What is the Impact of Interventions Targeted at Health Literacy on Patient Outcomes, Medication Adherence and Health Related Quality of Life?

A Systematic Review

Student Name: Suzanne Moore

Word Count: 27,974

Institution: School of Postgraduate Studies
           Royal College of Surgeons in Ireland
           123 St Stephen’s Green
           Dublin 2

Award: Higher Degree MSc

Supervisor: Dr Tom O’Connor

Date of Submission: October 2014
I declare that this thesis, which I submit to RCSI for examination in consideration of the award of a higher degree MSc is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research programme this is duly acknowledged in the text such that it is possible to ascertain how much of the work is my own. I have not already obtained a degree in RCSI or elsewhere on the basis of this work. Furthermore, I took reasonable care to ensure that the work is original, and, to the best of my knowledge, does not breach copyright law, and has not been taken from other sources except where such work has been cited and acknowledged within the text.

Signed: Suzanne Moore

RCSI Student Number: 12136042

Date: October 2014
Contents

Abbreviations List ................................................................. 12
Abstract ............................................................................. 13
Chapter 1 Background ......................................................... 17
  1.1 Literacy ......................................................................... 17
  1.2 What constitutes health literacy ...................................... 18
  1.3 Prevalence of limited health literacy ............................... 19
    1.3.1 European and International health literacy .............. 19
    1.3.2 Health literacy in the Irish context ......................... 19
  1.4 Patient information ..................................................... 20
  1.5 Patient information, medication and health literacy .......... 21
  1.6 Medication adherence ................................................ 22
  1.7 Pharmacy and health literacy ......................................... 24
  1.8 Health related quality of life ......................................... 25
    1.8.1 Health related quality of life and HIV ...................... 25
    1.8.2 Health related quality of life and cardiac conditions .. 26
    1.8.3 Health related quality of life and glaucoma ............. 26
    1.8.4 Health related quality of life and asthma ............... 27
    1.8.5 Health related quality of life and arthritis ............. 27
  1.9 Interventions for health literacy .................................... 28
    1.9.1 Simple interventions ............................................ 29
    1.9.2 Complex interventions ......................................... 29
  1.10 Tools for health literacy assessment ............................. 30
    1.10.1 TOFHLA ......................................................... 30
    1.10.2 REALM ......................................................... 31
  1.11 Ethical issues ............................................................ 32
    1.11.1 Communication .................................................. 32
    1.11.2 Consent .......................................................... 32
    1.11.3 Quality and safety .............................................. 33
  1.12 Aims and objectives .................................................. 33
  1.13 Summary ............................................................... 34
  1.14 Conclusion ............................................................. 36
Chapter 2 Methodological Issues in Systematic Reviews

2.1 Introduction

2.2 Research background

2.2.1 Research

2.2.2 Nursing research

2.2.3 Types of research

2.2.3.1 Quantitative research

2.2.3.2 Qualitative research

2.3 Systematic Reviews

2.4 Meta-analysis

2.5 Evidence based practice

2.6 The Cochrane Collaboration

2.7 The Campbell Collaboration

2.8 Randomised controlled trials

2.9 Development of a Systematic Review

- The Five Steps:

2.9.1 Formulation of a research question

2.9.2 Searching and identifying relevant literature

2.9.2.1 Published and unpublished literature

2.9.2.1.1 Published literature

2.9.2.1.2 Unpublished or Grey literature

2.9.2.2 Wording and synonyms

2.9.2.3 Inclusion and exclusion criteria

2.9.3 Appraising the quality of the studies sourced

2.9.3.1 Data analysis

2.9.4 Summarising the evidence

2.9.4.1 Heterogeneity

2.9.4.2 Tabular and graphical presentation

2.9.4.3 Narrative presentation

2.9.5 Interpreting the findings

2.10 Strengths and limitations of a Systematic Review

2.10.1 Strengths of Systematic Review

2.10.2 Limitations of Systematic Review
List of Figures

Figure 1: Venn Diagram of Search Strategy
Figure 2: Search Strategy Flow Diagram
List of Tables

Table 1: Data extraction table
Table 2: Risk of bias table for a single study
Table 3: Summary table
Table 4: List of excluded studies with reasons
Table 5: List of included studies and rationale for inclusion
Table 6: Sequence generation table
Table 7: Allocation concealment table
Table 8: Performance bias table
Table 9: Detection bias table
Table 10: Attrition bias table
Table 11: Reporting bias table
Acknowledgements

For all my family and friends, there is no possible way that this would have been achievable without you.

To Robbie, who has been essentially a single parent for the last few months. Thank you for the love, support, understanding and most importantly, cups of tea 😊 You are my rock and I don’t know what I would have done without you xxx

To my babies, Daniel and Katie who’s ‘help’ has been an invaluable source of distraction. I am so looking forward to making up for lost time and enjoying the family time I have so yearned for, for what feels like an eternity now xxx

To my Mammy! What can I say, my constant source of unconditional love and support. There are no words to describe how grateful I am for you xxx

To Ger, my editor extraordinaire. I am forever indebted for the academic, professional and personal advice. I am however, no longer able to associate with such a scholarly failure 😊 xxx

To my friends, especially my bestest Sue xxx For bearing with me while I ignored texts, phone calls and cancelled dates. But I’m back now, so look out!!

And finally, to the team in the RCSI. To Dr Helen McVeigh and Professor Niamh Moran in the School of Postgraduate Studies, who provided assistance and guidance in my time of need. To Professor Zena Moore and especially, Dr Tom O’Connor, who took over a sinking ship, restoring faith, hope and resolve. There is absolutely no way I would be here without your help and support.

Thank you all from the bottom of my heart xxxxx
Abbreviation List

ACQ7 – Asthma Control Questionnaire  
ACR – Albumin to Creatinine Ratio  
ACS – Acute Coronary Syndrome  
ADEs – Adverse Drug Events  
AEM – Avoidance Endurance Model  
AF – Arthritis Foundation  
A-fib – Atrial fibrillation  
AHL – Adequate Health Literacy  
AIDS – Acquired Immunodeficiency Syndrome  
AQOL – Asthma-Related Quality of Life Questionnaire  
A-REALM – Arthritis-Specific-Rapid Assessment of Adult Literacy in Medicine  
ART – Anti-Retroviral Therapy  
BP – Blood Pressure  
CALD – Culturally and Linguistically Diverse  
CD4 – A type of lymphocyte which is an important part of the immune system  
CHF – Chronic Heart Failure  
CI – Confidence Interval  
CIME – Clinically Important Medication Errors  
CKD – Chronic Kidney Disease  
CLBP – Chronic Low Back Pain  
COPD – Chronic Obstructive Pulmonary Disease  
CSO – Central Statistics Office  
CV – Cardiovascular Disease  
CVD – Cardiovascular Disease  
DM – Diabetes Mellitus  
DWM – Days Without Glaucoma Medicine  
EGFR – Estimated Glomerular Filtration Rate  
EBL – Evidence Based Learning  
EBP – Evidence Based Practice  
GEEs – Generalised Estimating Equations
HAART – Highly Active Antiretroviral Therapy
HAO – Health Assessment Questionnaire
HCP – HealthCare Professional
HeiQ – Health Education Impact Questionnaire
HF – Heart Failure
HIV – Human Immunodeficiency Virus
HL – Health Literacy
HSE – Health Service Executive
HTN – Hypertension
IHCAs – Interactive Health Communication Applications
IHL – Inadequate Health Literacy
IQR – Interquartile Range
IRRr – Incidence Rate Ratios
ITT – Intention To Treat
MASES – Medication Adherence Self-efficacy Scale
MDI – Metered-Dose Inhaler
MEMS – Medication Event Monitoring System
MeSH – Medical Subject Headings
MHL – Marginal Health Literacy
Mini-Cog – Cognitive Function Test
MMSE – Mini Mental State Exam
MPR – Medication Possession Ratio
NALA – National Adult Literacy Agency
NHS – National Health Service
NP – Nurse Practitioner
NVS – The Newest Vital Sign
OPD – Out Patients Department
PA – Psoriatic Arthritis
PACT – Patient Asthma Concerns Tool
P-ADEs – Potential Adverse Drug Events
PIH – Partners In Health
PILL-CVD – Pharmacist Intervention for Low Literacy in Cardiovascular Disease
QoL – Quality of Life
RA – Rheumatoid Arthritis
RCSI – Royal College of Surgeons in Ireland
RCT – Randomised Control Trial
REALM – The Rapid Estimate of Adult Literacy in Medicine
RIP – Rest In Peace
RNA – Ribonucleic Acid
SAS – Statistical Analysis Software
SPSS – Statistical Package for the Social Sciences
SR – Systematic Review
SSD – Sample Size Determination
S-TOFHLA – Shortened-Test of Functional Health Literacy
T2DM – Type 2 Diabetes Mellitus
TOFHLA – The Test of Functional Health Literacy
WHO – World Health Organisation
Abstract

Aim: To explore the impact of interventions targeted at health literacy on patient outcomes, medication adherence and health related quality of life.

Method: Systematic Review

Background: Health literacy has been identified as an essential competency for the maintenance of health and quality of life. Health literacy is an essential component of the skill base required of patients when they become ill and require professional intervention. Additionally, research suggests that an overwhelming 50% of patients do not take their medications as prescribed and that medication adherence or lack thereof, will have a greater impact on our future health than any specific medical treatment

Findings: Following a systematic search of the literature, seven studies were identified for inclusion in this review. Examination of the overall results identified that low health literacy levels do in fact negatively impact on a patients' ability to adhere to medication instructions. Results also established a link between lack of medication adherence and reduced health related quality of life.

Conclusion: Patient's with lower levels of health literacy have lower medication adherence and subsequently poorer health related quality of life prospects.
Chapter 1  Background

This chapter will define Literacy and Health Literacy (HL), and will highlight the differences between them. A picture of the current state of health literacy nationally and internationally will be drawn. Factors which influence health literacy within the healthcare environment will be identified. The interventions and tools used to assess and identify limited health literacy within the healthcare setting will be discussed in some detail. Ethical issues surrounding health literacy will be highlighted. Finally, the research question will be outlined together with the aims and objectives of the review.

1.1  Literacy

Literacy in its first and most basic sense is defined as a person's ability to read and write (Merriam-Webster 2014). A second and much more complex definition of literacy encompasses not only the basics of reading and writing, but also the ability of a person to develop knowledge and evolve themselves to the point where they can function as an individual, capable of making informed decisions and contributing to the wider community (UNESCO 2008, Keefe and Copeland 2011). As far back as 1966, UNESCO (2008) identified literacy as a topic which required investigation and established the Experimental World Literacy Programme. They acknowledged the importance of literacy by identifying it as a basic human right (UNESCO 2008). Literacy can be viewed as a source of not only individual, but also community growth. When people can, with confidence, interact with friends, family and the people in their community, it builds self-esteem, establishes relationships and can be a trigger for change. Keefe and Copeland (2011) recommend five core definitional principles for literacy. Firstly, they suggest that acquiring literacy is attainable by all and they also concur with UNESCO in recognising literacy as fundamental. Thirdly, they acknowledge that literacy is not achievable alone, but with interaction and communication with others. Finally, they place responsibility for literacy on the community as a whole, establishing a basis for teamwork in all aspects of life.
1.2 What constitutes health literacy

Health literacy is distinctive of basic literacy as it encapsulates a wider range of skills. It is, as its name suggests, literacy within the healthcare environment (Lambert and Keogh 2014a). Health literacy includes reading, writing and numeracy coupled with cultural experience, an understanding of health and wellbeing along with basic communication ability (Brown et al. 2011). Health literacy or lack thereof, is an area which is broadly acknowledged as being responsible for miscommunication and causing unnecessary angst among a large population of our community (Carmona 2006, Jordan et al. 2010).

Health literacy is an essential component of the skill base required of patients when they become ill and require professional intervention. Low or limited health literacy levels are associated with increased poverty, higher rates of acute presentations, higher readmission rates, increased risk of medication error, higher number of co-morbidities and financial implications for both the patient and the healthcare provider (Williams et al. 1995, Weiss et al. 2005, Carmona 2006, Davis et al. 2006, Bennett et al. 2009, Powers et al. 2010). It has been suggested (Williams et al. 1995, Brown and Bussell 2011, Martensson and Hensing 2012) that recognising there is a problem is the first step in tackling the significant problem that is health literacy. There is, however, a shortfall in knowledge on the part of healthcare professionals regarding how to identify and deal with the problem. Lambert and Keogh (2014b) and Mackert et al. (2014) imply that assuming understanding can have a detrimental effect on not only the doctor-patient relationship, but also the overall health and wellbeing of the patient, therefore advocating health literacy education of healthcare professionals.

The healthcare environment is constantly evolving and under pressure to reduce costs whilst maintaining safe and quality care. Carmona (2006) and Jordan et al. (2010) draw attention to the fact that health literacy has been
neglected and, as a result, is not benefiting from the rapid advances afforded to Medicine. There is a push towards patients taking ownership of their treatment (Lara and Salberg 2009, Brown and Bussell 2011), and the transfer of care from acute to outpatient settings (Davis et al. 2006, Shaw et al. 2009). This shift from the traditional, safe, assumed ‘patient role’, coupled with the mental and physical trauma of an acute illness, is understandably potentially unsettling for patients and carers. It is noted that being literate is not necessarily a precursor to being health literate (Ishikawa and Yano 2008). Furthermore, patients and carers who are usually health literate can, faced with the foreign terminology and concepts within the healthcare environment, find it challenging, overwhelming and sometimes even humiliating (Lambert and Keogh 2014b).

1.3 Prevalence of limited health literacy

1.3.1 European and International health literacy

Statistics illustrate that health literacy levels within Ireland are in keeping with European and International levels. In their study of health literacy and health promoting behaviors, von Wagner et al. (2007) identified that 11.4% of people in the United Kingdom had only limited health literacy. Maastricht University conducted a European health literacy survey in 2012. Results show a staggering 47.6%, virtually one in two people, are below an acceptable level of health literacy (Maastricht 2012). In America, Kutner et al. (2006) established that over half of the population or 53%, have only intermediate health literacy, 22% of people have basic health literacy, with a further 14% below basic levels of health literacy. Again, the results in Australia, although slightly higher, are consistent with the rest of the world, with 59% of the population on or below the minimal acceptable level (AUSSTATS 2006, Nutbeam 2009).

1.3.2 Health literacy in the Irish context

Research has identified that one in four Irish nationals are classed as illiterate (CSO 2012), with 40% of the population having unacceptable health literacy levels (Department of Health, 2012). These statistics,
coupled with the ever increasing numbers of foreign nationals, who do not speak English as a first language, settling in Ireland (CSO 2012) call upon renewed measures from healthcare providers to ensure that safe, competent and quality assured practice is available to all.

The data harvested both nationally and internationally provide concrete evidence of the scale of the problem. Given that the most vulnerable members of our society are already susceptible to being somewhat overlooked, the added burden of limited health literacy can be detrimental (Carmona 2006, Bennett et al. 2009).

1.4 Patient information

Patient information is an integral part of the patients' journey through the hospital process. Effective communication with patients encourages them to take ownership of their care (Hirsh et al. 2009) and improves the doctor-patient relationship (Kenny et al. 1998). Patient information when given and absorbed by the service user can also potentially reduce hospital costs by increasing understanding of appointment letters and prescription instructions. Specific verbal and written patient information are one of the many ways of communicating information to patients (Kenny et al. 1998, Gal and Prigat 2005, Shaw et al. 2009). The National Acuit Literacy Agency (NALA) has been raising awareness with regard to the deficits in adult literacy since 1980. The Health Service Executive (HSE 2009) and NALA collaborated to produce a document highlighting best practice relating to providing patient information, but to date there has been no national policy to ensure creators of patient information adhere to best practice. It is noted that the ability of a patient to respond to information given to them is directly linked to the way it is designed (Gal and Prigat 2005, Fuchs and Hippius 2007, Maat and Lentz 2010).

The National Health Service (NHS) in the United Kingdom has identified the various forms of written patient information as quality indicators. It has comprehensive guidelines on the production and development of written
patient information (NHS 2010). However the NHS only recommended that
the creators of written patient information follow these guidelines. The
United States Administration have made it illegal for personnel involved in
providing information to the public, not to use plain language (PLAIN 2011).
However, despite the policy and guidelines available internationally
concerning best practice when writing patient information, there are no
concrete indicators relating to information contained within specific patient
information.

There is a wealth of information, in multiple forms and on any given topic to
which patients can refer. There is however, a missing link in the chain as it
has been found that despite this, patients are unaware of where they can
get help (Jordan et al. 2010). Patient information leaflets and on-line
search engines provide a cost effective solution to patient education in a
time-pressured clinical environment (Shaw et al. 2009, Smith and
Koehlmoos 2011). What appears to have been overlooked however is the
patient, their abilities and their preferences. Jordan et al. (2010) stress that
a patient requires the capacity to process and retain information in order for
it to be utilised appropriately. While Shaw et al. (2009) found that patients
actually have a preference for, and respond more favorably to, face-to-face,
verbal communication, thus advocating the more traditional doctor patient
relationship.

1.5 Patient information, medication and health literacy
The use of written patient information is universal within the healthcare
setting (Gal and Prigat 2005) and there is extensive patient information
relating to medication. As far back as 1998, the European Commission
published guidelines on the readability of the label and packaging of
medicinal products for human use (Jordan et al. 2010). However, to date
there has been no national policy for the creators of written patient
information to reference.
Research suggests that an overwhelming 50% of patients do not take their medications as prescribed (Brown and Bussell 2011) and that medication adherence or lack thereof, will have a greater impact on our future health than any specific medical treatment (Sabate 2003). Several reasons for medication error have been identified, questioning both the accuracy of the information provided and the functional ability of the patient who was prescribed the medication. In their cross-sectional study of 395 patients, Davis et al. (2006) unearthed a number of barriers to medication adherence. They found that a large number of patients did not receive any type of information, verbal or written, about their medication. Variance between instructions about the same medication in different containers was also an issue which caused unnecessary confusion. There is a general acknowledgement that information and instructions provided with medication is far too complex for many patients, which is exacerbated by the presence of limited health literacy (Davis et al. 2006, Kripalani et al. 2007, Chi et al. 2012). Conversely, Davis et al. (2006) found that even perceived simple instructions such as ‘take one teaspoon’ led to medication error as patients often administered a ‘tablespoon’ instead. Whatever the reason for error, literature has identified an unsustainable level of inaccuracy. Lindquist et al. (2011) conducted a survey of 254 patients. After discharge, patients ‘take home prescription’ from their medical notes were accessed and patients were contacted by phone, following prior consent, and questioned about their medications. Results revealed that an unacceptable level of 56% of patients contacted had a medication error within 48 hours of discharge. They also determined however, that 39.3% of errors were in fact as a result of incorrect discharge information.

1.6 Medication adherence

Medication taking is however more intricate than the information contained within the instructions. It has been acknowledged within the literature that the topic of medication taking is so extensive that is has generated its own terminology (NCCSDO 2005). The terms compliance, concordance and adherence have all been coined to describe the same thing. The term compliance indicates a dictatorial instruction from a caregiver to a patient
Compliance can be described as a patient's obedience to medication instruction (Endrizzi and Rossi 2006). Concordance on the other hand is viewed as a partnership between the patient and the healthcare professional (Bell et al. 2007). Concordance involves interaction, discussion and mutual agreement on a way forward (NCCSDO 2005). Adherence attempts to recognise the freedom of choice on the part of the patient (NCCSDO 2005). It is suggested that patients who adhere to prescribed medications are more likely to have healthy behavior in general (Aronson 2007). Lack of medication adherence can be categorised as intentional and unintentional (NCCSDO 2005, DeMaria 2012). Intentional non-adherence is where the patient makes a conscious decision to omit or stop taking prescribed medications (Cortet and Benichou 2006). It is suggested that unintentional non-adherence to medications is a result of misunderstanding of instructions, the provision of incorrect information and/or confusion due to the prescription of multiple medications (Bell et al. 2007). Overall it has been established that adherence to medications prescribed for chronic illnesses is significantly lower than desired (Cortet and Benichou 2006).

A patient's cultural beliefs and attitudes also contribute to a decision to take medications or follow instructions correctly (Gatti et al. 2009, Brown and Bussell 2011). There is an unfounded belief that taking medication can lead to adverse effects and/or addiction (Brown and Bussell 2011). There is evidence presented by Fonarow (2003), which suggests that patients consider medications prescribed in hospital of higher importance than standard medical prescriptions, consequently they are more likely to adhere to instructions. Therefore, it is essential that medications are reconciled on discharge (Brown and Bussell 2011), together with protected time to ask questions and discuss medications with appropriate members of the multidisciplinary team (Gatti et al. 2009, Johnson et al. 2010, Brown and Bussell 2011). Furthermore, patients should be contacted post discharge so any questions can be clarified and any necessary reassurance provided (Lindquist et al. 2011).
Therefore, as a result of the above discussion and for the purposes of this systematic review, medication adherence will be the terminology referred to throughout the text.

1.7 Pharmacy and health literacy
Throughout the literature, there is extensive reference to the role of healthcare professionals, particularly the physician, in the education and prescription of medications for patients within the healthcare environment (DeWalt et al. 2004, Seligman et al. 2005, McCormack et al. 2010, Brown and Bussell 2011). Interestingly, very few references represent the pharmacist, who is essentially the only member of the multidisciplinary team, who is an expert in the field. Carlisle et al. (2011) state that the pharmacy is a vital part of the healthcare environment, which is reinforced by Emmerton et al. (2010) who state that pharmacists have a recognised role in education and promotion of appropriate and safe medication administration. As far back as the beginning of the 1970's, pharmacists have had a key role in patient education (Covington and Pfiffer 1972). This thinking is still endorsed by Carlisle et al. (2011) and Johnson et al. (2013), who recognise the responsibility of pharmacy and the pharmacist as a patient advocate, therefore being responsible for providing individual health literacy tailored information and advice.

It is acknowledged that the pharmacy, both as a department and as part of the extended multidisciplinary team, has an opportunity to change (Emmerton et al. 2010, Carlisle et al. 2011). This change requires the education of pharmacy staff in the multifaceted issue of health literacy and patient centered education and information (Carlisle et al. 2011, Johnson et al. 2013). Wolf et al. (2009) and Johnson et al. (2013) identify the lack of clarity and understanding of prescription labels and instructions as a health and safety risk, thus reinforcing the need for change.
1.8 Health related quality of life

Health related quality of life is perhaps one of the broadest concepts referred to within the healthcare community. Health related quality of life is individual to every patient, illness and healthcare professional (Guyatt et al. 1993, Romero et al. 2013, ATS 2014), with little common ground from which to establish a baseline (Chen et al. 2005, Imam et al. 2011). The concept of health related quality of life is multidimensional (Guyatt 1993) and encompasses an individual’s emotional mental, physical and social thoughts, actions and interactions (Romero et al. 2013, ATS 2014, ISOQOL 2014). Carr and Higgenson (2001) define it as a reflection of the gap between what an individual expects and what they experience. The term can be associated with healthy individuals as readily as those with an acute, chronic or terminal diagnosis. However, Khanna and Tsevat (2007) suggest that health related quality of life in those with chronic illnesses is invariably diminished. It is virtually impossible therefore, to determine an appropriate definition. To this end, health related quality of life could not be defined for the purposes of this systematic review. Consequently, health related quality of life will be discussed with reference to the co-morbidities identified for this systematic review, namely: HIV (Kalichman et al. 2013), heart failure (Morrow et al. 2007, Murray et al. 2007, Kripalani et al. 2012), glaucoma (Muir et al. 2012), asthma (Paasche-Orlow et al 2005) and arthritis (Rudd et al. 2009).

1.8.1 Health related quality of life and HIV

Health related quality of life and HIV was a feature of one of the included studies (Kalichman et al. 2013). Human Immunodeficiency Virus (HIV) is a chronic disease which causes healthy cells in an infected person’s body to change and ultimately destroy themselves (AIDS.gov 2014). Health related quality of life in HIV infected persons is difficult to quantify however (Campsmith et al. 2003, van der Kolk et al. 2010, Imam et al. 2011), as there are a number of influencing factors. Some of the evidence suggests a link between improved health related quality of life and prolonged survival (Mapes et al. 2003, Gotay et al. 2008, van der Kolk 2010). It is important to
note, and of significance to this particular systematic review, that health related quality of life in HIV participants is directly related to adherence to highly active antiretroviral therapy (HAART) (Flemming et al. 2004, van der Kolk et al. 2010, Imam 2011). Furthermore, a relationship between health related quality of life and limited health literacy was also established (Nojomi et al. 2008, Imam 2011). Conversely, Campsmith et al. (2003) found no correlation between the two.

1.8.2 Health related quality of life and cardiac conditions

Health related quality of life and cardiac conditions was a feature of three of the included studies (Morrow et al. 2007, Murray et al. 2007, Kripalani et al. 2012). Murray et al. (2007) discussed heart failure in their study. Morrow et al. (2007) referred to chronic heart failure in theirs. While Kripalani et al. (2012) examined acute coronary syndromes or acute decompensated heart failure in their study. Therefore for the purposes of this systematic review, the three conditions will be referred to in the same context. Heart failure is described as a prevalent debilitating clinical syndrome which can lead to progressive deterioration and consequently, reduced health related quality of life (Westlake et al. 2002, Polikandrioti 2008, Fotos et al. 2012). Heart failure is also responsible for the leading cause of morbidity and mortality in the United States (AHA 1998, Westlake et al. 2002). Polikandrioti (2008) and Fotos et al. (2012) advocate focusing on multidimensional management of the symptoms of heart failure in an effort to improve health related quality of life, rather than dwelling on a cure. Additionally the literature advocates the inclusion of mental health issues when addressing an individual’s health related quality of life (Westlake et al. 2002, Azevedo et al. 2008).

1.8.3 Health related quality of life and glaucoma

Health related quality of life and glaucoma was a characteristic of one of the included studies (Muir et al. 2012). Glaucoma is a result of optic nerve damage which can lead to visual loss and potentially blindness. Glaucoma has been identified as the leading cause of blindness in the world (Kellogg Eye Center 2014). The primary cause of diminished health related quality
of life in glaucoma sufferers is visual loss, which impacts on a person's ability to function alone (Aspinal et al. 2008, Skalicky and Goldberg 2013). In their study of 581 patients, Nordmann et al. (2003) found that deterioration in vision can be effectively managed with adherence to topical glaucoma treatment, therefore is of particular significance to the findings of this particular systematic review.

1.8.4 Health related quality of life and asthma

Health related quality of life and asthma was discussed in one of the included studies (Paasche-Orlow et al 2005). Asthma can be classified as a chronic disease whereby inflammation of the airways causes bronchoconstriction (Luyster et al. 2012) which poses a significant burden on the public health system in the United States. Furthermore, van Manen et al. (2001) state that patients with an airway obstructive disease such as asthma are also predetermined to suffer co-morbidities. To this end, health related quality of life can be a considerable problem within this cohort of patients. Ford et al. (2003) established that participants in their study were at risk of at least 10 days of impaired physical or mental health as a result of their asthma, reflecting an almost 50% increase in comparison to their counterparts. Strine et al. (2004) confirm this finding stating that participants with asthma are 50% more likely to report mental distress than those without. Of interest in relation to this particular systematic review, van Manen et al. (2001) established a link between participants in their study and low education levels. Therefore it could be hypothesised that the participants had low levels of literacy and health literacy in particular.

1.8.5 Health related quality of life and arthritis

The final included study health related quality of life and arthritis (Rudd et al. 2009). Arthritis is defined as a systemic, chronic inflammatory disease (Rupp et al. 2004) and is classified as one of the most prolific of the disability causing chronic diseases (Dominick et al. 2004). Health related quality of life and arthritis, in its many forms, has been extensively researched (Hurst et al. 1997, Dominick et al. 2004, Rupp et al. 2004, Pollard et al. 2005, Gratacos et al. 2013). The research concurs with that
of research into the previously discussed co-morbidites, implying that
disease and illness can have a dramatic effect on an individual’s health
related quality of life (Guyatt et al. 1993, Strombeck et al. 2000, Ford et al.
literature also unearthed evidence that adherence to an appropriate drug
regime was tantamount to the management of the debilitating side effects
of the disease (Gratacos et al. 2013, Heimans et al. 2013). Conversely,
Pollard et al. (2005) and Corbacho and Dapueto (2010) suggest that the
treatment available to patients with arthritis is not sufficient, resulting in a
deleterious impact on health related quality of life and suggest a review of
same.

The overall consensus is that regardless of the disease, health related
quality of life is always a casualty (Guyatt et al. 1993, Strombeck et al.
al. 2013, Skalicky et al. 2013). This discovery is confounded by the fact
that health related quality of life represents different things to different
people (Guyatt et al. 1993, Romero et al. 2013, ATS 2014). This section
highlights the importance of not only recognising it as a treatable symptom,
but the need to treat it differently for each patient.

1.9 Interventions for health literacy

Research has linked low health literacy with lower quality of life (Williams et
2009, Powers et al. 2010). Individuals with limited health literacy are more
prone to be smokers, excessive drinkers with a higher probability of
physical inactivity, depression, chronic diseases and ultimately a 75% higher
possibility of mortality (Weiss et al. 2005, Carmona 2006, Bostock and
Steptoe 2012). There have been several tools developed to measure
health literacy and a number of interventions developed as a result
(Pignone et al. 2005, Clement et al. 2009). There are, however, no
definitive answers to the best way to do either (Clement et al. 2009,
Sheridan et al. 2011).
1.9.1 Simple interventions

Interventions have been categorised as 'simple' and 'complex'. Simple interventions include altering the language, replacing text with pictures and providing audio-visual resources (Clement et al. 2009). The use of PLAIN English is becoming internationally recognised as best practice and a quality indicator. The PLAIN English Campaign is an organisation which actively promotes the removal of 'jargon' and 'gobbledygook' from not only medical, but all public information (PLAIN English Campaign 2011). Their 'Crystal Clear' mark is a coveted symbol of excellence with literacy agencies worldwide (PLAIN English Campaign 2011). NALA's 'Plain English' mark is also a symbol of excellence which indicates that international best practice standards have been met (NALA 2014). The increased shift towards the use of pictures and audiovisual information is advocated and vindicated given the volume of patients with limited health literacy (Brown and Bussell 2011, Carlisle et al. 2011, Johnson et al. 2013). In view of the relatively cost neutral change from current written patient information to the simple interventions discussed, it is hard to understand why healthcare organisations have not embraced them more fully, considering the potential improvement of patient care and reduced cost to the organisation due to fewer readmissions, co-morbidities and misinformation. This confirms Johnson et al. (2013) observation that despite the importance of oral communication, written communication is still the most prolific.

1.9.2 Complex interventions

More complex interventions target behaviors, delivery and the organisation (MRC 2000). Kane (2008) tackles the subject of behaviors in his review of patients with Ulcerative Colitis. It was found that empowering patients and promoting autonomy resulted in increased adherence to prescribed medication. Empowering patients and the promotion of autonomy are both interventions available free of charge to healthcare facilities, through appropriate and effective communication, but are consistently overlooked.
Organisational interventions incorporate the healthcare facility working as a
team, rather than the fractured individual departments which are a current
feature of most hospitals. Wolf et al. (2009) advocate the standardisation
of information, more training for healthcare professionals, further research
and regulatory guidance to ensure patients with limited health literacy are
not left behind.

Regardless of the intervention used, it is recommended that the 'Teach
Back' method is incorporated (Schillinger et al. 2003, DeWalt et al. 2004,
'Teach Back' requires to the patient to regurgitate information and
instructions received to determine their level of understanding about same.
The rationale behind 'Teach Back' is to overcome the presumption of
understanding (Davis et al. 2006).

There is ongoing research into the interventions and their effectiveness.
However the majority of studies focus on short-term effects. For their worth
to be truly evaluated, long-term studies and action plans are required

1.10 Tools for health literacy assessment

The literature has identified a number of tools utilised to assess health
literacy levels (DeWalt et al. 2004, Weiss et al. 2005, Davis et al. 2006,
McCormack et al. 2010, Powers et al. 2010). Although several tools were
identified, two tools were consistently prioritised for use, namely: The Test
of Functional Health Literacy (TOFHLA) and The Rapid Estimate of Adult
Literacy in Medicine (REALM). Therefore both these tools will be
discussed.

1.10.1 TOFHLA

The Test of Functional Health Literacy in Adults is widely recognised as the
most comprehensive indicator of a patient’s health literacy status (Parker et
al. 1995, Powers et al. 2010). An English and Spanish version of TOFHLA
are available. TOFHLA measures understanding of written instructions and numerical data and is carried out in two sections. The first section consists of three segments of written text contained within the patient’s personal written information and instructions, for example, pre-operative care and a prescription. This is followed by a comprehension test relating to the written information, which provides 50 questions with blank spaces, to which the patient must insert the correct multiple choice answer. Secondly, there is a 17-item numerical test, which relates to the patient’s ability to understand appointment dates, blood glucose readings, prescription instructions and financial information (Parker et al. 1995, Powers et al. 2010). There is however, some criticism of the TOFHLA process as it takes on average twenty two minutes to complete (Williams et al. 1995, Baker et al. 1999).

Baker et al. (1999) felt TOFHLA, although thorough, was excessively time consuming. They decided to develop a shortened version, the S-TOFHLA, successfully reducing it from approximately twenty two minutes to twelve minutes to complete. The first section was condensed to two segments of written text, followed by 36 questions. The second section was condensed from a 17 to a 4-item numerical test. Use of the S-TOFHLA is advocated within the time-restricted healthcare environment as it is more efficient and less intimidating (Baker et al. 1999, Keselman et al. 2007, Lindquist et al. 2011).

1.10.2 REALM
The Rapid Estimate of Adult Literacy in Medicine (REALM) tool is an assessment of the patient’s ability to read and articulate medical terminology (Powers et al. 2010). It consists of 66 medical words written in English in an increasingly difficult order. The patient is required to correctly pronounce each word. A score is given for each word pronounced properly. REALM is the shortest tool to administer, taking only 3 minutes to complete. The major drawback of REALM is the lack of comprehension assessment (Davis et al. 1993, Parker et al. 1995, Baker et al. 1999).
1.11 Ethical issues

Health literacy is, as previously noted, not as straightforward as it would appear. In fact, Martensson and Hensing (2012) describe it as a ‘complex phenomenon’, which is confirmed by Smith and Koehlmoos (2011). Despite the documented advantages of establishing patient’s health literacy levels, healthcare professionals need to be aware of all considerations.

1.11.1 Communication

Health literacy assessment has been hailed as the ‘newest vital sign’ (Powers et al. 2010). However the determination of a patient’s health literacy level can be a delicate subject (Williams et al. 1995, Seligman et al. 2005, Lambert and Keogh 2014b). Even though there is widespread agreement regarding the need to identify patients with low health literacy levels (Williams et al. 1995, Brown and Bussell 2011, Martensson and Hensing 2011), Powers et al. (2010) advice caution stating that routine health literacy testing can potentially have a negative effect. They imply that patients may feel they are being tested and categorised, thus leading to a breakdown in communication before a relationship has had time to become established. Healthcare professionals have a responsibility to foster relationships with the patients in their care. This promotes a forum for open and honest discussion regarding treatment, diagnosis and care. However, if the relationship is established on mistrust it may be very difficult to restore lost confidence.

1.11.2 Consent

It is universally accepted that nurses are patient advocates. Nurses assume responsibility for ensuring that patients receive appropriate information and education, thus providing them with the ability to make informed decisions (Williams et al. 1995, Gazmararian et al. 2005, Lambert et al. 2013). This duty of care does not negate the responsibility of other healthcare professionals however (Shaw et al. 2009, Jordan et al. 2010, Martensson and Hensing 2011). This can potentially lead to gaps in care when one member of the multidisciplinary team assumes another member has provided instruction. Informed consent is both time intensive and
difficult to achieve (Lara and Salberg 2009), which is perpetuated by the
frequency of patients misunderstanding the information and education
provided to them (Carmona 2006). This questions the validity and legality
of any consent, verbal or written.

1.11.3 Quality and safety

Communication and consent, or lack thereof, are essentially the
personification of quality and safety. To this end, as with other areas of
potential harm, such as infection control, there has been a call for the
introduction of ‘Universal Precautions’ for health literacy (Paasche-Orlow et
al. 2006, Johnson et al. 2013, Lambert and Keogh 2014b). It will however
require a greater understanding and acceptance of patient’s health literacy
levels to achieve this (Powers et al. 2010).

1.12 Aims and objectives

To date, the literature has identified an abundance of research. There is a
general consensus about health literacy, its effects and outcomes on
patient’s health and well being and its correlation with co-morbidities and a
less favorable overall conclusion (Williams et al. 1995, Weiss et al. 2005,
Carmona 2006, Bennett et al. 2009, Powers et al. 2010). There is
however, to the best of the author’s knowledge, no published systematic
reviews relating to the research question posed, namely: What is the
Impact of Interventions Targeted at Health Literacy on Patient Outcomes,
Medication Adherence and Health Related Quality of Life?

To this end, the aim of this systematic review is to explore health literacy,
its impact on medication adherence, chronic diseases and the overall
outcomes for patients burdened with this problem. The objectives of this
systematic review are:

- To explore the impact of interventions targeted at health literacy on
  medication adherence
- To explore the impact of interventions targeted at health literacy on
  health related quality of life
1.13 Summary

Literacy and health literacy have been identified as essential competencies for the maintenance of health and quality of life. Health literacy is an essential component of the skill base required of patients when they become ill and require professional intervention. Low or limited health literacy levels are associated with increased poverty, higher rates of acute presentations to hospitals, higher readmission rates, increased risk of medication error, higher number of co-morbidities and financial implications for both the patient and the healthcare provider. The healthcare environment is constantly evolving and under pressure to reduce costs whilst maintaining safe and quality care. It is often difficult for patients and carers to adapt to alien terminology and concepts within the healthcare environment.

Research has identified that one in four Irish nationals are classed as illiterate, with 40% of people having unacceptable health literacy levels. This is in keeping with European and International levels. In the United Kingdom, 11.4% of the population have limited health literacy, while in Europe an overwhelming 47.6% have low health literacy. In America, 53% of the population have only intermediate health literacy. In addition, the majority of the population, 59% are on or below the minimal acceptable threshold of health literacy in Australia. The data harvested both nationally and internationally provide concrete evidence of the scale of the problem.

Patient information is an integral part of the patient’s journey through the hospital process. Despite verbal and written patient information being one of the most common ways of communicating information to patients, there is, to date, no national policy to ensure creators of patient information adhere to best practice. In the United States, it is illegal for personnel involved in providing information to the public, not to use plain language. However, this has not transferred globally. Several reasons for medication error were identified, questioning both the accuracy of the information provided and the functional ability of the patient prescribed the medication.
There is a consensus that information and instructions provided with medication are far too complex for many patients, which is exacerbated by the presence of limited health literacy. Literature suggests that 56% of patients contacted had a medication error within 48 hours of discharge. Pharmacy and the pharmacist were identified as is a vital part of the healthcare environment, with a recognised role in education and the promotion of appropriate and safe medication administration.

Throughout the years, there have been countless studies conducted in an effort to determine the best interventions to use when dealing with patients with limited health literacy. To date, there is no definite consensus as to which intervention is best. Interventions can be grouped as ‘simple’ and ‘complex’. Simple interventions include altering the language, replacing text with pictures and providing audio-visual resources. Complex interventions target behaviors, delivery and the organisation. However, regardless of the intervention used, it is recommended that the ‘Teach Back’ method is incorporated.

There have also been a number of tools identified within the literature for identifying patients who may have a problem. The tools TOFHLA and REALM will be discussed in detail, as they were consistently referred to throughout the literature.

Issues relating to compliance, concordance and adherence were discussed and the level to which patients will adhere to what they have been instructed to do by a healthcare professional. Ethical considerations were also addressed as nurses have assumed responsibility for ensuring that patients receive appropriate information and education, thus providing them with the ability to make informed decisions. This has left a potential gap in care due to multidisciplinary team misunderstanding. To this end, as with other areas of potential harm, such as infection control, there has been a call for the introduction of ‘Universal Precautions’ for health literacy.
Finally, the aims and objectives of the present systematic review were identified and the relevance of the study to health literacy and its effects and outcomes on patient’s health and well being and its correlation with comorbidities and a less favorable overall conclusion were highlighted.

1.14 Conclusion

This chapter defined literacy and health literacy, and highlighted the differences between them. A picture of the current state of health literacy nationally and internationally was drawn. Factors which influence health literacy within the healthcare environment were identified. The interventions and tools used to assess and identify limited health literacy within the healthcare setting were discussed and ethical issues surrounding health literacy were highlighted. Finally, the research question for this particular systematic review was outlined together with the aims and objectives of the review.
Chapter 2  Methodological Issues in Systematic Reviews

2.1 Introduction

This chapter will firstly investigate the topic of research and nursing research and its relevance to the development of evidence based practice (EBP). The chapter will then discuss the concept of the systematic review (SR) as a research method. The strengths and weaknesses of SR will be critically appraised and a rationale given for the use of this method for this particular study.

2.2 Research background

2.2.1 Research

Research endeavours to extend available knowledge by systematically and scientifically interrogating the available literature (Clamp et al. 2004). Burns and Grove (2003) define research as a meticulous and systemic inquiry that reinforces and processes existing knowledge, while at the same time developing new knowledge. They go further saying that the ultimate goal of research is the development of quality evidence based practice, for use within the healthcare profession.

2.2.2 Nursing research

Nursing research is, by definition, the gathering of knowledge relating to the nursing profession. It is known that nursing research enables knowledge building, which in turn helps to improve practice and outcomes, by the promotion of evidence based practice (Knapp 1930, Watson and Keady 2008, Gerrish and Lacey 2010). Also Polit et al. (2001) define nursing research as a systematic investigation which endeavours to enhance nursing knowledge, including nursing practice, education, and administration. Burns and Grove (2003) simplify the definition stating that nursing research is the creation of a practical knowledge base, to which healthcare professionals can refer with confidence.
2.2.3 Types of research

Research can be divided into two methods: Quantitative research and Qualitative research.

2.2.3.1 Quantitative research

Quantitative research is defined as research which utilises traditional methods of study, for example, experiments, surveys, or correlation studies (Knapp 1930). Burns and Grove (2003) maintain that quantitative research is a systematic, robust and objective means of gathering knowledge about the world. Reliability and validity are essential to quantitative research. Without these essential traits, the essence of any research conducted is missing.

2.2.3.2 Qualitative research

Qualitative research is a broader method of research design which provides narrative data and is based on an interpretative philosophy (Topping 2010). Qualitative research concentrates on the lived experience. Its focus is on how people feel and experience different events (Nolan 2008, Bell 2010). Qualitative research must always demonstrate rigor and truth. These two elements are paramount to qualitative research. Any qualitative research study which omits rigor and truth may not be relied upon, thereby calling into question any conclusions reached.

2.3 Systematic Reviews

Systematic reviews can be catalogued as either Quantitative or Qualitative (Crowther and Cook 2007). They are however, more often than not, categorised under the Quantitative Methodology umbrella (Moore and Cowman 2008). As previously identified, quantitative research is concerned with the systematic gathering of information in order to answer a specific question. Quantitative research is built upon the foundations of reliability and validity. LoBiondo-Wood and Haber (2010) affirm quantitative research as looking to test a theory or answer research questions using statistical methods. This sentiment is echoed by Thomas and Harden (2008) and Timmins et al. (2012), who acknowledge the ever
erupting, and constant flow of available literature and the integration of systematic reviews as a reliable method of decanting same.

Systematic reviews are widely viewed as a source of evidence based research to which healthcare practitioners can refer, in the knowledge that the care they deliver is safe and quality driven (Harden et al. 2003, Smith et al. 2011). The processes of a systematic review are exact (Khan et al. 2003, Victor 2008), ensuring that the stringent, but necessary steps are followed in order to maintain their high standing (The Cochrane Collaboration 2014). A systematic review discovers, evaluates and distils any and all information available on a specific subject matter (Khan et al. 2003, Victor 2008), resulting in a body of evidence which is both reliable and of high quality (NHMRC 2000).

2.4 Meta-analysis

Meta-analysis is a quantitative research technique which can be incorporated into a systematic review (DiCenso et al. 2005). Meta-analysis involves the collation of comparable data within a number of different studies with the aim of showcasing the overall effect of an intervention in a statistical fashion (Macnee 2004, Roe 2007, Moore and Cowman 2008, Rumrill et al. 2010). The outcomes of meta-analysis refer to the statistical data in numerical and tabular form (Moore and Cowman 2008). The results of a systematic review can be presented in a narrative or statistical format (Macnee 2004). It is important however, that when offering results by way of meta-analysis, to ensure that it is appropriate to do so (Moore and Cowman 2008, Booth et al. 2010). There are several situations where the pooling of results would be inappropriate, for example, if the same outcomes have been measured differently within similar studies, if the included studies are not comparable in terms of population, setting and/or intervention or if not all studies have evaluated the effect of an intervention (Booth et al. 2008).
2.5 Evidence based practice

Evidence Based Practice (EBP) is a relatively new phenomenon (DiCenso 
et al. 2005). It denotes the development of quality research, which is 
subsequently merged with both clinical proficiency and patient standards 
(Sackett et al. 2000), with the aim of improving practice and establishing 
standards (Baigis and Hughes 2001, DiCenso et al. 2005). It is widely 
recognised that the provision of high quality, evidence based care is 
underpinned by, and dependant on, the ability of healthcare professionals 
to confidently discharge their duties in the knowledge that the care they 
provide has been established on a foundation of robust evidence (Gerrish 
2010). Evidence based practice is more and more frequently being sought 
by clinical decision makers and expected from healthcare professionals 
(Profetto-McGrath 2005, DiCenso et al. 2005, Polit and Beck 2012). In a 
constantly evolving profession, nurses are required to ensure that the care 
they provide is not only cost effective (Polit and Beck 2012), but of a high 
safety and quality standard (Burns and Grove 2003, Macnee 2004, Majid et 
 al. 2011).

It is important to be mindful however, that evidence based practice is only 
as reliable and trustworthy as the medium from which it is generated 
(Murphy and Cowman 2008, Gerrish 2010). The Hierarchy of Evidence 
provides guidance to researchers pertaining to each research methodology 
and its allocation to the hierarchy pyramid (Gerrish 2010). Muir Gray 
(1997) identified systematic reviews containing multiple randomised 
controlled trials as the top of their evidence pyramid. This is endorsed by 
Polit and Beck (2012), who state that systematic reviews and evidence 
based practice are intrinsically linked, especially when the systematic 
review is comprised of randomised control trials (RCT), which are widely 
viewed as the ‘Gold Standard’ research method (DiCenso et al. 2005, 
Moore and Cowman 2008).
2.6 The Cochrane Collaboration

Archie Cochrane (1909-1988), the inspiration for the establishment of The Cochrane Collaboration in 1993, was an epidemiologist and a medical researcher (Moore and Cowman 2008, The Cochrane Collaboration 2014). Cochrane recognised the negative impact of non-research based practice on the morbidity and mortality of pregnant women (The Cochrane Collaboration 2014). He understood the need for evidence based research and the importance of such literature being accessible to the care givers (Moore and Cowman 2008).

The Cochrane Collaboration is a not-for-profit, internationally recognised association (The Cochrane Collaboration 2014), and is a leader in the critical appraisal and synthesis of research evidence for the production of summaries of the strength of evidence to support or refute the specific intervention under exploration (Moore and Cowman 2008). The researched literature contained within The Cochrane Library is written for, and peer reviewed by, healthcare professionals at all levels. Recognised by, and in partnership with, the World Health Organisation (WHO), The Cochrane Collaboration is a leader in original, high quality, evidence based research (The Cochrane Collaboration 2014).

2.7 The Campbell Collaboration

Dr Donald Campbell (1916-1996), like Archie Cochrane, was a champion of evidence based change. Dr Campbell believed in the need for Government reform in order to improve people's well being through improved policy and practice (The Campbell Collaboration 2014). Although The Campbell Collaborations' roots are embedded in education, crime and justice, social welfare and international development rather than medical science, the ethos of the The Campbell and Cochrane Collaborations are synonymous and are considered sibling organisations (The Campbell Collaboration 2014).
Akin to the format of Cochrane systematic reviews, a Campbell systematic review is peer-reviewed. They have identified ten key principles on which they base their research, namely: collaboration, enthusiasm, avoiding duplication, minimising bias, keeping up to date, relevance, access, quality, continuity and wide participation (The Campbell Collaboration 2014). Their literature can be accessed online in the format of a monograph series.

2.8 Randomised controlled trials

Randomised control trials are globally considered to be the ‘gold standard’ research method (Moore and Cowman 2008). RCTs are traditionally regarded as a methodology utilised by the medical profession (Burns and Grove 2003, Smith 2008). However, more recently, nursing researchers have embraced their reliability and robustness, resulting in a high standard of evidence based care giving (Burns and Grove 2003, Smith 2008). The Cochrane and Campbell Collaborations both, for the most part, deal with the randomised controlled trials and controlled clinical trial, highlighting the importance of these methodologies, consequently ensuring a steadfast standard of excellence contained within their systematic reviews (Moore and Cowman 2008). Notwithstanding this, methodologies with less ‘notoriety’ should not be dismissed as they too have the potential to provide strong and reliable evidence.

Randomised control trials are conducted with the aim of establishing the effectiveness of an intervention (Nelson et al. 2010). Selected participants are randomly allocated into either an intervention or control group. This unique design of a randomised controlled trial ensures the maximum reduction in the possibility of bias, therefore strengthening the validity and generalisation of the results (Thomas et al. 2004, White and Schmidt 2005, Victor 2008). Thomas et al. (2004) have identified randomised controlled trials as the strongest study design methodology.
2.9 Development of a Systematic Review

– The Five Steps:

A systematic review is, by definition, a body of work which is methodical and efficient. Consequentially, there is a well established and widely recognised step by step approach which all systematic reviews must adhere to (Harden et al. 2004, White and Schmidt 2005, Liu et al. 2013), namely:

1. Formulation of a research question
2. Searching and identifying relevant literature
3. Appraising the quality of the studies sourced
4. Summarising the evidence
5. Interpreting the findings

2.9.1 Formulation of a research question

The formulation of a research question is the cornerstone of any piece of research (O’Mathuna 2010, Polit and Beck 2012). It is the first text that any reader is presented with, therefore it is essential to ensure that the question identifies the subject matter being researched (Khan et al. 2005, White and Schmidt 2005). Formulation of an appropriate research question can take time and requires an in-depth understanding of the subject matter being investigated (NHMRC 2000, Polit and Beck 2012). Khan et al. (2005) suggest that a free-form research question is plausible. However, they advocate the use of a structured question, encompassing the study population, design, intervention and outcomes. White and Schmidt (2005) and Manterola et al. (2013) also endorse this structured development of the research question. Furthermore, it is also imperative to establish that the topic of interest has not already been published (CRD 2008). This ensures that the research conducted is not only original, but worthy of publication (CRD 2008). To this end, Victor (2008) champions the involvement of appropriate stakeholders at this stage of the process and indeed throughout the development of the whole systematic review.
2.9.2 Searching and identifying relevant literature

Searching and identifying of relevant literature is not as straightforward as the instruction would suggest (Crowther and Cook 2007, Garg et al. 2008). A structured, comprehensive search is essential to identify all relevant studies (Khan et al. 2003, DiCenso et al. 2005, CRD 2008, Manterola et al. 2013), although it has been suggested that the identification of all appropriate literature is virtually impossible (NHMRC 2000). In addition, the search process should be documented at all stages. The rationale for this is to provide the author with a bank of literature from which to reference discussion (White and Schmidt 2005), in addition to supplying the reader with a retraceable search history in the event that further investigation is required (CRD 2008). However, there are several considerations to be made before any search is undertaken.

2.9.2.1 Published and unpublished literature

2.9.2.1.1 Published literature

Published literature can be accessed via the traditional routes of searching the electronic databases such as Medline, Pubmed, The Cochrane Library and Cinahl to name just a few (DiCenso et al. 2005, Bruce et al. 2008, Liu et al. 2013). Searching published literature can unearth further relevant literature via the reference list or bibliography of initial studies (CRD 2008). An author search following the identification of a study of particular interest can also assist in the search for pertinent literature (Polit and Beck 2012), as authors typically have an interest in a specialised area, thus exposing additional primary research studies (Polit and Beck 2012). Similarly, a citation search is another valuable tool whereby additional appropriate literature can be sourced following the detection of specific interest study (CRD 2008).

2.9.2.1.2 Unpublished or Grey literature

Unpublished or grey literature involves manual probing of all non-electronic data, including journals, unpublished reports and Government publications (Benzies et al. 2006, Polit and Beck 2012). Direct contact with authors to
request further information is also advocated (Garg et al. 2008), thus ensuring the inclusion of all appropriate literature, consequently increasing the reliability of the systematic review. Furthermore, searching beyond the electronic database is also perceived as essential (Bowling 2002, CRD 2008, Victor 2008).

2.9.2.2 Wording and synonyms

The chosen wording to be entered into any search engine is essential (DiCenso et al. 2005). Given the abundance of literature available on any given topic, it is imperative that the wording and synonyms selected reflect the research question appropriately (DiCenso et al. 2005, Polit and Beck 2012). The National Health and Medical Research Council (NHMRC 2000) advocate the use of a Venn diagram when conducting a literature search. They suggest that following the identification of a research question it is broken down into three separate components. Each of the components are searched independently, followed then with a more in-depth search combining each sphere using the words “AND” and “OR” (NHMRC 2000, Murphy and Cowman 2008). Therefore, by enhancing and extending the search enough it will ensure its reliability. The Venn diagram developed this particular systematic review and can be viewed in Figure 1.
Figure 1: Venn Diagram of search strategy

2.9.2.3 Inclusion and exclusion criteria

The identification of appropriate inclusion and exclusion criteria, otherwise referred to as sampling criteria is a basic but essential part of any research project. Burns and Grove (2003) imply that the list of characteristics required to conduct a research project are individual to each separate project. They advocate the use of strict inclusion and exclusion criteria in order to ensure the literature identified during a search is a true reflection of the target population required to answer the research question asked (Burns and Grove 2003).

Searching and identifying literature for any research project can be a long and arduous task (White and Schmidt 2005), which can be eased to some
degree by adopting the knowledge and expertise of a librarian (Burns and Grove 2003).

2.9.3 Appraising the quality of the studies sourced

The quality of literature available can vary dramatically (White and Schmidt 2005, CRD 2008). The tendency for the publication of literature with significant clinical findings and/or the preference for 'positive outcome' research conclusions cannot be ignored (Bowling 2002). The probability of bias, both negative and positive, has the potential to undermine the findings of any study (CRD 2008). Therefore, quality critical appraisal of all prose found is not only required, but a crucial step on the ladder (Khan et al. 2003, CRD 2008). The researcher is required to evaluate each individual aspect of the literature sourced (Khan et al. 2003). A quality appraisal tool, like that utilised by Thomas et al. (2004), assists in the identification of sourced literature under the headings of 'strong', 'moderate' and 'weak'. Following this, appropriate, quality articles can be incorporated into the review, leaving the more fragile behind (Thomas et al. 2004).

2.9.3.1 Data analysis

Data analysis has been identified as potentially the most critical step in the systematic review process (Lacey 2010). Appropriate analysis of the data sourced is essential to ensure that the results presented are accurate and reflective of the included studies (Kim and Choi 2008). Data analysis requires thorough reading and understanding of the included studies, coupled with the establishment of trustworthiness. This is ideally carried out by more than one researcher, to help ensure accuracy of data. Following this, the relevant data is extracted and assembled into a workable format. It is advised, when working with large numbers of studies to collaborate with a statistician to help guarantee accuracy of data collected (Lacey 2010). All steps of data analysis should be explicitly documented and transparent (Kim and Choi 2008, Lacey 2010).
2.9.4 Summarising the evidence

Following the identification of studies which are of high quality, the evidence unearthed then requires presentation. The National Health and Medical Research Council (2000) advocate the use of both tabular and graphical summaries. Systematic reviews however, also require a narrative synthesis of the data sourced (CRD 2008). Whether tabular, graphical or narrative, the literature should be summarised as separate entities.

2.9.4.1 Heterogeneity

Heterogeneity is the term used to describe divergence between similar literature sourced (Polit and Beck 2012, Moore 2012). Variables within literature can, depending on the circumstances, be viewed as negative or positive. Variances within the literature can be viewed as a pitfall when, following evaluation of the literature, the results of the studies are inconsistent (NHMRC 2000). Conversely, those same variances are seen as affirmative when the results present the same, despite the presence of variation in inclusion and exclusion criteria (NHRMC 2000).

2.9.4.2 Tabular and graphical presentation

The use of tables within the context of a systematic review, are key to the presentation of data and results (Polit and Beck 2012). Tables have the capacity to categorise data in a structured manner, thus visually regurgitating information in a simple form for the reader.

Graphical presentation of data can appear in multiple forms. Forest plots are most commonly utilised within the meta-analysis methodology (Polit and Beck 2012, Moore 2012). The identification of the confidence interval (CI) is visualised on a forest plot. The confidence interval specifies the strength and reliability of the data contained within the literature appraised (Macnee 2004, Watson 2008), thus illustrating the incidence of bias (Polit and Beck 2012, Moore 2012).
2.9.4.3  Narrative presentation

Despite the ease of data interpretation via tabular and graphical means, narrative presentation of the summarised data is a definitive piece of the systematic review jigsaw (Thomas et al. 2004, CRD 2008). This summary of the results is descriptive and contains information relating to the identified inclusion and exclusion criteria, identification of heterogeneity and outcomes (Thomas et al. 2004). The narrative presentation, although summarised, sets the tone for the dissemination of data in the final step of the ladder, for example, interpreting the findings (CRD 2008).

2.9.5  Interpreting the findings

The concluding step in the systematic review ladder is interpreting the findings (O'Mathuna 2010, Polit and Beck 2012). The previous step of summarising the results showcases the raw data discovered within the appropriate literature (Polit and Beck 2012). Interpreting the findings tasks the researcher with exploring the risk of bias and identifying any other issues which may tarnish the overall findings or recommendations of the review (Khan et al. 2003, Higgins and Green 2011).

2.10  Strengths and limitations of a Systematic Review

A systematic review is the end result of a process which endeavours to answer a specific research question by means of rigorous searching, analysing, evaluation and synthesis of a number of primary research articles on a topic of particular and explicit interest (Macnee 2004, Crowther and Cook 2007, Garg et al. 2008). Strengths and limitations are an inherent part of any research project (Garg et al. 2008). A systematic review, despite what its name suggests is as subject to perceived strengths and weakness as all other types of research. Critical appraisal is a crucial step on the ladder for the development of evidence based practice (Duffy 2005). Burns and Grove (2003) endorse the use of critical appraisal. They suggest that in spite of the use of the term critical, that critical appraisal is in fact a driving force behind quality and the identification of evidence based literature (Burns and Grove 2003). The strengths and weaknesses of a systematic review are discussed below.
2.10.1 Strengths of Systematic Review

The Cochrane Collaboration, an internationally recognised centre of excellence in the field of research, specialise in the production and dissemination of evidence based recommendations for practice where possible (DiCenso et al. 2005, The Cochrane Collaboration 2006). The Collaboration has throughout its history established a benchmark for researchers providing strict guidelines for the development of systematic reviews which endeavour to minimise bias and errors (Bowling 2002). Their worldwide reputation thus reinforces the perceived validity of the systematic review as a source of evidence based knowledge (Garg et al. 2008).

Systematic reviews are widely seen as an acceptable way in which healthcare professionals can keep abreast of up to date, evidence based practice (Collins and Fauser 2005, Crowther and Cook 2007, Garg et al. 2008, Faggion et al. 2010). Systematic reviews provide us with the ability to answer specific, often narrow questions (Crowther and Cook 2007, Polit and Beck 2012). Service users expect and deserve a high level of knowledge and expertise (Crowther and Cook 2007, Garg et al. 2008). However, Crowther and Cook (2007) imply that, healthcare professionals do not always have the time or the inclination to search, appraise, interpret and summarise data from the seemingly endless torrent of research articles. Healthcare professionals have in effect delegated the task to others in a bid to maintain the link between current research and optimal healthcare provision (Crowther and Cook 2007).

The utilisation of systematic reviews within the clinical setting also has an impact on cost (DiCenso et al. 2005). In an ever-increasing struggle to keep within budgets, while providing safe and quality care, evidence based guidelines provided by systematic reviews can help spread already stretched resources a little further (Crowther and Cook 2007).
2.10.2 Limitations of Systematic Review

While the advantages of systematic reviews appear to be set in stone, the disadvantages are as compelling.

The backbone of any systematic review is the formulation of a research question (White and Schmidt 2005, Victor 2008, O'Mathuna 2010, Polit and Beck 2012). The research question must be specific and focused (Crowther and Cook 2007, Garg et al. 2008, Nocini et al. 2010). The task of devising a question however, is in itself an arduous mission (NHMRC 2000). Crowther and Cook (2007) imply that if a question is not of a high enough quality, it will in turn reflect on the systematic review as a whole, thus reducing its reliability.

The search strategy is another area which despite having specific guidelines (The Cochrane Collaboration 2006) can be at the mercy of the researcher. Strict inclusion and exclusion criteria should be set prior to undertaking any search (Khan et al. 2003, Thomas et al. 2004, White and Schmidt 2005, O'Mathuna 2010). Collins and Fauser (2005) suggest that the preference of the researcher may alter, consequently swaying from being a strict and exclusive reviewer to a more liberal and inclusive reviewer. Both Crowther and Cook (2007) and Garg et al. (2008) highlight that the quality of a systematic review is wholly dependent on the quality of the contributing studies. Direct contact with the authors to request further information is also at the discretion of the researcher (Garg et al. 2008). To ensure the inclusion of all appropriate literature, thus increasing the reliability of the systematic review, searching beyond the electronic database is essential (Bowling 2002, CRD 2008).

The inclusion of unpublished literature is also a bone of contention (Benzies et al. 2006, Crowther and Cook 2007). Thomas et al. (2004) and Garg et al. (2008) endorse the inclusion of grey literature. Conversely, White and Schmidt (2005) and Crowther and Cook (2007) caution the use of grey literature as it is not peer-reviewed, therefore leaving it open to
interpretation and potentially reducing the quality of the literature, which in turn reduces the quality of the systematic review.

While organisations like The Cochrane Collaboration have set a standard for the development of systematic reviews, the potential for bias cannot be entirely ruled out (Bowling 2002, Garg et al. 2008, Nocini et al. 2010). Both DiCenso et al. (2005) and Garg et al. (2008) suggest that the title of systematic review does not guarantee ‘due rigor’. Nocini et al. (2010) endorse this thinking implying that while a systematic review can detect small but clinically significant effects of an intervention, if the results of those interventions are positive, they are more likely to be published, thus giving way to publication bias. Vickers et al. (1998) also agree with this school of thought, highlighting in their own systematic review that certain countries have a higher publication ratio for positive outcome research. Heterogeneity is natural variation, which arises between studies sourced (Moore 2012). A higher incidence of heterogeneity, gives way to lower quality and confidence in results found (DiCenso et al. 2005).

Finally, the emergence of the systematic review as the benchmark for sourcing quality, evidence based literature (Duffy 2005, DiCenso et al. 2005, Moore and Cowman 2008) appears to nullify the value and contribution of other properly designed and diligently researched literature (Crowther and Cook 2007). It is important not to lose sight of the original and still worthy role of the humble primary research article as an individual (Crowther and Cook 2007).

Strengths and limitations are an inherent part of any research project (Garg et al. 2008). Systematic reviews, as with all research, are subject to appraisal. This chapter has critically appraised the strengths and the limitations of the systematic review as a research method. The identification of strengths and limitations assists the researcher, highlighting areas which can potentially reduce the quality of their review. As Garg et al. (2008) suggest, it is wise for any researcher to carefully consider the quality of all literature prior to the inclusion of same in any body of work.
Overall however, in spite of the apparent abundance of limitations, the systematic review is a proven method of providing reliable, evidence based research, thus a worthy choice of methodology in this instance.

2.11 Summary

Research, both quantitative and qualitative, has been identified as a journey to find evidence based practice through the medium of a systematic and scientific interrogation (Clamp et al. 2004), that reinforces and processes existing knowledge, while developing new knowledge (Burns and Grove 2003). Nursing research is the gathering of nursing related knowledge, which ventures to improve practice and outcomes, by the promotion of evidence based practice (Knapp 1930, Polit et al. 2001, Burns and Grove 2003, Watson and Keady 2008, Gerrish and Lacey 2010).

Systematic reviews are for the most part categorised under the Quantitative Methodology umbrella (Begley 2008). Quantitative research is built upon the foundations of reliability and validity (LoBiondo-Wood and Haber 2010).

Systematic Reviews are widely viewed as providing evidence based research to which healthcare practitioners can refer, in the knowledge that the care they deliver is safe and quality driven (Harden et al. 2003, Smith et al. 2011). A systematic review can be presented in both narrative and statistical format (Macnee 2004). Meta-analysis involves the collation of comparable data within a number of different studies with the aim of showcasing the overall effect of an intervention in a statistical fashion (Macnee 2004, Roe 2007, Moore and Cowman 2008, Rumrill et al. 2010).

There are five specific steps involved in the generation of a systematic review namely:

1. Formulation of a research question
2. Searching and identifying relevant literature
3. Appraaising the quality of the studies sourced
4. Summarising the evidence
5. Interpreting the findings
Within each of the five steps, there are several additional steps which should be followed in order to ensure a quality and unbiased end product.

Finally, the strengths and limitations of a systematic review were critically appraised. As identified, strengths and limitations are an inherent part of any research project (Garg et al. 2008). The identification of strengths and limitations is essential to assist the researcher in highlighting areas of potential pitfalls (Garg et al. 2008).

2.12 Conclusion

The systematic review as a research method has been thoroughly discussed in this chapter. The strengths and limitations of the systematic review were critically appraised. Although the emergence of limitations appears to have outweighed the strengths, the author believes that in practice and with due diligence, the overall method of systematic review is in fact sound, resulting in a piece of work which is not only reliable, but potentially contributing to safe and quality patient care.
Chapter 3  Methodology

3.1  Introduction

This chapter will focus on the methods to be employed for the purpose of conducting this systematic review. Firstly, the objectives will be highlighted paying particular attention to the target population, interventions utilised and outcomes of same. Secondly, inclusion and exclusion criteria will be specified, providing specific details pertaining to participants, types of interventions used and the expected outcomes. The search strategy will then be discussed. The Medical Subject Headings (MeSH) and derivatives used to search for appropriate literature will be identified, along with any limits applied and the databases searched. Finally, in depth analysis of the data collection, extraction and appraisal will be provided.

3.2  Objectives

The question posed for the purpose of this systematic review is: What is the impact of interventions targeted at health literacy on patient outcomes, medication adherence and health related quality of life? Therefore, the function of this systematic review is to explore health literacy, its impact on medication adherence and the overall outcomes for patients burdened with this problem. The objectives of this systematic review are:

- To explore the impact of interventions targeted at health literacy on medication adherence
- To explore the impact of interventions targeted at health literacy on health related quality of life

3.2.1  Outcome measures

3.2.1.1  Primary outcomes

The primary outcome measure of this systematic review is to investigate the impact of the interventions targeted at health literacy on medication adherence.
3.2.1.2 Secondary outcomes

The secondary outcome measure will be to identify whether the primary outcome measure impacts on the health related quality of life of the patients within the studies.

3.3 Criteria for inclusion and exclusion of studies

3.3.1 Inclusion criteria

The inclusion criteria for the present systematic review was deliberately broad, to ensure the literature sourced encapsulated all available research on the topic in question. Inclusion criteria are as follows:

- All studies published in English, regardless of year published
- Minimum age of participants as over 18 years
- Studies which identified:
  - an intervention tool used to identify health literacy levels, and
  - participants with one or more chronic disease, and
  - the effectiveness of an intervention employed to improve medication adherence

3.3.2 Exclusion criteria

The exclusion criteria for this particular systematic review were minimalist. The rationale for this was the result of a scoping exercise carried out by the author on literature pertaining to the research question. It was established, following this exercise, that there was a mountain of literature on all of the related topics, namely: health literacy, medication adherence and health related quality of life. There was however, not such an abundance of literature when they were combined. This highlighted the importance of identifying all appropriate literature. The exclusion criteria were established as:

- Any study published in any language other than English - The rationale for this exclusion was because the author was not fluent in any language except English. Furthermore, the present systematic
review did not receive funding from any source, making it unfeasible to employ the skills of an interpreter.

- Studies with participants under the age of 18 years
- Studies including adult participants, not responsible for their own care - the justification for this exclusion was the scope for unacknowledged error on the part of the patient, therefore potentially distorting the results
- Studies which did not identify:
  - an intervention tool used to identify health literacy levels, and
  - participants with one or more chronic disease, and
  - the effectiveness of an intervention employed to improve medication adherence

3.4 Search strategy

The search strategy employed for use within this systematic review was a multiple step process. Firstly, a search using specific terminology was conducted, utilising the following terms and/or expressions:

- Literacy
- Health literacy
- Health education
- Patient education
- Illness
- Co-morbidities
- Comorbidities
- Medication error
- Medication adherence
- Interventions
- Outcomes

The MeSH headings which were used to search were dependent on the database being explored, as not all terms and/or expressions were recognised on all databases. Within each database, the relevant terms were searched individually, followed by combining the MeSH headings
using ‘AND’. A Venn diagram of the search strategy can be viewed in section 2.7.2.2.

The electronic databases which were searched for the purposes of this systematic review included The Cochrane Library, CINAHL, Embase, MEDLINE and Sciencedirect. Where possible, randomised control trials were identified, however this limitation was dependent on the database being explored. In the absence of a randomised control trial limiter, research articles were identified. A flow chart for the study selection process for each electronic database can be viewed in appendix 1-5.

Following detection of relevant articles, the reference list was surveyed for additional appropriate literature. These articles were retrieved, appraised and included or excluded as with all other material recovered.

The search strategy identified no grey literature or unpublished work. As a result, no further clarification was necessary regarding the studies for inclusion. Therefore, there was no requirement to contact any author or industry sources.

3.5 Data extraction and analysis

3.5.1 Data extraction

Data was extracted from the chosen articles via the data extraction table provided by the Royal College of Surgeons in Ireland (RCSI) (Table 1). This table was adapted slightly to incorporate relevant data required for this particular systematic review. The data captured included the following: author, title of study, source, date of study, geographical location, care setting, co-morbidities, inclusion and exclusion criteria, sample size, patient characteristics, study design and type, allocation and randomisation sequence, intervention details, outcome measures, analysis, results and conclusions.
Table 1: Data extraction table (RCSI 2014)

<table>
<thead>
<tr>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Co-morbidities</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Sample Size</th>
<th>Study Design Type</th>
<th>Allocation Randomised</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.5.2 Quality appraisal

Following examination of several published quality appraisal tools, it was decided that quality appraisal of the included studies would be conducted using the EBL Critical Appraisal Checklist (Appendix 6). The EBL Critical Appraisal Checklist encapsulates all required information identified in other tools and checklists, but is condensed into a single page document, thus making it more effective and efficient. Subsequently, each randomised controlled trial was evaluated using the ‘risk of bias table for a single study’ (Table 2).

Table 2: Risk of bias table for a single study (The Cochrane Collaboration 2013)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Judgement</th>
<th>Support for Judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.5.3 Quality appraisal of included quantitative study

The inclusion of a single quantitative study required it to be quality appraised as a separate entity. The prospective cohort study conducted by Paasche-Orlow et al. 2005) was appraised using the EBL Critical Appraisal Checklist. An in depth description of this checklist and results unearthed are discussed further on in chapter 4.4.7.2.

3.5.4 Data synthesis

As tabular synthesis will have been presented within the completed data extraction table (Table 1), data synthesis will be primarily narrative. A summary table containing the major study characteristics will be presented (Table 3). This will be followed by an initial narrative synthesis, which will provide a transparent descriptive summary of all included studies.
Subsequently, similarities between the retrieved studies will be identified and discussed. As a result of different intervention tools used within the studies, it was not possible to conduct a meta-analysis for this particular systematic review. As discussed in chapter 1.10, the literature has identified a number of tools utilised to assess health literacy levels (DeWalt et al. 2004, Weiss et al. 2005, Davis et al. 2006, McCormack et al. 2010, Powers et al. 2010). Although several tools were identified, two tools were consistently prioritised for use within this particular systematic review, namely: The Test of Functional Health Literacy (TOFHLA) and The Rapid Estimate of Adult Literacy in Medicine (REALM).
<table>
<thead>
<tr>
<th>Trial</th>
<th>(N)</th>
<th>Intervention</th>
<th>Population</th>
<th>Randomisation Procedure</th>
<th>Blinding</th>
<th>Follow up</th>
<th>Results – Relative Risk (RR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Summary table (NHRMC 2000)
3.6 Summary

This chapter highlighted the methods employed for the purpose of conducting this systematic review. The research question was identified as: What is the Impact of Interventions Targeted at Health Literacy on Patient Outcomes, Medication Adherence and Health Related Quality of Life? Following that, the function of this particular systematic review was established as being an exploration of health literacy, its impact on medication adherence, chronic diseases and the overall outcomes for patients burdened with this problem. The objectives of the systematic review are documented as:

- To explore the impact of interventions targeted at health literacy on medication adherence
- To explore the impact of interventions targeted at health literacy on health related quality of life

The primary outcome measure was acknowledged as providing evidence to corroborate the existing literature relating to the link between limited health literacy and medication adherence. The secondary outcome measure concerns itself with identifying whether the primary outcome measures impact on the quality of life of the patients within the studies.

The inclusion and exclusion criteria were then established. A rationale for the determination of each category was provided. This was followed by a description of the search strategy employed, including the search terminology, namely: literacy, health literacy, health education, patient education, illness, co-morbidities, co morbidities, medication error, medication adherence, interventions and outcomes.

An account of the electronic databases searched was provided. This was succeeded by the process used to identify additional appropriate literature. The data extraction, appraisal and synthesis were described, providing examples of tools used within the process.
3.7 Conclusion

This chapter discussed the methodological design by which the present systematic review will be conducted. The main objective of this systematic review will be to discover if patients with chronic diseases adhere to their medication and health promotion education following health literacy assessment and intervention. The secondary objective is to establish whether patients within the intervention group have an improved quality of life (QoL) following same.
Chapter 4  Results

4.1 Introduction

The purpose of this chapter is to provide an in depth description of the studies retrieved via the systematic approach illustrated in Chapter 3. To begin with, this chapter will provide an overview of the outcomes of the search strategy, identifying the number of studies included and those excluded. Following this, a narrative summary of each study will be given, including study design, population, geographical location, health literacy assessment tool used, intervention, sample size and co-morbidities. An overview of the quality appraisal applied to the retrieved studies will then be provided. Finally, the primary and secondary outcomes of the review will be discussed.

4.2 Search strategy

In order to conduct this systematic review, it was necessary to complete a search strategy. The intricacies of the search strategy conducted for this review are discussed in detail in the previous chapter, Chapter 3. The search strategy conducted for this particular systematic review disclosed 2,321 studies within the databases searched, see Figure 2. A number of duplicate studies were identified and removed, leaving a total of 1,573 potentially eligible studies. Following this, the titles of the studies were read and inappropriate articles were dismissed, which left 156. The abstracts of the remaining studies were examined and subsequently 27 studies were retrieved in full text. Of these 27 studies, 20 were excluded, as per criteria established within section 3.3. Therefore, 7 studies met the inclusion criteria and are the foundations of this systematic review (Paasche-Orlow et al. 2005, Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Muir et al. 2012, Kalichman et al. 2013). A summary of the data extracted from the 7 studies is provided in appendices 7-13. These studies will however, be narratively summarised and analysed within this chapter.
Figure 2: Search strategy flow chart, adapted from PRISMA (2009)
4.3 Review of the literature

The search strategy as described in detail in section 4.2 disclosed a considerable volume of literature pertaining to health literacy, medication adherence and health related quality of life. There will be a succinct discussion regarding each to assist the reader in understanding the complexity of the subject matter.

4.3.1 Health literacy

Within the sourced literature, health literacy is frequently partnered with patient information and education. There is a general consensus within the studies identified that the information we provide to patients is not fit for purpose (Garrud et al. 2001, Gal and Prigat 2005). Furthermore, the written information and instructions supplied to patients are frequently at a professional medical level rather than 'laymans terms', thus inadvertently alienating the target population (Dickinson et al. 2001, Gal and Prigat 2005, Hirsh et al. 2009, Maat and Lentz 2010). Health literacy in itself is a complex phenomenon (Williams et al. 1995, Paasche-Orlow et al. 2005, Powers et al. 2010, Martensson and Hensing 2011) and was discussed in detail in section 1.3.

4.3.2 Medication adherence

The complex phenomenon which is health literacy, is confounded by the complex phenomenon that is medication adherence. Neiheisel et al. (2014) refer to the magnitude of the medication adherence problem, suggesting that an understanding of the problem is key to finding a way forward. It is suggested that the average rate of non adherence to medication is about 24.8% (DiMatteo 2004). Wheeler et al. (2014) and Roberts et al. (2014) imply that despite the magnitude of the problem (Neiheisel et al. 2014), medication adherence or lack thereof should be tackled as an individual problem, with a trust based, patient centered approach. This thinking is endorsed by Matthes and Albus (2014) who also advocate reconciliation of medication, removing all non essential prescriptions (Strange et al. 2013). A more thorough discussion about medication adherence can be viewed in section 1.7.
4.3.3 Health related quality of life

The literature pertaining to health related quality of life and its relationship with co-morbidities is significant (Guyatt et al. 1993, Strombeck et al. 2000, Ford et al. 2003, Azevedo et al. 2008, Nojomi et al. 2008, Heimans et al. 2013, Skalicky et al. 2013). Health related quality of life has been identified as an all encompassing concept, which is individual to each person (Guyatt et al. 1993, ISOQOL 2014). Section 1.9 contains an in depth debate surrounding this topic.

4.4 Included and excluded studies

As demonstrated in figure 1, following initial screening, 27 studies were identified which contained potentially relevant literature pertaining to this particular systematic review. Following retrieval of the full text of the 27 potentially eligible studies, a more thorough appraisal was carried out. This resulted in the exclusion of 20 of the studies. Table 4, provides a list of excluded studies and a brief rationale for exclusion. As outlined in section 3.3, seven studies met the inclusion criteria. These studies were then subject to further analysis, via the data extraction table illustrated in table 1. A list of the 7 included studies can be viewed in table 5.

4.4.1 Excluded studies

There were 20 studies excluded from the final cohort from which this systematic review was developed. The titles of the excluded studies suggested the subject matter contained was that stipulated as an entry requirement of this particular review. However, a more scrupulous investigation of the studies did in fact highlight the lack of at least one of the inclusion criteria outlined in section 3.3, namely: the establishment of a physician confirmed diagnosis of a chronic disease, the evaluation of the participant’s health literacy by way of an established assessment tool, or failed to determine the effectiveness of an intervention. Ten of the studies assessed health literacy and its relationship with participants’ knowledge of illness and/or medications. None of the ten studies however included an intervention and reassessment of knowledge following same (Schillinger et al. 2002, Schillinger et al. 2003, Muir et al. 2006, Gordon and Wolf 2009, Kripalani et al. 2010, Waldrop-Valverde 2010, Green et al. 2011, Al Sayah
et al. 2012, Devraj et al. 2013, Westlake et al. 2013). Four of the studies did not assess health literacy (Williams et al. 2012, Freed et al. 2013, Goeman et al. 2013, Walker et al. 2013). Two of the studies were study protocols for proposed randomised controlled trials (Dirmaier et al. 2013, Weymann et al. 2013). In one study the participants had no illness and they were assessed on injection technique for potential illness such as diabetes. This study also lacked an intervention and assessment post same (Chew et al. 2004). Another study endeavoured to show the correlation between the provision of evidence based information, using patient education resources and an increase in self-care. There was however no assessment of health literacy and no intervention (Driscoll et al. 2009). While in another, participants did not have an illness (Smith and Wallace 2013). The final study, a systematic review, critically appraised instruments used to assess patients’ capacity to manage their own medications. This study did not specifically address health literacy (Elliott and Marriott 2009). Table 4 gives a breakdown of the reasons for exclusion for each of the 20 studies omitted following in depth and thorough analysis.

Table 4: List of excluded studies with reasons

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al Sayah et al. (2012)</td>
<td>A systematic review investigating the relationship between health literacy, numeracy and health outcomes in participants with diabetes. This study did not include an intervention</td>
</tr>
<tr>
<td>Chew et al. (2004)</td>
<td>Participants were assessed for health literacy, and its relationship to adherence to preoperative instructions. However, no illness were identified and the study did not include an intervention</td>
</tr>
<tr>
<td>Devraj et al. (2013)</td>
<td>This study discussed the correlation of low health literacy and understanding of pain and medication knowledge. There was however no intervention</td>
</tr>
<tr>
<td>Dirmaier et al. (2013)</td>
<td>This article was a study protocol of a randomised control trial</td>
</tr>
<tr>
<td>Driscoll et al. (2009)</td>
<td>This study did not assess health literacy. Furthermore it did not provide any intervention</td>
</tr>
<tr>
<td>Elliott and Marriott (2009)</td>
<td>This systematic review discussed published instruments designed to assess patients’ capacity to self-administer medication only. There was no mention of an intervention</td>
</tr>
<tr>
<td>Freed et al. (2013)</td>
<td>There was no assessment of health literacy</td>
</tr>
<tr>
<td>Goeman et al. 2013</td>
<td>There was no assessment of health literacy</td>
</tr>
</tbody>
</table>
Gordon and Wolf (2009) | Health literacy was measured against the participants' knowledge of having a kidney transplant. The study did not include an intervention
---|---
Green et al. (2011) | This study characterised the prevalence of and associations of demographic and clinical characteristics with limited health literacy in haemodialysis. There was however, no intervention
Kripalani et al. (2010) | This study measured health literacy and examined patients' use of medication management strategies. There was however, no intervention
Muir et al. (2006) | This study measured health literacy against participants' knowledge and adherence to Glaucoma therapy. The study did not include an intervention
Schillinger et al. (2002) | This study measured health literacy and outcomes for participants with Diabetes. There was however, no intervention
Schillinger et al. (2003) | This study observed patient education. There was no intervention
Smith and Wallace (2013) | Participants in this study did not have any illness
Waldrop-Valverde et al. (2010) | This study measured neurocognition, health literacy and numeracy in medication management for participants with HIV infection. There was however, no intervention
Walker et al. (2013) | There was no assessment of health literacy
Weymann et al. (2013) | This article was a study protocol of a randomised control trial
Westlake et al. (2013) | This study discussed health literacy and its influence on outcomes. However, no intervention was provided
Williams et al. (2012) | There was no assessment of health literacy

4.4.2 Included studies

The remaining 7 studies were deemed eligible for inclusion in this systematic review. An in depth description of all 7 studies will be discussed in the next section. Table 5 gives a brief breakdown of the reasons for inclusion for each of the 7 included studies.

Table 5: List of included studies and rationale for inclusion

<table>
<thead>
<tr>
<th>Study</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>This study was randomised clinical trial which assessed HIV treatment adherence and counselling interventions for people living with HIV and limited health literacy</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td>This study was a randomised controlled trial which investigated the effect of a pharmacist intervention on clinically important medication errors after hospital discharge</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Morrow et al. (2007)</td>
<td>This study was a randomised controlled trial which examined if participants health literacy and experience with instructions influenced their preference for heart failure medication instructions</td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td>This study was a randomised controlled trial which identified the influence of health literacy level on an educational intervention to improve glaucoma medication adherence</td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td>This study was a randomised controlled trial which evaluated a pharmacist intervention to improve medication adherence in heart failure</td>
</tr>
<tr>
<td>Paasche-Orlow et al. (2005)</td>
<td>This study was a prospective cohort study, which investigated if tailored education reduced health literacy disparities in asthma self-management</td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td>This study was a randomised controlled trial which assessed an intervention to reduce low literacy barrier in inflammatory arthritis management</td>
</tr>
</tbody>
</table>

4.5 Description of studies

4.5.1 Study design

Of the 7 studies eligible for inclusion in this systematic review, 6 were randomised control trials (Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Muir et al. 2012, Kripalani et al. 2012, Kalichman et al. 2013). The remaining study was a prospective cohort study (Paasche-Orlow et al. 2005).

4.5.2 Geographical location


4.5.3 Study settings

The study settings of the included study identified several sites. Two of the studies were conducted over two sites (Paasche-Orlow et al. 2005, Kripalani et al. 2012). Four studies were carried out in academically affiliated hospitals (Paasche-Orlow et al. 2005, Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2013). Two of the studies involved community dwelling participants (Morrow et al.
2007, Kalichman et al. 2013). Two studies enrolled participants attending speciality outpatient’s clinics (Rudd et al. 2009, Muir et al. 2012); while a further 2 were community based ambulatory centres (Paasche-Orlow et al. 2005, Murray et al. 2007). The final study included in-patient participants from a tertiary care hospital (Kri palani et al. 2012). Of the 7 studies, 2 identified the location of the study site to be in an urban (Rudd et al. 2009) or inner-city (Murray et al. 2007) area.

4.5.4 Populations and sampling

All studies had both male and female representation in their results. In one study however, there was a ratio of 126 men to 1 female (Muir et al. 2012). The participants in this study were veterans with Glaucoma. All studies excluded participants under the age of 18 years. Therefore, all studies were conducted with adults. None of the included studies represented carers or parents. As there are differences within the patient characteristics for each study, any further details can be sourced from appendices 7 to 13. As previously discussed in section 1.2, health literacy is an essential component of the skill base required of patients when they become ill and require professional intervention. Notwithstanding this, it has been suggested (Williams et al. 1995, Brown and Bussell 2011, Martensson and Hensing 2012) that recognising there is a problem is the first step in tackling the significant problem that is health literacy. To this end, having pre-established low health literacy levels was not a prerequisite for inclusion into this particular systematic review, in an attempt to reflect reality.

4.5.5 Sample size

There was a large variation between the sample size identified within the studies. The sample size ranged from 73 (Paasche-Orlow et al. 2005) to 851 (Kri palani et al. 2012) participants. The mean sample size was 236 participants.

4.5.6 Interventions

4.4.6.1 Intervention – Kalichman et al. (2013)

The first study was a randomised controlled trial conducted by Kalichman et al. (2013). The data extraction table for this study is presented in appendix 7. This
study focused on patients with limited health literacy, who are living with HIV. Four hundred and forty six participants, currently on anti-retroviral therapy (ART), were recruited from AIDS services and community outreach. Following recruitment and enrolment, participants were randomly assigned to 1 of 3 groups following baseline assessment and 3 unannounced phone assessments. The first group, consisted of \( n = 148 \) participants. This group was labelled the ‘pictograph-guided adherence counselling’. The intervention for this group relied on pictographic information, which was designed inclusive of particularly relevant information to each participant’s medication regimen. The information provided was designed specifically and excluded any non essential text. The intervention for the ‘pictograph-guided adherence counselling’ group, concentrated on providing the most relevant information, motivational enhancement techniques and training in self-monitoring skills. Medication instructions were individually tailored to each participant’s health literacy level. Adherence tools such as reminder alarms and pillboxes were provided. Counselling was provided and problem solving skills were developed.

The second group consisted of \( n = 157 \) participants. This group was labelled the ‘standard adherence counselling’ group. In addition to the standard interventions for this group and for the purposes of this study, Kalichman et al. (2013) incorporated interactive counselling. This counselling incorporated information and education relating to HIV, treatments and medication adherence. Adherence tools such as a pillbox and problem solving skills were also made available to this group. However, the written information provided did not include a reduction in text.

The third and final group, consisted of \( n = 141 \) participants. This group was labelled the ‘general health improvement counselling’ and represented the ‘control arm’ of the study. The intervention for this group provided counselling which focused on improving general health and well-being for people living with HIV. Education was provided about nutrition and diet.Unlike the other 2 groups, the control group was not given adherence tools, but rather expected to choose their own. Problem solving was only discussed in brief at a booster session.
The assessment of health literacy for all participants was assessed using the TOFHLA tool. In addition, further assessment was carried out which included determining numeracy literacy, vision, interviews and baseline viral load and CD4 counts.

4.4.6.2 Intervention – Kripalani et al. (2012)

The second study was a randomised control trial conducted by Kripalani et al. (2012). The data extraction table for this study is presented in appendix 8. This study consisted of \( n = 851 \) in-patient participants with cardiovascular disease. The intervention involved pharmacist tailored information aimed at reducing the number of adverse drug events (ADEs) during the first 30 days following discharge. Following recruitment, participants were randomised into either the ‘usual care’ or ‘usual care plus the intervention’ group. Randomisation was carried out by a computer program which maintained allocation concealment. There was one unblinded researcher at each study site. All other interventionists were blinded.

The ‘usual care’ group contained \( n = 428 \) participants. The intervention for this group consisted of 4 elements. The first element involved pharmacist-assisted medication reconciliation. Secondly, participants received tailored pharmacist counselling. This counselling was conducted over two sessions. Initial assessment established the participants understanding of medications and prescription labels and barriers to adherence and social support. The second session took part on discharge, where tailored counselling was geared towards discharge medication and previously identified needs. The ‘Teach Back’ technique was used to ensure participant understanding. The third element involved providing low-literacy adherence aids and individualised follow-up phone calls. Patients were also provided with medication adherence aids including a pillbox and an illustrated schedule of daily medications. Finally, participants received individualised post discharge follow-up via a telephone call. This conversation was used to address any questions about medication and, where
appropriate, the investigator discussed elements of care with the inpatient treating physician.

The second group, the ‘usual care plus the intervention’ contained $n = 423$ participants. The intervention for this group, was in line with the standard routine. However, participants in this group received medication reconciliation by a healthcare professional. Discharge counselling was also provided. Participants were not routinely supplied with medication adherence aids, graphical medication schedules or telephone follow-up.

The assessment of health literacy for all participants was assessed using the S-TOFHLA tool. Further assessment was carried out, which incorporated cognitive function assessment, self-reported medication adherence and establishing the participants understanding of their medication regimen.

4.4.6.3 Intervention – Morrow et al. (2007)

The third study was a randomised control trial conducted by Morrow et al. (2007). The data extraction table for this study is presented in appendix 9. This study was undertaken to examine whether older adults have a preference for a pharmacist based educational intervention on medication adherence to chronic heart failure (CHF) medication. The volunteer study sample consisted of $n = 83$ participants in the ‘intervention’ group and $n = 153$ participants in the ‘usual care’ control group, totalling $n = 236$. The discrepancy in the allocation of participants to groups was deliberate. The authors intended conducting a second study, of a prospective cohort methodology from the ‘usual care’ group. The intervention began with pharmacist based patient education over a 6 month period. Following this, patient’s preference for medication instructions was measured. To determine their preference, participants were asked to select one of two versions of diuretic medication instructions and complete a questionnaire. The questionnaire required participants to identify which version of diuretic medication instruction would provide the best information about taking a missed dose, side effects, purpose of the medication, medication name, drug interactions, medication
dosage and time of medication administration. In addition, participants were requested to indicate how familiar they were with the standard care instructions.

Following the intervention there was a redesign of the pharmacy instructions for frequently used chronic heart failure medications. Patient centered instructions were printed in 12-14 font size. The instructions featured improved readability, fewer words and included pictorials relating to specific medication. In addition, the instructions were tailored to each patient's established medication organisation schema. Furthermore, the intervention group participants were designated time with a pharmacist in order to facilitate clarification, if required, of the written instructions.

Standard pharmacy instructions for routinely prescribed chronic heart failure medications remained the same. These instructions contained a larger volume of written information relating to drug interactions and side effects.

The assessment of health literacy for all participants was conducted using the S-TOFHLA tool. Participants also completed a label reading test which focused on medication adherence and cardiovascular related visits to the emergency department. In addition, the visual acuity, verbal working memory and processing speed of participants were measured.

4.4.6.4 Intervention – Muir et al. (2012)

The fourth study was a randomised control trial conducted by Muir et al. (2012). The data extraction table for this study is presented in appendix 10. The purpose of this study was to analyse if health literacy level education can improve adherence to glaucoma medication, resulting in a fewer number of days without medication (DWM). The study was made up of n = 127 participants. The intervention group consisted of n = 67 participants. The standard care group contained n = 60 participants. Following assessment and recruitment, participants were randomly assigned to a group on a one-to-one basis. The intervention involved a preliminary one-to-one session lasting approximately 20 minutes, with a study coordinator. The study coordinator had a background in
ophthalmic research. The study coordinator received training regarding content and delivery of the intervention by an ophthalmologist. Participants in the intervention group were shown a patient specific, health literacy level, glaucoma tailored information video.

Drop instillation techniques were demonstrated and education was provided in relation to instillation of drops for the intervention group. Participants were required to display their technique to the study coordinator following same. Intervention participants received a monthly follow up phone call to address any problems. The participants’ medical records were reviewed to collect individual demographic information. Pharmacy records were monitored over a six month period, for the number of glaucoma mediation refills required with the aim of determining adherence.

The quality and consistency of the interventions was assessed by a glaucoma subspecialist. Furthermore, the glaucoma subspecialist authored the content of the intervention video.

The assessment of health literacy for all participants was assessed using the TOFHLA tool. In addition, cognitive function was evaluated using the mini mental state exam (MMSE). Participant self assessment of co-morbidities affecting their ability to administer eye drops, disease knowledge and satisfaction with care was also carried out.

4.4.6.5 Intervention – Murray et al. (2007)

The fifth study is a randomised control trial conducted by Murray et al. (2007). The data extraction table for this study is presented in appendix 11. This study was conducted to establish if a pharmacist intervention improves medication adherence and health outcomes in patients with heart failure. A total of $n = 314$ people were eligible for participation in the study. Participants were randomly assigned to the intervention group $n = 122$, or the usual group and $n = 192$. The slight imbalance in the number of participants within each group was intentional. This was done in order for the authors to conduct a separate prospective cohort
study. The intervention consisted of a pharmacist review of baseline medication history inclusive of anything the patient was taking. Supplements and non-prescribed medication were included in this review. The pharmacist then dispensed a 2 month supply of the participant’s medication. This was followed by a pharmacist led patient centered information session. This information session included the provision of verbal and written instructions concerning the participant's dispensed medications. Each of the participant’s medications were assigned a category and a corresponding icon. The same icon was consistently used in relation to the assigned medication. Written instructions were designed using easy-to-follow information and instructions. The information was also specifically targeted at the participant’s health-literacy level. Participant’s medication use, healthcare encounters, body weight, and other relevant data were remotely monitored by the pharmacist. Any concerns relating to the participant’s general health were referred to the appropriate healthcare professional, who followed up with the patient directly.

Pharmacists who dispensed medications to participants in the usual care group did not receive the same training as their counterparts. Furthermore, they were refused access to patient centered study materials. Medication history for the usual care group was assessed initially. However, following this, there was no further intervention. Participants in the usual care group were informed of the purpose of the study.

The assessment of health literacy for all participants was assessed using the S-TOFHLA tool. There was no discussion regarding any other assessments carried out.

4.4.6.6 Intervention – Paasche-Orlow et al. (2005)

The sixth study was a prospective cohort study conducted by Paasche-Orlow et al. (2005). The data extraction table for this study is presented in appendix 12. This study was conducted to investigate the relationship between health literacy and the ability to learn asthma self-management skills. Recruitment identified $n = 73$ eligible participants. Participants were enrolled on discharge from the study.
hospital. An interviewer administered survey was conducted to provide baseline personal and medical history for all participants. This survey requested information relating to age, sex, ethnicity, education, income, smoking history and asthma related healthcare use. Participant’s medical records were also consulted and any further details extracted. Following this, participant’s health literacy level and their understanding of asthma medications were tested. Participants’ understanding of asthma medications was conducted using a specifically developed 10 item questionnaire formulated by the authors.

The next step included observation of patients metered dose inhaler (MDI) technique. Participant’s technique was evaluated using six established criteria, namely: shaking the inhaler, exhaling before actuation, closing lips tightly around the mouthpiece, pressing down once on the canister, taking a full breath without triggering the ‘whistle’ indicator of the spacer and, holding breath for 5 seconds after inhalation (Barry and O’Callaghan 1996, Schillinger et al. 2003). All medications and spacers were provided free to the participants.

Following this, participants took part in a written and oral information session relating to discharge regimen, which included education and demonstration of correct MDI technique. Prior to discharge, participants were questioned regarding the names of each medication, the dose to be administered, the timing of administration and the duration of the prescription. The information session was repeated until the participants could demonstrate understanding of the above discharge regimen. Investigators took note of the number of information sessions each participant required. After 2 weeks participants returned and were reassessed on metered dose inhaler technique and knowledge of their asthma discharge regimen.

In addition to the above intervention, the authors allocated $n = 46$ participants to a substudy. Electronic measurement of these participants was carried out in order to identify their adherence to inhaled and oral medication post discharge.
The assessment of health literacy for all participants was assessed using the S-TOFHLA tool. There was no discussion regarding any other assessments carried out.

4.4.6.7 Intervention – Rudd et al. (2009)

The seventh and final study was a randomised control trial conducted by Rudd et al. (2009). The data extraction table for this study is presented in appendix 13. One hundred and twenty seven participants attending an arthritis centre in an urban teaching hospital were recruited for this study. Participants were randomly allocated to 1 of 3 groups, namely: standard care \(n=63\), plain English materials \(n=13\) or individualised care \(n=51\). The standard care group received routine rheumatology care and information from their rheumatologist. In addition the standard care group received an information pack from the Arthritis Foundation (AF) regarding their particular type of arthritis, relevant medications, examples of medication adherence aids and a map of the hospital. Arthritis Foundation information is targeted at 11th to 15th grade readers.

The intervention for the Plain English material group was almost identical to the standard care group, however the Arthritis Foundation information pack provided to participants contained information and education in Plain language, aimed at lower health literacy reading level. Information was provided regarding the following aspects of arthritis care, namely: what you need to know, treatment choices, medicine, therapy and exercise, surgery, patient specification medication information, information on how to get the most from your visit, examples of medication adherence aids and a map of, and information about, the hospital.

The third group was the individualised care group. The participants in this group received the same information and education as the plain English material group supplemented by two 20-minute appointments with an educator. The function of these appointments was to review all information and education and highlight patient specific details. Particular focus was given to the participant’s medication regimen, communication with members of the multidisciplinary team and barriers encountered within the healthcare facility, with participants given time to voice any
concerns. Participants were also encouraged to make contact, by whichever means preferred, by the participant, at any stage over the 6-month study period to ask questions or receive further information and/or education required.

The assessment of health literacy for all participants was assessed using the A-REALM tool.

4.4.7 Quality appraisal of included studies

4.4.7.1 Quality appraisal of included RCTs: risk of bias

4.4.7.1.1 Selection bias – sequence generation

Sequence generation was observed for all included studies. Participants in all cases were randomly assigned to an intervention group or standard/usual care group. Two of the studies however, conducted baseline screening prior to randomisation (Rudd et al. 2009, Kalichman et al. 2013). A sequence generation table is presented in table 6.

Table 6: Sequence generation table

<table>
<thead>
<tr>
<th>Study</th>
<th>Judgement</th>
<th>Selection bias – sequence generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>Low risk</td>
<td>All participants were randomly assigned to an intervention or standard/usual care group</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morrow et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.4.7.1.2 Selection bias – allocation concealment

Allocation concealment of the intervention was reported differently throughout the included studies. Three of the RCTs reported the use of participant allocation by means of a computer-generated programme (Murray et al. 2007, Kripalani et al. 2012, Kalichman et al. 2013). Another 2 studies did not elaborate further than documenting that participants were randomly assigned to a group (Morrow et al. 2007, Rudd et al. 2009). One study stated that participants were randomised on a one-to-one basis (Muir et al. 2012).
Four of the studies reported concealment of interventionists and/or participants (Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Kalichman et al. 2013). The other 2 studies did not refer to concealment at all (Morrow et al. 2007, Muir et al. 2012). An allocation concealment table is presented in table 7.

Table 7: Allocation concealment table

<table>
<thead>
<tr>
<th>Study</th>
<th>Judgment</th>
<th>Selection bias – allocation concealment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>Low risk</td>
<td>Allocation conducted by computerised randomisation generator</td>
</tr>
<tr>
<td></td>
<td>Low risk</td>
<td>Study blinded throughout. Interventionists never conducted assessments</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td>Low risk</td>
<td>Allocation conducted by computer program which maintained allocation concealment</td>
</tr>
<tr>
<td></td>
<td>Low risk</td>
<td>All investigators, statisticians and outcome assessors were blinded</td>
</tr>
<tr>
<td>Marrow et al. (2007)</td>
<td>Unclear risk</td>
<td>No reference to how allocation was conducted other than participants were randomly assigned</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>No reference to concealment or blinding</td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td>Unclear risk</td>
<td>Allocation conducted on a one-to-one basis</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>No reference to concealment or blinding</td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td>Low risk</td>
<td>Allocation conducted by computer</td>
</tr>
<tr>
<td></td>
<td>Low risk</td>
<td>Interviewers were blinded and no part in the intervention</td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td>Unclear risk</td>
<td>Allocation conducted by research assistant, no other details given</td>
</tr>
<tr>
<td></td>
<td>Low risk</td>
<td>All other study staff members were blinded</td>
</tr>
</tbody>
</table>

4.4.7.1.3 Performance bias

Table 8: Performance bias table

<table>
<thead>
<tr>
<th>Study</th>
<th>Judgment</th>
<th>Performance bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>High risk</td>
<td>No blinding reported</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marrow et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.4.7.1.4 Detection bias

In 4 of the 6 studies detection bias was discussed (Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Kalichman et al. 2013). In all 4 studies, baseline interviews and/or coordination of the study was conducted by an individual other than the interventionist, interviewer, statistician and/or outcome assessors. The remaining 2 studies did not refer to the subject of concealment at all (Morrow et al. 2007, Muir et al. 2012). The breakdown of detection bias is presented in table 9.

Table 9: Detection bias table

<table>
<thead>
<tr>
<th>Study</th>
<th>Judgment</th>
<th>Detection bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>Low risk</td>
<td>Assessment staff were blinded</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marrow et al. (2007)</td>
<td>High risk</td>
<td>No reference to concealment or blinding</td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td>High risk</td>
<td>No reference to concealment or blinding</td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td>Low risk</td>
<td>Assessment staff were blinded</td>
</tr>
</tbody>
</table>
4.4.7.1.5 Attrition bias

Attrition was reported for 5 of the 6 included studies (Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Muir et al. 2012, Kalichman et al. 2013). In all 5 of the studies attrition rates for both the intervention and standard/usual care groups were proportional, thus not effecting the reporting of results. Only one study did not report any dropouts at all, with results reported for the same number of participants recruited (Morrow et al. 2007). A table representing attrition bias is presented in table 10.

Table 10: Attrition bias table

<table>
<thead>
<tr>
<th>Study</th>
<th>Judgment</th>
<th>Attrition bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>High risk</td>
<td>8 participants did not complete the study for various reasons and were excluded from the results</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td>High risk</td>
<td>11 participants did not complete the study for various reasons and were excluded from the results</td>
</tr>
<tr>
<td>Marrow et al. (2007)</td>
<td>Low risk</td>
<td>No dropouts reported</td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td>High risk</td>
<td>4 participants did not complete the study for various reasons and were excluded from the results</td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td>High risk</td>
<td>44 participants did not complete the study for various reasons and were excluded from the results</td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td>High risk</td>
<td>22 participants did not complete the study, no reasons given for attrition. The 22 participants were excluded from the results</td>
</tr>
</tbody>
</table>

4.4.7.1.6 Reporting bias

For all of the 6 included RCTs, the results and outcome sections reported the outcomes under investigation. Thus, reporting bias was not a factor. Reporting bias is illustrated in table 11.
Table 11: Reporting bias table

<table>
<thead>
<tr>
<th>Study</th>
<th>Judgement</th>
<th>Reporting bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. (2013)</td>
<td>Low risk</td>
<td>For all studies the results and outcome sections reported the outcomes under investigation</td>
</tr>
<tr>
<td>Kripalani et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morrow et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muir et al. (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murray et al. (2007)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rudd et al. (2009)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.4.7.1.7 Other bias

Although none of the 6 included studies met all criteria set out for their particular methodology, no study indicated bias which could potentially influence the overall validity and generalisation of the results presented.

4.4.7.2 Quality appraisal of included quantitative study

For the purpose of this systematic review, the only included quantitative study was appraised using the EBL Critical Appraisal Checklist. This checklist involves appraisal of, section A: population – 6 items, section B: data collection – 8 items, section C: study design – 5 items and section D: results – 6 items. Overall validity is calculated by scoring each item Y – Yes, N – No, U – Unclear or N/A – Not applicable. If totals for Y & N/A are ≥ 75% or N & U are ≤ 25 %, the study can be deemed valid.

The included study applicable for this route of critical appraisal was a prospective cohort study conducted by Paasche-Orlow et al. (2005). Results of the scoring for this study can be viewed within appendix 14.

4.5 Outcomes

For the purposes of reporting, all included studies were analysed for outcomes achieved. However, due to the availability of a number of health literacy assessment tools, the data from all studies cannot be synthesised together.
Although 4 studies conducted health literacy assessment using the S-TOFHLA, they cannot be grouped together as the illness and outcomes being scrutinised were different in all (Paasche-Orlow et al. 2005, Morrow et al. 2007, Murray et al. 2007, Kripalani et al. 2012). Two studies used TOFHLA for health literacy assessment, but again illness and outcomes differed, therefore they cannot be pooled together for assessment (Muir et al. 2012, Kalichman et al. 2013). The final study is a stand alone study as it was the only one to use REALM, which had been adapted to A-REALM, making it arthritis specific for the study in question (Rudd et al. 2009). Tabular representation of the outcomes of each study can be viewed in appendices 15 to 21.

4.5.1 Outcomes – Kalichman et al. (2013)

In the first study, Kalichman et al. (2013) established that there was no difference in baseline assessment between participants. They also found that participants with marginal health literacy tended to be younger and had more years of education compared to those with lower health literacy. The hypothesised outcomes however were not reached and the study documented unexpected results. It was found that regardless of the intervention, participants with lower health literacy did not demonstrate improved outcomes. In addition, no added benefit was shown as a result of the intervention for those within the marginal health literacy. Thus, a more intensive provider-directed approach to ART adherence was recommended.

4.5.2 Outcomes – Kripalani et al. (2012)

Kripalani et al. (2012) established from the total $n = 851$ participants, that $n = 432$ (50.8%) had a clinically significant medication error within the first 30 days post discharge. The allocation of these errors was only slightly in favour of the intervention group at $n = 370$, as against $n = 407$ in the usual care group. Conversely, participants in the intervention group had a higher number, $n = 183$ of ADEs in comparison to the usual care group at $n = 170$. The most significant difference was observed within the potential ADEs category, where the intervention group had $n = 187$, compared with the usual care group at $n = 237$. However, none of the results are statistically significant with results highlighting the difficulty of improving medication safety.
4.5.3 Outcomes – Morrow et al. (2007)

Morrow et al. (2007) concluded that there were no significant differences between the two groups. Preference for the patient-centered instructions was dependant on the information being sought. For example, the patient centered approach was preferable when looking for information relating to adherence, such as dose and schedule. Conversely, the standard instructions were preferred when seeking details of drug interactions. Overall they did however identify that participants with lower health literacy levels showed a preference for the patient-centered instructions. They also discovered that participants in the intervention group were more likely to choose the patient-centered instructions. The study concludes that patients’ preferences are a valuable tool when considering the format of instructions aimed at patients, regardless of health literacy level.

4.5.4 Outcomes – Muir et al. (2012)

Muir et al. (2012) ascertained that of the total sample size of $n = 127$, $n = 72$ participants experienced DWM over a 6 month period. Days without medication ranged from one week to 549 days. In the case of the 549 days, the participant involved was prescribed three different medications over the 6 months. In general, it was noted that there was little difference between the two groups. The intervention group had 63 DWM, compared with 65 DWM for the standard care group. The results also found a correlation between inadequate or marginal health literacy and physical disability. This impacted on those participants’ ability to administer medication drops. There was also an association between lower health literacy and dissatisfaction with care. In conclusion, participants with inadequate health literacy in the intervention group had on average 30 less DWM than their counterparts in the standard care group. It is noted that Muir et al. (2012) recommend focusing future research and education on low health literacy, thus protecting the most vulnerable patients.

4.5.5 Outcomes – Murray et al. (2007)

In their results, Murray et al. (2007) found that of the dispensed medication, the intervention group had 81.7% adherence, compared with 78.7% of the usual care group, with overall adherence showing 78.8% in the intervention group and 67.9% in the usual care group during the intervention period. However, this dropped to
70.6% and 66.7% respectively at 3 months post intervention. Scheduling adherence was 53.1% in the intervention group compared to 47.2% in the usual care group. In the intervention group 37.5% of participants had a medication error and/or adverse events, compared with 47.4% of the usual care group. In terms of health outcomes, the study concluded that the intervention group had 19.4% fewer exacerbations. The intervention group also had fewer hospital admissions over the study period. Disease-specific quality of life improved in the intervention group, from baseline to 6 months, by 0.28 and to 12 months by 0.39, compared with 0.21 and 0.39 respectively in the usual care group. Overall satisfaction was also higher in the intervention group. Murray et al. (2007) concluded that participants in the intervention group were clinically and personally better off than participants in the usual care group.

4.5.6 Outcomes – Paasche-Orlow et al. (2005)

Paasche-Orlow et al. (2005) determined that, in general, a participant’s health literacy level did not determine the requirement for additional education sessions. They also found that, at baseline, inadequate health literacy was linked to inadequate asthma medication knowledge. The overall mean MDI technique score was 4.8, showing an increase of 1.1 from baseline. In conclusion, Paasche-Orlow et al. (2005) found that deficiencies in asthma medication knowledge, MDI technique and management of discharge regimen were more common for participants with lower health literacy, for example in inner city adults. However, this did not impede their ability to learn or retain information and education regarding medication or MDI technique. They recommend systematic assessment of patient comprehension of asthma instructions and medications with a tailored, teach-to-goal education programme to complement it.

4.5.7 Outcomes – Rudd et al. (2009)

Rudd et al. (2009) discovered that there was little change to mean scores at 6 and 12-months. There was an improvement in mental health in the intervention group, showing a 4.6% and 4.8% change compared with the standard care group showing a −4.3% and −0.8%. Self-efficacy in the intervention group also improved showing 1.5% and 3.6% change compared to −3.2% and −2.0% in the standard care group. This trend continued into medication adherence with –
4.76% and −12.21% for the intervention group compared with 0.25% and −3.12% for the standard care group – in this case decreased scores are representative of improvement. In conclusion Rudd et al. (2009) stated that although there were improvements in all variables studied, they were not significant. They recommend further research directed towards minimising the negative effects of limited health literacy.

4.6 Summary

This chapter provided an in depth description of the studies retrieved via the systematic approach illustrated in Chapter 3. Initially, the search strategy was discussed which identified that, following initial screening, 27 studies were identified which contained potentially relevant literature pertaining to this particular systematic review. Following a more thorough appraisal of the studies, 20 were excluded, leaving 7 studies, which met the inclusion criteria. A comprehensive appraisal of the included studies was then conducted. Study design highlighted the inclusion of 6 randomised control trials and 1 prospective cohort study.

Although all included studies originated from the United States of America, the study settings differed. Two studies were conducted over two sites. Four studies were carried out in academically affiliated hospitals. Two of the studies involved community dwelling participants. Two studies enrolled participants attending specialty outpatient’s clinics, while a further two were community based ambulatory centres. The final study included in-patient participants from a tertiary care hospital. Of the 7 studies, two identified the location of the study site to be in an urban or inner-city location.

All of the included studies had both male and female representation in their results. However, one study had a 99% male representative study sample. All studies excluded participants under the age of 18 years. All studies were therefore conducted with adults.

The population and sample size ranged from 73 to 851 participants. The mean sample size was 236 participants.
It was not possible to pool results of all the included studies. Although all studies required participants to have had their health literacy measured and medication adherence measured against same, no study included the same co-morbidity or measurement of adherence. The first study, conducted by Kalichman et al. (2013), found no difference in baseline assessment between participants. They found, to their surprise, that regardless of the intervention, participants with lower health literacy did not demonstrate improved outcomes. In addition, no added benefit was shown as a result of the intervention for those within the marginal health literacy. Thus, they recommended a more intensive provider-directed approach to ART adherence.

The second study, by Kripalani et al. (2012), established that despite improvements in both groups, none of the results are statistically significant with results highlighting the difficulty of improving medication safety.

The third study, by Morrow et al. (2007), concluded that there were no significant differences between the two groups. Preference for the patient-centered instructions was dependant on the information being sought. The study concludes that patients’ preferences are a valuable tool when considering the format of instructions aimed at patients regardless of health literacy level.

The fourth study, by Muir et al. (2012), also found that in general, there was little difference between the two groups. They did however find a correlation between inadequate or marginal health literacy and physical disability. There was also an association between lower health literacy and dissatisfaction with care. In conclusion, participants with inadequate health literacy in the intervention group had, on average, 30 less DWM than their counterparts in the standard care group. Recommendations suggest a focus on future research and education on low health literacy, thus protecting the most vulnerable patients.

The fifth study, by Murray et al. (2007), did find an improvement in their intervention group, with adherence showing 78.8%, compared with 67.9% in the usual care group during the intervention period. Disease-specific quality of life
improved in the intervention group, with overall satisfaction being higher in the intervention group. They conclude that participants in the intervention group were clinically and personally better off than participants in the usual care group.

The penultimate study, by Paasche-Orlow et al. (2005), determined that, at baseline, inadequate health literacy was linked to inadequate asthma medication knowledge. However this did not impede their ability to learn or retain information and education about asthma medication or MDI technique. In conclusion however, findings identified that deficiencies in asthma medication knowledge, MDI technique and management of discharge regimen were more common for participants with lower health literacy, for example in inner city adults. Recommendations suggest a systematic assessment of patient comprehension of asthma instructions and medications with a tailored, teach-to-goal education programme to complement it.

The final study, by Rudd et al. (2009), discovered that there was little change to mean scores at 6 and 12-months. In conclusion it was found that although there were improvements in all variables within the study, they were not significant. Further research directed towards minimising the negative effects of limited health literacy is recommended.

Quality appraisal of the included studies was then conducted. The following were examined in detail, namely: randomisation selection bias, allocation selection bias, performance bias, detection bias, attrition bias, reporting bias and finally, other bias. Quality appraisal of the single included quantitative study was appraised using the EBL Critical Appraisal Checklist. This checklist incorporates appraisal of population, data collection, study design and results.

An in depth analysis of the primary and secondary outcomes, as identified for this particular systematic review was then carried out and presented in tabular format within the appendices.
4.7 Conclusion

This chapter provided an in-depth description of the studies retrieved via the systematic approach illustrated in Chapter 3. To begin with, an overview of the outcomes of the search strategy, identifying the number of studies included and those excluded was provided. Following this, a narrative summary of each study was given, including study design, population, geographical location, health literacy assessment tool used, intervention, sample size and co-morbidities. The quality appraisal applied to the retrieved studies was then discussed. Finally, the primary and secondary outcomes of the review were highlighted and discussed.
Chapter 5  Discussion

5.1  Introduction

The purpose of this chapter is to debate the key findings of this systematic review. Initially, a concise summary of the key findings will be provided. The strengths and limitations of the studies included will be discussed. Following this, the primary and secondary outcomes will be examined in relation to both the studies individually and the systematic review as a whole. Any new and innovative research unearthed as a result of the review will be outlined. The potential overall contribution of the review to health and social gain will be highlighted. Finally the strengths and limitations of this particular systematic review will be argued.

5.2  Key findings

The key findings unearthed as a result of this systematic review are:

- The identification of patients with low health literacy is an essential element in the provision of safe and quality healthcare
- There are numerous interventions which can be employed to improve understanding of information and education provided within the healthcare environment
- In general, although not always statistically significant, participants who received health literacy appropriate interventions demonstrated improved medication adherence, thus leading to improved quality of life
- Low health literacy is not linked to the ability to learn and retain important information and education
- Patient satisfaction with the healthcare process is greater within populations who received health literacy appropriate interventions
- Health literacy appropriate interventions, although initially more labour intensive, are a cost neutral resource which healthcare providers are not utilising to their potential
5.3 Methodological issues of included studies

5.3.1 Overview

The included studies incorporated within this particular systematic review, as previously established, all contained similar and appropriate data relating to the research question. However, all studies differed in design, co-morbidity, health literacy assessment tool used and medication adherence intervention. To this end, it was not possible to synthesise the data together. Therefore, the methodological issues of the included studies have been discussed and a hypothesis reached regarding their possible overall quality and validity.

5.3.2 Study design

The strength of a review is dependent on the type of studies included (White and Schmidt 2005, CRD 2008). White and Schmidt (2005) suggest that any systematic review should include several trials which are clinically homogeneous and of high quality. Thomas et al. (2004) identify randomised controlled trials as the strongest study design methodology, followed by cohort analytic, case-control, cohort and interrupted time series designs with Thomas et al. (2004) deeming them as moderate strength. They also suggest that the lowest design methodology consist of all other research designs not previously mentioned.

For the purposes of this systematic review, there were 7 included studies. These studies consisted of 6 randomised control trials (Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Muir et al. 2012, Kripalani et al. 2012, Kalichman et al. 2013). The final included study was a prospective cohort study (Paasche-Orlow et al. 2005).

A prospective cohort study can be broken down into two separate parts. A prospective study enables a researcher to investigate what is likely to happen as a result of an intervention in a forward passage of time (McKenna et al. 2010). Although caution has been advised regarding the potential of attrition and learned responses (Nelson et al. 2010), the benefits of a prospective study have been acknowledged as reliable, as data are collected as it is produced (Smith 2008). A
cohort study is defined by its tracking of participants over a period of time, where results are obtained from a large sample of participants (Bruce et al. 2008). Thus, the inclusion of a prospective cohort study in the final results of this particular systematic review enhances the overall reliability of the outcomes achieved.

The majority, 99%, of the included studies for the purposes of this particular systematic review were randomised controlled trials. Randomised controlled trials are viewed as the 'gold standard' (Ostashkiewicz and O'Connell 2007, Victor 2008) or most ideal (NHMRC 2000) study design. The unique design of randomised controlled trials facilitates a reduction in the possibility of bias, therefore strengthening the validity and generalisation of the results (Thomas et al. 2004, White and Schmidt 2005, Victor 2008).

To this end, a positive assumption can be made about the quality and validity of the results and outcomes of the present review.

5.3.3 Sampling

As previously identified, the quality of the methodological design of included studies within a systematic review are directly related to the quality of the results obtained. This is also true of sampling (Bruce et al. 2008), which is viewed as an essential tool in medical research (Dahiru et al. 2006). With the exception of a census, the population in general is never studied as a whole (Procter et al. 2010). Therefore, a population sample is a representation of a group of interest. As a consequence it is fundamental that a sample group is of an appropriate size to reflect the topic being studied and to ensure generalisation of results (Bruce et al. 2008, Kim and Choi 2008, Procter et al. 2010). Sample size determination (SSD) helps guarantee the sample size is neither too large nor too small and can be achieved by employing power analysis (Dell et al. 2002, Hayat 2013). Establishing strict inclusion and exclusion criteria is the cornerstone of ensuring an appropriate representation of the population within the sample group (Ostashkiewicz and O'Connell 2007).
Of the included studies, only one did not refer to the employment of power analysis (Paasche-Orlow et al. 2005). Power analysis is defined as a statistical technique which is employed to estimate the minimum sample size required to ensure accuracy of results. Of the included studies, only one did not elaborate any further than to say that the sample size was sufficient to ensure adequate statistical power for regression analysis (Morrow et al. 2007). Another 3 of the included studies established an 80% (Kripalani et al. 2012), 90% (Kalichman et al. 2013) and 94% (Murray et al. 2007) chance respectively, of detecting differences between groups. The final 2 studies identified a value of 0.05 to determine statistical significance between groups (Rudd et al. 2009, Muir et al. 2012).

It is realistic therefore, to assume that the sampling measures contained within the included studies are statistically significant enough to reinforce the strength provided by the design of same studies.

5.3.4 Sequence generation

From the 7 studies identified for use in this particular systematic review, 6 were randomised control trials. Sequence generation was reported differently throughout the included studies. Three of the trials reported the use of participant allocation by means of a computer-generated programme (Murray et al. 2007, Kripalani et al. 2012, Kalichman et al. 2013). Another 2 studies did not elaborate further than documenting that participants were randomly assigned to a group (Morrow et al. 2007, Rudd et al. 2009), while one study stated that participants were randomised on a one-to-one basis (Muir et al. 2012).

As the majority of the included studies documented their sequence generation procedure, a positive assumption can be made that the probability of selection bias was minimal.

5.3.5 Allocation concealment

Allocation concealment is a process whereby it is unknown to which group participants are assigned (Akobeng 2005). Allocation concealment is paramount to ensuring that participants are not unfairly assigned to groups (Akobeng 2005, Nelson et al. 2010), resulting in invalid, unreliable outcomes (Bruce et al. 2008).
Hawthorne effect is a phenomenon whereby study results can be contaminated by the researcher and/or the participant being aware of the nature of the study, thus altering their behaviour and consequently the results (Smith 2008, Nelson et al. 2010).

In the present systematic review, allocation concealment of the intervention was reported differently throughout the included studies. Only 5 of the 7 included studies reported concealment of interventionists and/or participants (Paasche-Orlow et al. 2005, Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Kalichman et al. 2013). The other 2 studies did not refer to concealment at all (Morrow et al. 2007, Muir et al. 2012).

Allocation concealment was documented in the majority of the included studies. Once again, an affirmative hypothesis can be made that the probability of allocation bias and/or Hawthorn effect was nominal.

### 5.3.6 Blinding

Blinding, also known as detachment, is the process whereby the researcher and/or the participant remain unaware of who is receiving the intervention and who is not (Topping 2010). Blinding promotes anonymity between researcher and participant. This crucial step of the study design can occur as single blind, where just the participant is blinded or double blind where both the participant and the researcher are blinded (Smith 2008). Blinding is essential to ensure that results identified are not tainted by the opinion of, or manipulated by the persons involved (Bruce et al. 2008, Topping 2010).

Of the 6 included RCTs, none referred to blinding of the participants at any stage (Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Muir et al. 2012, Kripalani et al. 2012, Kalichman et al. 2013). Kalichman et al. (2013) did however refer to blinding of the intervention staff, stating they were blinded throughout the study.
The nature of the interventions utilised within this particular systematic review however, did not necessarily facilitate blinding. Participants had their health literacy assessed, a measure in itself that indicates a modification of normal procedure. This therefore, has the potential to alter results and outcomes reached within the studies.

5.3.6 Outcome assessment

5.3.6.1 Incomplete outcome data
The importance of study design, sampling, sequence generation and the efforts afforded to reduce the risk of bias are somewhat negated if there is a high instance of attrition within the groups (NHMRC 2000, Akobeng 2005). High attrition rates can potentially distort the randomisation process, thus introducing the risk of bias. Intention To Treat (ITT) is the process whereby despite participants being lost throughout the study, they are accounted for in the results in a bid to determine if the full cohort of participants would have changed the findings of the study (Roe 2007, Nelson et al. 2010).

Attrition was reported for 5 of the 6 included RCTs (Murray et al. 2007, Rudd et al. 2009, Muir et al. 2012, Kripalani et al. 2012, Kalichman et al. 2013). In all 5 of the studies attrition rates for both the intervention and standard/usual care groups were proportional, thus not effecting the reporting of results. Only one study did not report any dropouts at all, with results reported for the same number of participants recruited (Morrow et al. 2007).

Attrition bias did not therefore reflect negatively on the results established within this systematic review.

5.3.6.2 Selective outcome reporting
Selective outcome reporting is yet another potential source of bias (Chan et al. 2004, Chan and Altman 2005). Selective outcome reporting occurs when specific data are chosen for publication based on desired results (Dwan et al. 2010). In their study, Chan and Altman (2005) determined that over a third of 519 trials omitted at least two outcomes each, therefore favouring statistically significant
outcomes. Therefore, the consequences of selective outcome reporting, is reduced validity of results (Chan et al. 2004, Dwan et al. 2010).

The primary and secondary outcome measures for the included studies differed from those of the systematic review. However, for all of the 6 included RCTs, the results and outcome sections reported the outcomes highlighted for investigation.

The reporting of appropriate primary and secondary outcomes therefore confirms that reporting bias was not a factor in this particular systematic review.

5.3.7 Heterogeneity

Heterogeneity is the terminology used to describe the differences between specific studies (Bruce et al. 2008). The impact of heterogeneity on results established is directly related to the extent of the differences involved. For example, clinical diversity between patient characteristics, coupled with a variety of possible interventions, in addition to variability in study design and quality, can lead to insurmountable differences between studies (Pace and Stat 2011, Moore 2012). Where there is significant heterogeneity, meta-analysis cannot be conducted within a systematic review. However, as suggested by O'Mathuna (2010), a narrative systematic review is an alternative way of disseminating results.

Heterogeneity was identified in the present systematic review in the form of multiple health literacy assessment tools, thus data from all studies could not be synthesised together. For example, four studies conducted health literacy assessment using the S-TOFHLA (Paasche-Orlow et al. 2005, Morrow et al. 2007, Murray et al. 2007, Kripalani et al. 2012). Two studies used TOFHLA for health literacy assessment (Muir et al. 2012, Kalichman et al. 2013). The final study is a stand alone study as it was the only one to use REALM, which had been adapted to A-REALM, making it arthritis specific for the study in question (Rudd et al. 2009).
It is acknowledged that heterogeneity was identified with this systematic review. As previously discussed however, the differences between the studies did not represent true heterogeneity. Although there was divergence between included studies, this was not fundamentally significant as all studies, regardless of the tool used or intervention applied, effectively reported the same primary and secondary outcomes.

5.4 Discussion of Outcomes

5.4.1 Primary outcome – medication adherence

The primary outcome measures identified for the present systematic review was to provide evidence to corroborate the existing literature relating to low health literacy levels and lack of medication adherence. It has been established that low health literacy levels can be a barrier to the understanding of written instructions, along with an inability to interpret prescriptions (Davis et al. 2006, Powers et al. 2010), resulting in a higher probability of medication error (DeWalt et al. 2004, Lindquist et al. 2011). By definition, patients with lower health literacy levels are more likely to have a higher number of co-morbidities (Williams et al. 1995, Weiss et al. 2005, Carmona 2006, Bennett et al. 2009), thus predisposing those people to an increased volume of medications.

Examination of the overall results contained within the 7 included studies of this systematic review suggest that low health literacy levels do in fact negatively impact on a participants ability to adhere to medication instructions (Paasche-Orlow et al. 2005, Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Muir et al. 2012). On the contrary, the study by Kalichman et al. (2013), found that regardless of the intervention, participants with lower health literacy did not demonstrate improved outcomes. In addition, no added benefit was shown as a result of the intervention for those within the marginal health literacy group. However, given that the ratio of positive results for the primary outcomes far outweigh the negative results by 9:1, it can be concluded that the results of this particular systematic review concur with the view of the existing literature.
As highlighted in section 5.3.7, there was variation between the health literacy assessment tools employed within the included studies. Despite this variation in the assessment tool used, participants with low health literacy levels were identified in each study with ease. Furthermore, 99% of the included studies found a connection between the detection of participants with low health literacy, the provision of an individualised health literacy intervention and improved understanding of, and adherence to, prescribed medication. Although the findings were not necessarily statistically significant, the primary outcome results would advocate the routine use of health literacy assessment within the healthcare environment.

It is worth noting that the deviation between the health literacy assessment tools was not the only difference acknowledged between the included studies. The co-morbidities identified within the included studies varied dramatically. There was for example, representation of acute (Paasche-Orlow et al. 2005, Kripalani et al. 2012) and chronic (Morrow et al. 2007) conditions within the studies. Heart failure was the most prominent co-morbidity, accounting for 3 of the 7 included studies (Morrow et al. 2007, Murray et al. 2007, Kripalani et al. 2012). The 4 remaining studies involved participants with HIV (Kalichman et al. 2013), Glaucoma (Muir et al. 2012), Asthma (Paasche-Orlow et al. 2005) and Arthritis (Rudd et al. 2009). The differences in co-morbidities are important as it highlights the generalisation of the impact of health literacy assessment across a broad spectrum of participants, settings and diseases.

The most thorough way of presenting the established results of a systematic review is via narrative and tabular means. For the purposes of this particular systematic review however, presentation is exclusively narrative. The rationale for this is due to the heterogeneity identified between the included studies. Although all studies investigated the same theme, namely the effect of limited health literacy on medication adherence and subsequently health related quality of life, they used different assessment tools and intervention techniques. To this end it was not possible to present results as meta-analysis or in tabular form.
5.4.2 Secondary outcome – health related quality of life

Given that life expectancy is forecast to increase, it is not outlandish to predict an increase in chronic diseases (Shaw et al. 2009). Therefore, the secondary outcome measure of this systematic review was to identify if the primary outcome measures impact on the health related quality of life of the patients within the studies. An appropriate level of health literacy is inherently linked not only to improved health outcomes (Lindquist et al. 2011, Martensson and Hensing 2011, Lambert and Keogh 2014a), but overall quality of life (Lambert and Keogh 2014a). Powers et al. (2010) go a step further stating that low health literacy levels are detrimentally associated with an increase in mortality. However, medication taking behaviour is not as straightforward as it appears (Brown and Bussell 2011), with Sabate (2003) affirming that in the future, overall health will be determined by patients’ ability to adhere to medication.

The primary outcome of this particular systematic review does not show an improvement or impact on the secondary outcome identified, namely health related quality of life. For all of the 7 included studies however, an improvement in health related quality of life was inferred and assumed under different guises. Therefore, each study will be discussed with direct emphasis on the specific improvements noted within that particular study.

The first study, that of Kalichman et al. (2013) did not directly refer to health related quality of life within their participants. They did however discuss participants’ behavioural adherence strategies, which were assessed on a monthly basis for a period of 9 months post intervention. This allows hypothesis into the future of participants and their potential to sustain the improvement in their health. Kalichman et al. (2013) determined at their 9-month follow-up that participants with lower health literacy levels were more likely to demonstrate continued use of adherence strategies, thus affording the presumption of prospective health related quality of life.

The second study, that of Kripalani et al. (2012), again only alluded to the concept of health related quality of life. They identified their secondary outcomes as the
reduction of preventable and potential adverse drug events, including ameliorable adverse drug events deemed to be serious, life-threatening and/cr fatal. Kripalani et al. (2012) established that clinically significant medication errors within the first 30 days post discharge were higher in the usual care group. Potential adverse drug events were also higher in the usual care group. Conversely, participants in the intervention group had a higher number of actual adverse drug events than the usual care group. Once again, a hypothesis of improved health related quality of life can be reached based on the secondary outcomes identified in this study.

Morrow et al. (2007), the authors of the third study did not identify any type of long term quality of life issues. They did however identify that participants with lower health literacy levels showed a preference for the patient-centered instructions. They also discovered that participants in the intervention group were more likely to choose the patient-centered instructions. As a result, it is possible to assume that health literacy appropriate instructions and information could assist participants in establishing and maintaining prescribed medication adherence, thus improving quality of life.

Once again, in the fourth study, Muir et al. (2012) did not directly address the topic of health related quality of life. Nevertheless, they did discuss medication possession ratio (MPR) and days without medication (DWM), which are intrinsically linked. They found that, although not significant, the intervention group had fewer days without medication compared the standard care group. Overall, they identified that participants with adequate health literacy in the intervention group had on average 30 less DWM than their counterparts. Yet again, it can be presumed that in light of these outcomes, participants who have had health literacy assessment, followed by appropriate health literacy level interventions can expect an increased quality of life.

The fifth study by Murray et al. (2007) identified results in terms of health outcomes. The study concluded that the intervention group had 19.4% fewer exacerbations. In addition, the intervention group also had fewer hospital admissions over the study period. Disease-specific quality of life improved in the
intervention group from baseline to 6 months by 0.28 and 12 months by 0.39, compared with 0.21 and 0.39 respectively in the usual care group.

The penultimate study conducted by Paasche-Orlow et al. (2005) referred to health related quality of life by way of improved metered dose inhaler (MDI) technique. They found that the overall mean MDI technique score showed an increase of 1.1 from baseline. The results of this study are once again onlysuggestive of potential future quality of life. It can be hypothesised therefore, that going forward, the improvement in MDI technique will result in a greater concentration of medication administration, thus improved quality of life.

The final study, that of Rudd et al. (2009), revealed an improvement in both mental health and self-efficacy in the intervention group. In conclusion Rudd et al. (2009) stated that although there were improvements in all variables studied, they were not significant. To this end, as with the other 6 included studies, the presumption of health related quality of life can be extrapolated from the general improvement in self-care.

5.5 Strengths and limitations of this systematic review

Healthcare professionals are under increased pressure to improve the care they provide, while adhering to cost saving initiatives and budgets. Systematic reviews have been judged and found to be a timely source of safe, quality, evidence based literature (Crowther and Cook 2007, Garg et al. 2008). It has been established that systematic reviews enable already time-restricted healthcare professionals to access up to date, evidence based research, which can be integrated into their provision of care (Crowther and Cook 2007, Webb and Roe 2007, Nocini et al. 2010). It has been argued however, that systematic reviews are only as strong as the studies included within it (Garg et al. 2008). Strengths and limitations are an inherent part of any research project (Crowther and Cook 2007, Garg et al. 2008). This systematic review is subject to the same perceived strengths and limitations as all other studies. The strengths and limitations identified within this particular systematic review are discussed below.
5.5.1 Strengths

Randomised controlled trials have been universally acknowledged as the 'gold standard' in terms of research methodology, due to their ability to minimise bias and generate reliable, robust evidence based research (NH-MRC 2000, Nelson et al. 2010, Manterola et al. 2013). Randomised controlled trials are exclusively endorsed by The Cochrane Collaboration who have, in partnership with the World Health Organisation (WHO), driven the move towards safe, high quality, evidence based care (The Cochrane Collaboration 2014). With this in mind therefore, the main strength of this particular systematic review is the number of included randomised control trials. Six out of the seven included studies employed this methodology.

One of the most important reasons systematic reviews are held in such high regard is because of their rigorous and transparent development (Crowther and Cook 2007, Garg et al. 2008, Nocini et al. 2010). The ability of a systematic review to critically appraise and synthesise data from all included studies is a unique feature of their design (Collins and Fauser 2005, Crother and Cook 2007, Begley 2008). There are a number of explicit steps which contribute to the make up of a systematic review (Khan et al. 2003, Thomas and Harden 2008, Victor 2008, Booth et al. 2010). To this end all stages of this particular systematic review were thoroughly and transparently discussed, with results presented in both tabular and narrative format.

Another strength of this systematic review is the identification of an area of health, which has been somewhat overlooked. Low levels of health literacy, negatively impact on both patients and the healthcare facility. While the issue of health literacy, medication adherence and overall health related outcomes has been studied (Driscoll et al. 2009, Elliott and Marriott 2009, Green et al. 2011, Kripalani et al. 2010, Al Sayah et al. 2012, Devraj et al. 2013), there has not been, to the best knowledge of the author, a systematic review conducted around the topic. While it is acknowledged that the results of the included studies are not statistically significant as stand alone research articles, their combined results validate investigation into this topic.
5.5.2 Limitations

It is acknowledged by the author that despite their elevated position, systematic reviews are not infallible (Webb and Roe 2007, Dixon-Woods et al. 2008). Furthermore, Collins and Fauser (2005) suggest that strengths can evolve into weakness if a tapered angle contradicts comprehensive coverage of the topic of interest. To this end, the foremost limitation of this particular systematic review is the significant lack of relevant literature relating to the research question. Despite the discovery of a considerable amount of literature on the topics in question (Williams et al. 2012, Goeman et al. 2013, Walker et al. 2013, Westlake et al. 2013, Weymann et al. 2013), the inclusion and exclusion criteria set for the purposes of this systematic review restricted the use of sourced material significantly, resulting in a meagre 7 included studies. Notwithstanding this, Nocini et al. (2010) argue that the pooling of data from a number of studies augments the overall results. Additionally, they imply that small systematic reviews have the potential to be more statistically significant due to the detection of more subtle results.

Another limitation of the present systematic review is the exclusion of unpublished literature. The use of grey literature has been endorsed by Thomas et al. (2004) and Garg et al. (2008) who suggest that research conducted is not complete without all avenues of potential sources of evidence being explored. Conversely, White and Schmidt (2005) and Crowther and Cook (2007) caution the use of grey literature as it is not peer-reviewed, therefore leaving it open to interpretation and potentially reducing the quality of the review. Furthermore, the exclusion of literature not published in English compound this. The exclusion of grey literature, coupled with the exclusion of non English published literature can potentially alter the results of the study as there may have been statistically significant data contained within the excluded studies published.

5.6 Contribution to health and social gain

Although this particular systematic review has not identified any new information previously not well known, there is significant potential for a positive contribution to health and social gain.
5.6.1 Health literacy

Health literacy is an essential component of the skill base required of patients when they become ill and require professional intervention. Low or limited health literacy levels are associated with increased poverty, higher rates of acute presentations, higher readmission rates, increased risk of medication error, higher number of co-morbidities and financial implications for both the patient and the healthcare provider (Williams et al. 1995, Weiss et al. 2005, Carmona 2006, Davis et al. 2006, Bennett et al. 2009, Powers et al. 2010).

This systematic review has established that the assessment of health literacy within the healthcare setting does not have to be costly or time consuming. In fact, the initial cost of providing resources and training are overwhelmed by the overall health benefits to the patient and the cost savings to the healthcare facility. The results of this systematic review also revealed that health literacy assessment, followed by patient-centered information and instructions increased overall patient satisfaction (Murray et al. 2007, Kripalani et al. 2012).

5.6.2 Medication adherence

The primary outcome identified for this systematic review was the increased adherence to medication. Of the 7 included studies, 6 found a correlation between the detection of participants with low health literacy, the provision of an individualised health literacy intervention and improved understanding of, and adherence to, prescribed medication. These findings represent a potentially significant contribution to the overall health and social gain of the patient. The literature has found that health literacy appropriate interventions positively impact on patients, encouraging them to take ownership of their care, resulting in a reduction in hospital admissions and fewer exacerbations (Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Kalichman et al. 2013). This improvement in patient care has a knock on effect for the healthcare facility. As previously identified, there is a push towards a higher patient turnaround, and a more efficient use of staff and resources (Davis et al. 2006, Shaw et al. 2009, Lara and Salberg 2009, Brown and Bussell 2011). The results of this systematic
review provide evidence of the potential financial and personal gains available to all stakeholders.

5.6.3  Health related quality of life

The secondary outcome identified for this review was health related quality of life. This systematic review has established that health literacy assessment, coupled with patient-centered health literacy information and instructions, do positively impact on patients’ quality of life (Paasche-Orlow et al. 2005, Morrow et al. 2007, Murray et al. 2007, Rudd et al. 2009, Kripalani et al. 2012, Kalichman et al. 2013). Taking into consideration that research has identified one in four Irish nationals as illiterate (CSO 2012), with 40% of people having unacceptable health literacy levels (Department of Health, 2012), it is reasonable to assume that the contribution of this systematic review to health and social gain is significant.

5.7  Implications for future nursing practice

The integration of evidence based knowledge into nursing practice is the sole purpose of conducting nursing research. Nursing research is a rapidly expanding area of expertise (Hallberg 2009, Squires et al. 2011), which produces a larger volume of publications than any other speciality (Hallberg 2009). The universally acknowledged recognition of the requirement for the provision of safe and quality care has reinforced the need for conducting evidence based research (DiCenso 2003, Stevens 2013). Despite this, the literature has identified a discrepancy between the availability of this specialised knowledge and its dissemination into clinically based care (Crane 1995, DiCenso 2003, Lavin et al. 2007). This particular systematic review highlighted several areas to which the results are applicable.

5.7.1  Do Not Attend Rates (DNA’s)

Do Not Attend (DNA) rates within the healthcare setting are widely recognised as leading to a waste of time and money for both the patient and the health service (Kolawole and Bolaji 2002, Chung 2006, Molyneux and Griffith 2007, Trentman et al. 2010). Numerous studies have investigated DNAs and how to prevent patients from falling into this category (DOH 2001/2002, Chung and Newman 2005). However, there is little or no literature available to identify the reasons patients
give for missed appointments. It is thought that involving patients in their care (Chung and Newman 2005) and providing verbal and understandable written education about the day surgery process can help reduce these rates (Gal and Prigat 2005, Shaw et al. 2009 and Smith and Koehlmoos 2011). The results of this study recognise a communication gap not yet identified. It is possible however to hypothesise that patients do not understand their appointments, which leads to their non attendance.

5.7.2 Pre-Assessment

Pre-assessment is widely viewed as best practice for day surgery (DS) (Knox et al. 2009, Kluger et al. 2000, Thomson et al. 2004). Pre-assessment prior to day surgery can lead to reduced waiting times for the patient on the day of admission, by ensuring that relevant documentation is completed and any appropriate pre-operative tests have been carried out (Kluger et al. 2000, Knox et al. 2009, Swart and Houghton 2010). Pre-assessment can also help identify and reduce the number of adverse events and post operative unanticipated admissions (Kluger et al. 2000). Nurse lead pre-assessment can help reduce the workload of nursing and medical staff, while reducing costs for the hospital. This systematic review has identified the requirement for health literacy assessment of patients within the healthcare environment (Williams et al. 1995, Brown and Bussell 2011, Martensson and Hensing 2012). Given that one of the functions of pre-assessment is the provision of information and education, it is suggested by the author that this would be an ideal time to conduct health literacy assessment. This intervention would allow for the integration of patient centered, health literacy appropriate information and education, potentially reducing the DNA rates and increasing adherence to pre operative instructions such as fasting and bowel preparation.

The implications for future nursing practice identified within this systematic review are modest. Notwithstanding this, according to the principles of change management, before change can happen at any level, it is necessary to first identify areas for improvement (Jones et al. 2004, Cork 2005). The scope for
improvement at the most basic and holistic levels of care is significant, requiring healthcare professionals to further expand their knowledge and expertise.

5.5 Summary

The key findings established for this systematic review were: the identification of patients with low health literacy is an essential element in the provision of safe and quality healthcare; there are numerous interventions which can be employed to improve understanding of information and education provided within the healthcare environment; in general, although not always statistically significant, participants who received health literacy appropriate interventions demonstrated improved medication adherence, thus leading to improved quality of life; low health literacy is not linked to the ability to learn and retain important information and education; patient satisfaction with the healthcare process is greater within populations who received health literacy appropriate interventions; health literacy appropriate interventions, although initially more labour intensive, are a cost neutral resource which healthcare providers are not utilising to their potential.

Methodological issues which arise during the creation of a systematic review are extensive. They have been identified as sampling and population, participant selection, sequence generation, allocation concealment, blinding, incomplete data outcome, selective outcome reporting and heterogeneity.

The primary and secondary outcome measures identified for the present systematic review provide evidence to corroborate the existing literature relating to low health literacy levels, lack of medication adherence and the impact of same on health related quality of life.

Strengths and limitations have been identified as an inherent part of any research project (Crowther and Cook 2007, Garg et al. 2008). The strengths acknowledged for this particular systematic review included the volume in randomised controlled trials in the results. The methodology of the systematic review itself has been identified as a strong point. Systematic reviews have been established as a thorough and transparent process which efficiently appraises,
synthesises and decants evidence based literature (Crowther and Cook 2007, Garg et al. 2008, Nocini et al. 2010). The identification of an area of health, which has been somewhat overlooked, can also be viewed as a strength. Low levels of health literacy negatively impact on both patients and the healthcare facility.

It is also known however, that systematic reviews are also susceptible to limitations. The most prolific limitation of this review is the lack of relevant literature relating to the research question. Another potential limitation was the exclusion of unpublished literature. The use of grey literature is controversial, with arguments for and against inclusion of same. However, it is acknowledged that the exclusion of grey literature, coupled with the exclusion of non English published literature may have altered the results presented.

Results of this particular systematic review established that although it did not discover any new information previously not well known, the results established significant potential for a positive contribution to health and social gain. For example, the results of this systematic review confirmed that health literacy assessment, followed by patient centered information and instructions increased medication adherence and as a result health related quality of life.

Finally, implications for future nursing practice were discussed, with specific focus on DNA rates and pre assessment.

5.6 Conclusion

The purpose of this chapter was to debate the key of findings of this systematic review. Initially, a concise summary of the key findings was given. The strengths and limitations of the studies included were discussed. Following this, the primary and secondary outcomes were examined in relation to both the studies individually and the systematic review as a whole. The strengths and limitations of this particular systematic review were argued. Finally, the potential for overall contribution of this systematic review to health and social gain and implications for future nursing practice were highlighted.
Chapter 6  Summary and Conclusion

6.1  Introduction

This chapter will present an overall summary of this systematic review. A final conclusion will then be reached.

6.2  Summary

The function of this systematic review was to assess the impact of low health literacy levels on medication adherence and ultimately health related quality of life.

It defined literacy and health literacy, and highlighted the differences between them. A picture of the current state of health literacy nationally and internationally was drawn. Factors which influence health literacy within the healthcare environment were identified. The interventions and tools used to assess and identify limited health literacy within the healthcare setting were discussed and ethical issues surrounding health literacy were highlighted. Furthermore, the research question, aims and objectives for this particular systematic review were outlined.

The systematic review as a research method has been thoroughly discussed. The strengths and limitations of the systematic review were critically appraised. Although the emergence of limitations appears to have outweighed the strengths, the author believes that in practice and with due diligence, the overall method of systematic review is in fact sound, resulting in a piece of work which is not only reliable, but potentially contributing to safe and quality patient care.

There was in depth discussion regarding the methodological design by which the present systematic review was conducted. The main objective of this systematic review was to discover if patients with chronic diseases adhere to their medication and health promotion education following health literacy assessment and intervention. The secondary objective was to establish whether patients within
the intervention group have an improved health related quality of life following same.

Following this, in depth description of the studies retrieved via the systematic approach were discussed. To begin with, an overview of the outcomes of the search strategy, identifying the number of studies included and those excluded was provided. Following this, a narrative summary of each study was given, including study design, population, geographical location, health literacy assessment tool used, intervention, sample size and co-morbidities. The quality appraisal applied to the retrieved studies was then discussed. Finally, the primary and secondary outcomes of the review were highlighted and discussed.

The key of findings of this systematic review were identified and debated. Initially, a concise summary of the key findings was given. The strengths and limitations of the studies included were discussed. Following this, the primary and secondary outcomes were examined in relation to both the studies individually and the systematic review as a whole. The strengths and limitations of this particular systematic review were argued.

The methodological issues of the included studies were discussed. These included an in depth appraisal of the study design, sampling, sequence generation, allocation concealment and blinding.

A thorough outcome assessment was then conducted. This incorporated debate relating to incomplete outcome data, attrition and the potential impact of both, on the overall results and generalistion of the review. Selective outcome reporting, which was identified as another potential source of bias was also discussed. Heterogeneity and its potential impact on results established was then examined.

A discussion of outcomes followed. The primary outcome measures were identified for the present systematic review concluding that the overall results contained within the 7 included studies of this particular systematic review suggest that low health literacy levels do in fact negatively impact on a
participant's ability to adhere to medication instructions. These results correspond with the view of the existing literature. The secondary outcome measure was to identify if the primary outcome measures impact on the health related quality of life of the patients within the studies. Of the 7 included studies, the suggestion of health related quality of life was assumed under different guises. However, it can be extrapolated from the results that regardless of the intervention, co-morbidity or population, health related quality of life improved for all participants.

Strengths and limitations of this particular systematic review were identified. This review has the benefit of several strengths, primarily: the majority inclusion of randomised controlled trials. Strength is the rigorous and transparent development of the conducting of the review, adhering to the explicit steps outlined in the literature, which contribute to the make up of a systematic review. Another strength of this systematic review is the identification of an area of health, which has been somewhat overlooked, namely health literacy. While it is acknowledged that the results of the included studies are not statistically significant as stand alone research articles, their combined results validate investigation into this topic.

The limitations of this systematic review were also identified. The foremost limitation was established as the significant lack of relevant literature relating to the research question, despite the discovery of a considerable amount of literature on the topics in question. Another limitation of this review was the exclusion of unpublished literature and studies not published in English. These exclusions could have the potential to alter the overall results of the study.

The contribution of this systematic review to health and social gain was discussed. It was established that the assessment of health literacy within the healthcare setting does not have to be costly or time consuming. On the contrary, the cost benefits far outweigh the perceived losses.
The results also reveal that health literacy assessment, followed by patient centered information and instructions increased overall patient satisfaction. As identified in the literature, there is a correlation between the detection of participants with low health literacy, the provision of an individualised health literacy intervention and improved understanding of, and adherence to, prescribed medication.

Finally, it was ascertained that health literacy assessment, coupled with patient centered health literacy information and instructions do positively impact on patients quality of life. The results of this systematic review therefore, provide evidence of the potential financial and personal gains available to all stakeholders.

6.3 Conclusion

This systematic review has identified that in accordance with the literature, patients with lower levels of health literacy have lower medication adherence and subsequently poorer heath related quality of life prospects. Although there were only 7 included studies in the results, the data collected all pointed to the same outcome. It is essential for healthcare professionals to recognise the impact of low health literacy levels on, not only the patient, but the health service as a whole. Furthermore, it is imperative that healthcare professionals undergo the appropriate training and education to ensure that the emergence of this issue is forcefully dealt with.
Reference List


Department of Health (2012). The European health literacy survey: Results from Ireland.


Bibliography List


Appendix 1
Cochrane Library Search Flow Chart

Health literacy  n = 565
Medication     n = 40,171
Comorbidities  n = 1,548

Health literacy AND Medication n = 139
Health literacy AND Comorbidities n = 9
Medication AND Comorbidities n = 396

Health literacy AND Medication AND Comorbidities n = 6

All titles read, none suitable
Appendix 2
CINAHL Search Flow Chart

Health literacy
n = 6,439

Medication
n = 211,223

Medication errors
n = 211,223

Co morbidities
n = 8,013

Health literacy AND Medication n = 609
Health literacy AND Medication errors n = 78
Health literacy AND Co morbidities n = 7
Medication AND Co morbidities n = 497
Medication errors AND Co morbidities n = 15

Health literacy AND Medication AND Co morbidities n = 1
Health literacy AND Medication errors AND Co morbidities n = 1
-> Duplicate article

Article not suitable
Appendix 3
Embase Search Flow Chart

Health literacy. MeSH: health'/exp OR health AND ('literacy'/exp OR literacy) 
n = 14,726

Medication 
 n = 215,398

Medication error 
 n = 15,941

Comorbidities 
 n = 46,796

Co morbidities 
 n = 16,543

↓

Health literacy AND Medication n = 1,029
Health literacy AND Medication error n = 121
Health literacy AND Comorbidities n = 98
Health literacy AND Co morbidities n = 46
Medication AND Comorbidities n = 3,274
Medication AND Co morbidities n = 1,141
Medication error AND Comorbidities n = 78
Medication error AND Co morbidities n = 29

↓

Health literacy AND Medication AND Comorbidities n = 27
Health literacy AND Medication AND Co morbidities n = 10
Health literacy AND Medication errors AND Comorbidities n = 1
Health literacy AND Medication errors AND Co morbidities n = 2

⇒ 1 duplicate article, none suitable
Appendix 4
PubMed Search Flow Chart

Health literacy ↓ n = 7,636

Low health literacy ↓ n = 2,029

Medication ↓ n = 215,398

Medication error ↓ n = 14,263

Co morbidity ↓ n = 96,052

Comorbidity ↓ n = 86,546

Health literacy AND Medication n = 599
Low health literacy AND Medication n = 209
Health literacy AND Medication error n = 86
Low health literacy AND Medication error n = 25
Health literacy AND Comorbidity n = 65
Low health literacy AND Comorbidity n = 20
Health literacy AND Co morbidity n = 78
Low health literacy AND Co morbidity n = 26
Medication AND Comorbidity n = 5,500
Medication AND Co morbidity n = 6,054
Medication error AND Comorbidity n = 143
Medication error AND Co morbidity n = 158

Health literacy AND Medication AND Comorbidity n = 14
Health literacy AND Medication AND Co morbidity n = 16
Low health literacy AND Medication AND Comorbidity n = 3
Low health literacy AND Medication AND Co morbidity n = 5
Health literacy AND Medication errors AND Comorbidity n = 1
Health literacy AND Medication errors AND Co morbidity n = 1
→ duplicate article
Low health literacy AND Medication errors AND Comorbidity n = 0
Low health literacy AND Medication errors AND Co morbidity n = 0

154
Appendix 5
ScienceDirect Search Flow Chart

Health literacy ↓
n = 26,712

Low health literacy ↓
n = 22,164

Medication ↓
n = 571,338

Medication error ↓
n = 114,188

Comorbidity ↓
n = 87,723

Co morbidity ↓
n = 265,799

Health literacy AND Medication n = 5,430
Low health literacy AND Medication n = 4,838
Health literacy AND Medication error n = 1,831
Low health literacy AND Medication error n = 1,672
Health literacy AND Comorbidity n = 1,201
Low health literacy AND Comorbidity n = 3,024
Health literacy AND Co morbidity n = 3,188
Low health literacy AND Co morbidity n = 3,024
Medication AND Comorbidity n = 37,953
Medication AND Co morbidity n = 76,571
Medication error AND Comorbidity n = 10,048
Medication error AND Co morbidity n = 18,436

Health literacy AND Medication AND Comorbidity n = 695
Health literacy AND Medication AND Co morbidity n = 1,363
Low health literacy AND Medication AND Comorbidity n = 658
Low health literacy AND Medication AND Co morbidity n = 1,299
Health literacy AND Medication errors AND Comorbidity n = 251
Health literacy AND Medication errors AND Co morbidity n = 522
Low health literacy AND Medication errors AND Comorbidity n = 246
Low health literacy AND Medication errors AND Co morbidity n = 502

Limited to = 502
Appendix 6
## EBL Critical Appraisal Checklist

<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Population</strong></td>
<td>Is the study population representative of all users, actual and eligible, who might be included in the study?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are inclusion and exclusion criteria definitively outlined?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is the sample size large enough for sufficiently precise estimates?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is the response rate large enough for sufficiently precise estimates?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is the choice of population bias-free?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If a comparative study:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Were participants randomised into groups?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Were the groups comparable at baseline?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If groups were not comparable at baseline, was incomparability addressed by the authors in the analysis?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Was informed consent obtained?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B. Data Collection</strong></td>
<td>Are data collection methods clearly described?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If a face-to-face survey, were inter-observer and intra-observer bias reduced?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is the data collection instrument validated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If based on regularly collected statistics, are the statistics free from subjectivity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Does the study measure the outcome at a time appropriate for capturing the intervention’s effect?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is the instrument included in the publication?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are questions posed clearly enough to be able to elicit precise answers?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Were those involved in data collection not involved in delivering a service to the target population?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C. Study Design</strong></td>
<td>Is the study type / methodology utilised appropriate?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is there face validity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is the research methodology clearly stated at a level of detail that would allow its replication?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Was ethics approval obtained?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are the outcomes clearly stated and discussed in relation to the data collection?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D. Results</strong></td>
<td>Are all the results clearly outlined?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are confounding variables accounted for?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Do the conclusions accurately reflect the analysis?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is subset analysis a minor, rather than a major, focus of the article?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are suggestions provided for further areas to research?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is there external validity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Calculation for section validity: \((Y+N+U=T)\)

If \(Y/T < 75\%\) or if \(N+U/T > 25\%\) then you can safely conclude that the section identifies significant omissions and that the study's validity is questionable. It is important to look at the overall validity as well as section validity.

- **Section A validity calculation:** \(1/4 = 25\%\) not valid
- **Section B validity calculation:** \(5/7 = 71\%\) not valid
- **Section C validity calculation:** \(1/5 = 20\%\) not valid
- **Section D validity calculation:** \(4/6 = 67\%\) not valid

### Calculation for overall validity: \((Y+N+U=T)\)

If \(Y/T \geq 75\%\) or if \(N+U/T \leq 25\%\) then you can safely conclude that the study is valid.

- **Overall validity calculation:** \(11/22 = 50\%\) not valid

---

**EBLIP Critical Appraisal Checklist**
Lindsay Glynn, MLIS
Memorial University of Newfoundland
lglynn@mun.ca
Appendix 7
### Data Extraction Table: Kalichman et al. (2013)

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Co-morbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al.</td>
<td>Randomised Clinical Trial of HIV Treatment Adherence Counseling Interventions for People Living With HIV and Limited Health Literacy</td>
<td>Journal of Acquired Immune Deficiency Syndromes</td>
<td>2013</td>
<td>America</td>
<td>AIDS services and community outreach</td>
<td>1. HIV</td>
<td>Inclusion criteria: 1. HIV positive 2. Taking ART 3. TOFHLA score &lt; 90% Exclusion criteria: Not discussed</td>
<td>1,385 screened</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Study Design and Type</th>
<th>Allocation</th>
<th>Tools Used</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) 46.7 in pictograph guided group, 47.8 in health improvement group and 47.0 in control group; male 310, female 136; African American 137, 132 and 152; unemployed 42, 38 and 50; income of &lt; $10,000 per year 101, 105, 111;</td>
<td>RCT</td>
<td>Recruitment, screening, office-based assessment and telephone assessment 1. After baseline assessment and 3 unannounced phone assessments, the Project Manager randomly assigned participants to conditions. 2. Randomisation was done via an</td>
<td>Recruitment, screening, office-based assessment and telephone assessment 1. TOFHLA</td>
<td>Two 60-minute one-to-one counselling sessions and one 30 minute booster session</td>
<td>Primary outcomes: 1. HIV RNA Viral Load 2. ART adherence</td>
<td>Differences between conditions were measured using analyses of variance for continuous measures and contingency table X² Baseline equivalence between conditions</td>
<td>Primary outcomes: 1. No differences from baseline measures of viral load 2. No differences from baseline measures of adherence</td>
<td>Participants with lower health literacy did not demonstrate positive outcomes with either intervention, which was unexpected. Results encourage screening patients for basic health literacy skills in risk</td>
</tr>
<tr>
<td>Mean years of education: 12.0, 11.9 and 12.0; mean years since diagnosis: 14.0, 13.0 and 13.6; CD4 cell count: 411, 437 and 404; mean number of pills a day: 3.0, 2.8 and 2.8; correct reading literacy: 72.2%, 72.4% and 73.9%; correct numeracy literacy: 64.1%, 64.3 and 67.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Automated randomisation generator 3. Randomisation was not breached throughout the trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Importance of following prescribed instructions 3. Motivational enhancement techniques, including direct feedback on participant health status and training in self-monitoring skills 4. Medication instructions were tailored, including memory cues</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>And effects of attrition on dependent measures were also measured. Generalised estimating equations (GEEs) were used to analyse adherence and viral load</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary outcomes: 1. No differences from baseline measures at 3- and 9-months post intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessments for difficulties adhering to treatment. Interventions are required to achieve optimal ART adherence and positive treatment outcomes for patients with lower health literacy skills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 8
<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Co-morbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
</table>
Exclusion criteria: 1. If being discharged within 3 hours 2. Too ill to participate 3. Unable to communicate in English or Spanish 4. Active psychosis, bipolar disorder, delirium or severe dementia 5. Hearing or vision impairment 6. Did not manage their own medication 7. Unlikely discharge home 8. No telephone 9. Police custody | 6,416 screened 5,565 excluded 851 eligible 423 in intervention group 428 in control group |
<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Study Design and Type</th>
<th>Allocation</th>
<th>Tools Used</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) 60; mean years of education 14; male 499, female 352; primary language English 414 in intervention group and 425 in control group; primary language Spanish 9 and 3; white 319 and 335, black 77 and 71, other 27 and 22; median length of education (IQR) 14 and 14; annual household income &lt; $10,000, 20 and 17; inadequate 47 and 39, marginal 36 and 38, adequate 331 and 340; impaired cognition 52 and 46; has primary care provider 386 and 392; median preadmission medications (IQR) 8 and 7</td>
<td>RCT Randomisation Sequence: 1. Participants randomly assigned to either intervention or usual care group 2. Randomisation was stratified by study site and diagnosis, in permuted blocks of 2 to 6 patients, by a computer program that maintained allocation concealment</td>
<td>One unblended research coordinator at each site administered the randomisation, contacted study pharmacists who then delivered the intervention to eligible patients and participated in the individualised telephone follow-up. All investigators, statisticians and outcome assessors were blinded</td>
<td>1. s-TOFHLA 2. Mini-Cog 3. Self-reported medication adherence (Morisky scale) 4. Medication Understanding Questionnaire</td>
<td>1. Pharmacist-assisted medication reconciliation 2. Tailored inpatient counselling by a pharmacist 3. Provision of low-literacy adherence aids 4. Individualised telephone follow-up after discharge</td>
<td>Primary outcomes: 1. The number of clinically important medication errors per patient within 30 days of discharge Secondary outcomes: 1. Preventable ADEs 2. Potential ADEs due to discrepancies or non-adherence 3. Preventable ADEs judged to be serious, life-threatening or fatal</td>
<td>Sample size was calculated on the basis of achieving a 25% reduction in the percentage of patients who would have at least 1 clinically important medication error after discharge.</td>
<td>1,432 (50.8%) had 1 or more clinically important medication errors during the 30 days after hospital discharge. The mean number of clinically important medication errors was similar in the intervention 0.87 (per patient) and the control 0.95 (per patient) groups. Treatment effect favoured the intervention, but not significantly</td>
<td>Overall, health-literacy-sensitive pharmacist intervention does not significantly reduce clinically important medication errors or ADEs. Results highlight the difficulty of improving medication safety during the transition from hospital to home.</td>
</tr>
<tr>
<td>Limitations</td>
<td>Control group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>---------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADEs were</td>
<td>1. PILL-CVD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>found among%</td>
<td>treated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>253 patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>errors by</td>
<td>showing 187 in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>group</td>
<td>29.7% in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>group and 237</td>
<td>hospitals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>intervention</td>
<td>making it</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>showed an</td>
<td>difficult to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>incremental</td>
<td>support the</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>benefit from</td>
<td>study,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the PILL-CVD</td>
<td>resources to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>intervention</td>
<td>out in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. On average</td>
<td>hospitals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the study</td>
<td>had 1074</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. The literacy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. The</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>literacy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>were</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>educated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>about side</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>effects,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>therefore</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>may alter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>responses in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>their flavour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Negative binomial regression was used to assess the adjusted effect of the intervention through multivariable analysis. Significant adherence-threatening life-threatening discrepancies were showed as having a relatively low prevalence of inadquate health literacy. The participants had intact and educated.
Appendix 9
## Data Extraction Table: Morrow et al. (2007)

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Co-morbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morrow et al.</td>
<td>Patients' Health Literacy and Experience With Instructions. Influence Preferences for Heart Failure Medication Instructions</td>
<td>Journal of Aging and Health</td>
<td>2007</td>
<td>America</td>
<td>Urban Hospital</td>
<td>CHF</td>
<td>Inclusion Criteria: 1. Taking at least one CHF medication Exclusion Criteria: 1. Not discussed</td>
<td>236 Total</td>
</tr>
</tbody>
</table>

### Patient Characteristics

<table>
<thead>
<tr>
<th>Study Design And Type</th>
<th>Allocation</th>
<th>Tools Used</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>Not discussed</td>
<td>1. s-TOFHLA</td>
<td>Patient-centered instructions developed, which included: 1. Larger font 2. Less information 3. Medications organised with patients' schemas for organising 4. Inclusion of pictorials</td>
<td>Primary outcomes: To identify patients' preference for medication instructions Secondary outcomes: To identify if patient preferences varied with patient demographics Preference for patient-centered information was higher for participants with lower health literacy levels, lower education, race, lower mental-processing speed and the type of information sought. Participants in the</td>
<td>Primary outcomes: Patients with CHF preferred the patient-centered instructions for issues relating to adherence, but preferred standard instructions for details of drug interactions Secondary outcomes: Impact of patient-centered instructions on</td>
<td>Results suggest that patient-centered instructions help those patients most in need of clear and accurate information about self-care. However, it might be beneficial to integrate the patient-centered instructions with the standard</td>
<td></td>
</tr>
<tr>
<td>intervention group also showed preference for patient-centered information, suggesting familiarity with the instructions increased preference</td>
<td>QoL not discussed</td>
<td>instructions to ensure a balance. The study suggests that patients' preferences are a valuable tool for the development of any information and instructions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Data Extraction Table: Muir et al. (2012)

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Comorbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muir et al.</td>
<td>The influence of health literacy level on an educational intervention to improve glaucoma medication adherence</td>
<td>Patient Education and Counseling</td>
<td>2012</td>
<td>America</td>
<td>Veterans Affairs Medical Center</td>
<td>1. Glaucoma</td>
<td>Inclusion criteria: 1. All patients eligible to participate 2. A score of 18 or higher on the MMSE</td>
<td>131 Enrolled</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Exclusion criteria: 1. Visual acuity less than 20/200 in the better seeing eye 2. Eye surgery in the past month</td>
<td>2 Withdraw</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>127 Total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Study Design and Type</th>
<th>Allocation</th>
<th>Tools Used</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) 66; male 126, female 1; caucasian 37, African American 89, other 1; primary open angle glaucoma 68; open angle glaucoma not otherwise specified 39; normal tension glaucoma 9; pigment dispersion</td>
<td>RCT</td>
<td>Not discussed</td>
<td>1. Mini Mental State Exam (MMSE) 2. The Test of Functional Health Literacy in Adults (TOFHLA)</td>
<td>1. A one to one session with the study coordinator 2. A tailored, health literacy level appropriate, informational video about glaucoma was shown to each participant. Drop instillation</td>
<td>Primary outcomes: To compare the effectiveness of an educational intervention targeted to an individual's health literacy level to routine care in improving glaucoma medication 67 of the intervention and 60 of the control group had Days Without Medicine (DWM) over the 6 months from the start of the study. Intervention group participants experienced 41 fewer</td>
<td>Primary outcome: For each literacy level, the number of DWM was lower in the intervention group than in the control group. Participants who received health literacy level appropriate</td>
<td>Future research and educational efforts should focus on the problem of low health literacy. Health literacy encompasses a variety of experiences, which may change over time.</td>
<td></td>
</tr>
<tr>
<td>Techniques were demonstrated, taught and participants asked to demonstrate proper technique</td>
<td>Adherence, evaluated by identifying the number of days without medication (DWM)</td>
<td>DWM over the study period than the control group. There was little difference between groups for the Medication Possession Ratio (MPR). Participants with low health literacy were more likely to report the presence of a physical disability — affecting ability to administer drops. Low health literacy participants were less satisfied with care, with marginal health literacy participants being 2.5 times more likely to be satisfied with care</td>
<td>Education experienced more than 30 days less without medication than their counterparts in the control group. There was very little difference between the groups when participants had a higher health literacy level</td>
<td>It is predicted that a sample size of 97 in each group would be required to detect a significant difference in DWM. A limitation of the study was the sample being 99% male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. All intervention participants received a follow up phone call once a month to provide support and answer any questions. The study coordinator was trained on the delivery and content of the intervention by an ophthalmologist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 11
<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Co-morbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. ≥ 50 years of age</td>
<td>1.2 excluded</td>
<td>314 total</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. Clinically stable</td>
<td>2 included</td>
<td>122 intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3. Planned to have all treatment within the care practice, including prescribed medications</td>
<td>3 included</td>
<td>192 in control group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4. Diagnosis of heart failure confirmed by their primary care physician</td>
<td>4 excluded</td>
<td>Follow up at 6 months:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5. At least 1 cardiovascular medication for heart failure</td>
<td>5 excluded</td>
<td>107 in intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3. Were not using or planning to use a medication dispenser box</td>
<td>Exclusion criteria:</td>
<td>Follow up at 12 months:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. Dementia</td>
<td>1. Dementia</td>
<td>106 in intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. State funded medications, as no deterrent to adherence</td>
<td>2 excluded</td>
<td>164 in control group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Completed trial, included in analysis:</td>
<td>164 in control group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>106 in intervention group</td>
<td></td>
</tr>
<tr>
<td>Patient Characteristics</td>
<td>Study Design and Type</td>
<td>Allocation</td>
<td>Tools Used</td>
<td>Intervention Details</td>
<td>Outcome Measures</td>
<td>Analysis</td>
<td>Results</td>
<td>Conclusions</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------</td>
<td>------------</td>
<td>------------</td>
<td>----------------------</td>
<td>------------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
</tbody>
</table>
| Mean age (years) 62; male 104, female 210; black 155, white 156, other 199; mean education years intervention 11 and control 11; health literate 88 and 136; HTN 114 and 186; Coronary artery disease 77 and 14; DM 74 and 131; Stroke 16 and 29; COPD 39 and 67; A-fib 14 and 27; mean BP 132.9/68.9 and 135.4/70.5 | RCT Randomisation sequence: Participants were randomly assigned without blocking or stratification. More patients were randomly assigned to the control group in order to study the risk factors associated with the clinical deterioration of heart failure | Interviews were blinded to patients' study status and played no role in the delivery of the intervention. Interviewers contacted a centralised data manager at the end of each interview to determine the patients' study assignment, which was otherwise concealed | Not discussed | 1. Pharmacist delivered intervention including: baseline medication history, prescription taking skills, communication skills, supervision, perceived health, cognitive function, coping, poor vision and poor hearing. When medicine dispensed, patient-centred verbal instructions and written materials about the medications given. 3. Each medication category given an icon, which appeared on the container label, lid and on the written | Primary outcomes: 1. Medication adherence 2. Exacerbations requiring Emergency Department (ED) care or hospital admission | Primary outcomes: 1. Medication adherence was assessed using Medication Event Monitoring System (MEMS) v's prescription container lids. Refill adherence was measured using prescription records. ED data was used to assess exacerbations. Secondary outcomes: Disease-specific quality of life was analysed using the Chronic Heart Failure Questionnaire, which includes | Primary outcomes: 1. Medication adherence was 78.8% in the intervention group, compared with 67.9% in the control group. 2. The intervention group had 19.4% fewer exacerbations requiring ED care or hospital admission | The pharmacist intervention used in this study improved adherence to medications, including proportion taken, reliability of scheduling and amount of refills. Patients in the intervention group had fewer exacerbations and were more satisfied with their pharmacist. Costs were lower and disease-specific QoL were greater in the intervention group. Continued intervention is required to ensure maintenance of intervention. Limitations: Population

---

174
<table>
<thead>
<tr>
<th>Patient Instructions</th>
<th>Questions about fatigue, dyspnoea, emotion and mastery. Satisfaction with pharmacy services was assessed using an internally developed and validated 12-item instrument. Healthcare costs were measured by using fixed-training of pharmacist, material development, programming and equipment, and variable-time spent administering the intervention and written materials, intervention costs compared with 0.7.</th>
<th>The total direct costs were estimated at $17,215 for the intervention group, compared with $23,672 for the control group.</th>
<th>Predominantly indigent. Patients who use special pill box adherence aids were excluded. Single pharmacist intervention – cannot assess pharmacist attitudes or behaviors. Due to multi-intervention technique, unable to attribute intervention effects to any single component.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Written instructions were at low health literacy level.</td>
<td>5. Medication use, healthcare encounters, body weight and other relevant data monitored.</td>
<td>6. Intervention pharmacist studied relevant guidelines and was trained by an interdisciplinary team of investigators specialising in cardiovascular pharmacotherapy, a geriatrician, a cardiologist, a behavioural scientist and a cognitive psychologist.</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 12
<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Comorbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Exclusion criteria: 1. Other chronic lung diseases 2. Contraindication to corticosteroids 3. Patients or physicians who did not consent 4. Investigators patients</td>
<td>63 excluded</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>56 participants returned for 2-week follow-up visit</td>
<td>73 enrolled</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Study Design and Type</th>
<th>Allocation</th>
<th>Tools Used</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) 40.9; male 25, female 48; African American 58, White 15; inadequate health literacy 16; high school graduate 44; income ≥ $19,999 36; physician for asthma care 37; asthma knowledge score (SD) 6.9</td>
<td>Prospective Cohort Study</td>
<td>Not discussed</td>
<td>1. s-TOFHLA 2. 10-item assessment of patients' understanding of asthma medications</td>
<td>1. Patients health literacy was established 2. Patients were also assessed about their understanding of their asthma medications 3. Participants were asked to demonstrate their metered-dose inhalers</td>
<td>Primary outcomes: 1. Examined the relationship between inadequate health literacy and difficulties learning and retaining instructions about discharge medications and</td>
<td>Wilcoxon rank sum were used in bivariate analyses. Logistic regression models were used to determine if inadequate health literacy was an independent predictor of better</td>
<td>Primary outcomes: 1. Observed deficiencies in asthma self-management skills were common and that inadequate health literacy is associated with worse asthma medication knowledge and</td>
<td>This study presents evidence that inadequate asthma self-management skills are common and that inadequate health literacy is associated with worse asthma medication knowledge and</td>
</tr>
<tr>
<td>4. Standardised asthma discharge regimen, including both oral and inhaled corticosteroids and a short-acting bronchodilator.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. One-to-one, 30-minute, guideline-based, written and oral asthma education session about the discharge regimen.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Teach-back method was used to ensure understanding.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Education repeated until patient could prove understanding.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Knowledge and technique re-evaluated at 2 week follow-up visit.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>appropriate MDI technique</th>
<th>outcomes.</th>
<th>MDI technique.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results suggest the need for a systematic assessment of patient comprehension of discharge instructions and medications at hospital discharge and where deficits are identified, this study recommends a tailored, teach-to-goal, asthma education program.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 13
<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Source</th>
<th>Date of Study</th>
<th>Geographical Location</th>
<th>Care Setting</th>
<th>Co-morbidities</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rudd et al.</td>
<td>A randomised controlled trial of an intervention to reduce low literacy barriers in inflammatory arthritis management</td>
<td>Patient Education and Counseling</td>
<td>2009</td>
<td>America</td>
<td>Arthritis centre in an urban teaching hospital</td>
<td>1. RA</td>
<td>Inclusion criteria: 1. At least one visit with a Rheumatologist who gave permission to recruit their patient</td>
<td>2,559 identified</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. PA</td>
<td>2. Post graduate degree</td>
<td>1,480 approved by Rheumatologist</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3. Inflammatory polyarthritides</td>
<td>3. Visual impairment affecting reading ability</td>
<td>1,145 received letter requesting participation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4. Not comfortable with spoken and written English</td>
<td>679 screened by phone</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>464 excluded</td>
<td>464 excluded</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>215 total included</td>
<td>215 total included</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>134 consented</td>
<td>134 consented</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>127 randomised</td>
<td>127 randomised</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>51 in intervention group</td>
<td>51 in intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13 in Plain English group</td>
<td>13 in Plain English group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>63 in control group</td>
<td>63 in control group</td>
</tr>
<tr>
<td>Patient Characteristics</td>
<td>Study Design and Type</td>
<td>Allocation</td>
<td>Tools Used</td>
<td>Intervention Details</td>
<td>Outcome Measures</td>
<td>Analysis</td>
<td>Results</td>
<td>Conclusions</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>---------------------</td>
<td>-----------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Mean age (years) 57.6 in intervention/plain English group and 59.5 in control group; male 26 and female 101; less than high school education 31 and 33; working 32 and 23; disease duration &lt;5 years 17 and 16; annual income &lt;30k 12 and 24</td>
<td>RCT</td>
<td>Study staff members were blinded to participant’s group assignment. Recruitment logs and tracing system were kept separate from the Study Educator’s logs and appointment schedule</td>
<td>1. REALM 2. HAQ 3. Medical Interview Satisfaction Scale 4. Lorig’s self-efficacy scale 5. Levine’s 4-item measure based questionnaire 6. Mental Health Index</td>
<td>Individualised group: 1. Usual Rheumatology care supplemented by plain language materials 2. Two meetings with an educator, where information reviewed, highlighting of material directly effecting the participant 3. Personalisation of medication calendar, communication with caregivers and discussion about specific challenges facing the participant 4. Second meeting with study educator 5. Encouraged to contact study</td>
<td>Primary outcomes: 1. Adherence to treatments 2. Self-efficacy 3. Satisfaction with medical care 4. Appointment keeping</td>
<td>Baseline variables were compared between the two groups. Means were compared using two independent sample t-tests for continuous variables. Longitudinal data was analysed as percentage change between baseline and six months and between baseline and one year. All statistical analysis were performed at a 5% level of significance using SAS statistical software version 9.1</td>
<td>Primary outcomes: 1. Medication adherence showed – 12.21 in the intervention group and – 3.12 in the control group – scales show improvement with decreased scores 2. Self-efficacy increased in the intervention group, showing 3.57, compared with –2.04. 3. Satisfaction with medical care improved in the intervention group, showing 1.38, compared with –0.43 in the control group 4. No differences were seen between groups relating to appointment keeping</td>
<td>The intervention developed in this study did have an effect, but nothing of significance. The improvement in reported mental health in the intervention group could be linked to reduced anxiety. The improvements in mental health may advocate further research in this area</td>
</tr>
</tbody>
</table>
educator if any questions

Plain English group:
1. Usual Rheumatology care supplemented by notebook containing all information material in Plain language at appropriate health literacy level
2. Notebook contained information about arthritis and 'how to get the most from a visit to the doctor, medicine calendars and reminder cues, a map of the hospital and information about the hospital

For the purpose of data presentation, details from the Intervention

Secondary outcomes:
1. Self-reported health status showed −0.79 in the intervention group, compared with 1.33 in the control group. scales show improvements with decreased scores
2. Participants in the intervention group showed a 4.79% improvement in mental health, compared with −0.78% in the control group
and Plain English groups were pooled
Appendix 14
<table>
<thead>
<tr>
<th>Section A: Population</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Unclear (U)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the study population representative of all users, actual and eligible, who might be included in the study?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are inclusion and exclusion criteria definitively outlined?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the sample size large enough for sufficiently precise estimates?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the response rate large enough for sufficiently precise estimates?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the choice of population bias-free?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If a comparative study:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were participants randomised into groups?</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Were the groups comparable at baseline?</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>If groups were not comparable at baseline, was incomparability addressed by the authors in the analysis?</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Was informed consent obtained?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Section B: Data Collection</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Unclear (U)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are data collection methods clearly described?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If a face-to-face survey, were inter-observer and intra-observer bias reduced?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the data collection instrument validated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If based on regularly collected statistics, are the statistics free from subjectivity?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the study measure the outcome at a time appropriate for capturing the intervention's effect?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the instrument included in the publication?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are questions posed clearly enough to be able to elicit precise answers?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were those involved in data collection not involved in delivering a service to the target population?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Section C: Study Design</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Unclear (U)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the study type / methodology utilised appropriate?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is there face validity?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the research methodology clearly stated at a level of detail that would allow its replication?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was ethics approval obtained?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are the outcomes clearly stated and discussed in relation to the data collection?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Section D: Results</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Unclear (U)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are all the results clearly outlined?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are confounding variables accounted for?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do the conclusions accurately reflect the analysis?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is subset analysis a minor, rather than a major, focus of the article?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are suggestions provided for further areas to research?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is there external validity?</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Calculation for section validity: \((Y+N+U=T)\)

- If \(Y/T < 75\%\) or if \(N+U/T > 25\%\) then you can safely conclude that the section identifies significant omissions and that the study's validity is questionable. It is important to look at the overall validity as well as section validity.

- Section A validity calculation: \(1/4 = 25\% \text{ not valid}\)
- Section B validity calculation: \(5/7 = 71\% \text{ not valid}\)
- Section C validity calculation: \(1/5 = 20\% \text{ not valid}\)
- Section D validity calculation: \(4/6 = 67\% \text{ not valid}\)

Calculation for overall validity: \((Y+N+U=T)\)

- If \(Y/T \geq 75\%\) or if \(N+U/T \leq 25\%\) then you can safely conclude that the study is valid.

- Overall validity calculation: \(11/22 = 50\% \text{ not valid}\)
Appendix 15
### Outcome measures – Kalichman et al. 2013

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>TOFHLA score</th>
<th>Marginal health literacy – viral load</th>
<th>Low health literacy – viral load</th>
<th>Marginal health literacy – medication adherence</th>
<th>Low health literacy – medication adherence</th>
<th>Marginal health literacy – health related quality of life</th>
<th>Low health literacy – health related quality of life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalichman et al. 2013</td>
<td>446 Total</td>
<td>M = 86% SD = 58</td>
<td>Baseline: M = 2.10; SD = 0.72</td>
<td>Baseline: M = 2.08; SD = 0.81</td>
<td>Baseline: n = 19; SD = 30%</td>
<td>Baseline: n = 28; SD = 33%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>148 Pictograph Guided</td>
<td></td>
<td>9-months: M = 2.07; SD = 0.95</td>
<td>9-months: M = 2.29; SD = 1.19</td>
<td>9-months: n = 20; SD = 45%</td>
<td>9-months: n = 28; SD = 45%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>157 Standard</td>
<td>M = 84% SD = 53</td>
<td>Baseline: M = 2.18; SD = 0.98</td>
<td>Baseline: M = 2.23; SD = 1.00</td>
<td>Baseline: n = 25; SD = 34%</td>
<td>Baseline: n = 28; SD = 34%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9-months: M = 2.08; SD = 0.90</td>
<td>9-months: M = 2.25; SD = 1.14</td>
<td>9-months: n = 22; SD = 37%</td>
<td>9-months: n = 30; SD = 44%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>141 General Health Improvement</td>
<td>M = 57% SD = 40</td>
<td>Baseline: M = 1.98; SD = 0.64</td>
<td>Baseline: M = 2.10; SD = 0.81</td>
<td>Baseline: n = 18; SD = 34%</td>
<td>Baseline: n = 33; SD = 39%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9-months: M = 2.25; SD = 0.96</td>
<td>9-months: M = 2.00; SD = 0.88</td>
<td>9-months: n = 21; SD = 45%</td>
<td>9-months: n = 39; SD = 57%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

*a Low health literacy scored as <85%; Marginal literacy scored as between 85% and 90%*
Appendix 16
## Outcome measures – Kripalani et al. 2012

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>s-TOFHLA score</th>
<th>Baseline</th>
<th>Systematic Review Primary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kripalani et al. 2012</td>
<td>851 Total</td>
<td>Not reported</td>
<td>AHL(^a), n = 331; 80.0%</td>
<td>CIME(^d) at 30 Days: n = 370; 87.5%</td>
</tr>
<tr>
<td></td>
<td>423 Intervention</td>
<td></td>
<td>MHL(^b), n = 36; 8.7%</td>
<td>ADEs(^d) at 30 Days: n = 183; 43.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IHL(^c), n = 47; 11.4%</td>
<td>P-ADEs(^d) at 30 Days: n = 187; 44.2%</td>
</tr>
<tr>
<td>428 Usual care</td>
<td>Not reported</td>
<td></td>
<td>AHL: n = 340; 81.5%</td>
<td>CIME at 30 Days: n = 407; 95%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MHL: n = 38; 9.1%</td>
<td>ADEs at 30 Days: n = 170; 40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IHL: n = 39; 9.4%</td>
<td>P-ADEs at 30 Days: n = 237; 55.4%</td>
</tr>
</tbody>
</table>

\(^a\) AHL – Adequate Health Literacy  
\(^b\) MHL – Marginal Health Literacy  
\(^c\) IHL – Inadequate Health Literacy  
\(^d\) CIME – Clinically Important Medication Errors  
\(^e\) ADEs – Adverse Drug Events  
\(^f\) P-ADEs – Potential Adverse Drug Events
## Outcome measures – Morrow et al. 2007

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>s-TOFHLA score</th>
<th>% Inadequate literacy as per s-TOFHLA</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morrow et al. 2007</td>
<td>236 Total</td>
<td>$M = 26.7$</td>
<td>14%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>83 Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>153 Usual care</td>
<td>$M = 25.4$</td>
<td>22%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Appendix 18
### Outcome measures – Muir et al. 2012

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>TOFHLA score</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muir et al. 2012</td>
<td>127 Total</td>
<td>Not reported</td>
<td>Days without medication over 6 months</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>67 Intervention</td>
<td></td>
<td>AHL:\textsuperscript{a} ( M = 74; 110(\text{SD}) )</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 Usual care</td>
<td>Not reported</td>
<td>MHL:\textsuperscript{b} ( M = 85; 120(\text{SD}) )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IHL:\textsuperscript{c} ( M = 51; 83(\text{SD}) )</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} AHL – Adequate Health Literacy
\textsuperscript{b} MHL – Marginal Health Literacy
\textsuperscript{c} IHL – Inadequate Health Literacy
Appendix 19
### Outcome measures – Murray et al. 2007

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>s-TOFHLA score</th>
<th>Health literate</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murray et al. 2007</td>
<td>270 Total 106 Intervention</td>
<td>Not reported</td>
<td>n – 88; 72%</td>
<td>Adherence</td>
<td>Health Related Quality of Life:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Taking adherence:</td>
<td>Emergency department visits:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n – 122; 78.8%</td>
<td>M – 2.16; 3.31 (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Scheduling adherence:</td>
<td>Hospital admissions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n – 122; 53.1%</td>
<td>M – 0.78; 1.66 (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Combined outcome:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M – 2.94; 4.69 (SD)</td>
</tr>
<tr>
<td></td>
<td>164 Usual care</td>
<td>Not reported</td>
<td>n – 138; 71%</td>
<td>Taking adherence:</td>
<td>Emergency department visits:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n – 192; 67.9%</td>
<td>M – 2.68; 4.87 (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Scheduling adherence:</td>
<td>Hospital admissions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n – 192; 47.2%</td>
<td>M – 0.97; 1.78 (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Combined outcome:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M – 3.65; 6.26 (SD)</td>
</tr>
</tbody>
</table>
Appendix 20
### Outcome measures – Paasche-Orlow et al. 2005

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>s-TOFHLA score</th>
<th>Literacy level</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paasche-Orlow et al. 2005</td>
<td>73 Total</td>
<td>Not reported</td>
<td>Inadequate health literacy: N = 16; 22%</td>
<td>Improvement of MDI(^a) technique at 2 weeks</td>
<td>Health Related Quality of Life: Not discussed</td>
</tr>
</tbody>
</table>

\(^a\) MDI – Metered-Dose Inhaler
### Outcome measures – Rudd et al. 2009

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>A-REALM score</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rudd et al. 2009</td>
<td>127 Total</td>
<td>$M = 10$; 16% (SD)</td>
<td>Medication Adherence</td>
<td>Health Related Quality of Life – HAQ$^b$</td>
</tr>
<tr>
<td></td>
<td>64 Plain English and Individualized Care</td>
<td></td>
<td>Baseline -&gt; 0.40</td>
<td>Baseline -&gt; $M = 0.92$; 0.62 (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 months -&gt; 0.23; % change -&gt; -4.76$^a$</td>
<td>6 months -&gt; 0.85; % change -&gt; -0.30$^a$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 year -&gt; 0.17; % change -&gt; -12.21</td>
<td>1 year -&gt; 0.84; % change -&gt; -0.79</td>
</tr>
<tr>
<td></td>
<td>63 Standard Care</td>
<td>$M = 12$; 21% (SD)</td>
<td>Baseline -&gt; 0.40</td>
<td>Baseline -&gt; $M = 0.91$; 0.66 (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 months -&gt; 0.23; % change -&gt; 0.25</td>
<td>6 months -&gt; 0.92; % change -&gt; 3.30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 year -&gt; 0.17; % change -&gt; -3.12</td>
<td>1 year -&gt; 0.89; % change -&gt; 1.33</td>
</tr>
</tbody>
</table>

$^a$ – Scales show improvement with decreased scores

$^b$ – Health Assessment Questionnaire. Scale from 0-3, where 0 is best