supplementary Figure 1. We included nine studies assessing rHBPC, five included in the original review (Harding et al., 2004; Hudson et al., 2005; McMillan et al., 2006; Rabow et al., 2004; Walsh et al., 2007) and four newly identified through our updated searches (Greene et al., 2012; Hudson et al., 2013; McMillan et al., 2013; Meyers et al., 2011). The studies differed widely with regard to the study setting, population, intervention, comparison and outcomes, and detailed information on these aspects is provided in Supplementary Table 1.

The harvest plots provide an overall summary of the effect estimates of included primary studies across all outcomes. For caregiver outcomes, the majority of the nine studies showed no greater benefit for rHBPC than for standard non-reinforced home-based interventions; a small number of studies showed some positive effects (Figure 1). Although rHBPC interventions focused mostly on lay caregivers, five studies also assessed patient outcomes (Figure 2). For pain, QoL, hospitalization, patient response and satisfaction of care, there appeared to be no difference between rHBPC and non-rHBPC interventions. Symptom control and psychological health displayed a mix of positive intervention effects and no effect.

Through the gap analysis, the review team identified four emerging aspects, which potentially influenced the effectiveness of the included rHBPC interventions or the assessment of effectiveness (Table 1; 'Emerging aspect' column). These included i) the heterogeneity and ambiguity of the primary study comparator, non-reinforced care, against which rHBPC interventions were compared; ii) the potential lack of individually tailored care based on

patient and caregiver needs; iii) the appropriateness of outcomes used in the review, as well as in primary studies; and iv) the primary study designs with which these interventions are usually evaluated.

In the subsequent consultations, experts highlighted both clinical and methodological aspects, such as the need to embrace more tailored, evolving care, the use of more responsive outcomes and more appropriate study designs, and overall better reporting in primary research. A summary of the findings of these consultations is provided in Table 1 ('Expert consultations' column).

Discussion

As we felt that statistical aggregation was unlikely to be appropriate given expected heterogeneity in populations, interventions, outcomes and study methods, the graphical summary provided by the harvest plots allowed us to produce evidence on effectiveness that is accessible to and informative for decision-makers (Pettman et al., 2011). The harvest plots show, for example, that rHBPC interventions were, for the most part, not effective in improving patient or lay caregiver outcomes. Harvest plots, however, do not tell the entire story; presenting the evidence in such an overview manner can obscure critical differences in individual studies, and recognizing such differences may require looking beyond the overall summary of evidence. At this stage, rather than concluding that rHBPC does not work, it may be valuable to examine both the factors that may have led to some interventions being more effective than others (Anderson et al., 2013; Squires et al., 2013), and to step outside of the conventional systematic review and explore this heterogeneity from a broader perspective.

Thus, we consulted experts with the aim of supplementing the summary of evidence generated through the systematic review with more detailed information regarding the assessed populations, interventions and outcomes, and potentially the effects (or lack thereof) of individual studies. The inclusion of expert input in systematic reviews of effectiveness has been shown to add value, both at the planning stage to define the scope of the review (Burns et al., 2014a; Higgins and Green, 2011; von Philipsborn et al., 2016), and at the evidence synthesis stage, for example, through Bayesian meta-analysis (Woertman et al., 2013). Our application of gap analysis and expert consultations as a supplement to the more traditional evidence synthesis likewise aimed to go beyond the conduct and reporting of any individual study, to enrich the results of the review with the knowledge and experience of experts. These experts did, in fact, highlight both clinical and methodological aspects, which could potentially be helpful in the further adaptation and testing of existing rHBPC interventions or the development and evaluation of new ones. For example, rHBPC interventions could be designed to be more tailor-fit to patients and their lay caregivers; or in evaluating interventions, researchers could look at outcomes and study designs that are more responsive in this population.

There were, of course, limitations in the application of this combination of methods. Harvest plots allow the presentation of a bulk of evidence, but readers may need some time to 'orient'

themselves. Another criticism of graphical summary techniques is that they could potentially encourage ‘vote-counting’ practices, if readers or decision-makers attempt to quantitatively compare the frequency of effect directions (Thomson and Thomas, 2013), but this should be explicitly discouraged in association with harvest plots. The information gained from the expert consultations is useful, but is based on personal experiences and is exploratory in nature, and thus should not be taken as hard evidence. Additionally, due to time and resource constraints, we were only able to conduct four consultations with experts from three countries and we did not involve other stakeholders (i.e. patients, lay caregivers or other interested parties). Hence, further applications of these or similar methods would benefit from consulting a larger, more diverse base of stakeholders.

For the purposes of assessing the effectiveness of rHBPC, this combination of harvest plots, followed by a gap analysis and expert consultations proved to be useful both in summarizing the evidence and identifying evidence gaps, as well as in looking beyond the aggregate level at how these findings may be explained. We would welcome applications of this approach or similar approaches to a range of interventions in health and other disciplines, potentially consulting a larger, more diverse base of stakeholders, to learn from the insights gained. In addition, it would be worth examining whether decision-makers find such a combination of methods accessible, understandable and useful in informing decisions.

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DISCLAIMER: The sole responsibility for the content of this presentation lies with the authors. It does not necessarily reflect the opinion of the European Union. The European Commission is not responsible for any use that may be made of the information contained therein.

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Accepted Article

Table 1: Findings of gap analysis and expert consultations

Emerging aspect	Gap analysis	Expert consultations	Potential implications for research and practice
<p>Primary study comparator (non-reinforced care)</p>	<p>The type of care, against which reinforced care was assessed, was poorly described in most included studies. Caregivers may be receiving substantial support through standard home-based services. Usual care, and especially the extent to which caregivers are supported as part of usual care, likely varies widely among included studies.</p>	<p>Usual care varies from place to place - not only from country to country, though there are very substantial differences to be seen at that level, but also within countries from one location to another.</p> <p>The support that caregivers receive as part of usual care is extremely heterogeneous. Some caregivers receive structured support throughout the illness trajectory, while others receive help only when they are overwhelmed by problems and seek care themselves.</p> <p>The extent to which caregivers are involved in decisions regarding patient care differs within “usual care”, from virtually none, to playing a part in care-planning discussions.</p>	<p>In determining what care may be appropriate in a given setting, a clear understanding of what type of support patients and caregivers receive as part of usual care is likely to be critical to identifying whether rHBPC could be effective, and which additional, alternative or complementary services could be warranted.</p>
<p>Lack of tailored care</p>	<p>Although some of the included interventions did offer some flexibility, it could be that for reinforced palliative care to be effective, targeted and tailored care should be more strongly emphasized, and delivered to those patients and caregivers assessed as needing it most.</p>	<p>Care tailored to the individual patient and caregiver, at least to a certain extent, is seen as the best practice - this could be based on diagnosis, age, illness trajectory, social surrounding, etc., and the recognition of such indicators is important.</p> <p>Being able to assess the needs of patients and/or lay caregivers, and to inform them of (evidence-based) options is essential. The</p>	<p>As changes in patient and caregiver needs occur frequently in relation to the illness trajectory, assessing these needs frequently and reacting to them through tailored care may be an important means to design more effective interventions.</p>

		<p>health and social care professional, however, should not make assumptions about what patients and/or caregivers need or want, and they should be involved in these discussions.</p> <p>The needs of caregivers and patients are not static, and will likely change over time and trajectory of the illness. This makes repeated assessments through ongoing communication important.</p>	
Appropriateness of assessed outcomes	<p>All of the outcomes assessed in this review have been used in the primary literature, and are thought to be important for patients and caregivers. It should be considered, nevertheless, whether these are most appropriate, and whether certain additional or alternative outcomes should have been assessed, both in the primary literature and in this review.</p>	<p>Hard outcomes used in palliative care may only tell part of the story, and meaningful effects can potentially be hidden among the noise, e.g. in a population so severely burdened, it may be unrealistic to expect clinically significant differences in quality of life. It is important, therefore, to ask patients and caregivers if their care has improved, and specifically what the benefits of care were.</p> <p>Outcome importance may differ between subgroups, and it is important to recognize this when evaluating services.</p>	<p>The outcomes used to assess rHPBC interventions should also be revisited, and standardized health outcomes such as QoL and psychological health, should be supplemented with more qualitative accounts of patients' and caregivers' perceptions and experiences.</p>
Primary study design	<p>Included studies encountered a range of problems when implementing and assessing palliative care services – e.g. attrition. Study designs, other than those included, may be more appropriate for assessing the effectiveness of reinforced home-</p>	<p>Mixed-methods and qualitative research should play a large role in assessing the effectiveness of services in a meaningful way - it is important to see what exactly is happening, to hear what patients and caregivers feel they are receiving, as opposed to assuming, based on the intervention design.</p>	<p>Researchers should also revisit which research approaches are most appropriate for answering a given question in primary studies and systematic reviews. For effectiveness, they could consider designs other than the RCT, such as N-of-1 studies; for questions beyond effectiveness,</p>

	based palliative care services.	If care is truly based on caregiver/patient assessment, and therefore truly tailored to the individual, and because the goals of individual participants will be different, evaluation of care becomes very difficult, especially in a randomized trial. Other study designs – e.g. process evaluations, qualitative studies, participative approaches, N-of-1 studies – should be considered.	qualitative studies, mixed-method studies or process evaluations are likely to be valuable.
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Figure 1

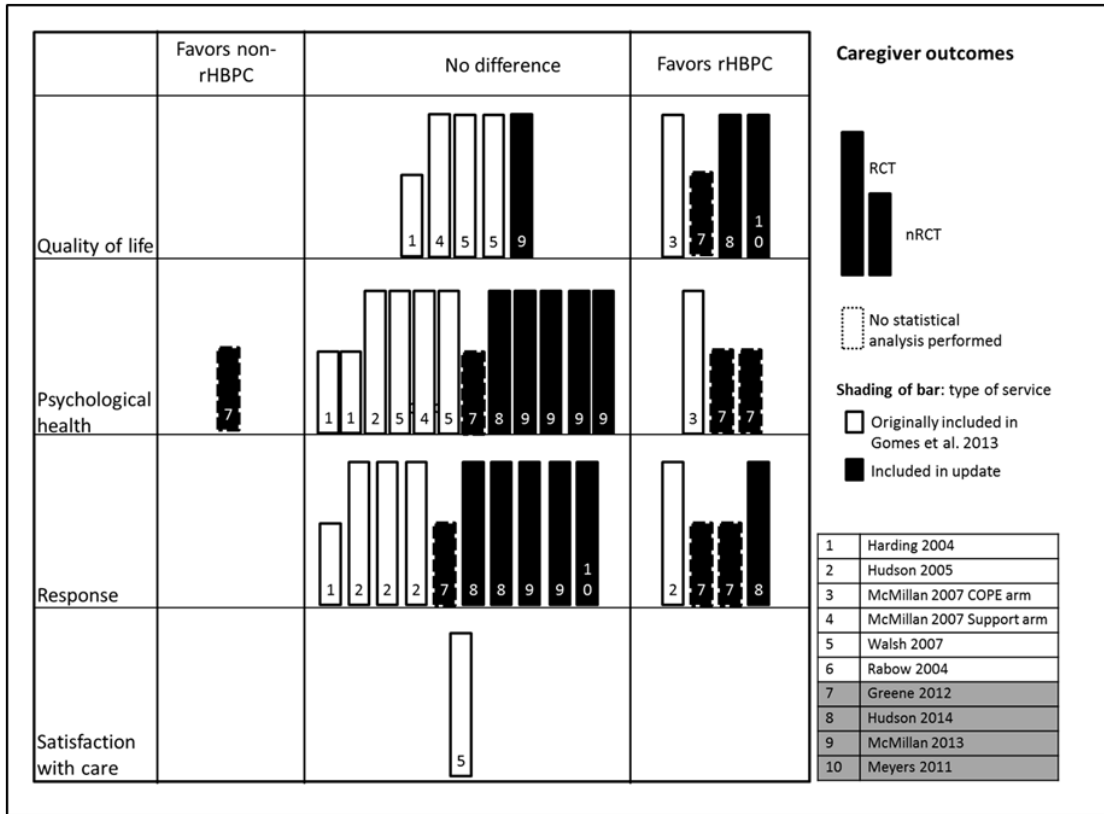


Figure 1: Effect estimates of included rHBPC interventions for lay caregiver outcomes.

Accepted

Figure 2

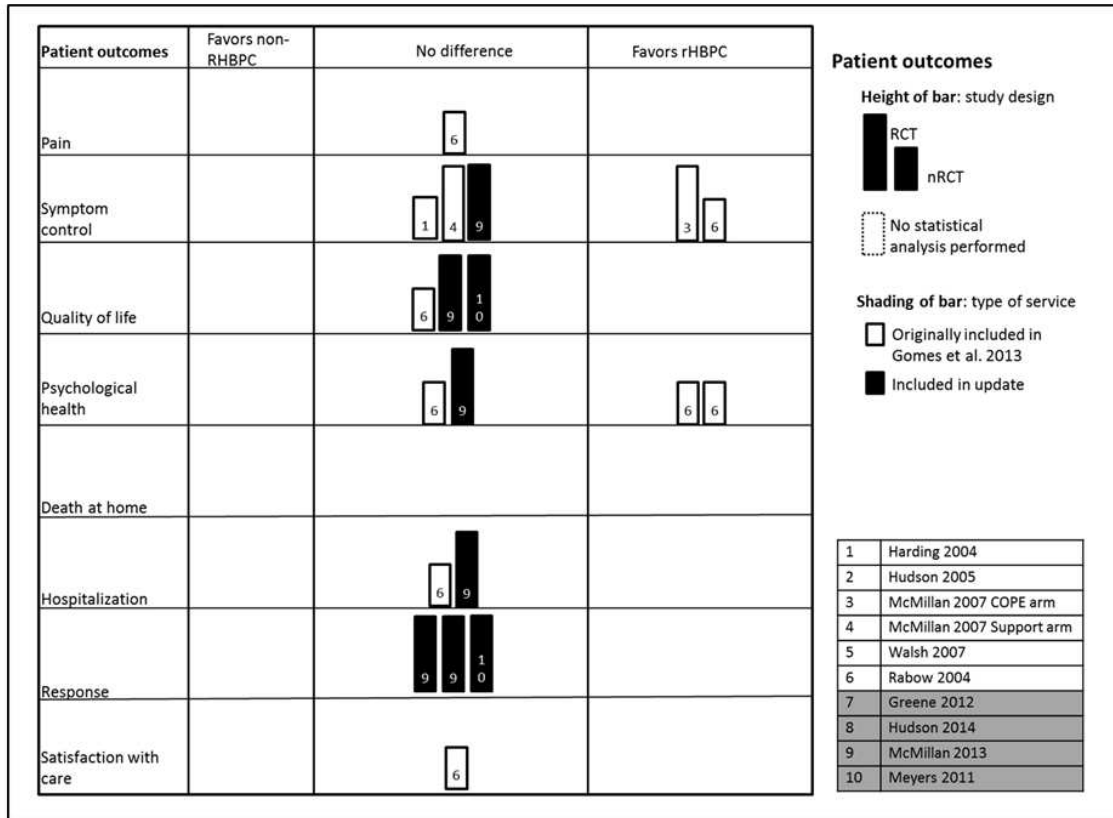


Figure 2: Effect estimates of included rHBPC interventions for patient outcomes.

Accepted