

Abstract

Context Treatment burden, the burden associated with the treatment and management of chronic illness, has not yet been well articulated.

Objective Using Rodgers' (1989) method of concept analysis, this review describes the ways in which treatment burden has been conceptualized, in order to define the concept and develop a framework for understanding its attributes, antecedents and consequences.

Methods Leading databases were searched electronically between the years 2002 to 2011. To ensure the review focused on actual observations of the concept of interest, articles that did not measure treatment burden (either qualitatively or quantitatively) were excluded. An inductive approach was used to identify themes related to the concept of treatment burden.

Main results Thirty articles, identified from 1557 abstracts, were included in the review. The attributes of treatment burden include burden as a dynamic process, as a multidimensional concept, and comprising of both subjective and objective elements. Prominent predisposing factors (antecedents) include the person's age and gender, their family circumstances, possible comorbidity, high use of medications, characteristics of treatment, and their relationship with their healthcare provider. The most dominant consequences are poor health and wellbeing, non-adherence to treatment, ineffective resource use and burden on significant others. Furthermore, many of these consequences can also become antecedents, reflecting the cyclic and dynamic nature of treatment burden.

Conclusion The findings underscore the need for researchers and healthcare professionals to engage in collaborative discussions and make cooperative efforts to help alleviate treatment burden and tailor treatment regimens to the realities of people's daily lives.

Keywords: treatment burden, chronic illness, concept analysis, medication burden, health professional

Burden of treatment for chronic illness: A concept analysis and review of the literature

Introduction

Chronic diseases are the leading cause of death in the world, largely associated with 63% of the 57 million deaths that occurred in 2008.¹ The majority of these deaths are attributed to cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes.¹ Although the burden associated with chronic illness is well documented, the burden associated with the treatment and management of chronic illness has not been well defined. Related terms such as disease burden and symptom burden have been well articulated,^{2,3} but the definition of treatment burden has remained elusive and confusing. Although treatment burden is often inseparable from disease burden, it is not based on the natural history of the disease, but on the need to treat the disease in order to change its course or ameliorate its effects. Treatment burden is, therefore, an important concept that is distinct from disease burden, symptom burden and other related terms.

Treatment of chronic illness comes in many forms including surgery, physical therapy, psychological therapy, and radiotherapy. However, one of the most common treatment forms is the use of medication. In Australia, as in many developed nations, the use of medications represents one of the largest components of health expenditure; accounting for 13% of the total health expenditure in 2006-07.⁴ There were 262 million prescriptions filled in 2008,⁴ many of which were used to treat chronic illness. The prevention and treatment of chronic illness, especially when involving multiple medications, can become burdensome.

Few validated instruments have been developed to assess the experiences of treatment burden on patients.⁵⁻¹⁶ In some cases however, the concept of treatment burden has been included as one domain within a multi-dimensional instrument designed to assess health-related quality of life or treatment satisfaction.^{5-12,17,18} These measures reflect wide variation in terms of the dimensions of treatment burden and its definition. One team of researchers explored the experience of treatment burden with the purpose of identifying its core components.³⁷ These researchers identified four main tasks that contributed to the sense of

burden, namely learning about treatments and their consequences, engaging with others and mobilizing support, adhering to treatment and lifestyle changes and monitoring treatments. Although the most useful conceptualization of treatment burden in the literature, this analysis was not intended to provide a concept analysis. Instead, it was focused on the utility of an existing theoretical framework as a tool for identifying burden. Thus, it is important to conduct further empirical investigation of this concept to enhance our knowledge and draw coherent conclusions about its prevalence and impact..

The lack of a clear conceptual model of treatment burden has contributed to our inability to measure its impact or identify people most at risk, thereby obscuring the health professional's role in assisting people to alleviate this burden. It has generated confusion and misinterpretation that detracts from appropriate and timely management or prevention. A crucial first step in assessing treatment burden and articulating the role of health professionals is defining the concept itself and developing a framework for understanding its occurrence and impact.

The purpose of this review is to comprehensively analyse the concept of treatment burden to enable informed recommendations for health professionals who wish to alleviate its impact. This analysis aims to outline the ways in which treatment burden has been conceptualized and operationalized, by identifying and discussing the critical attributes of treatment burden, exploring the factors that can lead to treatment burden (antecedents), and highlighting its consequences. Antecedents are predisposing events that occur prior to the concept whereas consequences are events that occur as a result of the concept.¹⁹ Furthermore, attributes are at the heart of a concept, providing insight into its occurrence.¹⁹ A thorough knowledge of the attributes, antecedents, and consequences of treatment burden is important from a health practice perspective because without such knowledge, health professionals will not be able to provide services that alleviate such burden among people with chronic illness.

Methods

Rodgers'²⁰ evolutionary method of concept analysis was used to comprehensively analyse the concept of treatment burden. This particular method is well suited to the concept of treatment burden because of its changing and dynamic nature (e.g. the emergence of new health technologies leading to possible burden). The evolutionary view of concept analysis indicates that concepts are influenced by contextual factors and may change over time.²¹

Data sources and search strategy

A systematic search was conducted using the terms *treatment burden*, *burden of treatment*, *medication burden*, and *burden of medication* as keywords in the following databases: Medline, PsychINFO, Cinahl, Cochrane, Scopus, Health Reference Centre (HRC), PsychEXTRA, Informit, the System for Information on Grey Literature in Europe (SIGLE), and National Technical Information Service USA (NTIS). A sensitivity analysis conducted prior to the search suggested that these key search terms encompassed most of the research within the field. In particular, the sensitivity analysis confirmed that medication was the most prominent form of treatment for chronic illness, necessitating the inclusion of this search term. Although the use of broader terminology may have identified other bodies of literature, restricting the search to these specific terms ensured that the overlap with other forms of burden was minimized.

To ensure a contemporary exploration of this concept, the search was limited to articles published from 2002 to 2011 with human subjects and a focus on the major chronic illnesses that have been named as priorities in Australia: asthma, diabetes, cardiovascular disease, musculoskeletal illness, cancer, and mental health. According to the World Health Organization, these conditions contribute a significant burden in terms of mortality and/or morbidity globally.¹ After this search, 1157 abstracts were identified.

These abstracts were reviewed by two members of the research team. Abstracts without a substantial focus on treatment burden were excluded, along with those that emphasized disease or symptom burden. If both researchers were uncertain about whether the abstract met the inclusion criteria or were not in agreement, the full article was retrieved and reviewed. As a result of this process, 170 articles were thoroughly reviewed by two researchers, leading to the exclusion of a further 140 articles (Figure 1). Further exclusions were applied to ensure the review focused on articles that actually measured a person's experience of treatment burden. Specifically, articles that did not measure treatment burden (either qualitatively or quantitatively) were excluded (i.e., opinion pieces or theoretical articles). Thirty articles met the inclusion criteria and were included in the concept analysis (Table 1). Most of these studies were conducted in the United States of America (USA) and included self-report survey questionnaires to assess the level of treatment burden among patients and their carers. A number of inter-related themes were identified from the review relating to the antecedents, attributes and consequences of treatment burden.

Data extraction and analysis

An initial coding framework was developed based on the questions in Table 2. These questions reflected Rodgers' method of concept analysis, which involves a multidisciplinary literature review to identify the common attributes, antecedents and consequences of the concept.³

Five researchers independently extracted data from the selected articles in accordance with the review questions in Table 2 and coded the data within the initial framework, expanding the subthemes as required. Each coding framework was then reviewed by two researchers for recurring themes, which were placed into categories (attributes, antecedents, and consequences).

Results

Attributes of treatment burden

The defining attributes of treatment burden were chosen due to their frequent occurrence in the literature. Treatment burden emerged as a dynamic multidimensional concept that comprized of both subjective and objective elements.

A Dynamic Process

Treatment burden changed over time²² in response to disease severity and control^{23,24} and the development of comorbidities.^{25,26} It is possible that that either familiarity with, or acceptance of, treatment lessens the experience of burden through a process of adjustment. In patients with diabetes, longer duration of disease was associated with less burden.⁸ Despite changing over time, some degree of burden appeared to persist.²⁷ Treatment burden also had a cyclic aspect, with many of the consequences of treatment burden also being antecedents. For example, increased burden could result in non-adherence to medication which may then lead to further burden.²⁸

A Multidimensional Concept

Treatment burden emerged as a multidimensional concept, including physical, financial, temporal, and psychosocial time demands.

Physical side effects²⁹ were a significant source of treatment burden,^{13,23,28,30} arising in particular from medications or drug interactions.²⁸ Side effects could occur at any stage of treatment. For example, they could be more acute at the commencement of therapy, they could be ongoing, or they may result from cumulative toxicity in the later stages of treatment.²⁸ Side effects varied in nature and severity, from minor hypoglycaemic events and weight gain,⁸ to those that are so unpleasant that the possibility of experiencing them frightened some patients.⁸

Experiencing more than one side effect contributed to overall treatment burden.¹³ Some side effects may be preventable especially those related to the use of medications that were no longer required.³¹

The cost of treatment could be high²³ contributing to overall treatment burden.^{27,28,32} Even when treatment was subsidized the out-of-pocket costs could be intolerable.³³ The cost of travel was one of the greatest out-of-pocket expenses, especially for patients from non-metropolitan areas,³⁴ although this was often obscured by the rhetoric of ‘free’ hospital care. Inpatient treatment was also associated with financial burden.³⁵ Personal medical costs competed with other living expenses, such as, food, clothing and housing.²⁵

The time required to plan and organize travel for treatment,³⁶ receive treatment,^{34,37,38} learn about treatments and their potential outcomes,³⁷ monitor treatment,^{36,39} and manage side effects⁴⁰ were related to treatment burden. As well as consuming financial resources, travel required a great deal of time, especially for patients who lived in outer regional areas.³⁴ A substantial time burden for family and carers as well as for patients themselves was evident.⁴⁰ One study reported families of children with chronic illnesses may already be under considerable time pressure and the increased use of long-term home-based care for these children adds to this burden over time.³⁸

The psychological and social aspects of treatment burden were closely linked, often because additional support is needed to manage treatment²⁷ or day-to-day tasks or both. Some patients had difficulties managing home responsibilities as a consequence of treatment^{32,34,40} and often, household and personal tasks, normally completed by the patient, were carried out by other family members.³³ Parents needed to accompany, administer medication to, and monitor a child receiving treatment. However, many families seemed to adapt well to treatment tasks.⁴¹ When children attended school, the burden of administering medications was likely to be borne by the child or a staff member, which may explain why some children experience

more burden than their parents.³⁸ Older adults generally relied on family for assistance and support.⁴² Family members or carers also at times needed to accompany or support patients receiving invasive or lengthy treatments such as cancer treatment.⁴⁰ The impact of treatment on significant others added to the burden experienced by the patient.⁴³ Family members could perceive themselves as being incompetent or not able to care for the patient due to a lack of personal or economic resources.²⁷ These perceptions could also add to the patient's sense of burden.²⁷ Thus, there is a need for adequate information to be provided by healthcare professionals about treatment and its consequences in order to address these perceptions.³²

Treatment tasks that interfered with daily activities²³ or lifestyle^{5,41,43} also contributed to treatment burden.^{35,41} For instance, it was inconvenient to transport treatment equipment or medications (e.g., insulin injections or metered dose inhalers) and embarrassing to use (medication) in public.⁹ More invasive treatments such as dialysis were even more inconvenient and restrictive.^{5,9} Interestingly, new technologies (e.g., new forms of blood glucose monitoring) did not emerge as a significant source of distress or burden,⁴⁴ but this area requires further investigation.

Both subjective and objective burden

Some elements of treatment burden such as the number of medications,^{23,28,31,35,37,45,46} and time to administer or monitor treatment,³⁷ could be measured objectively. Patients and carers however, were not homogenous and therefore could have different perceptions concerning the burden related to similar tasks.³⁸ This subjective aspect of treatment burden was associated with a number of factors^{13,23,43} and therefore may be predictable. However, as it includes elements of an intangible nature, for example, guilt, hopelessness, and fear,³² its quantification could be difficult. Subjective aspects, such as fear of medication supply running out, the meaning attributed to side effects,¹⁶ beliefs about a medication's effectiveness^{30,31} beliefs about

the impact of medication on health and wellbeing (e.g., believing that medication is harmful and addictive) were associated with increased levels of treatment burden.⁹

Antecedents of treatment burden

Although a large number of antecedents of treatment burden were identified, there was minimal information about their particular influence on treatment burden, reflecting the lack of theoretical development within the research field. Antecedents were associated with characteristics of the patient, the disease, the treatment, the family or support network, and the healthcare system.

Patient characteristics

Gender seemed to be a key antecedent of burden because men and women experienced treatment burden differently. Women experienced more treatment burden than men and also reported more caregiver burden when their children were sick, possibly as a result of their traditional homemaker roles.^{13,40,41} A strong positive correlation was apparent between unemployment and treatment burden.^{34,40} A strong relationship between age and treatment burden also emerged.^{40,16,47} Elderly people seemed to experience more treatment burden than young people, as might be expected given the likelihood of illness and multiple conditions.

Disease conditions

As expected, comorbidity was associated with increased burden.²⁵ The presence of particular comorbidities,^{26,35} especially psychological illnesses such as anxiety or depression,⁴⁰ were associated with high levels of treatment burden.^{27,35,36} Particular chronic conditions such as diabetes³⁶ and schizophrenia³⁵ were associated with greater levels of treatment burden. Finally,

functional capacity, poor symptom control²³ and longer duration of illness⁸ could also lead to treatment burden.³⁹

Treatment characteristics

Treatment characteristics, particularly medications,^{8,13,30} were an important antecedent of burden. Using a high number of medications^{23,28,31,37,45,46} emerged as the most common antecedent in the literature. Particular dosage forms (e.g., injections as opposed to oral tablets), were also considered to be burdensome. Finally, changes to medication regimens were also a key antecedent of burden and have been attributed to a lack of continuity of healthcare.³⁷

Family support and engagement

Availability of extended family networks and support from an appropriate social network could lead to lower treatment burden.³² However, the support and assistance provided by a caregiver could also result in treatment burden for both the patient and the carer.²⁷ One way of reducing burden, particularly for carers, was to introduce an intervention designed to support family members to understand, communicate and participate in treatment decisions.²⁷

Healthcare systems

An aspect of healthcare that emerged frequently was the health practitioner-patient relationship.^{28,36} Failure of healthcare practitioners to provide adequate information regarding treatment was associated with treatment burden.³⁶ Poor communication between patients and healthcare providers about medication adherence was likely to result in the use of multiple medications (polypharmacy), which was associated with treatment burden.²⁸ The location of the healthcare centre also emerged as an antecedent of financial and time burden, caused by

long travel distances.³⁴ This issue was further complicated by a lack of financial reimbursement for travel of this kind.³⁴

Consequences of treatment burden

The concept analysis identified a number of consequences of treatment burden including poor adherence, reduced health and wellbeing, ineffective use of health resources, reduced employment and low productivity, and negative health impacts on family and carers.

Adherence

One of the most widely cited consequences of treatment burden was non-adherence to treatment. Non-adherence^{26,36,37,48} was then related to sub-optimal health outcomes,^{28,36} including disease relapse,^{30,35} decreased quality of life²³ and the unscheduled use of more expensive healthcare resources, such as increased emergency department visits and hospitalisation.³⁰ Non-adherence was also associated with increased school absences.²³

Non-adherence was most often linked to treatment burden resulting from medication characteristics, including the number of medications, their frequency of administration,⁴⁵ side effects²³ and perceived lack of efficacy.²³ As the number of medications being used increased, the rate of non-adherence associated with the addition of each additional medication decreased.⁴⁵ Hence, there appeared to be a threshold of treatment burden where additional medications did not add further burden. However, the addition of each additional medication did nevertheless add to the financial cost of treatment.²⁶ This was a concerning finding given that the elderly and welfare recipients were found to reduce their use of medications in response to the introduction of prescription co-payments and subsequently experienced an increase in serious adverse events.³³

Health and wellbeing

The health and wellbeing consequences of treatment burden were many and varied. Treatment burden affected patient choices about treatment,³⁶ with some patients who were recommended insulin refusing this therapy.³⁶ Such a choice was associated with poor glycemic control.³⁶ However, opting for a less efficacious alternative treatment could be a reasonable course of action given that ‘...difficult or demanding treatment regimens may appreciably lower treatment effectiveness, which may be possible to achieve with less burdensome treatment’.^{5:573} In other words, whilst a treatment might appear to have superior efficacy in the controlled setting of a clinical trial, in reality, the interaction between treatment regimen and treatment burden could create difficulties. Thus, patients may choose to select a less effective, but less burdensome treatment to suit their daily lives, which ultimately may result in better health outcomes.

Treatment burden was associated with a number of negative health outcomes including specific symptoms,^{16,28} recurrence of disease,^{27,35,43} decline in health,^{28,35} reduced survival,⁴³ decreased treatment satisfaction,²² and reduced quality of life.^{24,40} Treatment-related side effects were often found to have a marked impact on quality of life¹⁶ which was also affected by perceived treatment burden, disease severity²⁴ and disruption of lifestyle.⁴⁸ Finally, as well as increasing the risk of adverse outcomes, which was mediated by non-adherence, greater prescription co-payment burden was associated with increased self-reported psychological distress and attempted suicide in patients with schizophrenia.²⁶

Resource use

Ineffective use of resources has been attributed to treatment burden.³⁷ Unfortunately, a reduction in scheduled care (i.e., non-adherence) may result in a demand for unscheduled care (i.e., hospital admission), creating avoidable resource use.^{23,30} Perceived financial burden,

caused by prescription co-payments resulted in the increased self-reported use of unscheduled care, such as emergency room visits and hospitalisation.²⁶ Polypharmacy complicated therapy and healthcare delivery,²⁸ which added to unnecessary use of resources. Moreover, polypharmacy was accompanied by an increased risk that medications included in the treatment regimen were unnecessary and therefore a waste of resources.³¹

Employment

The burden of treatment had a marked impact on the patient's ability to attend work and maintain productivity. In a cancer clinic, patients who were still employed were absent for an average of 12.6 days during the month.³³ Absences from work were related to prescription co-payment burden,²⁶ the need to travel,³⁴ and side effects,^{33,40} including fatigue associated with chemotherapy. The latter resulted in the loss of 4.2 sick or vacation days per month.⁴⁰ In some instances, patients needed to change employment status in order to manage treatment burden.^{33,40} Caregivers also needed to take time off work to care for cancer patients.³³ Unfortunately, work absences could lead to feelings of guilt among patients about burdening their co-workers and lost productivity,⁴⁰ which added to burden.

Family and carers

Treatment burden was related to carer burden and fatigue,⁴³ causing patients to forgo caregiver support.³³ The distress caused by treatment burden was found to flow in both directions in that seeing a significant other (i.e., patient or carer) suffer could lead to further burden and distress,⁴² especially in the case of parents.^{24,41} There was evidence that effective treatment of a loved one resulted in significant benefits for carers.⁴²

Discussion

This concept analysis provides a much needed theoretical framework for understanding the dynamic, multidimensional and cyclic nature of treatment burden. We found that treatment burden is a dynamic process, evolving with the emergence of new treatment options and symptoms. It persisted over time, but perhaps reached a subjective threshold beyond which perceptions of burden no longer increase. The dimensions of treatment burden include undesirable physical effects of treatment (side effects), the economic burden imposed by treatment (financial burden), time required to obtain, administer and manage treatment (time burden), and the psychosocial aspects of burden including the impact on family and lifestyle (personal burden). Treatment burden has both subjective and objective elements including number of medications, time to administer and monitor treatment (objective) versus feelings of guilt, hopelessness, and fear relating to treatment (subjective). A range of antecedents and consequences were identified, although many of the consequences could also become antecedents, reflecting the cyclic nature of treatment burden. The attributes, antecedents and consequences emerging from the review of treatment burden are summarized in Figure 2, which also highlights the cyclic nature of the concept. As an outcome of this concept analysis, we define treatment burden *as a person's subjective and objective overall estimation of the dynamic and multidimensional burden that their treatment regimen for chronic illness has imposed on them and on their family members. It is influenced by a person's characteristics, disease duration/severity, treatment circumstances, level of family support and engagement and also the overall healthcare systems, in which the person obtains treatment.*

The health consequences of treatment burden are particularly concerning given that treatment burden has been associated with specific symptoms, recurrence of disease, decline in health, reduced survival, decreased treatment satisfaction, and reduced quality of life. There is a clear need to implement services that help alleviate the burden of treatment experienced by patients in order to improve their health and wellbeing. Another alarming consequence of

treatment burden, particularly from a public health perspective, was the ineffective use of resources. In an era of cost efficiency, poor use of health resources is particularly undesirable. By addressing poor adherence and consequently, treatment burden, it may be possible to identify ways of minimizing the use of more costly resources such as hospital admissions. The World Health Organization indicates that poor adherence to the treatment of chronic illness is a global problem averaging almost 50% in developed countries.⁴⁹ Strategies which increase adherence are urgently needed if we are to optimize health outcomes. However, these strategies must take into account the subjective aspect of treatment burden and its important cyclic nature.

Research implications

The attributes, antecedents and consequences identified in this review also have clear implications for all healthcare professionals to alleviate the burden of treatment for patients. As the perception of treatment burden could be subjective, strategies to alleviate its impact need to be individualized, reflecting the individual's circumstances and preferences. This review has reinforced the fact that it is not just health outcomes that are important for patients and their family, but also the way in which how health professionals achieve those outcomes for patients. Further, the dynamic nature of treatment burden means that for any one individual patient, their capacity to manage new and multiple treatments may vary over time. The complexity of this concept can best be managed through individualized and holistic care and ongoing evaluation that is responsive to the needs of each person.

The analysis has highlighted the fact that burden can also be a result of interactions with healthcare professionals. Poor health professional-patient relationships and a lack of adequate information regarding treatment were associated with high levels of treatment burden. As Moss and Crane²⁸ argued, poor communication between patients and healthcare providers about medication use may result in the provision of multiple medications, which could then lead to

treatment burden. Healthcare professionals need to develop a relationship that is sensitive to patient's preferences and offer explanations of treatment options that include their potential side effects. This type of relationship will enable patients to become more actively involved in decision making and integrate treatment with their daily lives, ultimately improving adherence and treatment outcomes.

Despite the variety of settings and methods used in the studies included in this concept analysis, treatment burden resulting from medication use emerged as a key theme. This finding is not surprising given that medication is one of the most common forms of treatment for chronic conditions. In Australia, reports indicate that Australians between the ages of 65 and 75 were taking an average of four medications in 2009 and will be taking, on average, six medications by 2019.⁵⁰ The findings present clear opportunities for health professionals who are prescribing or dispensing medications to engage in greater discussions and improve medication management among patients. Community pharmacists, in particular, are accessible and well placed to support medication management so that patients with chronic conditions receive the maximum benefit from their treatment.

Interestingly, the tasks of self-management (e.g., organizing treatment, monitoring symptoms, changing lifestyle) were identified as a major source of treatment burden. Similar to the findings of Gallacher et al.,³⁷ our study revealed a set of tasks associated with learning about treatments, engaging with and organizing the treatment, altering routines and monitoring symptoms and progress. It is ironic that these core tasks of self-management represent a significant burden for patients despite being seen as a solution for the long-term management of chronic illness in society. Gallacher et al.³⁷ were able to clearly distinguish between treatment burden and illness or disease burden, suggesting that our response to chronic illness generates a great deal of distress that is independent of that which might be experienced otherwise. It is not surprising that Gallacher et al. refer to treatment burden as the “work” of

chronic disease management. Our study has confirmed the important role this “work” plays in generating a sense of burden. This review identified many negative consequences of treatment burden some of which may result in the continued escalation of burden over time because they also act as antecedents. Breaking this cycle is important, as is the identification of the factors that have the greatest impact on treatment burden and those that can be most easily modified. Clearly, health professionals have a major role alongside patients and their families in alleviating the burden associated with the treatment of chronic illness.

Research limitations

Like any research, this review also has limitations that must be considered. Only research published in the decade between 2002 and 2011 was included in the analysis. These dates were chosen because treatment burden is a relatively new and evolving concept and therefore research conducted prior to this date was deemed inappropriate for the purposes of this review. Furthermore, the articles used in the concept analysis focused on selected chronic illnesses known to be associated with high burden of disease. We acknowledge that there may be high levels of treatment burden associated with other ongoing health conditions. Given the importance of treatment burden for patients and their family and lack of clarification of the concept to date, the insights from this review provide a valuable foundation on which to further develop this concept.

Conclusion

Given the potential negative impacts of treating a chronic illness(s), researchers and healthcare professionals need to engage in collaborative discussions and make cooperative efforts to help alleviate treatment burden in order to optimize health outcomes. Continued research into

treatment burden, its definition, assessment and impact, is needed in order to understand people's burden experience and implement treatment that suits the realities of daily life.

References

1. World Health Organization. *Noncommunicable diseases country profiles 2011*. Geneva: Switzerland, 2011.
2. Mathers CD, Vos ET, Stevenson CE *et al*. The burden of disease and injury in Australia. *Bulletin of the World Health Organization*, 2001; **79**: 1076-1084.
3. Gapstur RL. Symptom burden: a concept analysis and implications for oncology nurses. *Oncology Nursing Forum*, 2007; **34**: 673-680.
4. Australian Institute of Health and Welfare. *Australia's health, 2010. Australia's health series no. 12. Cat. no. AUS 122*. In: Australian Institute of Health and Welfare, ed. Canberra: Commonwealth of Australia; 2010.
5. Anderson RT, Skovlund SE, Marrero D *et al*. Development and validation of the insulin treatment satisfaction questionnaire. *Clinical Therapeutics*, 2004; **26**: 565-578.
6. Béchetille A, Arnould B, Bron A *et al*. Measurement of health-related quality of life with glaucoma: Validation of the Glau-QoL © 36-item questionnaire. *Acta Ophthalmologica*, 2008; **86**: 71-80.
7. Brod M, Hammer M, Kragh N *et al*. Development and validation of the Treatment Related Impact Measure of Weight (TRIM-Weight). *Health and Quality of Life Outcomes*, 2010; **8**: 19-30.
8. Brod M, Valensi P, Shaban JA *et al*. Patient treatment satisfaction after switching to NovoMixReg. 30 (BIAsp 30) in the IMPROVETM study: an analysis of the influence of prior and current treatment factors. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation*, 2010; **19**: 1285-1293.
9. Campbell JL, Kiebert GM, Partridge MR. Development of the satisfaction with inhaled asthma treatment questionnaire. *European Respiratory Journal*, 2003; **22**: 127-134.
10. Chen H, Cisternas MG, Katz PP *et al*. Evaluating quality of life in patients with asthma and rhinitis: English adaptation of the rhinasthma questionnaire. *Annals of Allergy, Asthma, & Immunology*, 2011; **106**: 110-118.
11. Henry B, Aussage P, Grosskopf C *et al*. Development of the Cystic Fibrosis Questionnaire (CFQ) for assessing quality of life in pediatric and adult patients. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation*, 2003; **12**: 63-76.
12. Modi AC, Quittner AL. Validation of a disease-specific measure of health-related quality of life for children with cystic fibrosis. *Journal of Pediatric Psychology*, 2003; **28**: 535-546.
13. Bernhard J, Maibach R, Thurlimann B *et al*. Patients' estimation of overall treatment burden: why not ask the obvious? *Journal of Clinical Oncology*, 2002; **20**: 65-72.
14. Oude Elberink JNG, van der Heide S, Guyatt GH *et al*. Analysis of the burden of treatment in patients receiving an EpiPen for yellow jacket anaphylaxis. *Journal of Allergy and Clinical Immunology*, 2006; **118**: 699-704.
15. Wilcox AR, Dragnev MCC, Darcey CJ *et al*. A new tool to measure the burden of Crohn's disease and its treatment: Do patient and physician perceptions match? *Inflammatory Bowel Diseases*, 2010; **16**: 645-650.
16. Ribí K, Bernhard J, Bohme C *et al*. Endocrine symptom assessment in women with breast cancer: what a simple "yes" means. *Supportive Care in Cancer*, 2007; **15**: 1349-1356.
17. Bailie GR, Cardone KE, Grabe DW *et al*. Quantifying home medication regimen changes and quality of life in patients receiving nocturnal home hemodialysis. *Hemodialysis International*, 2011; **15**: 234-242.

18. Corona J, Matsumoto H, Roye DP *et al.* Measuring quality of life in children with early onset scoliosis: development and initial validation of the early onset scoliosis questionnaire. *Journal of Pediatric Orthopedics*, 2011; **31**: 180-185.
19. Walker LO, Avant KC. Strategies for theory construction in nursing. Upper Saddle River, NJ: Pearson Prentice Hall, 2005.
20. Rodgers BL. Concepts, analysis and the development of nursing knowledge: the evolutionary cycle. *Journal of Advanced Nursing*, 1989; **14**: 330-335.
21. Rodgers BL, ed. Concept analysis: An evolutionary view. Philadelphia: Saunders; 2000.
22. Brod M, Christensen T, Bushnell D. Maximizing the value of validation findings to better understand treatment satisfaction issues for diabetes. *Quality of Life Research*, 2007; **16**: 1053-1063.
23. Graves MM, Adams CD, Bender JA *et al.* Volitional nonadherence in pediatric asthma: parental report of motivating factors. *Current Allergy and Asthma Reports*, 2007; **7**: 427-432.
24. Fiese BH, Wamboldt FS, Anbar RD. Family asthma management routines: connections to medical adherence and quality of life. *Journal of Pediatrics*, 2005; **146**: 171-176.
25. Rodbard HW, Green AJ, Fox KM *et al.* Impact of type 2 diabetes mellitus on prescription medication burden and out-of-pocket healthcare expenses. *Diabetes Research & Clinical Practice*, 2010; **87**: 360-365.
26. Kim E, Gupta S, Bolge S *et al.* Adherence and outcomes associated with copayment burden in schizophrenia: a cross-sectional survey. *J Med Econ*, 2010; **13**: 185-192.
27. Gutierrez-Maldonado J, Caqueo-Urizar A. Effectiveness of a psycho-educational intervention for reducing burden in Latin American families of patients with schizophrenia. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation*, 2007; **16**: 739-747.
28. Moss L, Crane PB. Exploring polypharmacy in elderly women after myocardial infarction. *Journal of Women and Aging*, 2010; **22**: 22-33.
29. World Health Organization. *Diagnosis and management of adverse drug reactions*. Geneva: Switzerland, World Alliance for Patient Safety, 2007.
30. Thomas P. The stable patient with schizophrenia - from antipsychotic effectiveness to adherence. *European Neuropsychopharmacology*, 2007; **17**: 115-122.
31. Tjia J, Micco E, Armstrong K. Interest in breast cancer chemoprevention among older women. *Breast Cancer Research and Treatment*, 2008; **108**: 435-453.
32. Ow R. Burden of care and childhood cancer: experiences of parents in an Asian context. *Health and Social Work*, 2003; **28**: 232-240.
33. Longo CJ, Fitch M, Deber RB *et al.* Financial and family burden associated with cancer treatment in Ontario, Canada. *Supportive Care in Cancer*, 2006; **14**.
34. Zucca A, Boyes A, Girgis A *et al.* Travelling all over the countryside: travel-related burden and financial difficulties reported by cancer patients in New South Wales and Victoria. *Australian Journal of Rural Health*, 2011; **19**: 298-305.
35. Nicholl D, Akhras KS, Diels J *et al.* Burden of schizophrenia in recently diagnosed patients: healthcare utilisation and cost perspective. *Current Medical Research and Opinion*, 2010; **26**: 943-955.
36. Vijan S, Hayward RA, Ronis DL *et al.* Brief report: the burden of diabetes therapy: implications for the design of effective patient-centered treatment regimens. *Journal of General Internal Medicine*, 2005; **20**: 479-482.

37. Gallacher K, May CR, Montori VM *et al.* Understanding patients' experiences of treatment burden in chronic heart failure using normalization process theory. *Annals of Family Medicine*, 2011; **9**: 235-243.
38. Ziaian T, Sawyer MG, Reynolds KE *et al.* Treatment burden and health-related quality of life of children with diabetes, cystic fibrosis and asthma. *Journal of Paediatrics and Child Health*, 2006; **42**: 596-600.
39. Brod M, Cobden D, Lammert M *et al.* Examining correlates of treatment satisfaction for injectable insulin in type 2 diabetes: lessons learned from a clinical trial comparing biphasic and basal analogues. *Health & Quality of Life Outcomes*, 2007; **5**: 8.
40. Henry DH, Viswanathan HN, Elkin EP *et al.* Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. *Supportive Care in Cancer*, 2008; **16**: 791-801.
41. Haugstvedt A, Graue M, Rokne B *et al.* Perceived family burden and emotional distress: similarities and differences between mothers and fathers of children with type 1 diabetes in a population-based study. *Pediatric Diabetes*, 2011; **12**: 107-114.
42. Martire LM, Gildengers AG, Karp JF *et al.* Treatment of late-life depression alleviates caregiver burden. *Journal of the American Geriatrics Society*, 2010; **58**: 23-29.
43. de Kraker J, Graf N, Van Tinteren H *et al.* Reduction of postoperative chemotherapy in children with stage I intermediate-risk and anaplastic Wilms' tumour (SIOP 93-01 trial): a randomised controlled trial. *Lancet*, 2004; **364**: 1229-1235.
44. Wysocki T, Gavin L. Paternal involvement in the management of pediatric chronic diseases: associations with adherence, quality of life, and health status. *Journal of Pediatric Psychology*, 2006; **31**: 501-511.
45. Benner JS, Chapman RH, Petrilla AA *et al.* Association between prescription burden and medication adherence in patients initiating antihypertensive and lipid-lowering therapy. *American Journal of Health-System Pharmacy*, 2009; **66**: 1471-1477.
46. Robertson TA, Cooke CE, Wang J *et al.* Effect of medication burden on persistent use of lipid-lowering drugs among patients with hypertension. *American Journal of Managed Care*, 2008; **14**: 710-716.
47. Yoon J, Adams JL, Ganz PA *et al.* Symptoms after breast cancer treatment: are they influenced by patient characteristics? *Breast Cancer Research and Treatment*, 2008; **108**: 69-77.
48. Olinder AL, Kernell A, Smide B. Missed bolus doses: devastating for metabolic control in CSII-treated adolescents with type 1 diabetes. *Pediatric Diabetes*, 2009; **10**: 142-148.
49. World Health Organization,. Adherence to long-term therapies: evidence for action. 2003. Available at: http://www.who.int/chp/knowledge/publications/adherence_full_report.pdf, accessed 11 May 2012,
50. Australian Department of Health and Ageing,. Evaluation of the DAA/PMP Programs. 2010. Available at: [http://www.health.gov.au/internet/main/publishing.nsf/Content/5B1B138DA00BB9C7CA2578150083984E/\\$File/DAA%20PMP%20Report.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/5B1B138DA00BB9C7CA2578150083984E/$File/DAA%20PMP%20Report.pdf), accessed 11 May 2012,
51. Fried TR, Bradley EH, Towle VR. Assessment of patient preferences: integrating treatments and outcomes. *The Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*, 2002; **57B**: S348-S354.