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Are all outcomes in chronic heart failure rated equally? An argument for a patient-centred approach to outcome assessment

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Abstract Chronic heart failure (CHF) is a multi-dimensional and complex syndrome. Outcome measures are important for determining both the efficacy and quality of care and capturing the patient's perspective in evaluating the outcomes of health care delivery. Capturing the patient's perspective via patient-reported outcomes is increasingly important; however, including objective measures such as mortality would provide more complete account of outcomes important to patients. Currently, no single measure for CHF outcomes captures all dimensions of the quality of care from the patient's perspective. To describe the role of outcome measures in CHF from the perspective of patients, a structured literature review was undertaken. This review discusses the concepts and methodological issues related to measurement of CHF outcomes. Outcome assessment at the level of the patient, provider and health care system were identified as being important. The perspectives of all stakeholders should be considered when developing an outcomes measurement suite to inform CHF health care. This paper recommends that choice of outcome measures should depend on their ability to provide a comprehensive, comparable, meaningful and accurate assessment that are important to patient.

Keywords Outcome assessment · Patient-centred · Chronic heart failure · Patient important outcome · Outcome measurement · Composite endpoints

Introduction

Chronic heart failure (CHF) is a common, complex syndrome occurring most commonly in the elderly [1]. Recent

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innovation, driven largely by pharmaceutical agents, devices and disease management programs, has led to improved survival [2]. But longevity often comes with an increased burden of disease [3]. Living with CHF is often associated with limited physical, psychosocial and economic capacity [4, 5]. Symptom burden and lengthy, costly re-hospitalisations are defining characteristics of the CHF trajectory [6]. People with CHF often have multiple medical conditions and live with debilitating symptoms such as fatigue and breathlessness. Therefore, the primary objective in the management of CHF is to optimise patient well-being in the context of longer-term survival. Balancing these two perspectives is challenging and requires an understanding of the individual's values and wishes, juxtaposed with those of health professionals and society at large.

Outcome measurement makes an important contribution to describing, interpreting and predicting the effects of disease and the influence of health care interventions. Outcome assessment can be used not only to evaluate the efficacy of interventions but also to describe the impact of care on patients (e.g. patient satisfaction), to support evidence-based clinical decision-making at the individual patient level, and to identify aspects of care for further improvement [7]. Consequently, the concept of outcomes naturally directs attention to the needs of patients and their well-being [8]. The selection of outcome measures should be undertaken and aligned to those important to the patients.

Choosing inappropriate outcome measures may lead to unimportant or misleading information, wasted resources and a loss of opportunity to demonstrate potential benefits. Despite debate on perspectives of management in CHF [9–12], choosing which outcomes to measure from the large range available remains challenging, and researchers and clinicians alike require further guidance [13]. At the same time, there are calls from agencies such as the Food and Drug Administration in the United States for researchers to generate endpoint models that clearly explain the roles and relationships between outcomes in providing an evidence base [14]. As individuals live longer with chronic conditions, the burden from comorbidities increases and assessing the relative contributions of different conditions and treatments becomes increasingly complex [15].

With a growing interest in patient-centred care, seeking to measure outcomes that are important to patients is a natural consequence [14]. Outcomes that are important to patients are those that patients notices, cares about and for which they would be willing to undergo a treatment with associated risk, cost or inconvenience for it to be the only thing that changed [16]. Process measures are those that assess characteristics of care that would influence ultimate outcomes (e.g. medication adherence). Surrogate outcomes are those that are known to predict important outcomes but are easier and quicker to measure (e.g. exercise capacity in CHF). Clinicians and health service managers, planners and policy makers often need intermediate and surrogate measures to monitor progress, understand causal relationships and evaluate cost-effectiveness. But it is important to emphasise that these outcomes should be supportive of, rather than alternative to outcomes that are important to patients.

The purpose of this paper is to review patient important outcome measures used in CHF and discuss methodological issues. The advantages and disadvantages of approaches to outcome measures are included and recommendations for a comprehensive, patient-centred outcome assessment suggested.

Methods

Information sources and search

Electronic databases Medline, Cumulative Index to Nursing & Allied Health Literature (CINAHL) and EMBASE were searched in addition to the World Wide Web using the Google Search Engine. Medical Subject Heading (MeSH) terms and keywords used in this search related to CHF and outcome assessment, outcome classification, health care outcomes and patient outcomes. Searches were not limited to any date range to enable insights into changes that may have occurred in outcome concepts or methods. Further additional data sources, such as clinical guidelines and policies, were hand searched for information relevant to the review. The search was limited to reviews, editorials or comments on outcomes in CHF published in English. Methodological issues pertaining to adverse events [17] and burden of disease (e.g. frequency of tests, clinician assessment of disease burden) [18] were also identified.

Data extraction and synthesis

Data were summarised and managed using Endnote XV (Thomson Reuters, New York) software. Articles retrieved were analysed to identify issues in methodological assessment and relevance to patients. In addition, those outcomes deemed to be important to patients were analysed for their relevance to clinicians and health care systems.

Eligibility criteria

Articles were eligible if they considered concepts and methodological issues related to measurement of outcomes in CHF.

The following questions drove the selection of articles and information.

- What are the measures of health outcomes in CHF?

- What are the outcome measures that have been identified as important to patients in clinical trials and outcome assessment?

Results

The following numbers of references were retrieved for this review: CHF and outcome assessment ($n = 107$), outcome classification ($n = 2$), health care outcomes ($n = 4$) and patient outcomes ($n = 65$) (see supplementary material).

Which measures of health outcomes in CHF are important to patients?

Outcome measures assessed at the individual level in CHF have included survival (mortality) [10], event-free survival, hospitalisation [10], PROs (e.g. symptoms, QOL) [10] and economic outcomes (e.g. cost and resource use per patient) [18]. Outcome measures such as mortality, morbidity as well as PROs such as symptom burden, functional status, psychological state, compliance with a therapeutic regimen, self-management and quality of life are also identified by the American College of Cardiology/American Heart Association (ACC/AHA) as important data elements for assessing the clinical management and outcome of patients with CHF [19].

Mortality

Mortality is a critical outcome measure in CHF especially when it is unexpected, premature or avoidable. Unexpected death may be a result of both cardiac and non-cardiac cause. To be a reliable and valid outcome at the system level, appropriate casemix and severity adjustments need to be made to adjust for these differences [20].

In CHF clinical trials, all-cause mortality has been found favour to be an unbiased and unambiguous endpoint [10] and has been used as a sole primary outcome [9]. However, as CHF care improves, mortality is becoming a less frequent event in some clinical trials, with the result that large sample sizes are required to detect differences between intervention and control groups [10]. This has led in mortality being included as part of a composite endpoint (usually with hospitalisation). This is controversial because of the potential for unequal weighting of events [21].

The choice of all-cause versus cause-specific mortality is also contested [22]. Although all-cause mortality will result in a higher event rate, the inclusion of deaths not the result of cardiovascular disease will invariably reduce sensitivity and therefore power to detect an intervention effect [22]. Assessment of cause-specific mortality improves precision but presupposes no impact on non-cause-specific mortality, which may not necessarily be true.

As well as providing a clearer indication of the effects of management, cause-specific mortality can also provide insights into a broader concept of chronic condition and its mechanism. However, a focus on cause-specific mortality requires researchers to distinguish between cardiovascular death and death caused by comorbidity. The difficulty of adjudicating the cause of death may depend on the quality of documentation provided on the death certificate, particularly for community-based deaths [22]. Furthermore, although cause-specific mortality may provide clinicians and health service operatives with important information to improve care and service delivery, it may not be meaningful to patients or their families for whom the impacts will be the same regardless of cause [22].

Hospitalisation

Data on hospitalisation (e.g. cause of admission, length of stay) provide useful information on prognosis, allow inference regarding the burden of CHF and management on patients and their families, and inform cost-effectiveness analysis [21]. But, despite its utility, hospitalisation as an outcome measure has limitations. Admission to the hospital is influenced by patient and social preference and differences in practice patterns, with thresholds determining admission and length of stay varying according to country, region and even institution [9]. The use of "observational stays" in some institutions and "short stay" [9] holding units in emergency departments further confounds comparison between studies. As with mortality, there is also the dilemma of whether to choose all-cause or cause-specific hospitalisation, with advantages and disadvantages to each [22]. When adjudicating the reason for hospitalisation, the definition of CHF hospitalisation is likely to vary depending on severity of CHF, comorbidities and related admission policies [12].

Patient-reported outcomes (PROs)

Over the past two decades, there has been a growing interest in collecting outcomes that are important to patients to ensure clinical care is person-centred [23]. Implicit in this process is obtaining the perspective of the patient through the use of patient-reported outcome (PRO). PRO is an umbrella term used to capture any outcome relying on patients' perception, interpretation or evaluation of their condition and care [24]. This may include multidimensional constructs such as patient preferences, symptoms, functional status, psychological well-being, quality of life (QOL) and satisfaction with care. Importantly, PROs provide patients with a voice to identify impacts of disease

and care that are important to them [25]. PROs include "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else" [26]. In CHF, the majority of PROs identified were health-related quality of life (HRQoL) and depression [27].

In clinical practice, PROs can be used to inform health decisions in a wide range of applications from individual patient decision-making through to developing health policy aimed at improving population health [28]. Routine administration of questionnaires to measure PROs can be used to screen for unmet needs [8] or problems such as depression and anxiety [29]. Evaluating satisfaction with treatment may assist providers in understanding the issues influencing treatment adherence and may help identify aspects of management linked to long-term treatment outcomes [30]. PROs can also facilitate communication amongst the health care team by providing a common language amongst professions from different clinical backgrounds [31]. Finally, established discrepancies between clinician and patient perceptions of symptoms and treatment effectiveness mandate collection of patient-reported data to inform future practice [31]. Adding an additional dimension of patient preference and prioritisation of outcomes may be a useful conceptual advance to PROs.

In clinical trials, PROs provide a number of advantages over and above traditional outcomes such as mortality. They offer a way to differentiate benefits when two or more treatments present with similar clinical efficacy [32]; they measure the benefit of "add-on" therapy that has the primary objective of providing an incremental benefit to QOL rather than substantial impact on survival [33]; and they can be used to examine long-term impacts of treatment on daily life in the context of lengthy survival, increasingly an issue in CHF [34]. Adding the additional aspect of a prioritised outcome can potentially lead to informed quality decision-making.

PROs usually reflect unobserved (latent) concept which may manifest themselves in different observable ways depending on the condition or treatment of interest. There is a challenge in selecting the most appropriate measure that would fulfil the objectives of the outcome assessment. It must also be guided by the severity and nature of CHF and ensure PROs measure selected would measure benefits/side effects of the therapy as well as the change in patients as CHF progress [35]. PROs are inherently subjective and rely on patient's self-report [36]. This means it is also imperative for PROs measure to be reliable and valid as well as responsive and relevant [37]. In addition, relying on self-report means PROs data are more prone to missing data than other clinical outcomes [38]. This is an important issue especially in many CHF studies where elderly patients may often drop out of the study due to severe illness or even death. Consequently missing data may lead to bias which may result in an erroneous conclusion [38].

In evaluating PROs, the timing of the outcome assessment is crucial. In most situations, the timing of the assessment of PROs will depend on disease progression, the therapy response, the risk of premature death or adverse events and the respondent burden [37]. Incorrect timing of PROs assessments could potentially jeopardise the reliability and the validity of the PROs findings [39] by biasing the treatment effect. If an evaluation of PROs measure took place outside an accepted time window, the result may be different. In addition, choosing appropriate timing of PROs assessments requires careful consideration of the transient effect of therapy on PROs measure.

PROs data especially quality of life comprise multiple components such as individual's perceived physical, psychological and social well-being [40]. Statistical analyses of these data often result in false significant results due to multiple tests. Several methods have been suggested to address the multiplicity issues such as comparing only the summary score, adjusting p values or to analyse only selected domains [38, 40].

In interpreting PROs, there is a need to determine the minimal important difference (MID). This measure enables interpretation of outcome assessment beyond statistical significance. However, it can be argued a meaningful change is a subjective concept may differ depending on different perspective. There is clearly a need for a comprehensive interpretation strategy that incorporates different anchors, each having its own metric that is meaningful to a given audience [41]. Works have been carried out to establish MID for Minnesota Living With Heart Failure Questionnaire [25] and the Kansas City Cardiomyopathy Questionnaire [42], two most popular HRQoL measures used in CHF.

Adverse events

An adverse event is defined as an unintended harm due to medical management or lack thereof in contrast to complication arising from the underlying disease [17]. Although adverse events may be linked with quality of care and patient safety, presence does not necessarily indicate poor quality, nor their absence indicate good quality [17]. Most patients with CHF have one or more comorbid condition that will potentially cause treatment conflict, [43] especially when multiple medicines are prescribed. This places patients with CHF at risk of adverse outcomes which may be captured by mortality, hospitalisation and PROs (e.g. side effects and symptoms).

Burden of disease

Burden refers to the demands experienced by patients, caregivers, clinicians, the health care system and society [44]. Patients' and carers' burden can be expressed as

mortality, hospitalisation and PROs such as symptom burden [45]. In some instances, economic burden is also described at an individual level. This may include lost productivity as well as direct and indirect costs of care such as hospital transportation [46]. Patients' and carers' burdens are usually linked with expectations of and satisfaction with care [44] as measured via PROs. The burden of CHF at a system level has generally been measured with traditional indices such as incidence, mortality and morbidity and increasingly health services utilisation, particularly hospitalisations [47]. One definition of the burden of disease is a measure of the years of healthy life that an individual or population loses as the result of disease. Generic outcomes that combine both mortality and morbidity into a single index such as disability-adjusted life years have also been used [48]. Identifying the outcomes important to patients such as quality of life is an important consideration in determining disease burden.

Several reviews exploring different endpoint/outcomes in CHF and cardiovascular clinical trials have demonstrated the lack of consensus on appropriate measures [9, 10, 21]. In some CHF clinical trials, there is a recognition that treatment efficacy needs to be measured by multiple outcomes, especially where management or the outcomes of interventions have multiple components [49]. Composite endpoints are useful both for capturing multiple components and additive effects of interventions and also for reducing sample size due to increased event capture.

Composite endpoints

Implicit in applying a composite endpoint is the premise that each of the component endpoint would measure the same underlying pathophysiological process, but be different enough that they add a dimension to the measurement of the disease process that has not been contributed by any other component endpoint [50]. Composite endpoints may include more than one clinical outcome (e.g. major acute coronary event), surrogate outcomes and/or PROs, or a combination of all three [51]. In CHF trials, most commonly used composite primary endpoint is mortality and hospitalisation with or without worsening HF. By combining multiple endpoints with low event rates such as incidence of mortality and morbidity into a single composite endpoint increases the event rate and in turn reducing the sample size to achieve required power [52]. As a result, the trials will become smaller, less costly and the result will be available earlier [52]. However, some argue this comes at a cost of precision and sensitivity [53].

Examples of composite endpoints in CHF trials include Packer's ordinal composite score (improved, unchanged or worse) [54], Cleland's 'patient journey' [55], Braunwald's "weighted unsatisfactory outcome" [56], composite endpoint used in the African American Heart Failure Trial (A-HeFT) [57] and global ranking endpoint [58]. All of these endpoints make an important point in conceptualising the complexity of a multidimensional approach to management and importance of each component to the patient. For example, in Packer's score, patients are classified as "better, the same, or worse" depending on the patient's vital status and their symptoms. Patients who died or were hospitalised due to worsening heart failure or experienced worsening HF were classified as worse. Patients with improved symptoms and no worsening were classified as better. Patients classified as neither better nor worse were classified as unchanged. Packer's composite endpoint effectively weighs death, hospitalisation and symptoms equally. Another weighting scheme is based on hierarchical endpoints based on ranking of events or global rank approach. In this type of scheme, all patients are ranked on the basis of pre-specified hierarchy of events. For example death would be ranked worst, then hospitalisation and so forth. An alternative to above weighting of schemes is a score calculated for A-HeFT trial. In this scoring system, death is counted as -3, a first hospitalisation from HF is counted as -1 and change in quality of life varies from -2 to 2 depending on the degree of worsening or improvement. This weighting scheme assigns a numeric value to all patients and each patient's experience contributes directly to the total score. A challenge with this weighting scheme is establishing consensus amongst patients, clinicians and regulators on what constitutes a MID. In addition, the relative importance assigned to each component may not achieve agreement amongst all stakeholders. This would create a problem in interpretation when the components are not moving in the same direction.

Outcome assessment in clinical management

In clinical management, the purposes of outcome measurement typically include monitoring and support of patient progress, diagnosis, treatment and communication [59]. Outcomes assessment in clinical management can be targeted at either or both of two levels: at an individual patient care level and/or at an aggregated system level [60]. Information at the system level can be collected and analysed at either the clinic or group practice level.

In clinical management, outcome assessments typically use routine data to avoid undue burden on patients that may not have immediate consequences for their own personal care. Routine outcomes data are subject to numerous biases and are unlikely to be of sufficient quality for rigorous evaluation of treatment efficacy [61]. Nonetheless, outcome data can be utilised in measuring the quality of care, designing system interventions, reallocating resources and research efforts, training health care personnel and characterising a patient population to better understand their needs.

Discussion

The current review has found a range of commentaries and reviews concerning outcomes measures important to patients in CHF yet no gold standard exists. While there was a general agreement that outcomes assessment is essential in improving care, a number of strengths and limitations were highlighted in each of outcome measures important to patients.

Outcomes in CHF are used to describe the impact of treatment/care on patients' lives. Incorporating patients' perspective in the form of PROs means an essential element [62] of patient-centred care is being practiced. Indeed, there has been a call to include PROs in routine clinical practice [33]. Therefore, choosing outcome measures that are meaningful to patients is essential. Traditionally, patient outcomes in CHF have been mortality, hospitalisation and avoiding or decreasing adverse events of care [11]. With debilitating symptoms including fatigue and breathlessness, improving functional status and health-related quality of life (HRQoL) has become patient important outcomes. Patients with CHF often experience multiple medical conditions with unpredictable prognosis with limited physical, psychosocial and economic capacity [4, 5]. Increasingly, patients' perspective as expressed in PROs such as HRQoL, functionality, symptoms (and symptom management) and more recently quality of death have become patient focused outcomes [63].

Increasingly, there is a recognition that patients' desired outcomes may change as the patients and their careers evolve as the disease progresses and treatment/care becomes familiar [64]. Undoubtedly, for many patients, outcomes such as mortality and morbidity/hospitalisation would play a central role and override any consideration for other outcomes. This would be the case, especially in patients with mild symptoms where their prime objective would be to improve survival [65]. However, in more severely ill patients with distressing and in times disabling symptoms, this may not be so; an improvement in their quality of life or symptom relief may be more important [66]. Consequently, in examining patient level outcomes, PROs need to be considered in conjunction to clinical outcomes such as mortality and rehospitalisation [67]. In order to consider the justification for this, it is useful to consider patient, clinician and system perspectives in CHF outcome assessment and these are summarised in Table 1.

Clinician level

In providing care to patients with CHF, clinicians aim to increase survival and improve QOL both by managing current problems and preventing future morbidity. To achieve this, clinicians need to monitor the processes and results of care to inform future improvements to care and support shared decision-making with patients [68]. Process measures include patient understanding of self-management advice, availability of support and adherence to treatment as well as vital signs, laboratory and diagnostic test results and response to medications [13]. Physiological and elemental outcomes such as changes in pulmonary capillary wedge pressure and natriuretic peptide levels may be disease rather than patient-centred but are nonetheless an important part of CHF patient management. They inform clinicians of the status of disease process as well as the mechanism related to the patient problem and a better understanding of the way a treatment works [69]. Process measures should ideally require minimal additional resources and minimal disruption to the delivery of care. Furthermore, they should be clinically useful and acceptable to patients [60]. As much as possible, they should inform concrete action (e.g. provision of information) [67] to improve patient care.

System level

At a system level, outcomes evaluate changes in health of a defined population as a result of health care or health system activity. Outcome measures at this level assist in establishing and evaluating health policies that may benefit CHF communities [27]. Such methods of assessment are critical in informing policy decisions. As demands on resources increase, outcome measures are increasingly needed to enable disparities in burden to be highlighted across different health conditions and geographical regions as well as over time. Outcome measures have an important part to play in examining accessibility of quality CHF care across the population. These applications are needed to ensure the health care system is suitably responsive to the needs of different groups.

Given the escalating health care cost associated with CHF and other chronic conditions, it is important to balance societal benefits with expenditure to allocate care and resources judiciously. There is a need to understand the relative benefits of the various treatment options for CHF in terms of clinical and economic outcomes. The quality adjusted life year (QALY) is widely used for economic evaluation across health care [70]. QALYs combine information on both quantity and quality of life and offer a standard unit for comparison across different interventions and places on the disease trajectory [71]. That said, there have been numerous criticisms of QALYs, especially concerning the methods used to generate their utility weights and the use of QALYs for informing allocation of health care funds between disparate conditions [72]. A broader assessment at system level would include cost-benefit analyses [73] and loss of productivity as possible societal outcomes.

Table 1 Patient, clinician and system perspectives in chronic heart failure outcome assessment

	Perspective		
	Patient	Clinician	System
Reason for interest in outcomes	Minimise risk of CHF Restore to "health" in timely way Ability to live a normal life	Assess patient needs Provide appropriate care/treatment Monitor quality of care/treatment provided	Plan services Monitor the quality of care/ treatment provided Justify cost of care Improve population health Reduce health disparities
Desired outcomes	Timely access to quality care Minimise symptom burden and 'functional limitation Survival Avoid major clinical events such as hospitalisation Self-management of CHF Feel safe and secure and satisfied with care	Patient adherence/ satisfaction Improved self-management of CHF Appropriateness of treatment/care provided Avoid adverse events Good liaison with other health care team	Reduce incidence/prevalence of CHF Appropriate service provision Improved knowledge and understanding of CHF and related risks. Population-based surveillance system
Possible outcome measures	Mortality QOL (Re)hospitalisation Functional status Patient satisfaction	Mortality Symptoms (e.g. dyspnoea) LVEF Patient satisfaction	Mortality Incidence/prevalence Hospital days Cost of treatments Workforce implications

CHF chronic heart failure, *QOL* quality of life, *LVEF* left ventricular ejection fraction

Two-thirds of the economic burden of CHF can be accounted for by admissions to hospital alone [74], making interventions that avoid (re)admission a priority from the system perspective. At the same time, there is a need to measure hospitalisation and other system outcomes in terms of their impact on the patient [75]. While we may assume that patients generally wish to avoid hospitalisation, it may be that this is a preferred outcome for some people who lack support in the community [76]. PROs such as psychological well-being, unmet needs and satisfaction with care have so far had a limited influence at the systems level. Future work is needed to integrate these measurements into the systems level model.

Moving towards a prioritised, integrative model of outcomes assessment

This review has considered outcome measures of importance to patients and considered their importance at clinician and health care systems level. Mortality, hospitalisation and PROs are outcomes that are relevant and important to all stakeholders of CHF care and have wide application in research and clinical practice. If standardised, this "core set" of outcomes has potential to enable both evaluation of health care effectiveness and monitoring of population health [77]. Identifying consensus in outcomes between patients, providers and health systems is important in generating an integrative model of health care assessment that has utility and relevance. Furthermore, as evaluation metric is often a driver of service organisation and delivery, having a genuinely person-centred outcome goal is likely to alter service provision.

The critical issue is whether this should be approached by developing a single measure, by measuring a core set of outcomes and trying to combine the results as a composite outcome, or by keeping them as a set of individual outcomes. To varying degrees, any single outcome may be inadequate to capture important differences [71]. However, comparability and interpretability of outcome assessment will be greatly facilitated by a simple measure of outcome [78] such as a composite outcome. Combining multiple outcomes into a single summary measure is a useful approach for defining 'net benefit' [79].

In using a composite outcome, we would also circumvent the need to make an allocation for multiple hypotheses testing, as one is essentially dealing with a single endpoint [51]. In addition, the problem of competing risks can be avoided especially if a clinical outcome such as mortality is combined with morbidity (in the form of hospitalisation) [52] and PROs. With the core set of outcomes forming a composite will ensure each component of this outcome is relevant and includes an outcome considered to be important

to the patient. Ensuring reliability, validity and acceptability is critical, and ideally, this composite outcome would lead to greater efficiency and higher quality of care.

To ensure the utility of the composite outcome at all levels of care, each component (from the core set of outcomes) should be appropriately weighted, depending on the purpose and the goal of outcome assessment. Currently, in most studies with composite endpoints, the components are assigned equal weights even though stakeholders, particularly patients, may not consider them equally important. Weighting needs to be undertaken carefully because, if the balance is inappropriate, reduced power may arise [11]. In addition, the problem associated with the interpretation of the treatment effect occurs when the components are moving in different directions, especially when a less frequent endpoint, such as mortality, with much more frequent endpoints such as symptom improvement [52] are combined. Standardising the weights of composite endpoints will allow the patients, providers and health care system to agree on defining a clinically meaningful effect on composite scores [44].

Conclusion

Although the literature challenges conceptual and methodological assumptions of conventional endpoint assessment methods, to date there has been limited application on non-traditional measures [21]. Choosing measures must depend on the capacity to provide comprehensive, comparable, meaningful and accurate reflection of outcomes as well as the capacity for data collection. Measurement issues require issues of reliability, validity and utility in meeting the needs of a range of stakeholders. Importantly, ensuring these metrics needs to meet the priorities of patients. While it is likely that utility will vary from the perspective of patient, clinician and health care system, the needs of clinicians and the system should be seen as supportive of rather than alternative to those important to patients, a core set of outcomes with broad-scale application and appeal. A composite endpoint combining these outcomes offers promise if it is reliable, valid and acceptable to patients, providers and policy makers.

Conflict of Interest Ms S. Chang, Drs P. Newton, S. Inglis, T. Luckett., Profs H. Krum, P. Macdonald and P. Davidson have no conflict of interest or financial ties to disclose.

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