Literature review using systematic approaches to explore physical illness co-morbidity among people with serious mental illness and related healthcare interventions

<table>
<thead>
<tr>
<th>Item type</th>
<th>Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Nash, M; Bracken-Scally, M; Smith, V; Higgins, A; Eustace-Cook, J; Monahan, M; Callaghan, P; Romanos, M.T.</td>
</tr>
<tr>
<td>Publisher</td>
<td>Health Service Executive (HSE)</td>
</tr>
<tr>
<td>Downloaded</td>
<td>2-Dec-2016 09:15:02</td>
</tr>
<tr>
<td>Link to item</td>
<td><a href="http://hdl.handle.net/10147/620897">http://hdl.handle.net/10147/620897</a></td>
</tr>
</tbody>
</table>
Literature review using systematic approaches to explore physical illness co-morbidity among people with serious mental illness and related healthcare interventions
Acknowledgements

The research team, commissioned by the Health and Wellbeing Directorate, Health Service Executive, undertook the work described in this report. We thank the Steering Group for this project and for their insight and support throughout the conduct of this work.

About the authors

Dr Michael Nash is an Assistant Professor in Mental Health at the School of Nursing and Midwifery, Trinity College Dublin.

Dr Mairéad Bracken-Scally is a Postdoctoral Researcher at the School of Nursing and Midwifery, Trinity College Dublin.

Dr Valerie Smith is an Assistant Professor in Midwifery at the School of Nursing and Midwifery, Trinity College Dublin and a Research Associate, School of Nursing and Midwifery, NUI Galway.

Professor Agnes Higgins is a Professor in Mental Health at the School of Nursing and Midwifery, Trinity College Dublin.

Jessica Eustace-Cook is Subject Librarian for the School of Nursing and Midwifery, Trinity College Dublin.

Professor Patrick Callaghan is Professor of Mental Health Nursing and Head of School, School of Health Sciences, Faculty of Medical and Health Sciences, University of Nottingham

Dr Mark Monahan is an Assistant Professor in mental health at the School of Nursing and Midwifery, Trinity College Dublin.

Dr Maria Romanos is a Consultant Forensic Psychiatrist, St John of God Hospital, Stillorgan, Dublin.
This report should be cited as:

## Contents

List of Tables................................................................................................................................. i
List of Figures..................................................................................................................................... ii
Executive Summary ............................................................................................................................. 1

1. Background ...................................................................................................................................... 8
   1.1 Defining co-morbidity .................................................................................................................. 8
   1.2 Serious mental illness and physical health co-morbidity .............................................................. 8
   1.3 Reduced life expectancy ............................................................................................................ 10
   1.4 Impact of co-morbidity ............................................................................................................. 11

2. Review Methodology ....................................................................................................................... 12
   2.1 Aim of project ............................................................................................................................ 12
   2.2 Specific objectives ...................................................................................................................... 12
   2.3 Criteria for including studies in the review .............................................................................. 13
   2.3 Search and selection strategy .................................................................................................... 14
   2.4 Quality assessment of included studies ...................................................................................... 16
   2.5 Data extraction and analyses .................................................................................................... 16

3. Prevalence ....................................................................................................................................... 17
   3.1 Description of included studies .................................................................................................. 17
   3.2 Schizophrenia ............................................................................................................................ 19
   3.3 Bipolar Disorder ......................................................................................................................... 21
   3.4 Depression ................................................................................................................................. 23
   3.5 Situating prevalence rates in an Irish context ............................................................................ 25

4. Risk Factors for Co-morbidities ...................................................................................................... 26
   4.1 Description of included studies .................................................................................................. 26
   4.2 Prevalence rates of biological/lifestyle risk factors .................................................................... 27
       4.2.1 Schizophrenia .................................................................................................................... 27
       4.2.2 Bipolar Disorder ................................................................................................................ 28
4.2.3 Depression................................................................. 29
4.2.4 Schizophrenia, Bipolar Disorder and Depression combined........... 30
4.3 Physical ill-health conditions proportionate to risk factors............... 31
4.4 Less conventional risk factors for co-morbidity in SMI .................. 33
  4.4.1 Practitioner specific factors........................................... 34
  4.4.2 Organisation specific .................................................... 35
  4.4.3 Medication side effects .................................................. 38

5. Interventions for addressing physical illness co-morbidity in SMI........ 39
  5.1 Systematic Reviews .......................................................... 40
    5.1.2 Weight management..................................................... 40
    5.1.3 Smoking cessation/reduction ........................................ 42
  5.2 Controlled studies (randomised and controlled clinical trials)......... 43
    5.2.1 Exercise programme for reducing cardiovascular risk ............... 44
    5.2.2 Self-management programme for reducing cardiovascular risk .... 44
    5.2.3 Weight management in people with diabetes........................ 45
    5.2.4 Nicotine-patch therapy for smoking cessation/reduction ............ 45
  5.3 Non-randomised studies ................................................... 46
    5.3.1 Weight management programme .................................... 46
    5.3.2 Supportive group psychotherapy and adjunctive sustained-release bupropion for nicotine addiction .................................. 47

6. Results summary .................................................................. 48

7. Study strengths and limitations ............................................... 50

8. Recommendations for co-morbidity and SMI ............................... 52
  8.1 Recommendation for future research....................................... 52
    8.1.1 Service User Involvement ............................................. 53
    8.1.2 Healthcare provider/practitioner Involvement ...................... 54
    8.1.3 National Administrative/Policy level involvement ................. 55
8.2 Recommendations for practice and organisation of care ............................................ 55

8.2.1 Tobacco Use ........................................................................................................... 55

8.2.2 Monitoring physical effects of psychotropic medication ........................................ 56

8.2.3 Developing care pathways ...................................................................................... 57

8.3 Recommendations for practitioner education ............................................................ 57

8.4 Recommendations for moving forward ........................................................................ 58

9. Conclusion .................................................................................................................. 58

References ....................................................................................................................... 60

List of Appendices .......................................................................................................... 66

Appendix 1 Project Search Strategy .................................................................................. 67

Appendix 2 – Prevalence and risk factor studies- data extraction and study characteristics .......................................................................................................................... 71

Appendix 3- Effectiveness studies- data extraction and study characteristics ...... 79

Appendix 4 – Prevalence and risk factor studies- study references ................................. 82

Appendix 5- Prevalence and risk factor studies- supplementary tables ......................... 86

Appendix 6 – Effectiveness studies- study references ..................................................... 89

Appendix 7- Effectiveness studies- supplementary tables .............................................. 90

Appendix 8- Physical co-morbidity in SMI: Research in Ireland .................................... 92
List of Tables

Table 1: Instruments used for the quality assessments of the included studies .... 16

Table 2: Outcomes - Weight and BMI ................................................................. 41

Table 3: Outcomes - smoking abstinence and reduction.............................. 43

Table 4: Differences between high intensity training and CG at end of programme. 44

Table 5: Differences between LGCC and enhanced usual care at 12 and 24-month follow-ups .............................................................................................................. 45

Table 6: Additional weight management outcome measures.......................... 47
List of Figures

Figure 1: Illustrating co-morbidity in people with severe mental illness ................... 9

Figure 2: Illustrating risk factors for co-morbidity in SMI ........................................ 10

Figure 3: Flow diagram of search and selection strategy ............................................ 15

Figure 4: Comparison of prevalence of selected physical illness in SMI versus Irish general population ........................................................................................................... 19

Figure 5: Prevalence of physical ill-health conditions in people with schizophrenia . 20

Figure 6: Prevalence of selected physical illness in schizophrenia versus Irish general population ........................................................................................................... 21

Figure 7: Prevalence of physical ill-health conditions in people with bipolar disorder ......................................................................................................................... 22

Figure 8: Prevalence of selected physical illness in bipolar disorder versus Irish general population ........................................................................................................... 23

Figure 9: Prevalence of physical ill-health conditions in people with depression ...... 24

Figure 10: Prevalence of selected physical illness in depression versus Irish general population ........................................................................................................... 25

Figure 11: Prevalence of risk factors in people with schizophrenia ......................... 28

Figure 12: Prevalence of risk factors in people with bipolar ..................................... 29

Figure 13: Prevalence of risk factors in people with depression .............................. 30

Figure 14: Prevalence of risk factors in people with serious mental illness .......... 31
Figure 15: Association between dyslipidaemia and hypertension in people with schizophrenia ............................................................ 32

Figure 16: Association between smoking and diabetes in people with schizophrenia .................................................................................. 32

Figure 17: Association between dyslipidaemia and diabetes in people with schizophrenia .................................................................................. 32

Figure 18: Association between dyslipidaemia and diabetes in people with bipolar disorder .................................................................................. 32

Figure 19: Explaining risk factors for poor physical health in SMI ........................................ 33

Figure 20: Change from baseline BMI.................................................................................. 45

Figure 21: Change from baseline in nicotine dependency at 3-months: Intervention group .................................................................................. 46

Figure 22: Body weight mean reduction between baseline and follow-up .................... 47

Figure 23: Change in carbon monoxide level between baseline and follow-up at 14 weeks ........................................................................... 48
Executive Summary

International evidence indicates that the physical health of Mental Health Service Users (MHSUs), especially those with serious mental illness (SMI)\(^1\), is often sub-optimal (Parks et al., 2006; DeHert et al., 2011). Over the past number of years, physical illness co-morbidity (from here on referred to as ‘co-morbidity’) in people with SMI, has become an area of concern for key stakeholders such as policy makers, healthcare practitioners, healthcare providers, service users and family.

Aim/objective

The aim of this project was to bring together the available and relevant published literature on physical illness co-morbidity in adults aged between 18 and 65 years with SMI, and related healthcare interventions.

Method

Robust systematic review methodological approaches were adopted with a focus on studies reporting on populations of people with SMIs and commonly occurring co-morbidities.

- **Population**: Individuals, 18 to 65 years, diagnosed with a SMI
- **Exposure**: Individuals with physical ill-health co-morbidities and commonly associated biological and lifestyle risk factors
- **Intervention/Comparators**: Studies reporting on any intervention to promote physical health or treat physical ill-health co-morbidities in people with SMI
- **Outcomes**: Prevalence rates of physical ill-health co-morbidities, prevalence rates of biological and lifestyle risk factors, correlations between risk factors and co-morbid conditions, and effectiveness of any interventions or treatments
- **Study types**: Retrospective and prospective observational cohort studies, cross-sectional surveys, non-randomised studies, randomised studies and systematic reviews

---

\(^1\) Serious Mental Illness in this report has been defined as Schizophrenia, Schizoaffective Disorder, Bipolar disorder, Mania and Major Depressive Disorder.
Prevalence of physical health co-morbidities in those with an SMI

- **Schizophrenia**: Of the physical health conditions examined, chronic lung disease occurred most frequently, followed by cancer, cardiovascular disease, and hypertension.
- **Bipolar disorder**: Of the physical health conditions examined, hypertension occurred most frequently, followed closely by chronic lung disease and cancer.
- **Depression**: Of the physical health conditions examined, obesity occurred most frequently, followed by hypertension and cancer.

In the context of the general prevalence in the Irish population:
- Stroke prevalence was much higher in people with SMI than in the Irish general population, despite the age range for the current study being 18-65 years. This suggests that stroke is more common in younger age groups in people with SMI than in the Irish general population.
- The prevalence of cardiovascular disease was much higher than in the Irish general population indicating that this area should be targeted as a priority for early screening and identification.
- The diabetes prevalence was just over double the Irish general population indicating that this area should be targeted as a priority for early screening and identification.

Biological and lifestyle risk factors for physical health co-morbidities

- **Schizophrenia**: The most commonly occurring risk factors for physical health co-morbidity were smoking, impaired fasting glucose\(^2\) and dyslipidaemia\(^3\).
- **Bipolar Disorder**: The most commonly occurring risk factors for physical health co-morbidity were smoking, hyperglycaemia, and pre-diabetes.
- **Depression**: The most commonly occurring risk factors for physical health co-morbidity were smoking and dyslipidaemia.
- Positive correlations\(^4\) between the following: dyslipidaemia and hypertension; smoking and diabetes; and dyslipidaemia and diabetes were found.

---

\(^2\) Impaired fasting glucose (IFG) is where fasting blood glucose levels are consistently higher than normal, but not high enough to be diagnosed as diabetes. This is also referred to as **pre-diabetes**.

\(^3\) Dyslipidaemia is a term used to describe an imbalance in fat levels in the blood. This is usually hyperlipidaemia, high cholesterol, which is a main risk factor for cardio-vascular disease.

\(^4\) Indicating that an increase in one was associated with an increase in the other e.g. higher levels of smoking associated with higher levels of diabetes.
• Smoking rates in people with SMI are more than double the Irish general population rate.

Less conventional risk factors for physical health co-morbidities

Less conventional risk factors, is a term used here, to refer to factors that can increase the risk of physical co-morbidity in people with SMI. These risk factors are important in the area of co-morbidity in SMI, but are under-researched and can play a part in the late diagnosis or duration of untreated physical illness in SMI.

Figure A provides an overview of the person, practitioner, organisation and treatment specific risk factors for poor physical health in SMI.

Person specific risk factors refer to lifestyle and behavioural factors that are detrimental to physical health.

In a specific SMI context we find that, smoking prevalence is up to three times higher than that of the general population (McNeill, 2001), people with SMI tend to make poorer dietary choices (McCreadie et al., 1998) and are less physically active (Daumit et al 2005).

There may also be a genetic pre-disposition to conditions such as diabetes as first-degree relatives of people with SMI were found to have higher rates on impaired fasting glucose (Spelman et al 2007).

• The following practitioner specific factors are highlighted:
  o Lack of knowledge, skills and confidence in physical healthcare
  o Diagnostic overshadowing

• The following organisation specific factors are highlighted:
  o Low quality of physical healthcare
  o Lack of care pathways
  o Lack of action
  o Inequalities in access to services

---

5 Diagnostic Overshadowing is where legitimate symptoms of physical illness are recast as a manifestation of mental illness e.g. referred to as psychosomatic rather than a genuine physical complaint.
- **Treatment specific factors** include medication side effects, for example, the low priority given to monitoring medication side effects by practitioners.

**Figure A:** Explaining risk factors for poor physical health in SMI

**Interventions for physical health co-morbidities**
- Notably, no economic data within the Irish context were found.
- A number of systematic reviews of weight management programmes (exercise, cognitive/behaviour therapy, pharmacological interventions alone, pharmacological interventions in combination with lifestyle management, and behaviour and dietary interventions) demonstrated that in the majority of cases, the intervention decreased weight and BMI.
- In a systematic review of smoking cessation studies, bupropion, varenicline, the American Lung Association (ALA) programme, as well as CBT combined with motivational interviewing, were shown to increase smoking abstinence.
- Individual studies demonstrated the following:
- An exercise intervention\(^6\) improved maximal oxygen uptake.
- A self-management programme\(^7\) was shown not to have any effect on BMI.
- A weight management programme\(^8\) was shown to reduce BMI.
- A nicotine patch therapy intervention\(^9\) was shown to increase nicotine abstinence.
- A combined weight management programme\(^10\) was shown not to have any effect on weight or BMI.
- Support group psychotherapy and bupropion\(^11\) was shown to reduce carbon monoxide levels.

**Study strengths and limitations**

- The review was limited to specific SMIs and specific co-morbidities.
- The age range used (18-65 years) increases the strength of the review’s findings.
- Clinical heterogeneity identified across the included prevalence and risk factor studies (i.e. in terms of population, methods of data collection, locations, and results) in this review was a limitation of the study.
- The majority of included studies had a moderate to high quality rating (a strength), with a small number of intervention studies of low to moderate quality (a minor limitation).

**Recommendations**

As set out in Figure A, the risk factors for physical illness in SMI fall within in a number of key areas, and the following recommendations attempt to contribute to each of these areas.

---

\(^6\) 4x4-min interval training on a treadmill interspersed with 3 min of active resting periods. Training sessions 3 times per week for 8 weeks.

\(^7\) Self-management sessions by health specialist (4 group sessions), care management by health specialist, clinical registry tracking, and guideline support.

\(^8\) 24-week intervention with three modules: basic diabetes education; nutrition; and lifestyle exercise.

\(^9\) 8-week program of nicotine-patch therapy.

\(^10\) 24-week program of diet (1600 & 2000 calorie diet for women & men respectively), exercise (45 minute sessions of individualised fitness training) and nutritional counselling (45 minutes sessions), with sessions twice weekly.

\(^11\) 14-week treatment phase: nine sessions of weekly group therapy led by clinic nurses trained in the educational model of the American Cancer Society Fresh Start Program, modified for patients with schizophrenia.
• Recommendations for practice and organisation of care
  o Establish a system to identify and record the smoking status of all clients on admission and incorporate into overall client care plans, including specific smoking cessation techniques.
  o Introduction of smoking cessation champions in mental health settings.
  o Development of a coherent approach to monitoring the adverse effects of prescribed psychotropic medication.
  o Development of clear and coherent care pathways for referral and treatment of co-morbid conditions.

• Recommendations for practitioner education
  o Education and training of the workforce in the area of documentation and reporting of risk factors for physical illness.
  o The issue of medical co-morbidity and SMI to be made more explicit in undergraduate education curricula for nursing curricula, medical practitioners in psychiatry and trainee GPs.

• Recommendations for moving forward
  o Co-morbidity and SMI should be incorporated into the HSE Mental Health Division Service Priorities plan.
  o Development of an action plan, time frame for achievement and working group to move all recommendations forward.

• Recommendations for future research
  o Conduct a high quality prospective national survey by age category of individuals with a known SMI, in order to identify the prevalence and type of co-morbidity(ies).
  o Based on the findings of the national survey of service users, conduct interviews on a purposively sampled cross-sectional sub-group of respondents with diverse self-reported co-morbidities.
  o Conduct a high quality, prospective national survey, categorised by primary, secondary and acute care sectors.
  o Conduct a high quality, prospective national inter-professional survey of healthcare providers/practitioners to identify current practices and attitudes towards including physical health care for people with SMI as a dimension of practice and their education and training needs.
- Develop a national database of specific mortality and co-morbidity data for people with SMI.
- Based on Irish prevalence rates, conduct a methodologically robust economic analysis of the impact of co-morbidity in people with SMI on individuals, local healthcare service provision and healthcare expenditure at large.
- Design and implement, a multi-centre/regional randomised trial targeted at preventing the leading co-morbidity in people with SMI in the Irish context.
1. Background

International evidence indicates that the physical health of Mental Health Service Users (MHSUs), especially those with serious mental illness (SMI)\textsuperscript{12}, is often sub-optimal (Parks et al., 2006; DeHert et al., 2011). Over the past number of years, physical illness co-morbidity (from here on referred to as ‘co-morbidity’) in people with SMI, has become an area of concern for key stakeholders such as policy makers, healthcare practitioners, healthcare providers, service users and family.

1.1 Defining co-morbidity

Co-morbidity, simply described, refers to the simultaneous presence of at least two long term ill-health conditions. In mental health settings, dual diagnosis, or the presence of a mental health disorder and a substance use disorder, for example, is a traditional conceptualisation of co-morbidity. Degenhardt et al. (2003) suggested that co-morbidity can be defined most generally as the co-occurrence of two or more mental health problems. However, in the context of this report, co-morbidity specifically refers to a primary serious mental illness and a secondary physical health condition; for example, schizophrenia and type-2 diabetes or bipolar disorder and hypertension.

1.2 Serious mental illness and physical health co-morbidity

Typically, when compared with the general population, MHSUs suffer from poorer physical health, have an increased prevalence of physical illness, have an increased exposure to public health risk factors and have poorer health outcomes. This is illustrated by an increased prevalence of conditions such as obesity and type-2 diabetes and poor health outcomes such as higher mortality levels when compared with the general population (see Figure 1). Thakore (2005) suggested that over 50% of those with schizophrenia have a general medical condition, but adds that this may be an underestimate.

\textsuperscript{12} Serious Mental Illness in this report has been defined as Schizophrenia, Schizo-affective Disorder, Bipolar disorder, Mania and Major Depressive Disorder.
Reasons for poor physical health in people with SMI are broadly similar to those in the general population, involving lifestyle factors and choices, such as poor diet, low levels of physical activity and smoking. However, those with SMI have an increased prevalence of, and exposure to, lifestyle and health risk factors in comparison to the general population (see Figure 2). Individuals with schizophrenia are more likely than the general population to have lifestyle risk factors for cardiovascular disease and mortality (de Leon & Diaz, 2005; McCreadie, 2003; Osborn et al., 2006). Furthermore, in many cases people with SMI register more than one co-morbid physical illness (Carney et al., 2006a; O’Brien et al., 2007; Udo et al., 2011; Woodhead et al., 2014).
The complexity of co-morbidity in people with SMI goes beyond lifestyle risk factors when the risks associated with the side effects of psychotropic medications are included. Psychotropic medications are the front line treatment for many mental health problems, yet most of these medications list adverse metabolic reactions in their side effect profiles. Taylor et al. (2012) list common metabolic reactions such as hyperlipidaemia (high cholesterol), increased Low Density Lipoprotein (LDL) and decreased High Density Lipoprotein (HDL), type-2 diabetes and obesity or severe weight gain. These in turn are key risk factors for cardiovascular disease. This makes medication side effects a unique risk factor for this group.

The combination of lifestyle risk factors and the unique risk factor of medication side effects can impact on pathways to wellness, as Glover et al. (2013) found that the combination of medication side effects, symptoms of illness and existing physical co-morbidities were barriers to exercise among people with mental illness.

1.3 Reduced life expectancy
The most critical expression of poor physical health outcomes in MHSUs can be seen in mortality data. Saha et al. (2007) suggested that the association between mental illness and increased mortality rates has long been recognised. Harris and Barraclough
(1998) found much higher standardised mortality ratios (SMRs) in people with schizophrenia when compared with the general population for the same physical ill-health conditions. In a 13-year follow-up study, of 370 patients with schizophrenia, Brown et al. (2000) found an all-cause SMR of 298 (95% confidence interval (CI) 236-372) and a natural cause SMR of 232 (95% CI 176-300). An increased risk of death from coronary heart disease and stroke in those with SMI was also reported by Osborn et al. (2007).

Internationally, people with SMI have a significantly reduced life expectancy compared to the general population. While no firm data exists in Ireland, UK research suggests that life expectancy can be 20% shorter in people with schizophrenia than the general population (Thornicroft, 2011). Chang et al. (2011) found UK male and female MHSUs have lower life expectancy - 8.0 to 14.6 life years lost for men and 9.8 to 17.5 life years lost for women, while in the USA, Parks et al. (2006) found service users die on average 25 years earlier than the general population.

While there is an increased mortality risk from suicide among people with mental health problems, the recent focus on co-morbid physical problems has shown a higher mortality risk from physical conditions, most notably cardiovascular illnesses, than from suicide (Newcomer & Hennekens 2007). Furthermore, the World Health Organisation (WHO) (not dated) recognised that the majority of premature deaths in people with SMI were due to physical medical conditions that are preventable with more attentive checks for physical illness, side effects of medicines and suicidal tendencies.

### 1.4 Impact of co-morbidity

Co-morbidity is associated with worse health outcomes, more complex clinical management, and increased health care costs (Valderas et al., 2009). Naylor et al. suggested that between 12 per cent and 18 per cent of all NHS expenditure on long-term conditions is linked to poor mental health and wellbeing – between £8 billion and £13 billion in England each year. However, this research relates to the increased costs of mental health problems in people with physical conditions e.g. co-morbid depression in diabetes. Unfortunately, we could find no cost benefit analyses that address the specific subject of costs of treating co-morbid physical conditions in people with SMI. This suggests that this area is largely un-researched and that such economic analysis would be a welcome addition to knowledge development in this
area. However, financial cost is matched by the emotional cost for MHSUs and family/carers living with co-morbidity, such as the increase in the burden of illness, decreased quality of life for service users and an increased burden of care for family/carers.

This literature review focuses on mental illness to include what is sometimes referred to as severe and enduring disorders such as schizophrenia, bipolar disorder/mania and depression. Most international literature identifies greater health disparities, inequality and poor health outcomes in these groups.

2. Review Methodology

2.1 Aim of project
The aim of this project was to bring together the available and relevant published international literature, in one report, so that the totality of the evidence on physical illness co-morbidity in people with severe mental illnesses, and related healthcare interventions, is made available.

2.2 Specific objectives
The objectives of this project were:

1. To illustrate the prevalence of physical ill-health co-morbidities in people with schizophrenia, bipolar disorder and depression;

2. To describe clinical/socially common important biological and lifestyle risk factors for these physical ill-health co-morbidities;

3. To evaluate interventions that have been used in promoting health or treating physical ill-health in these populations;

4. To describe physical health research that has been done in this area in Ireland;

5. To make recommendations for practice and future research.
2.3 Criteria for including studies in the review

In meeting the aim of the project, robust systematic review methodological approaches were adopted. Due to the breadth of the subject material, and to ensure depth in analyses, a pragmatic decision was made to focus the review on studies reporting on populations of people with SMI and commonly occurring co-morbidities. The criteria for considering studies for inclusion in the review was determined using an agreed PEOS (Population, Exposure, Outcomes, Study type) or PICO (Population, Intervention/Comparator, Outcome, Study type), as follows:

- **Population:** Individuals, between the ages of 18 and 65 years\(^\text{13}\), diagnosed with a SMI of schizophrenia, bipolar disorder or depression
- **Exposure:** Individuals with physical ill-health co-morbidities and commonly associated biological and lifestyle risk factors

The WHO Non-communicable Diseases Country Profiles (WHO, 2014) demonstrated that 88% of deaths in Ireland (n=27,000) were caused by conditions such as cardiovascular illness (32%), cancer (30%), chronic respiratory diseases (7%) and diabetes (2%). These non-communicable diseases are classified by the WHO (2008) as the leading threat to human health. Furthermore, the Health Service Executive, (HSE, 2008b) reported that data from SLÁN 2007 indicated a rising trend in key risk factors for chronic illness such as smoking, overweight and obesity, lack of physical activity, lack of adequate nutrition and diet, and a high prevalence of untreated high blood pressure and high cholesterol levels. In light of this, this review explores the prevalence of co-morbidity of cardiovascular disease, cancer, respiratory disorders, obesity (defined as a BMI ≥ 30) and diabetes in people with SMI and endeavours to contextualise this within an Irish context.

- **Intervention/Comparators (for effectiveness studies only):** Studies reporting on any intervention (e.g. exercise, counselling, education, dietary, etc.) to promote physical health or treat physical ill-health co-morbidities in people with schizophrenia, bipolar disorder or depression
- **Outcomes:** The outcomes of interest to the review were prevalence rates of physical ill-health co-morbidities, prevalence rates of biological and lifestyle risk

\(^{13}\) Data on those aged 18-65 was extracted, where possible, from studies with a broader participant age range.
factors, correlations between risk factors and co-morbid conditions, and effectiveness of any interventions or treatments for promoting physical health or treating physical ill-health in people with schizophrenia, bipolar disorder or depression.

- **Study types:** To meet the objectives of the review, including a broad range of study types was necessary. These were retrospective and prospective observational cohort studies, cross-sectional surveys, non-randomised studies, randomised studies and systematic reviews.

### 2.3 Search and selection strategy

Given the potential breadth of information available on the topic, a broad, pragmatic approach to searching the literature was adopted. Decision rules, as per funder requirements, were applied to the search strategy as follows:

- Peer-reviewed;
- Published in an academic/scientific journal;
- Published in the past 15 years - a date range of 2000 to 2015 was applied to all searches;
- National and international in origin;
- Primary studies, review papers and/or meta-analyses.

In addition, due to limited budget to fund translation services, and the relatively short time-frame to complete the project, searches were limited to English-language publications. Population and age filters were applied, also, as follows; Humans; Adult: 18-44 years; Middle Aged + Aged: 45+ years; Middle Aged: 45-64 years; Adult: 19+ years.

Searches of the following scientific databases were completed during the week of the 11\textsuperscript{th} May 2015:

- Cochrane Database of Systematic Reviews (CDSR)
- National Library of Medicine (PubMed)
- The Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Exerpta Medica Database (EMBASE)
- PsycINFO - American Psychological Association
Appendix 1 provides full details of the search strategy including the search terms used and the numbers of citations retrieved at each search.

To ensure a robust and systematic selection processes, retrieved citations were screened independently by two reviewers (MN and MB) according to the pre-specified inclusion criteria. Any disagreements between the reviewers were resolved through discussion and consensus. Studies that were selected for inclusion in the review were subsequently categorised according to their study design and their resulting contributions (i.e. prevalence rates of co-morbidities; information on risk factors or effectiveness studies). Figure 3 provides a flow diagram of the search and selection process.

Figure 3: Flow diagram of search and selection strategy
2.4 Quality assessment of included studies

The strength of the evidence from primary studies is highly dependent on the methodological quality of the study, in both conduct and reporting. For this reason, it is important, in reviews using systematic methods, to conduct a formal assessment of the methodological quality of the included studies, using previously validated tools. Due to the differing nature of the study designs, diverse, but well-recognised, tools were used to perform the methodological quality assessment of the included studies (Table 1). The assessment process was performed independently by two pairs of reviewers (MN and MB; VS and MB), with any disagreements resolved through discussion and consensus.

Table 1: Instruments used for the quality assessments of the included studies

<table>
<thead>
<tr>
<th>Study category</th>
<th>Critical appraisal instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational studies; survey, retrospective or prospective cohort studies</td>
<td>Newcastle Ottawa Scale for cohort studies (modified as necessary)</td>
</tr>
<tr>
<td>Non-randomised retrospective or prospective cohort studies, correlational studies</td>
<td>Newcastle Ottawa Scale for cohort studies (modified as necessary)</td>
</tr>
<tr>
<td>Randomised controlled trials</td>
<td>Cochrane Risk of Bias tool (Higgins &amp; Green 2008)</td>
</tr>
<tr>
<td>Non-randomised controlled trials (NRCTs); Controlled before-after (CBA) studies</td>
<td>Risk of bias criteria for Cochrane Effective Practice and Organisation of Care (EPOC) reviews (Higgins &amp; Green 2008)</td>
</tr>
<tr>
<td>Systematic reviews</td>
<td>AMSTAR-R (Shea et al, 2009)</td>
</tr>
</tbody>
</table>

2.5 Data extraction and analyses

Data extraction tables were specially pre-designed to extract the relevant data from the included studies. Tables were developed to meet the requirements of the differing study designs, as follows:

Descriptive studies (prevalence & risk factors):
- Study setting;
- Participant characteristics and numbers;
- Type of SMI;
- Use of antipsychotic medication;
- Reported physical ill-health conditions;
- Reported biological and lifestyle risk factors.

Effectiveness studies:
- Study design (systematic review, RCT, etc.);
- Study setting/location;
• Participant characteristics and numbers;
• Intervention(s);
• Comparator(s);
• Outcome measures;
• Effect estimates (based on the number of specific outcome events and total number of participants in each group for each intervention and comparator groups).

Appendix 2 (descriptive studies) and Appendix 3 (effectiveness studies) illustrate the data extraction tables and present details of the characteristics of the included studies. For prevalence rates of co-morbidities and risk factors, data were analysed using descriptive statistics (proportions, range, medium, etc.) by pooling prevalence rates across studies. For effectiveness studies, it was planned to perform statistical meta-analysis on outcomes (e.g. weight loss, smoking cessation, etc.), however, due to the diverse nature of the included interventions, meta-analysis was not possible, and a narrative synthesis of the results was provided, with measures of relative risk (RR), mean differences (MD), odds ratios (OR) and 95% confidence intervals (CI) presented, where available and appropriate to do so.

3. Prevalence

3.1 Description of included studies
Forty three studies contributed data to the prevalence of co-morbidities for the major SMI s of schizophrenia, bipolar disorder and depression. The majority of included studies reported on more than one physical ill-health condition in their paper, however, ten studies reported on obesity only, ten reported on diabetes only and one reported on cardiovascular disease only. The study references are listed in Appendix 4. Appendix 2 provides full details of the characteristics of the included studies, including their methodological quality assessment scores; in brief, however, the studies were conducted between the years 2000 and 2015; 12 were conducted in the US, five in the Netherlands, four in Canada, four in Taiwan, three in Spain, two in Belgium, two in Japan, and one in each of Czech Republic, Croatia, Italy, Norway, France, Brazil,
Singapore, Malaysia, and Korea. A further two studies were a European wide study, and a world-wide study, respectively.

Recruitment and data collection strategies varied across the studies, ranging from in-patient care facilities, long- and short-stay facilities, out-patient departments, administrative databases, medical charts, survey (national/local) and medical and pharmacy claims records.

In seven studies all participants were on antipsychotic medication/mood stabilisers, in 14 studies the majority of participants were on antipsychotics and/or mood stabilisers, one study recruited participants who were medication free for a 2-week period, and the remaining 21 studies did not outline the medication profile of participants.

In 37 studies, the type of reported prevalence, that is point prevalence, lifetime prevalence or period prevalence, was not explicitly stated. In two of the included studies, lifetime prevalence was reported (Argo et al., 2011; Goldstein et al., 2011) and in four of the included studies period prevalence was reported (Bresee et al., 2010; Protopopova et al., 2005; Seldenrijk et al., 2015; Yang et al., 2014).

In this section the pooled prevalence of co-morbidity in SMI is reported. The SMI group as a whole is first examined and then the pooled prevalence of co-morbidity by each separate mental illness is then explored. Notably, pooled prevalence figures are calculated using international data, Figure 4 provides a simple comparative illustration of selected co-morbidities in people with SMI. Statistics from various health reports in Ireland are used to offer a comparison between prevalence in people SMI and the Irish general population. As indicated in Figure 4, the prevalence of cardiovascular disease, diabetes and stroke is higher in those with SMI than the general population.
Figure 4: Comparison of prevalence of selected physical illness in SMI versus Irish general population

*Importantly, there is an apparent aberration in the prevalence of obesity in SMI versus the Irish general population. This is explained, at least in part, by a small number of studies which reported low prevalence of obesity which skewed the overall mean prevalence. Six studies reported low prevalence of obesity (M=2.09%), eight studies reported moderate prevalence of obesity (M=17.6%), whilst ten studies reported a high prevalence of obesity (M=29.9%). This signifies a high level of heterogeneity in study findings. This means the pooled prevalence of obesity of 13% should be viewed with some caution. Further research into this discrepancy is required.

3.2 Schizophrenia

Twenty-five studies that explored the prevalence of co-morbidities in people with schizophrenia were included in the review. The prevalence of diabetes was the most commonly reported condition (20 studies), followed by obesity (12 studies) and hypertension/hypertensive disease (10 studies). Ischemic heart disease, stroke, congestive heart failure and chronic lung disease (including COPD) were each reported across two of the included studies. For the remaining physical ill-health conditions, one study only reported on each of these conditions (Appendix 5, Table 5.1).

The analyses demonstrated that, of these conditions, chronic lung disease occurs most frequently in people with schizophrenia (25.0%, 2 studies, 4037 participants), followed closely by cancer, cardiovascular disease and hypertension/hypertensive disease (24.0%, 1 study, 2963 participants; 17.6%, 2 studies, 22540 participants, and 17.1%, 10 studies, 31005 participants, respectively). Myocardial infarction (MI), alone,
and peripheral vascular disease (PVD) were found to have the lowest prevalence rates in people with schizophrenia (0.5%, 1 study, 2963 participants and 0.9%, 1 study, 1074 participants, respectively) (Figure 5; Appendix 5, Table 5.1). The prevalence of a number of key physical ill-health conditions in people with schizophrenia, as compared to the general population is presented in Figure 6.

Considerable variations in study sample sizes were evident across the included studies; for example, from 32 participants to 145718 participants in studies reporting on diabetes. Moreover, considerable differences were found in the individual prevalence rates across the included studies; for example, from 1% to 59% across studies reporting on obesity. This latter issue, in particular, should be considered when interpreting the overall pooled prevalence rates of physical health-illness conditions in people with schizophrenia, with possible causes/reasons for these differences requiring further exploration.

*Notably, the mean prevalence of obesity (8%) differed greatly from the median prevalence value for this condition (18.9%) and these values are greatly skewed by outliers with a large number of studies providing a much higher prevalence of obesity. Three studies reported low prevalence of obesity (M=2%), six studies reported moderate prevalence (M=17%), and three studies reported high prevalence (M=39%), demonstrating the variability in prevalence across studies.

Figure 5: Prevalence of physical ill-health conditions in people with schizophrenia
Fourteen studies that explored the prevalence of co-morbidities in people with bipolar disorder were included in the review. The prevalence of diabetes and obesity were the most commonly reported physical ill-health conditions (reported each in 9 studies), followed by hypertension/hypertensive disease (5 studies). For the remaining co-morbidities, all were reported in either one or two studies only (Appendix 5, Table 5.2).

The analyses demonstrated that, of these conditions, hypertension/hypertensive disease occurs most frequently in people with bipolar disorder (31.1%, 5 studies, 10950 participants), followed closely by chronic lung disease and cancer (30.3%, 2 studies, 8669 participants; 28.3%, 2 studies, 8669 participants, respectively). These results are somewhat similar to those found in people with schizophrenia, where chronic lung disease, cancer, and hypertension/hypertensive disease occurrence were identified as three of the most commonly occurring physical ill-health conditions.

MI alone, and PVD were found to have the lowest prevalence rates in people with bipolar disorder (0.9%, 2 studies, 7017 participants and 1.2%, 1 study, 3557 participants, respectively) (Figure 7; Appendix 5, Table 5.2). These results compare favourably to the prevalence rates of co-morbidities in people with schizophrenia where MI and PVD were also found to have the lowest prevalence rates. The
prevalence of a number of key physical ill-health conditions in people with bipolar disorder, as compared to the general population is presented in Figure 8.

As with studies on people with schizophrenia, considerable variations in study sample sizes were evident across the studies reporting on physical ill-health conditions in people with bipolar disorder; for example, from 50 participants to 6490 participants in studies reporting on obesity. Considerable differences were also found in the individual prevalence rates across the included studies; for example, from 3.3% to 45.6% across studies reporting on cancer. This heterogeneity requires further exploration and should be considered when interpreting the overall pooled prevalence rates of physical health-illness conditions in people with bipolar disorder.

*Again, as in the schizophrenia group, the mean prevalence of obesity differed greatly from the median value of the prevalence rate for this condition, and again, these values were skewed by outliers. Three studies reported low prevalence of obesity (M=2%), one study reported moderate prevalence of obesity (M=23%), whilst five studies reported high prevalence of obesity (M=32%), demonstrating high heterogeneity across studies.

Figure 7: Prevalence of physical ill-health conditions in people with bipolar disorder
3.4 Depression

Nine studies that explored the prevalence of co-morbidities in people with depression were included in the review. The prevalence of diabetes was the most commonly reported conditions (4 studies), followed by cardiovascular disease, hypertension/hypertensive disease and obesity (reported each in 3 studies). For the remaining co-morbidities, all were reported in one study only (Appendix 5, Table 5.3).

The analyses demonstrated that, of these conditions, obesity occurs most frequently in people with depression (28.9%, 3 studies, 8866 participants), followed by hypertension and cancer (21.5%, 3 studies, 8866 participants and 15.8%, 1 study, 76 participants, respectively). These results are somewhat different from the results of studies of people with schizophrenia and bipolar disorder where prevalence rates for obesity were 8% or less, indicating perhaps, that the physical ill-health condition of obesity is more specific to people with depression compared to people with other SMIs. Cancer rates, while moderate to high at 15.8%, are somewhat lower in people with depression compared to people with schizophrenia (24.0%) and people with bipolar disorder (28.3%). None of the studies reported on chronic lung disease in people with depression, which is limiting, as given the high prevalence rates in people with schizophrenia (25%) and bipolar disorder (30.3%) it would have been useful to have prevalence rates of this condition in people with depression for comparative purposes.
Asthma and stroke were found to have the lowest prevalence rates in people with depression (1.4%, 1 study, 76 participants and 4.3%, 1 study, 1003 participants, respectively) (Figure 9; Appendix 5, Table 5.3). These results are moderately comparable to the rates of these physical ill-health conditions in people with schizophrenia (3.0% and 1.9%, respectively) and in people with bipolar disorder (7.3% and 1.9%, respectively). The prevalence of a number of key physical ill-health conditions in people with depression, as compared to the general population is presented in Figure 10.

As with studies on people with schizophrenia and bipolar disorder, considerable variations in study sample sizes were evident across the studies; for example, from 76 participants to 6831 participants in studies reporting on cardiovascular disease. Considerable differences were also found in the individual prevalence rates across the included studies; for example, from 6.1% to 46.0% across studies reporting on cardiovascular disease. This heterogeneity requires further exploration and should be considered when interpreting the overall pooled prevalence rates of physical health-illness conditions in people with depression.

Figure 9: Prevalence of physical ill-health conditions in people with depression

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>28.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21.5</td>
</tr>
<tr>
<td>Cancer</td>
<td>15.8</td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td>7.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6.8</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.3</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.3</td>
</tr>
</tbody>
</table>
3.5 Situating prevalence rates in an Irish context

Saha et al. (2007), in a systematic review of mortality in people with schizophrenia, suggested not only that a substantial gap exists between the health of people with schizophrenia and the general community, but that the mortality gap has increased in recent decades. Holt (2012) reaffirms this, suggesting that while the rates of cardiovascular disease and mortality have fallen in the general population over the last 20 years similar benefits have not been shared by people with SMI, resulting in a widening gap in health inequality. In an Irish context, between 1985 and 2000 the Republic of Ireland experienced a 47% reduction in deaths from heart disease (CHD) amongst those aged 25–84 years, in the Irish general population (Balanda et al., 2010). However, there was no data available to determine if people with SMI in Ireland made similar health gains from public health initiatives as the general population. A comparative study of health gains between people with SMI and the general population would be one way of determining this.

Diabetes prevalence (Type-1 and Type-2 combined) in adults in the Republic of Ireland is 4.5% and by 2020 this is expected to rise to 5.9% (Balanda et al., 2010). The pooled prevalence of diabetes in people with SMI, from the international studies in the current report is 9.1%, just over double the Irish general population. This is already well in excess of the projected general population figure of 5.9% for 2020. This would indicate that this area should be targeted as a priority for screening and early identification. Similar to the current study findings, Ryan et al. (2003), reported impaired fasting
glucose tolerance, higher insulin resistance, and higher plasma glucose, insulin, and cortisol in schizophrenia patients. Other Irish research has examined the genetic and environmental risk for physical ill-health in SMI. Spelman et al. (2007) reported high levels of impaired glucose tolerance in unaffected relatives of schizophrenia patients, pointing towards either a shared environmental or genetic predisposition to impaired glucose tolerance. This highlights the importance of screening of relatives of individuals with SMI and also of assessing family history of physical conditions.

Balanda et al. (2010) predicted that stroke prevalence in the Irish general population is expected to increase from 1.7% in 2007 to 1.9% in 2015 and to 2.1% in 2020. In the current study, the pooled prevalence rate for stroke in SMI aged between 18 - 65 years is 4.75%. This is substantially greater than the predicted levels in 2020 but more importantly in this review age was capped at 65 years. This suggests that stroke is more common in younger age groups in people with SMI than in the Irish general population, where the upper age limit included in prevalence estimates is 75 years+.

This review shows that people with SMI have an increased prevalence of stroke risk factors such as diabetes and cardiovascular disease. Li et al (2014) in a meta-analysis of stroke in schizophrenia suggest that the presence of risk factors such as diabetes and hypertension may link to the development of atherosclerosis and the pathogenesis of stroke event.

By illustrating only two conditions, diabetes and stroke, the extent of the challenge ahead for co-morbidity in SMI in Ireland can be seen. The WHO (2008) suggested that up to 80% of heart disease, stroke, and type-2 diabetes and over a third of cancers could be prevented by eliminating shared risk factors, mainly tobacco use, unhealthy diet, physical inactivity and the harmful use of alcohol.

4. Risk Factors for Co-morbidities

4.1 Description of included studies

Twenty-four international studies contributed data to the analyses of clinically/socially common biological and lifestyle risk factors, for the development of co-morbidities, in people with the SMI of schizophrenia, bipolar disorder and depression. The study references are listed in Appendix 6. Nineteen of the included studies reported on one
risk factor only, and the remaining four reported on two risk factors only. Dyslipidaemia (encompassing hyperlipidaemia, high cholesterol, lipid disorder and hypercholesterolemia) was most commonly reported (15 studies), followed by smoking (8 studies). Impaired fasting glucose was reported in three studies, hyperglycaemia was reported in two studies and lipid disorder and pre-diabetes were each reported in one study. Appendix 2 provides full details of the characteristics of the included studies, including their methodological quality assessment scores. In brief, however, the studies were conducted between the years 2000 and 2015; eight were conducted in the US, three in Canada, two in Spain, two in the Netherlands, and one study was conducted in each of the following countries; Norway, Czech Republic, Malaysia, Brazil, Korea, Taiwan, Japan, Croatia and Belgium. The methodological quality of the included studies was assessed as being moderate to high in the majority of the included studies, with eight studies scoring 6/6, six scoring 5/6, nine scoring 4/6, and one study scoring 2/6, on a modified Newcastle Ottawa Scale.

Recruitment and data collection strategies varied across the studies, ranging from in-patient care facilities, long- and short-stay facilities, out-patient departments, administrative databases, medical charts, survey (national/local) and medical and pharmacy claims records. Sixteen studies recruited participants on antipsychotic medication and/or mood stabilisers; for the remaining seven studies participant medication consumption activity was not stated.

The analyses of the data on risk factors were conducted in two ways; i) pooled prevalence rates of specific clinically/socially common risk factors, by individual SMI, were calculated and ii) where five or more of the same studies reported prevalence rates for both a risk factor and a physical health condition, in individuals with the same SMI, a correlation co-efficient, to determine possible associations between the risk factor and the condition, was calculated.

4.2 Prevalence rates of biological/lifestyle risk factors

4.2.1 Schizophrenia

Fourteen of the 24 included studies contributed data to the prevalence rates of risk factors for developing physical ill-health co-morbidity in people with schizophrenia. Dyslipidaemia was the most commonly reported risk factor across the studies (8
studies), followed by smoking (5 studies), impaired fasting glucose/glucose tolerance (3 studies), and hyperglycaemia (1 study) (Appendix 7, Table 7.1).

The analyses demonstrated that, of these risk factors smoking was the most commonly occurring risk factor (58.1%, 5 studies, 2508 participants), followed by impaired fasting glucose (16.1%, 3 studies, 1162 participants), and dyslipidaemia (14.9%, 8 studies, 38303 participants). Hyperglycaemia was the least frequently occurring biological risk factor in people with schizophrenia (7.0%, 1 study, 200). (Figure 11; Appendix 7, Table 7.1). Notably, the rate of smoking was substantially larger than in the general population in Ireland (19.5%).

Considerable variations in study sample sizes were evident across the included studies; for example, from 32 participants to 22434 participants in studies reporting on dyslipidaemia. The ranges across the studies for smoking and impaired fasting glucose were moderately narrow and narrow, respectively; however, the range across the studies for dyslipidaemia was considerably wide (4.0% to 69.8%) and should be considered when interpreting the overall pooled prevalence rates of risk factors for physical health-illness conditions in people with schizophrenia.

![Figure 11: Prevalence of risk factors in people with schizophrenia](image)

**4.2.2 Bipolar Disorder**

Eight of the 23 included studies contributed data to the prevalence rates of risk factors for developing co-morbidity in people with bipolar disorder. Dyslipidaemia was the
most commonly reported risk factor across the studies (5 studies), followed by smoking (3 studies), pre-diabetes (1 study), and hyperglycaemia (1 study) (Appendix 7, Table 7.2).

The analyses demonstrated that, of these risk factors smoking was the most commonly occurring risk factor (48.5%, 3 studies, 2174 participants), followed closely by hyperglycaemia (43.5%, 1 study, 184 participants). As with schizophrenia, the rate of smoking was substantially larger than in the general population in Ireland (19.5%). Pre-diabetes occurred in 23.3% of 60 participants (1 study), and dyslipidaemia in 5.9% of 10527 people with bipolar disorder (Figure 12; Appendix 7, Table 7.2).

The range of prevalence rates for smoking, across studies, was moderately narrow (27.0% to 50.1%), although wider than in studies reporting on people with schizophrenia and depression, indicating that smoking is a common lifestyle choice and considerable risk factor for ill-health in people with these SMI's. Dyslipidaemia prevalence, contrastingly, varied considerably across the included studies, from 1.1% to 36.5%, and should be considered when interpreting the overall pooled prevalence rates of this risk factor for physical health-illness in people with bipolar disorder.

![Figure 12: Prevalence of risk factors in people with bipolar](image)

### 4.2.3 Depression

Four of the 23 included studies contributed data to the prevalence rates of risk factors for developing physical ill-health co-morbidity in people with depression.
Dyslipidaemia and smoking only were reported, each in two of the included studies (Appendix 7, Table 7.3).

The analyses demonstrated similar findings to the findings of the analyses of risk factors in people with schizophrenia and bipolar disorder, with smoking reported in 43.4% of the studied population of (2 studies, 1079 participants). Again, the rate of smoking was substantially larger than in the general population in Ireland (19.5%). Dyslipidaemia occurred less frequently at 13.8% (2 studies, 1079 participants) (Figure 13; Appendix 7, Table 7.3).

![Figure 13: Prevalence of risk factors in people with depression](image)

### 4.2.4 Schizophrenia, Bipolar Disorder and Depression combined

Combining the three SMI s of schizophrenia, bipolar disorder and depression, smoking was strikingly evident as the most frequently occurring lifestyle risk factor in these populations (47.9%), much higher than the prevalence of this risk factor in the Irish general population (19.5%). Hyperglycaemia collectively occurred in approximately one-quarter of these populations, and dyslipidaemia collectively occurred in just over one-tenth (13%) of people with these SMI s (Figure 14; Appendix 7, Table 7.4).
4.3 Physical ill-health conditions proportionate to risk factors

Very few studies contributed data to analyses on associations between co-morbidities and biological/lifestyle risk factors. Of the analyses that were possible to perform, the results demonstrated a strong positive correlation between the numbers of people with dyslipidaemia and the numbers of people with hypertension, in people with schizophrenia ($r = 0.99$, 7 studies) (Figure 15). This indicates that as the numbers of people with dyslipidaemia increases, there is likely also to be an associated increase in the numbers of people experiencing hypertension. A strong positive correlation was also found between the numbers of people smoking and the numbers of people with diabetes in people with schizophrenia ($r = 0.98$, 5 studies), (Figure 16) and between the numbers of people with dyslipidaemia and the numbers of people with diabetes in people with schizophrenia ($r = 0.95$, 8 studies) (Figure 17). Finally, a moderate positive correlation between the numbers of people with dyslipidaemia and the numbers of people with diabetes in people with bipolar disorder ($r = 0.60$, 5 studies) was found (Figure 18).

These results, although they do not imply causation, do indicate that as the numbers of people experiencing the risk factor increases, it is likely that associated increases in the numbers of people with the co-morbidity would be seen.
Hypertension

Figure 15: Association between dyslipidaemia and hypertension in people with schizophrenia

Diabetes

Figure 16: Association between smoking and diabetes in people with schizophrenia

Diabetes

Figure 17: Association between dyslipidaemia and diabetes in people with schizophrenia

Dyslipidaemia

Figure 18: Association between dyslipidaemia and diabetes in people with bipolar disorder
4.4 Less conventional risk factors for co-morbidity in SMI

Less conventional risk factors, is a term used here, to draw attention to factors that have the potential to increase the risk of physical co-morbidity in people with SMI. The purpose of this section is to raise awareness of factors that may not normally be considered as risk factors for physical illness, but that can contribute to their presence. For example, risk factors for poor physical health in SMI are not confined to more conventional lifestyle or behavioural risk factors related to individual choices. Less conventional risk factors, i.e. risk factors that are important in the area of co-morbidity in SMI, but are under-researched, can play a part in the late diagnosis or duration of untreated physical illness in SMI.

Figure 19 illustrates some less conventional risk factors that can contribute to the increased co-morbidity of physical illness in SMI. The relative risk of each of these risk factors is not known. For interpretation these risk factors have been grouped into headings to illustrate how practitioner issues, issues around healthcare organisation and medication side effects, can contribute to the risk of co-morbidity. Often these risk factors are present in conjunction with person specific risk factors, however, the emphasis during the patient encounter often predominately falls on lifestyle and behavioural choices.

<table>
<thead>
<tr>
<th>Person Specific</th>
<th>Practitioner Specific</th>
<th>Organisation Specific</th>
<th>Treatment Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Lifestyle Choices</td>
<td>Lack of knowledge, skills and confidence in physical healthcare</td>
<td>Lack of action e.g. diagnosed conditions untreated</td>
<td>Medication side effects</td>
</tr>
<tr>
<td>Genetic/Family history of physical illness</td>
<td>Lack of specific training</td>
<td>Unclear care pathways e.g. responsibility issues between primary care and mental health services</td>
<td></td>
</tr>
<tr>
<td>Severity of mental health symptoms e.g. factors preventing physical activity</td>
<td>Role ambiguity - lack of clarity on whose role physical health monitoring is</td>
<td>Inequalities in access to services e.g. screening</td>
<td></td>
</tr>
<tr>
<td>Poor health literacy</td>
<td>Diagnostic overshadowing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 19: Explaining risk factors for poor physical health in SMI
4.4.1 Practitioner specific factors

4.4.1.1 Lack of knowledge, skills and confidence in physical healthcare

Phelan et al. (2001) suggest that many mental health practitioners have little training in physical care, and that the physical assessments of psychiatric inpatients by junior psychiatrists are poor. Nash (2005) found that mental health nurses required more training in the area of physical health and, in particular, in the area of diabetes (Nash, 2009).

4.4.1.2 Diagnostic overshadowing

Stigma not only negatively impacts on the social standing of people with mental health problems, it can also negatively impact on their physical health. In England, Rethink Mental Illness, a mental health charity, released a report entitled “Lethal Discrimination” (Rethink Mental Illness, 2013). A key finding of this report was that “many health professionals are failing to take people with mental illness seriously when they raise concerns about their physical health” (p1).

Diagnostic Overshadowing (DO) is linked to stigma and is essentially a judgement bias where healthcare practitioners misattribute legitimate symptoms of physical illness to a manifestation of mental illness rather than a genuine physical complaint (Nash, 2013). Basically, physical symptoms may be classified as ‘psychosomatic’ and this runs the risk of non-intervention. This subsequently increases the risk of service users having a period of untreated illness.

In a qualitative study of 20 service users’ perceptions of barriers to primary care, McCabe & Leas (2008) found that a considerable barrier to care was not having their physical health concerns taken seriously by health-care providers. Similarly, DeCoux (2005) found that the main barriers encountered by MHSUs when trying to access physical care included problems with credibility; nine out of ten participants perceived that staff at hospitals, mental health programs, prisons, or other treatment facilities thought they were “faking” or did not care when they complained of symptoms of illness. MHSUs also complained of not being taken seriously, inadequate access to information and education, and disrespectful behaviour on the part of clinicians.
4.4.2 Organisation specific

4.4.2.1 Low quality of physical healthcare

In a retrospective cohort study using medical chart data from acute care settings in the USA, Druss et al. (2000) explored post-MI care in people with mental disorders. They found that people with a mental disorder were significantly less likely to undergo percutaneous transluminal coronary angiography or coronary artery bypass graft surgery and that people with schizophrenia were less likely to undergo cardiac catheterisation as those without a diagnosis of mental disorders.

In 2001, Druss et al. explored care of those with a mental disorder hospitalised for MI. Compared with those without a diagnosis of a mental disorder, people with schizophrenia were less likely to have reperfusion, beta-blockers and angiotensin-converting enzyme inhibitors. People with a diagnosis of affective disorders were less likely to have reperfusion and aspirin. They suggested that “deficits in quality of medical care seem to explain a substantial portion of the excess mortality experienced by patients with mental disorders after myocardial infarction” (p565).

Kisely et al. (2009) in a population-based study of administrative data investigating the treatment of people with psychosis admitted for ischaemic heart disease or stroke found this group was less likely to receive guideline-consistent treatment such as coronary artery bypass grafting, beta-blockers and statins. Those with a history of stroke were found to be less likely to receive cerebrovascular arteriography or warfarin.

In a case-note review of 50 newly referred consecutive adult inpatients and 50 newly referred consecutive adult outpatients, Dale et al. (2008) showed a poor level of consideration of basic physical examinations and investigations and a poor level of record keeping in relation to physical examinations or investigations.

4.4.2.2 Unclear care pathways

While care pathways and guidelines exist for a range of physical conditions e.g. NICE guidelines, there is little evidence available of how they are incorporated into managing co-morbid medical conditions in SMI; if at all. Frayne et al. (2005) examined quality measures for diabetes care in MHSUs and found disparities in diabetes screening procedures between service users and non-mental health service users which
included under performance of haemoglobin A1c testing, low-density lipoprotein cholesterol testing and eye examinations.

Howard and Gamble (2011) in an exploration of mental health nurses practice in physical care of patients found that the majority of MHN in their sample were not familiar with any guidelines or policies relating to the physical health needs of individuals with SMI. This is despite the UK having implemented National Service Frameworks and NICE clinical guidelines for a wide range of complex conditions such as diabetes, coronary heart disease, obesity and stroke.

Crawford et al. (2014) in a national audit of care received by people with schizophrenia found that the documented evidence of monitoring for physical health problems falls well below agreed standards. Only in a few instances did they find local agreements on responsibility for treating and managing physical health care in SMI, but mostly there were no local agreements in place.

Many guidelines propose the locus of care for co-morbidity and SMI lies in primary care, where the expertise and traditional practice resides. However, this is not always the case. For example, Crawford et al. (2014) proposed that secondary care services retain responsibility for monitoring and treating the physical health problems of all in-patients, and for monitoring physical health in the community within 6 months of initiation of antipsychotic medication or major changes in the use of these drugs, and that primary care services take responsibility for assessing physical health at all other times.

4.4.2.3 Lack of action e.g. under treatment of co-morbid physical health conditions

Emerging evidence indicates that people with mental health conditions (MHCs) may receive less intensive medical care (Frayne et al., 2005). Nash (2014) suggested that it is a curious fact that even when a physical condition has been diagnosed in someone with a SMI, appropriate treatment may not follow. This can also extend to a lack of intervention in reducing physical health risk factors in this group. For example, two studies by Kendrick (1993, 1996) found that while people with long term mental health problems were frequently seen in primary care, GPs had made few attempts to address cardiovascular and respiratory risk factors, even though these risk factors were, in most cases, usually recorded in clinical notes.
Furthermore, the Royal College of Psychiatrists (RCP 2012) were concerned to find low rates of physical care interventions in people observed with abnormal blood pressure (only 25% had treatment), abnormal lipid levels (20%) and abnormal blood glucose or HbA1c (53%). In the CAITE study, involving people with a diagnosis of schizophrenia, Nasrallah et al. (2006) found a lack of appropriate treatment in 30% of people with diabetes, 62% with hypertension and 88% with high cholesterol.

With regard to smoking cessation, the Royal College of Psychiatrists (RCP, 2012) also found that only 57% of service users with schizophrenia were recorded as having an intervention to stop smoking in the last 12 months.

Manderbacka et al. (2012) used a cohort study to examine equity in access to coronary care among persons with a history of severe mental disorder in 1998–2009 in Finland. They found poor access to coronary revascularisation, according to need, among people with severe mental disorders and especially poor access to hospital care and revascularisations among people with psychotic disorders.

4.4.2.4 Inequalities in access to services e.g. under-screening and disparities in screening procedure

Inequalities in the provision of, and access to, screening or routine health check-ups in primary care settings can impact on physical health outcomes. While the prevalence of co-morbid conditions such as cardiovascular disease and diabetes or risk factors such as smoking and hypertension are greatly increased in people with SMI, research suggests that they are less well monitored than in the general population.

In a case-matched retrospective case note review, involving twenty-two general practices in the Birmingham area of the UK, Roberts et al. (2007) compared the proportions of patients with schizophrenia (n=195), matched controls with a diagnosis of asthma (n=390) and general control patients (n=390), for six pre-defined routine health checks (blood pressure, weight, cholesterol, smoking status, alcohol consumption and family history of heart disease) in a 3 year period. They found that people with schizophrenia were half as likely as asthma controls to have blood pressure and cholesterol levels recorded and were also less likely to have smoking status noted. Furthermore, patients with schizophrenia were significantly less likely than general population controls to have either blood pressure or cholesterol recorded. Therefore, while co-morbidity and exposure to poor health risk factors in people with
schizophrenia is increased, they were significantly less likely than other patient groups to receive some potentially important basic health checks, particularly blood pressure and cholesterol measurement.

While people with schizophrenia are at increased risk of developing cardio-metabolic disorders, a national audit of people with a diagnosis of schizophrenia carried out by the Royal College of Psychiatrists in the UK (RCP, 2012), found that only 29% of this population (approximately 6000 participants) received a fully comprehensive assessment of important cardio-metabolic risk factors. Research by the Disability Rights Commission (2006), shows that MHSUs receive less cholesterol checks and statins or spirometry for respiratory illness in comparison to others without a diagnosis of mental illness.

4.4.3 Medication side effects
Most psychotropic medications prescribed for the treatment of mental disorders have metabolic factors and weight gain listed in their side effect profiles. However, Holt & Peveler (2006) characterise the state of research into psychotropic drugs causing diabetes as confusing and inconsistent with a causative link inconclusive. Indeed, some research has reported lower mortality associated with long-term cumulative exposure to antipsychotic medication (Tiihonen et al., 2009). Medications may provoke weight gain and type-2 diabetes, but the mechanisms for these interactions are not yet fully clear.

4.4.3.1 Low priority given to monitoring medication side effects by practitioners
While the overall picture regarding the role of psychotropic medication in co-morbidity in SMI is unclear and very complex, there is evidence that indicates a lack of effective monitoring of prescribed medications. De Hert et al. (2011) observed that neither psychiatrists nor primary care physicians carefully screen service users for metabolic risk factors associated with anti-psychotic medication.

Bennett et al. (1995) found that Community Psychiatric Nurses held an unfavourable attitude towards their involvement with medication monitoring, with some perceiving this role negatively. Taylor et al. (2004) found low levels of testing for diabetes 41% (250/606) in patients prescribed antipsychotics. They also found testing more common in those receiving atypical antipsychotics. Apparent differences in claimed causal
association of the use of some antipsychotics with diabetes may in part reflect different rates of testing.

An audit of mental health services across the United Kingdom (Barnes et al., 2007) revealed low levels of physical health monitoring; for example, 26% of patients had blood pressure recorded, 17% for obesity, 28% for blood glucose (or HbA1c) and 22% for plasma lipids. Of concern to the researchers was the non-treatment of diagnosed medical conditions. In people with diabetes, 38% (n=46) had no record of medication being prescribed to treat the condition, for dyslipidaemia 36% (n=76) and for hypertension 52% (n=60). The authors suggest that non-pharmacological treatments may have been recommended but that this was not recorded in the notes.

Barnes et al. (2007) also investigated practitioner’s experiences of physical health monitoring and found that obstacles to screening in routine practice included uncertainty about whose responsibility this was, a lack of confidence about the interpretation of abnormal screening results, and limited access to basic equipment. However, monitoring of physical health parameters did improve following this clinical audit when a specific monitoring form was implemented.

Therefore, while the science behind medication being a causative factor in co-morbidity may be uncertain, evidence would appear to suggest that the monitoring of medication side-effects, especially regarding cardio-metabolic risk and the screening of factors such as type-2 diabetes could be improved. There is no clear evidence regarding the practices in medication monitoring from an Irish perspective.

Psychotropic medications such as clozapine (atypical anti-psychotic) and lithium (mood stabilizer) require regular blood monitoring due to the risks associated with reduced white blood cell count (clozapine) and toxicity (lithium). Service users taking these medications will therefore have more regular monitoring of medication side effects than service users who do not take them.

5. Interventions for addressing physical illness co-morbidity in SMI

Three types of international study publications, assessing the effectiveness of interventions or treatments for reducing physical ill-health morbidity in people with SMIs were included in the review; i) systematic reviews, ii) randomised studies, and
iii) non-randomised studies. Appendix 3 provides full details of the characteristics of the included reviews/studies, including descriptions of the interventions or treatments, descriptions of the target conditions, outcomes of interest and methodological quality assessment scores. Interventions targeted at general or mixed psychiatric populations (i.e. encompassing a combination of two or more of the SMIAs focused on within this review), for example, Daumit et al. (2013)\textsuperscript{14}, were not included in the review.

### 5.1 Systematic Reviews

Five systematic reviews, published between 2003 and 2015 were included in the analyses (Faulkner et al., 2003; Faulkner et al., 2007; Firth et al., 2015; Hjorth et al., 2014; Tsoi et al., 2013). All five reviews targeted individuals with schizophrenia. Two of the reviews were Cochrane Systematic reviews (Faulkner et al., 2007; Tsoi et al., 2013). Four reviews focused on interventions to reduce obesity or control weight gain (Faulkner et al., 2003; Faulkner et al., 2007; Firth et al., 2015; Hjorth et al., 2014). The remaining review focused on interventions for smoking cessation/reduction (Tsoi et al., 2013). The interventions were of varying types in some of these reviews (see Appendix 3 for further details), and narrative syntheses, rather than statistical pooling of data, were applied.

#### 5.1.2 Weight management

Table 2 presents the results for the primary outcomes of weight management and BMI. In the majority of cases, all of the different intervention types demonstrated reductions in both weight and BMI in people with schizophrenia, at varying follow-up time-points post-intervention. These reductions were significant for cognitive/behaviour therapy interventions, pharmacological interventions, alone and in combination with lifestyle management, and for behavioural and dietary interventions. Exercise programmes alone were found to significantly reduce weight in the intervention groups; however, this did not translate to a decreased BMI (Table 2).

\textsuperscript{14} However, the Daumit et al. (2013) study does merit a mention because their study showed that a behavioural weight-loss intervention significantly reduced weight over an 18 month period in overweight and obese adults with SMI)
### Table 2: Outcomes - Weight and BMI

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced weight</td>
<td>Pharmacological interventions</td>
<td>Treatment interventions only</td>
<td>Combined programmes of exercise, diet and CT/BT</td>
<td>Exercise interventions</td>
</tr>
<tr>
<td></td>
<td>5/8 studies; weight loss in favour of pharmacological intervention</td>
<td>3-4 months: $\Delta$MD -1.69; 95% CI -2.8 to -0.6; 3 studies, 129 participants</td>
<td>5/11 studies; weight loss in the intervention groups and weight gain in the control groups</td>
<td>Significant reduction in weight in favour of intervention = 4/6 RCT studies</td>
</tr>
<tr>
<td></td>
<td>2/8 studies; weight loss in favour of control treatment</td>
<td>Anti Obesity Agents +/- Lifestyle Management</td>
<td>Exercise programme only</td>
<td>No change in weight between intervention and control groups = 2/6 RCT studies</td>
</tr>
<tr>
<td></td>
<td>1/8 studies; no difference in weight loss between groups</td>
<td>Medium term: $\Delta$MD -4.58; 95% CI -5.2 to -4.0; 1 study, 37 participants</td>
<td>4/5 studies; reduction in weight in favour of intervention</td>
<td></td>
</tr>
<tr>
<td>Behavioural &amp; dietary interventions</td>
<td>8/8 studies; weight loss in favour of behavioural intervention</td>
<td>H2 Antagonists</td>
<td>CT/BT interventions only</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 weeks: $\Delta$MD -5.3; 95% CI -8.4 to -2.2; 2 studies, 59 participants</td>
<td>1/3 studies; weight loss in the intervention group (by 0.5kg) and weight gain in the control group (by 0.5kg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Appetite suppressant</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 months: $\Delta$MD -2.6; 95% CI -5.1 to -0.1; 1 study, 16 participants</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticonvulsants</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 months: $\Delta$MD -1.38; 95% CI -4.2 to 1.5; 1 study, 36 participants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduction in BMI</td>
<td>Results not reportable</td>
<td>CT/BT intervention</td>
<td>Combined programmes of exercise, diet and CT/BT</td>
<td>Exercise interventions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-4 month follow-up: $\Delta$MD -0.66; 95% CI -1.1 to -0.3; 3 studies, 129 participants</td>
<td>1/11 studies; weight loss in the intervention groups and weight gain in the control groups</td>
<td>$\Delta$MD -0.98kg/m$^2$; 95% CI -3.17 to 1.22 kg/m$^2$; 4 RCT studies, 80 participants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti Obesity Agents +/- Lifestyle Management</td>
<td>Exercise programme only</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium term: $\Delta$MD -0.17; 95% CI -1.3 to 1.0; 2 studies, 41 participants</td>
<td>2/5 studies; reduction in BMI in favour of intervention group</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H2 Antagonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 weeks: $\Delta$MD -1.51; 95% CI -2.5 to -0.6; 2 studies, 59 participants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^2$Result significant (p < 0.05) favouring intervention; $^*$Result significant favouring control; $^*$Non-significant result
5.1.3 **Smoking cessation/reduction**

A variety of interventions, pharmacological and non-pharmacological, targeting smoking cessation were evaluated in the review. Table 3 presents the results for the outcome measures of smoking abstinence at longest follow-up, smoking abstinence at end of the intervention and reduction of smoking behaviour or dependence, according to intervention type.

In brief, the results demonstrated that those receiving Bupropion\(^\text{15}\) were almost three times more likely to be abstinent from smoking at 3-months follow-up compared to those receiving a placebo. For a transdermal nicotine patch intervention smoking abstinence at end of treatment was significant in favour of the intervention with almost three times as many people in the patch group abstinent at the end of the treatment period, compared to those in the non-patch group.

Varenicline\(^\text{16}\) was found to be effective for smoking abstinence at the end of treatment and for a reduction in smoking behaviour at 12-weeks follow-up, compared to placebo; however, it was ineffective for abstinence at 6-months follow-up.

No differences were found between groups receiving a ‘Treatment of Addiction to Nicotine in Schizophrenia’ (TANS) intervention and a Medication Management (MM) control in abstinence rates at 6 and 12-month follow-ups or in a reduction in smoking behaviour.

The American Lung Association (ALA) programme, compared to group therapy, was ineffective for smoking abstinence and a reduction of smoking behaviours (measured by carbon monoxide levels) at the end of treatment period; however, it was significantly effective for abstinence at 6-months follow-up; indicating, perhaps, that the beneficial effects of this programme are experienced by participants more-so after the programme is complete, rather than during it.

A CBT and motivational interview intervention, compared to no intervention/usual care, was effective for reduction in smoking behaviour (OR 3.96; 99% CI 1.53 to 10.23) but was ineffective for abstinence at follow-up.

\(^{15}\) Bupropion is a prescription medication used in smoking cessation. It reduces the cravings and withdrawal symptoms from nicotine

\(^{16}\) Varenicline is a prescription medication used in smoking cessation by reducing the urge to smoke
### Table 3: Outcomes - smoking abstinence and reduction

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Smoking abstinence at longest follow-up</th>
<th>Smoking abstinence at end of the intervention</th>
<th>Reduction of smoking behaviour or dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bupropion</strong></td>
<td>6-months: (^*)RR 2.78; 95% CI 1.02 to 7.58; 5 studies, n = 214</td>
<td>End of treatment: (^*)RR 3.03; 95% CI 1.69 to 5.42; 7 studies, n = 340</td>
<td>End of treatment: (^<em>)MD - 10.77; 95% CI -16.52 to -5.01; 3 studies, n = 184 3-months: (^</em>)MD -2.61, 95% CI -7.99 to 2.77; 2 studies, n = 93</td>
</tr>
<tr>
<td><strong>Transdermal Nicotine Patch (TPN)</strong></td>
<td>High dose vs Low dose, 8 weeks; 7 day abstinence rates: (^*)32% vs 23%; 1 study, n = 51</td>
<td>Abstinence (^*)higher in those with TPN vs those with no TPN</td>
<td>No differences between groups in CO levels at end of treatment</td>
</tr>
<tr>
<td><strong>Varenicline</strong></td>
<td>6-months: (^*)RR 5.06, 95% CI 0.67 to 38.24; 1 study; n = 128</td>
<td>End of treatment: (^*)RR 4.74, 95% CI 1.34 to 16.71; 2 studies, n = 137</td>
<td>12 weeks: (^*)3 fewer cigarettes/day in treatment compared placebo group (95% CI 0.4 to 6.1)</td>
</tr>
<tr>
<td><strong>American Lung Association (ALA) programme</strong></td>
<td>6-months: (^*)17.6% (ALA) vs 10.7% (group therapy)</td>
<td>(^*)23.5% (ALA) versus 32.1% (group therapy)</td>
<td>No difference between groups in CO levels at end of treatment</td>
</tr>
<tr>
<td><strong>‘Treatment of addiction to nicotine in schizophrenia’ (TANS) and Medication Management (MM)</strong></td>
<td>6 months: (^<em>)14% (TANS) vs 16% (MM) 12 months: (^</em>)12% (TANS) vs 12% (MM)</td>
<td>NR</td>
<td>No differences in reduction in cigarettes/day CPD between the two groups</td>
</tr>
<tr>
<td><strong>CBT and motivational interview</strong></td>
<td>No differences between groups at 3, 6 &amp; 12-months and four years</td>
<td>NR</td>
<td>3-months: (^*)OR 3.96; 99% CI 1.53 to 10.23, p&lt; 0.001; however non-significant at 6 &amp; 12-months and 4-years</td>
</tr>
</tbody>
</table>

n = number of participants; RR = Relative risk; CI = Confidence Interval; NR = not reported; OR = Odds Ratio  
\(^*\)result significant (p < 0.05) favouring intervention; 
\(^\dagger\)result significant favouring control; 
\(^*\)non-significant result

5.2 Controlled studies (randomised and controlled clinical trials)

Three randomised controlled trials (RCTs) (Chou et al., 2004; Kilbourne et al., 2013; McKibbin et al., 2010) and one clinical controlled trial (CCT) (Heggelund et al., 2011) were included in the analyses. Three of the studies targeted individuals with a diagnosis of schizophrenia (Chou et al., 2004; Heggelund et al., 2011; McKibbin et al., 2010) and one targeted individuals with bipolar disorder (Kilbourne et al., 2013). Of the three studies targeting individuals with schizophrenia, one focused on an exercise programme for reducing cardiovascular risk (measured primarily by \(\text{VO}_{2}\text{peak}\) (Heggelund et al., 2011), one focused on a Diabetes Awareness and Rehabilitation
Training (DART) for weight management in people with diabetes (McKibbin et al., 2010), and one focused on nicotine patch therapy (Chou et al., 2004). The one study targeting individuals with bipolar disorder evaluated a self-management programme, Life Goals Collaborative Care (LGCC), for reducing cardiovascular risk. Appendix 3 provides the full details of the characteristics of the included studies, including descriptions of the interventions and risk of bias (methodological quality) assessment scores.

Due to the differing natures of the interventions and populations in the included studies, a meta-analysis on outcomes was not appropriate; rather a narrative synthesis of the findings is presented.

5.2.1 Exercise programme for reducing cardiovascular risk
Individuals with schizophrenia receiving a high intensity training programme, compared with individuals who were inactive in the form of playing computer games (CG) had significantly improved VO$_{2\text{peak}}$ levels at the end of the programme (MD 0.33, 95% CI 0.07 to 0.58, 1 study, 19 participants). No differences were evident in any other outcome measures of cardiovascular risk at the end of the programme (Table 4).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>12-month follow-up</th>
<th>MD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure</td>
<td>0.0 (-15.0 to 16.0)</td>
<td></td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>3.0 (-5.0 to 12.0)</td>
<td></td>
</tr>
<tr>
<td>Body weight</td>
<td>-2.8 (-0.2 to 0.5)</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-0.9 (-2.0 to 0.1)</td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>0.1 (-0.5 to 0.7)</td>
<td></td>
</tr>
</tbody>
</table>

5.2.2 Self-management programme for reducing cardiovascular risk
Individuals with bipolar disorder who underwent a 12-month LGCC programme, compared to those who received enhanced usual care, were significantly more likely to have reduced diastolic blood pressure at 12-months follow-up, but not at 24-months. No differences in systolic blood pressures, BMI or total cholesterol levels were found between the groups at either 12 or 24-month follow-ups (Table 5).
Table 5: Differences between LGCC and enhanced usual car at 12 and 24-month follow-ups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>12-month follow-up MD (95% CI)</th>
<th>24-month follow-up MD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure</td>
<td>-6.5 (-15.0 to 2.01)</td>
<td>-3.2 (-9.8 to 3.4)</td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>-5.2 (-10.1 to -0.34) $^*$</td>
<td>-2.6 (-7.3 to 2.1)</td>
</tr>
<tr>
<td>BMI</td>
<td>-1.7 (-4.4 to 1.0)</td>
<td>-2.16 (-4.9 to 0.5)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>-8.2 (-28.46 to 12.06)</td>
<td>3.0 (-17.0 to 23.0)</td>
</tr>
</tbody>
</table>

$^*$significant difference (p < 0.05)

5.2.3 Weight management in people with diabetes

Individuals with schizophrenia who received the DART intervention, compared to individuals receiving usual care + information, were statistically significantly more likely to have reduced BMI (change from baseline at 12 months follow-up; 6-months from end of treatment, MD 2.4; 95% CI 1.95 to 2.85; 1 study, 52 participants) (Figure 20).

![Figure 20: Change from baseline BMI](image)

5.2.4 Nicotine-patch therapy for smoking cessation/reduction

Individuals with schizophrenia who were treated with nicotine-patch therapy for smoking were more likely to be abstinent from smoking in the medium term (i.e. 3-months follow-up) than those not treated with nicotine-patch therapy (point prevalence: 27% versus 0%, intervention versus control, respectively, 1 study, 66 participants). Additionally, nicotine-patch therapy significantly reduced nicotine dependency, measured by the Fagerstrom Tolerance Questionnaire, from baseline (pre-treatment) to 3-months follow-up in the intervention group (MD 4.60; 95% CI 3.63 to 5.57, intervention group, 26 participants, Figure 21), and the differences in dependency between groups was also significant at 3-months follow-up (z = -11.5, p < 0.0001).
5.3 Non-randomised studies

Two non-randomised studies, published between 2001 and 2006, were included in the analyses (Centorrino et al., 2006; Weiner et al., 2001). Both studies targeted individuals with schizophrenia, however, the treatment in the studies focused on diverse physical ill-health issues. Centorrino et al. (2006) focused on a combined programme of diet, exercise and counselling for managing weight in individuals with diagnosed schizophrenia, and, a weight gain of ≥ 4.5kg and an increase in BMI of ≥ 5%, since starting antipsychotic treatment. Weiner et al. (2001), alternatively, examined the efficacy, tolerability, and safety of supportive group psychotherapy and adjunctive sustained-release bupropion for nicotine addiction in people with schizophrenia. Appendix 3 provides full details of the characteristics of the included studies, including methodological quality assessment scores. In brief, both studies, with a total of 25 participants, were conducted in the US. Baseline outcome measurements were collected in both studies prior to introducing the treatments with follow-ups ranging from 48 weeks for the weight management programmes and 14 weeks for the smoking cessation programme. Due to the differing nature of the interventions in the studies, the results for each study are presented separately.

**5.3.1 Weight management programme**

The results for the combined weight management programme, although favouring the programme slightly for reducing body weight, demonstrated no statistically significant difference in mean body weight reduction between baseline and follow-up at 24 weeks (MD -6.00; 95% CI -17.2 to 5.72), and between baseline and follow-up at 48 weeks (MD -6.30; 95% CI -18.02 to 5.42) (Figure 22).
For the weight management indicators of BMI, Blood Pressure (BP), serum cholesterol and serum glucose, statistically significant differences between baseline and follow-up were observed, in favour of the weight management programme, for reduced systolic and diastolic blood pressure at 24 weeks and 48 weeks, only. No significant reductions were observed for any of the remaining outcomes at either of the two follow-up time-points (Table 6).

Table 6: Additional weight management outcome measures

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Follow-up: 24 weeks MD (95% CI)</th>
<th>Follow-up: 48 weeks MD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>-2.1 (-5.1 to 0.9)§</td>
<td>-2.0 (-20.2 to 16.2)$</td>
</tr>
<tr>
<td>Systolic BP (mm/Hg)</td>
<td>-14.0 (-21.7 to -6.3)'</td>
<td>-14.0 (-23.2 to -4.8)'</td>
</tr>
<tr>
<td>Diastolic BP (mm/Hg)</td>
<td>-9.3 (-14.1 to -4.55)'</td>
<td>-9.4 (-13.7 to -5.1)'</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td>-13.0 (-34.6 to 8.6)'</td>
<td>-9.0 (-44.1 to 26.1)'</td>
</tr>
<tr>
<td>Serum glucose (mg/dl)</td>
<td>-4.4 (-14.1 to -5.3)'</td>
<td>-2.8 (-13.3 to 7.7)'</td>
</tr>
</tbody>
</table>

MD = Mean difference between baseline and follow-up; CI = confidence interval
§statistically significant result (p < 0.05);
§non-significant result

5.3.2 Supportive group psychotherapy and adjunctive sustained-release bupropion for nicotine addiction

In Weiner et al. (2001), a measure of end expired breath carbon monoxide levels was used to obtain an objective indicator of cigarette consumption, rather than participant self-report, which is known to be unreliable. At baseline, the Fagerstrom Test for Nicotine Dependence (a revised version of the Fagerstrom Tolerance Questionnaire) indicated a high nicotine dependency in the study population (M 6.13, SD, 2.10; 8
participants). The only meaningful reportable outcome measure for this analysis was a change in carbon monoxide level between baseline and follow-up at 14 weeks. The results demonstrated a statistically significant reduction, in favour of the smoking cessation programme, in mean carbon dioxide levels between baseline and follow-up at 14 weeks (Figure 23).

<table>
<thead>
<tr>
<th>Study</th>
<th>Post-programme Mean</th>
<th>SD</th>
<th>Pre-programme Mean</th>
<th>SD</th>
<th>Total Mean</th>
<th>Total SD</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (95% CI)</td>
<td>8</td>
<td></td>
<td>8</td>
<td></td>
<td>8</td>
<td></td>
<td>-21.06 [-37.99, -4.13]</td>
<td>-21.06 [-37.99, -4.13]</td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect: Z = 2.44 (P = 0.01)

Figure 23: Change in carbon monoxide level between baseline and follow-up at 14 weeks

6. Results summary

Prevalence of physical health co-morbidities

- Schizophrenia: Of the physical health conditions examined, chronic lung disease occurred most frequently, followed by cancer, cardiovascular disease, and hypertension.
- Bipolar disorder: Of the physical health conditions examined, hypertension occurred most frequently, followed closely by chronic lung disease and cancer.
- Depression: Of the physical health conditions examined, obesity occurred most frequently, followed by hypertension and cancer.
- In the context of the general prevalence in the Irish population:
  - Stroke prevalence was much higher in people with SMI than in the Irish general population, despite the age range for the current study being 18-65 years. This suggests that stroke is more common in younger age groups in people with SMI than in the Irish general population.
  - The prevalence of cardiovascular disease was much higher than in the Irish general population indicating that this area should be targeted as a priority for early screening and identification.
The diabetes prevalence was just over double the Irish general population indicating that this area should be targeted as a priority for early screening and identification.

**Biological and lifestyle risk factors for physical health co-morbidities**

- **Schizophrenia**: The most commonly occurring risk factors for physical health co-morbidity were smoking, impaired fasting glucose and dyslipidaemia.

- **Bipolar Disorder**: The most commonly occurring risk factors for physical health co-morbidity were smoking, hyperglycaemia, and pre-diabetes.

- **Depression**: The most commonly occurring risk factors for physical health co-morbidity were smoking and dyslipidaemia.

- Positive correlations between the following: dyslipidaemia and hypertension; smoking and diabetes; and dyslipidaemia and diabetes were found.

- Smoking rates in people with SMI are more than double the Irish general population rate.

**Less conventional risk factors for physical health co-morbidities**

- The following practitioner specific factors are highlighted:
  - Lack of knowledge, skills and confidence in physical healthcare
  - Diagnostic overshadowing

- The following organisation specific factors are highlighted:
  - Low quality of physical healthcare
  - Lack of care pathways
  - Lack of action
  - Inequalities in access to services

- Treatment specific factors include medication side effects, for example, the low priority given to monitoring medication side effects by practitioners.

**Interventions for physical health co-morbidities**

- A number of systematic reviews of weight management programmes (exercise, cognitive/behaviour therapy, pharmacological interventions alone, pharmacological interventions in combination with lifestyle management, and behaviour and dietary interventions) demonstrated that in the majority of cases, the intervention decreased weight and BMI.
• In a systematic review of smoking cessation studies, bupropion, varenicline, the American Lung Association (ALA) programme, as well as CBT combined with motivational interviewing, were shown to increase smoking abstinence.

• Individual studies demonstrated the following:
  o An exercise intervention improved maximal oxygen uptake.
  o A self-management programme was shown not to have any effect on BMI.
  o A weight management programme was shown to reduce BMI.
  o A nicotine patch therapy intervention was shown to increase nicotine abstinence.
  o A combined weight management programme was shown not to have any effect on weight or BMI.
  o Support group psychotherapy and bupropion was shown to reduce carbon monoxide levels.

7. Study strengths and limitations

Developing a search strategy for the current study was challenging due to the wide range of terms needed to capture the relevant populations and multiple study types. However, following a number of scoping searches to assist with determining appropriate search terms and combinations for the strategy proper, a pragmatically based search was developed using the key SMI, co-morbid and study designs terms. This, we believed, would optimise retrieval of relevant literature, as it increased the specificity of the search, while recognising also that using a study design filter is not without its limitations, as not all studies are appropriately described by design in their text. The review was limited to both specific SMIs and specific co-morbidities. This might be viewed as a limitation to the study as it limits information at a broader mental health level and it does not facilitate exploring multiple co-morbidities specifically. However, it also provides strength to the review, as it provides information focused to specific SMIs and conditions, which will have specific meaning for clinical practice and in clinical decision making in these defined populations.

This review also has a number of other important strengths and limitations that require noting. The age range used (18-65 years) increases the strength of the review’s
findings, as wide age limits will limit the clinical application of results as the needs of an adult population (as investigated here) contrasts sharply to the needs of children and the elderly. Indeed, the search strategy used in this study resulted in a large number of studies with populations having a very wide age limit that could not be included on this basis. This would emphasise the need to conduct further investigative research specific to the child and adolescent and older persons populations which would be more clinically applicable and meaningful. A significant number of studies included in the meta-analysis for prevalence of physical ill-health conditions (21 studies), did not provide a participant age range; rather, mean age and standard deviation were provided and were deemed to be within the study age limit of 18-65 years based upon these descriptive statistics.

The clinical heterogeneity identified across the included prevalence and risk factor studies (i.e. in terms of population, methods of data collection, locations, and results) in this review, needs to viewed with caution, as it has the potential to heavily influence and limit the pooled prevalence results. The limited time frame for review did not allow deeper exploration of the causes of heterogeneity, but this has been identified as warranting further exploration in order to reduce this in future research, thus potentially facilitating homogeneity and optimising opportunities for improved evidence synthesis in studies of these types. Notably, the importance of the current study from a methodological, as well as a clinical, perspective is highlighted here.

The strength of the evidence of the review findings are influenced considerably by the methodological quality of the included studies. Based on formal quality assessments, using previously used, validated tools, the majority of included studies had a moderate to high quality rating, with a small number of intervention studies of low to moderate quality. This increases, overall, the strength of the review, for informing practice and clinical decision making; however, low-quality effectiveness studies (considered as ‘gold-standard’ for informing practice change and treatment), is limiting and indicates a need for high quality prospective randomised controlled trials in this area.
8. Recommendations for co-morbidity and SMI

The HSE is committed to delivering high quality healthcare services and recognises that healthcare reform means that service design and practice “…move away from simply treating sick people to keeping people healthy” (HSE, 2015a, p6). Reducing the burden of chronic disease is one of the three priority areas in the Healthy Ireland Health Services National Implementation Plan 2015 – 2017 (HSE, 2015b). Reducing Chronic Disease is recognised as the greatest challenge facing the health services in Ireland because it represents the biggest risk to our population’s health. This report illustrates that these policy aspirations are timely in light of the prevalence of co-morbid chronic disease and their risk factors in people with SMI.

In 2013 the Irish Government produced a series of goals to accompany the Healthy Ireland Framework Document (DH&C, 2013) that include:

- Increase the proportion of people who are healthy at all stages of life;
- Reduce health inequalities;
- Protect the public from threats to health and wellbeing;
- Create an environment where every individual and sector of society can play their part in achieving a healthy Ireland.

These goals should be at the heart of any strategy that aims to promote the physical health and wellbeing of mental health service users. To this end the Irish Institute of Public Health (Balanda et al., 2010) recommendation of a stronger focus on prevention, tackling inequalities of health and building appropriate information systems to support the monitoring and evaluation of strategies in effectively managing co-morbidity and SMI is echoed here.

8.1 Recommendation for future research

Recommendations for future research arising from this review are multi-fold, requiring MHSUs (self-report), healthcare provider/practitioner (self- and secondary-report) and national administrative/policy level involvement e.g. inclusion of physical health outcomes as a key quality indicator. Recognising that future research activity is resource intensive, and aspects require planning over long periods of time, our recommendations for future research are described as immediate (I), interim (IM) and longer-term (LT). These recommendations are:
8.1.1 Service User Involvement

In the absence of extensive, reliable Irish data, there is a need to:

I. (I) Conduct a high quality prospective national survey (service user self-report), by age category (e.g. aged 19-64 years and aged 65 years or older), of individuals with a known SMI, in order to identify the prevalence and type of co-morbidity(ies) in this population in an Irish context. Within this survey the following data should additionally be captured, as a sub-section for those answering positively to the presence of co-morbidity:

a. Biological and lifestyle risk factor self-reported prevalence data (e.g. rates of dyslipidaemia and smoking, which have been shown in this review to be highly correlated with diabetes and hypertension in people with schizophrenia and bipolar disorder). Although self-report, of prevalence of lifestyle risk factors in particular, in populations with SMI, is not without its challenges, it is important to capture this information from the perspective of the users themselves, and to assess against national general health information data.

b. Treatment/non-treatment of co-morbid condition(s)

c. Compliance with treatments

d. Point of treatment/locus of care (e.g. GP, other primary care centre, general hospital, mental health institution, etc.)

e. Satisfaction with the treatment/management of their co-morbidity, using a validated (or modified, as appropriate) satisfaction scale for use in selected populations of people with SMI

II. (IM) Based on the findings of the national survey of service users, conduct interviews on a purposively sampled cross-sectional sub-group of respondents with diverse self-reported co-morbidities to:

a. Explore barriers/facilitators, from the perspective of service users, to physical health care

b. Explore service-users experiences of treatment and management options, and care, in the context of users’ perspectives on current health care provision, options for care and organisation of care that meets both their mental and physical health needs.
Information on experiences from the perspectives of users is of vital importance for forward planning care provision and organisation of care for people with a dual diagnosis of SMI and physical health co-morbidity, so that the specific needs of these individuals as a select group will be better met. Data collection on the prevalence rates of physical ill-health in the first degree relatives of those with SMI would also be beneficial.

8.1.2 Healthcare provider/practitioner Involvement

I. (IM) Conduct a high quality, prospective national survey, categorised by primary, secondary and acute care sectors, to determine:
   a. The current point prevalence (using anonymous medical record data collection methods) of co-morbidities in people with SMI by category of healthcare provision
   b. Geographical prevalence spread (diversity, clustering, etc)
   c. Identifiable clinical/social biological/lifestyle risk factors associated with identified co-morbidity, as per medical data records

National surveys from a healthcare provider/practitioner perspective, in addition to a service user perspective, are necessary to firmly explore the existence and extent of co-morbidities from these two discrete, yet highly intertwined, perspectives and data sets, in order to establish potential disparities between the two. This is necessary to obtain a complete understanding of and clarity on the extent of the potential challenges presented by the existence, extent and reporting of co-morbidity in people with SMI in Ireland.

II. (I) Conduct a high quality, prospective national inter-professional survey of healthcare providers/practitioners (in all sectors; GPs, psychiatrists, nurses, primary, acute and secondary care services) to identify current practices and attitudes towards including physical health care for people with SMI as a dimension of practice and their education and training needs. Knowledge of the health and social care workforce needs is essential to ensure workforce preparedness for the challenges that may arise from implementing programmes aimed at tackling co-morbidity and SMI.
8.1.3 National Administrative/Policy level involvement

I. (I) Develop a national database of specific mortality and co-morbidity data for people with SMI. This could be facilitated by developing links to established studies such as the SLÁN (2007) Survey of Lifestyle, Attitudes & Nutrition in Ireland, if it is to be recommissioned, or the Healthy Ireland study.

II. (IM to LT) Based on Irish prevalence rates, once captured, (as recommended above), conduct a methodologically robust economic analysis of the impact of co-morbidity in people with SMI on individuals, local healthcare service provision and healthcare expenditure at large. This analysis should be encompassing and include; (i) healthcare resource use and expenditure in people with SMI and co-morbidity, including costs associated with direct medical resource use (staff time, education input, additional referrals), indirect costs (associated with lost or reduced productivity) and other non-medical costs (such as patient out of pocket expenses), and (ii) measures of cost savings or cost effectiveness (e.g. incremental cost-effectiveness ratios (ICERs) and quality adjusted life years (QALYs)) of effective co-morbidity prevention or treatment practices (e.g. screening, etc.).

III. (LT) Design and implement, a multi-centre/regional randomised trial targeted at preventing the leading co-morbidity (as identified in the national surveys as recommended at I and IM priorities, as above) in people with SMI in the Irish context. Such a trial may be informed by the findings of this review, (i.e. identified interventions which were shown to be effective in reducing co-morbidity or risk factors (e.g. weight management and smoking cessation programmes), as appropriate. Any such trial, in the future, should include a health economic component to consider the economic impact (cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis), of implementing a tested intervention, compared to more standard treatment, if the intervention is shown to be effective.

8.2 Recommendations for practice and organisation of care

8.2.1 Tobacco Use

Tobacco use is a significant cause of ill health and mortality in the Irish population (HSE, 2010). This report has illustrated the high prevalence of smoking in people with
SMI – across the three conditions explored. This was almost three times higher than the Irish general population and therefore warrants urgent attention. Smoking is a major physical health risk factor and in this review was highly correlated with diabetes in people with schizophrenia.

I. This review has found that interventions, such as nicotine patch therapy, and others, in people with schizophrenia, were shown to be effective in smoking abstinence and change in smoking behaviour. The Health Service Executive has been proactive in addressing the issue of tobacco use in mental health facilities. In the *Best practice guidelines for tobacco management in mental health settings*, the HSE (2008a, p7) recommend establishing “a system to identify and record the smoking status of all clients on admission and incorporate into overall client care plans, including specific smoking cessation techniques.”

II. This report would endorse this recommendation and suggest the introduction of smoking cessation champions in mental health settings. Smoking cessation champions can raise awareness of health related issues of tobacco use, the benefits of reduced tobacco intake and abstinence and inform service users of the national QUIT campaign.

8.2.2 Monitoring physical effects of psychotropic medication

III. The development of a coherent approach to monitoring the adverse effects of prescribed psychotropic medication. This can take two forms; (i) the initial screening when psychotropic medication is prescribed and (ii) ongoing monitoring of physical medication side effects.

The adoption of the NICE (2014A,B) guidelines, which recommend that prior to commencing psychotropic medication a baseline physical health check is complete and ongoing screening for indicators of key physical health issues undertaken e.g.

I. weight and waist measurements
II. pulse and blood pressure
III. general health (including some blood tests and asking whether you eat healthily and take regular exercise).
IV. an electrocardiogram (ECG)
Ongoing screening or medication monitoring for key physical conditions is also recommended e.g. in NICE guidelines for Bipolar Disorder (2014) the recommendation is to, at the earliest opportunity, “…identify people with bipolar disorder who have:

I. hypertension  
II. have abnormal lipid levels  
III. are obese or at risk of obesity  
IV. have diabetes or are at risk of diabetes (as indicated by abnormal blood glucose levels)  
V. or are physically inactive.”

The Department of Health and Children in their report *Building a Culture of Patient Safety* (DH&C 2008) concluded that clinical audit should be viewed as an essential and integral component of professional practice and thus contribute to improved patient outcomes. To ensure high standards of practice and quality of care in this area, clinical audit of practice is recommended.

**8.2.3 Developing care pathways**

I. The development of clear and coherent care pathways for referral and treatment of co-morbid conditions such as type-2 diabetes and dyslipidaemia. The development of practice care registers to monitor the physical health of those with SMI in primary care is recommended by NICE (2014A,B) as this not only helps monitor physical health but also facilitates communication and support across service boundaries so that gaps in service provision and follow-up can be narrowed.

**8.3 Recommendations for practitioner education**

As a priority we recommend the education and training of the workforce in the area of documentation and reporting of risk factors for physical illness. The importance of accurate and timely screening and documentation of physical health risk factors feeds back into other recommendations in this report.

We recommend that the issue of medical co-morbidity and SMI be made more explicit in undergraduate education curricula for nursing curricula, medical practitioners in psychiatry and trainee GPs.
8.4 Recommendations for moving forward

The issue of co-morbidity in SMI has been the subject of some research in Ireland (see Appendix 8 for a short review). Co-morbidity and SMI should be incorporated into the HSE Mental Health Division Service Priorities plan. We therefore recommend the development of an action plan, time frame for achievement and working group to move all recommendations forward.

Consensus building in this area is urgently needed and setting up a working group would combine the expertise and experience of primary care and mental health practitioners in the development of a strategy for the management of co-morbidity in SMI. This would explore models of service organisation and delivery and clarification of roles and responsibilities. A key outcome of this group would be the development of SMI co-morbidity practice registers to monitor the physical health of those with SMI and to help facilitate communication and support across service boundaries to reduce potential gaps in service provision.

9. Conclusion

The DRC (2006) stated that an individual with a major mental health problem is more likely to develop a significant illness such as diabetes, CHD, stroke or respiratory disease than other citizens, more likely to develop it before 55, and – once they have it – more likely to die of it within five years. In light of this, the issue of co-morbidity of physical health in people with SMI is related to Tudor Hart’s (1971, p405) “inverse care law”, which states that “the availability of good medical care tends to vary inversely with the need for the population served.” Worryingly, therefore, despite the high levels of physical health co-morbidity in people with SMI, the level of medical care available to address these issues is limited.

This report has illustrated the increased levels of co-morbidity of physical conditions in people with SMI and endeavoured to contextualise this within an Irish context. What was found was that there are potentially higher levels of conditions such as type-2 diabetes, stroke and hypertension in people with SMI, but that these occur at a much younger age than the Irish general population. Exposure to risk factors such as
smoking is also increased in people with SMI when compared to the Irish general population.

Higher mortality rates are not confined to unnatural causes such as suicide, but result from natural causes also. Osborn (2001) notes increased mortality rates from natural causes in people with mental health problems such as schizophrenia and affective disorders including depression.

There is a great opportunity to now address these health inequalities in this marginalised and often socially excluded group through the recommendations outlined within this report.
References


## List of Appendices

<table>
<thead>
<tr>
<th>Appendix One</th>
<th>Project search strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix Two</td>
<td>Prevalence and risk factor studies- data extraction and study characteristics</td>
</tr>
<tr>
<td>Appendix Three</td>
<td>Effectiveness studies- data extraction and study characteristics</td>
</tr>
<tr>
<td>Appendix Four</td>
<td>Prevalence and risk factor studies- study references</td>
</tr>
<tr>
<td>Appendix Five</td>
<td>Prevalence and risk factor studies- supplementary tables</td>
</tr>
<tr>
<td>Appendix Six</td>
<td>Effectiveness studies- study references</td>
</tr>
<tr>
<td>Appendix Seven</td>
<td>Effectiveness studies- supplementary tables</td>
</tr>
<tr>
<td>Appendix Eight</td>
<td>Physical co-morbidity in SMI: Research in Ireland</td>
</tr>
</tbody>
</table>
Appendix 1 Project Search Strategy

Search Terms for Prevalence and Risk Factor Studies

As both prevalence and risk factor data overlapped between prevalence and risk factor studies, search terms were similarly developed for these two types of study categories. These studies were then collectively screened for eligibility for inclusion in the review, and tagged appropriately as prevalence only data, risk factor only data and both prevalence and risk factor data.

**Pubmed MeSH Search:**
1. ((("Affective Disorders, Psychotic"[Mesh]) OR "Depressive Disorder"[Mesh]) OR "Schizophrenia and Disorders with Psychotic Features"[Mesh])
   AND
2. ((("Cardiovascular Diseases"[Mesh]) OR "Diabetes Mellitus"[Mesh]) OR "Respiration Disorders"[Mesh]) OR "Neoplasms"[Mesh]) OR "Obesity"[Mesh])
   AND
3. (Prevalence OR Prevalences OR Occurrence OR occurrences OR incidence OR incidences OR frequency OR instance OR instances OR occurred OR occurring OR existent OR extent)[tiab]
   AND
4. #1 AND #2 AND (predictive OR prediction OR correlation OR observational OR Expected OR expectation OR observed OR predictive OR predicting OR expecting OR observing)[tiab]

**CINAHL Search:**
1. (MH "Psychotic Disorders+") OR (MH "Depression+")
   AND
2. (MH "Cardiovascular Diseases+") OR (MH "Diabetes Mellitus+") OR (MH "Respiration Disorders+") OR (MH "Neoplasms+") OR (MH "Obesity+")
   AND
3. (Prevalence OR Prevalences OR Occurrence OR occurrences OR incidence OR incidences OR frequency OR instance OR instances OR occurred OR occurring OR existent OR extent)[tiab]
   AND
4. #1 AND #2 AND (predictive OR prediction OR correlation OR observational OR Expected OR expectation OR observed OR predictive OR predicting OR expecting OR observing)[tiab]

**PsychInfo Search:**
1. DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Catatonic Schizophrenia" OR DE "Childhood Schizophrenia" OR DE "Paranoid Schizophrenia" OR DE "Process Schizophrenia" OR DE "Schizophrenia (Disorganized Type)" OR DE "Schizophreniform Disorder" OR DE "Undifferentiated Schizophrenia" OR DE "Major Depression" OR DE "ANAclitic Depression" OR DE "Dysthymic Disorder" OR DE "Endogenous Depression" OR DE "Postpartum Depression" OR DE "Reactive Depression" OR DE "Recurrent Depression" OR DE "Treatment Resistant Depression" OR DE "Bipolar Disorder" OR DE "Cyclothymic Personality"

AND

3. (Prevalence OR Prevalences OR Occurrence OR occurrences OR incidence OR incidences OR frequency OR instance OR instances OR occurred OR occurring OR existent OR extent)[tiab]

4. #1 AND 2 AND (predictive OR prediction OR correlation OR observational OR Expected OR expectation OR observed OR predictive OR predicting OR expecting OR observing)[tiab]

**Embase Search:**

1. 'depression'/exp OR 'psychosis'/exp OR 'schizophrenia'/exp

AND

2. 'cardiovascular disease'/exp OR 'diabetes mellitus'/exp OR 'breathing disorder'/exp OR 'neoplasm'/exp OR 'obesity'/exp

AND

3. (Prevalence OR Prevalences OR Occurrence OR occurrences OR incidence OR incidences OR frequency OR instance OR instances OR occurred OR occurring OR existent OR extent)[tiab]

4. #1 AND #2 AND (predictive OR prediction OR correlation OR observational OR Expected OR expectation OR observed OR predictive OR predicting OR expecting OR observing)[tiab]

**Searches Terms for Effectiveness Studies**

**Pubmed MeSH Search:**

1. ((("Affective Disorders, Psychotic"[Mesh]) OR "Depressive Disorder"[Mesh]) OR "Schizophrenia and Disorders with Psychotic Features"[Mesh]))

AND

2. ((("Cardiovascular Diseases"[Mesh]) OR "Diabetes Mellitus"[Mesh]) OR "Respiration Disorders"[Mesh]) OR "Neoplasms"[Mesh]) OR "Obesity"[Mesh])

AND

3. Intervention OR interventions OR “alternative intervention*” OR “standard care” OR “no intervention*” OR monitor*OR manage* OR psychosocial OR psycho-social OR education* OR “medication type” OR “health promotion*”

AND

4. “Randomized Controlled Trial*” OR “cluster trial*” OR “systematic review*” OR “random allocation*” OR “non-randomised controlled trials*” OR “controlled clinical trial*” OR “Clinical Trial*” OR “controlled before-and-after studies” OR “controlled before-and-after study” OR “Pragmatic Clinical Trial*” OR randomly[tiab] OR “randomly allocated” OR allocated OR randomly OR randomly
CINAHL Search:
1. (MH "Psychotic Disorders+") OR (MH "Depression+)")
AND
2. (MH "Cardiovascular Diseases+") OR (MH "Diabetes Mellitus+") OR (MH "Respiration Disorders+") OR (MH "Neoplasms+") OR (MH "Obesity+")
AND
3. Intervention OR interventions OR “alternative intervention**” OR “standard care” OR “no intervention**” OR monitor* OR manage* OR psychosocial OR psycho-social OR education* OR “medication type” OR “health promotion**”
AND
4. “Randomized Controlled Trial***” OR “cluster trial***” OR “systematic review***” OR “random allocation***” OR “non-randomised controlled trials***” OR “controlled clinical trial” OR “Clinical Trial***” OR “controlled before-and-after studies” OR “controlled before-and-after study” OR “Pragmatic Clinical Trial***” OR randomly[tiab] OR “randomly allocated” OR allocated OR randomly OR “random allocation” OR (random* AND trial*) OR “clinical trials randomized” [tiab] OR randomised [tiab]

PsychInfo Search:
1. DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Catatonic Schizophrenia" OR DE "Childhood Schizophrenia" OR DE "Paranoid Schizophrenia" OR DE "Process Schizophrenia" OR DE "Schizophrenia (Disorganized Type)" OR DE "Schizophreniform Disorder" OR DE "Undifferentiated Schizophrenia" OR DE "Major Depression" OR DE "Anxiety Disorders" OR DE "Dysthymic Disorder" OR DE "Major Depression" OR DE "Postpartum Depression" OR DE "Reactive Depression" OR DE "Recurrent Depression" OR DE "Treatment Resistant Depression" OR DE "Bipolar Disorder" OR DE "Cyclothymic Personality"
AND
AND
3. Intervention OR interventions OR “alternative intervention**” OR “standard care” OR “no intervention**” OR monitor* OR manage* OR psychosocial OR psycho-social OR education* OR “medication type” OR “health promotion**”
AND
4. “Randomized Controlled Trial***” OR “cluster trial***” OR “systematic review***” OR “random allocation***” OR “non-randomised controlled trials***” OR “controlled clinical trial” OR “Clinical Trial***” OR “controlled before-and-after studies” OR “controlled before-and-after study” OR “Pragmatic Clinical Trial***” OR randomly[tiab] OR “randomly allocated” OR allocated OR randomly OR
“random allocation” OR (random* AND trial*) OR “clinical trials randomized” [tiab] OR randomised [tiab]

Embase Search:
1. 'depression'/exp OR 'psychosis'/exp OR 'schizophrenia'/exp
   AND
2. 'cardiovascular disease'/exp OR 'diabetes mellitus'/exp OR 'breathing disorder'/exp OR 'neoplasm'/exp OR 'obesity'/exp
   AND
3. Intervention OR interventions OR “alternative intervention*” OR “standard care” OR “no intervention*” OR monitor* OR manage* OR psychosocial OR psycho-social OR education* OR “medication type” OR “health promotion*”
   AND
4. Randomized Controlled Trial OR cluster trial OR systematic review OR random allocation OR non-randomised controlled trials OR controlled clinical trial OR Clinical Trial OR controlled before-and-after studies OR controlled before-and-after study OR Pragmatic Clinical Trial OR randomly:ab OR randomly allocated:ab OR allocated:ab OR randomly:ab OR random allocation:ab OR (random* AND trial*) OR clinical trials randomized:ab OR randomise:ab

Results of Searches (i.e. number of citations)

<table>
<thead>
<tr>
<th>Study Categories</th>
<th>Pubmed</th>
<th>CINAHL</th>
<th>PsychInfo</th>
<th>Embase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence (strings combined and limiters applied)</td>
<td>1428</td>
<td>390</td>
<td>910</td>
<td>1510</td>
</tr>
<tr>
<td>Risk Factors (strings combined and limiters applied)</td>
<td>905</td>
<td>302</td>
<td>683</td>
<td>920</td>
</tr>
<tr>
<td>Effectiveness (strings combined and limiters applied)</td>
<td>285</td>
<td>182</td>
<td>199</td>
<td>44</td>
</tr>
</tbody>
</table>
### Appendix 2 – Prevalence and risk factor studies - data extraction and study characteristics

<table>
<thead>
<tr>
<th>Author</th>
<th>Population (hospital, out-pt etc)</th>
<th>N</th>
<th>Age (M, SD, range)</th>
<th>Sex</th>
<th>Country</th>
<th>Medication</th>
<th>Mental Illness &amp; risk factors</th>
<th>Physical Illness(es)</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aquila (2000)</td>
<td>Residents in an adult care facility for formerly homeless persons with SMI</td>
<td>32</td>
<td>24.6-65.7, M=46.9, SD=9.1</td>
<td>19/32 male (59%)</td>
<td>USA</td>
<td>All taking atypical antipsychotics</td>
<td>Schizophrenia</td>
<td>Hypertension, DM, Obesity, Smoking, Dyslipidaemia,</td>
<td>2/6</td>
</tr>
<tr>
<td>Argo (2011)</td>
<td>Outpatients at Adult Psychiatry Clinic</td>
<td>202</td>
<td>&gt;=18, M=38.0, SD=10.8</td>
<td>135/192 male (70.3%)</td>
<td>USA</td>
<td>All taking atypical antipsychotics</td>
<td>Schizophrenia</td>
<td>Hypertension, DM, dyslipidaemia</td>
<td>4/6</td>
</tr>
<tr>
<td>Bell (2009)</td>
<td>Collection of clinical information from pts enrolled in OPD clinics</td>
<td>819</td>
<td>M=47.1, SD=12.2</td>
<td>573/819 male (70%)</td>
<td>USA</td>
<td>All taking second generation antipsychotics</td>
<td>Schizophrenia</td>
<td>Hypertension, DM, obesity, dyslipidaemia, impaired fasting glucose</td>
<td>6/6</td>
</tr>
<tr>
<td>Bernardo (2009)</td>
<td>In-patients of short-stay hospitalisation units</td>
<td>733</td>
<td>&gt;=18, M=37.8, SD=11.3</td>
<td>526/733 male (71.8%)</td>
<td>Spain</td>
<td>Second generation antipsychotics</td>
<td>Schizophrenia</td>
<td>CVD, DM, obesity, smoking</td>
<td>5/6</td>
</tr>
<tr>
<td>Birkenaes (2007)</td>
<td>Clinical groups from Oslo TOP study (patients with severe mental disorders from all health care sectors)</td>
<td>110 (BP) 163 (scz)</td>
<td>18-65, M=38.7, SD=11.9 (BP) 18-65, M=33.6, SD=10.3 (scz)</td>
<td>43/110 male (39.1%; BP) 94/163 male (57.7%; scz)</td>
<td>Norway</td>
<td>45.5% min. 1 antipsychotic (BP) 92% min. 1 antipsychotic (scz)</td>
<td>Bipolar disorder and schizophrenia</td>
<td>DM, obesity, smoking</td>
<td>6/6</td>
</tr>
<tr>
<td>Bresee (2010)</td>
<td>Population based cohort from Alberta administrative databases</td>
<td>287552 (24347 aged 20-59)</td>
<td>&gt;=20, 20-107, M=47.6, SD=16.7: data extracted for those aged 20-59yrs where possible</td>
<td>14596/28755 male (50.8%)</td>
<td>Canada</td>
<td>Not stated</td>
<td>Schizophrenia</td>
<td>CVD, hypertension, stroke, MI/IHD/arrhythmia, DM, dyslipidaemia</td>
<td>6/6</td>
</tr>
<tr>
<td>Author</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>Age</td>
<td>Sex</td>
<td>Country</td>
<td>Diagnosis</td>
<td>Other Conditions</td>
<td>Morbidity</td>
<td>Reference</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-------------</td>
<td>-----</td>
<td>-----</td>
<td>---------</td>
<td>-----------</td>
<td>-----------------------------------------------------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Callaghan (2009)</td>
<td>Based upon inpatient discharge records</td>
<td>11392</td>
<td>&gt;=18, M=41.0, SD=14.0</td>
<td>7399/11392 male (64.9%)</td>
<td>Canada</td>
<td>Schizophrenia</td>
<td>DM, obesity, lipid disorder, smoking</td>
<td>6/6</td>
<td></td>
</tr>
<tr>
<td>Callaghan (2010)</td>
<td>Based upon hospital discharge records</td>
<td>6490</td>
<td>&gt;=18, M=42.0, SD=14.4</td>
<td>2756/6490 (40.5%)</td>
<td>Canada</td>
<td>Bipolar</td>
<td>DM, obesity, dyslipidaemia</td>
<td>5/6</td>
<td></td>
</tr>
<tr>
<td>Carney (2006a)</td>
<td>Subjects with schizophrenia or schizoaffective disorder who filed at least 1 claim for medical services, 1996-2001</td>
<td>1074</td>
<td>18-64, M=40.2, SD=11.9</td>
<td>505/1074 male (47%)</td>
<td>USA</td>
<td>Schizophrenia</td>
<td>Hypertension, IHD, stroke, heart failure, cardiac arrhythmia, peripheral VD, DM, COPD, asthma, obesity, dyslipidaemia</td>
<td>6/6</td>
<td></td>
</tr>
<tr>
<td>Carney (2006b)</td>
<td>Sample of administrative claims from Wellmark Blue Cross Blue Shield, 1996-2001</td>
<td>3557</td>
<td>18-64, M=39.3, SD=11.8</td>
<td>1395/3557 male (39.2%)</td>
<td>USA</td>
<td>Bipolar</td>
<td>Hypertension, IHD, stroke, heart failure, cardiac arrhythmia, peripheral VD, valvular disease, DM, asthma, chronic lung disease, cancer, lymphoma, obesity, dyslipidaemia</td>
<td>6/6</td>
<td></td>
</tr>
<tr>
<td>Chien (2010)</td>
<td>Subjects with primary diagnosis of bipolar disorder with at least one service claim during 2005 from National Health Research Institute database</td>
<td>1848 (1516 aged 18-59)</td>
<td>&gt;=18: data extracted for those aged 18-59 where possible</td>
<td>806/1848 male (43.6%)</td>
<td>Taiwan</td>
<td>Bipolar</td>
<td>DM</td>
<td>5/6</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Patients</td>
<td>Demographics</td>
<td>Diagnosis</td>
<td>Country</td>
<td>Other Conditions</td>
<td>N/A</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>
<td></td>
</tr>
<tr>
<td>Chien (2012)</td>
<td></td>
<td>Subjects with primary diagnosis of MDD with at least one service claim during 2005 from National Health Research Institute database</td>
<td>4593 (3531 aged 18-59)</td>
<td>1646/4593 male (35.8%)</td>
<td>Taiwan</td>
<td>Not stated</td>
<td>MDD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohen (2006a)</td>
<td></td>
<td>Patients from 5 different long-stay wards</td>
<td>266 (222 aged 20-59)</td>
<td>172/266 male (64.7%)</td>
<td>The Netherlands</td>
<td>40.7% on typical antipsychotics 59.3% on atypical antipsychotics</td>
<td>Schizophrenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohen (2006b)</td>
<td></td>
<td>Unselected in- and out-patients</td>
<td>200</td>
<td>140/200 Male (70%)</td>
<td>The Netherlands</td>
<td>N=55 typical N=133 atypical</td>
<td>schizophrenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coodin (2001)</td>
<td></td>
<td>Patients received treatment in a hospital-based program for persons with schizophrenia</td>
<td>183</td>
<td>120/183 men (65.6%)</td>
<td>Canada</td>
<td>Not stated</td>
<td>Schizophrenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darba (2013)</td>
<td>Retrospective, cross-sectional multicenter study of patients receiving oral antipsychotic treatment</td>
<td>1452</td>
<td>863/1452 men (60.9%)</td>
<td>Receiving oral antipsychotic treatment &gt;=12 weeks</td>
<td>Spain</td>
<td>Schizophrenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fagiolini (2002)</td>
<td>Data from the Pittsburgh Study of Maintenance Therapies in Bipolar Disorder, a randomised controlled long-</td>
<td>50</td>
<td>22/50 male (44%)</td>
<td>94% lithium in acute treatment 90% lithium in maintenance treatment</td>
<td>USA</td>
<td>Bipolar</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>term treatment</th>
<th>study/trial</th>
<th>sample size</th>
<th>M, SD</th>
<th>% male</th>
<th>country</th>
<th>medication</th>
<th>diagnosis</th>
<th>adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fairuz (2007)</td>
<td>Cross sectional study of hospital patients</td>
<td>85</td>
<td>18-65, M=37, SD=11</td>
<td>45/85 male (53%)</td>
<td>Malaysia</td>
<td>40/85 atypical antipsychotics 41/85 conventional antipsychotics</td>
<td>Schizophrenia</td>
<td>DM, impaired fasting glucose</td>
</tr>
<tr>
<td>Fiedorowicz (2008)</td>
<td>Outpatients seen for a primary diagnosis of bipolar disorder from an adult OPD psychiatry clinic at a tertiary care hospital</td>
<td>217</td>
<td>M=46.3, SD=15</td>
<td>80/217 male (37%)</td>
<td>USA</td>
<td>Mood stabilisers and antidepressants prescribed to majority of patients</td>
<td>Bipolar</td>
<td>Hypertension, DM, obesity, dyslipidemaemia</td>
</tr>
<tr>
<td>Fleischhack (2013)</td>
<td>First-episode, partially antipsychotic-naïve pts with scz</td>
<td>498</td>
<td>18-40, M=m25.6, SD=5.5 Female M=26.5, SD=5.7</td>
<td>298/498 male (59.8%)</td>
<td>Europe</td>
<td>Not stated</td>
<td>Schizophrenia</td>
<td>Hypertension, DM, obesity</td>
</tr>
<tr>
<td>Goldstein (2009)</td>
<td>Respondents of the cross sectional National Epidemiologic Survey on Alcohol and Related Conditions</td>
<td>1411 (BP) 6831 (MDD)</td>
<td>&gt;=18 BP: M=38.1, SE=0.2 MDD: M=43.8, SE=0.1</td>
<td>BP: 648/1411 male (45.9%) MDD: 2295/6831 male (33.6%)</td>
<td>USA</td>
<td>Not stated</td>
<td>Bipolar and MDD</td>
<td>CVD, hypertension, obesity, smoking</td>
</tr>
<tr>
<td>Goldstein (2011)</td>
<td>Respondents of the cross sectional National Epidemiologic Survey on Alcohol and Related Conditions</td>
<td>1905 (BP) 5695 (MDD)</td>
<td>&gt;=18 BP: M=37.15, SE=0.41 MDD: M=43.97, SE=0.26</td>
<td>BP: 854.1905 male (44.8%) MDD: 1860/5695 male (32.7%)</td>
<td>USA</td>
<td>Not stated</td>
<td>Bipolar and MDD</td>
<td>Hypertension, MI, angina, atherosclerosis, tachycardia, other heart disease, obesity, smoking</td>
</tr>
<tr>
<td>Gomes (2013)</td>
<td>Cross-sectional recruited from the Bipolar Research</td>
<td>159</td>
<td>&gt;=18, M=43.5, SD=12</td>
<td>52/159 male (32.7%)</td>
<td>Brazil</td>
<td>Any mood stabiliser 88%</td>
<td>Bipolar</td>
<td>Hypertension, DM, obesity</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Design</td>
<td>Sample</td>
<td>Mean Age</td>
<td>Gender</td>
<td>Country</td>
<td>Diagnoses</td>
<td>Medications</td>
<td>Other Conditions</td>
</tr>
<tr>
<td>-------------</td>
<td>--------</td>
<td>--------</td>
<td>----------</td>
<td>--------</td>
<td>---------</td>
<td>-----------</td>
<td>-------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Jerrell (2010)</td>
<td>Medical and pharmacy claims</td>
<td>2231</td>
<td>18-54, 51% &gt;= 40 yrs</td>
<td>USA</td>
<td>Newly prescribed one of seven antipsychotic medications</td>
<td>Schizophrenia</td>
<td>Hypertension, DM, obesity, dyslipidaemia</td>
<td>5/6</td>
</tr>
<tr>
<td>Kim (2009)</td>
<td>Patients hospitalised for treatment of acute mood disorders</td>
<td>184</td>
<td>19-64, M=38.0, SD=13.2</td>
<td>Korea</td>
<td>114/184 on psychotropic medications (62%)</td>
<td>Bipolar</td>
<td>Dyslipidaemia, hyperglycaemia</td>
<td>4/6</td>
</tr>
<tr>
<td>Levitan (2012)</td>
<td>Data from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions</td>
<td>5092</td>
<td>18-65 Classic: M=42.0, SD=12.1 Atypical: M=39.3, SD=12.6 Undifferentiated: M=41.3, SD=12.4</td>
<td>USA</td>
<td>Not stated</td>
<td>Depression</td>
<td>Obesity</td>
<td>5/6</td>
</tr>
<tr>
<td>Li (2012)</td>
<td>Cohort study using a nationwide database</td>
<td>1003</td>
<td>M=41.22, SD=14.51</td>
<td>Taiwan</td>
<td>Not stated</td>
<td>Depression</td>
<td>Hypertension, stroke, DM, dyslipidaemia</td>
<td>6/6</td>
</tr>
<tr>
<td>Limosin (2008)</td>
<td>Baseline data from a national survey</td>
<td>5692</td>
<td>M=37.1, SD=11.8</td>
<td>France</td>
<td>1358/5962 no treatment</td>
<td>schizophrénia</td>
<td>Obesity</td>
<td>5/6</td>
</tr>
<tr>
<td>Authors</td>
<td>Study details</td>
<td>Sample size</td>
<td>Mean Age (SD)</td>
<td>Gender</td>
<td>Country</td>
<td>Diagnosis</td>
<td>Comorbidities</td>
<td>Notes</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-------------</td>
<td>---------------</td>
<td>--------</td>
<td>----------</td>
<td>----------------------------</td>
<td>----------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Maina (2008)</td>
<td>Data retrospectively obtained from clinical charts of drug-naïve patients</td>
<td>76</td>
<td>M=26.5, SD=4.8</td>
<td>33/76 male (43.4%)</td>
<td>Italy</td>
<td>Drug naive</td>
<td>Bipolar</td>
<td>Obesity</td>
</tr>
<tr>
<td>Mookhoek (2011)</td>
<td>Residential patients in a psychiatric center (data extracted for schizophrenia pts only where possible)</td>
<td>256</td>
<td>M=48, SD=12.2</td>
<td>177/256 male (69.1%)</td>
<td>The Netherlands</td>
<td>Not stated</td>
<td>Schizophrenia</td>
<td>DM, obesity</td>
</tr>
<tr>
<td>Ono (2013)</td>
<td>Inpatients</td>
<td>258</td>
<td>18-65, M=40.0, SD=12.8</td>
<td>146/256 male (57.0%)</td>
<td>Japan</td>
<td>All receiving antipsychotics during the 3-week period before the study</td>
<td>Schizophrenia</td>
<td>DM, impaired fasting glucose</td>
</tr>
<tr>
<td>Papakostas (2005)</td>
<td>Outpatients enrolled in a medication trial</td>
<td>369</td>
<td>18-65, M=39.8, SD=10.4</td>
<td>170/369 male (46.1%)</td>
<td>USA</td>
<td>Medication free for at least 2 wks</td>
<td>Depression</td>
<td>Obesity</td>
</tr>
<tr>
<td>Protopopova (2012)</td>
<td>Subjects treated in outpatient clinic that specialised in psychoses</td>
<td>129</td>
<td>M=36, SD=11.9</td>
<td>77/129 (60%)</td>
<td>Czech Republic</td>
<td>96% (n=125) treated with antipsychotics 89% used atypical antipsychotics</td>
<td>Schizophrenia</td>
<td>CVD, hypertension, DM, dyslipidaemia, smoking</td>
</tr>
<tr>
<td>Seldenrijk (2015)</td>
<td>Longitudinal study of depression and</td>
<td>2510, of which</td>
<td>18-65, M=41.7, SD=12.7</td>
<td>93/261 male (35.6%)</td>
<td>The Netherlands</td>
<td>62.1% no or infrequent use</td>
<td>Depression</td>
<td>Hypertension, DM, smoking</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Mean Age</td>
<td>% Male</td>
<td>Country</td>
<td>Diagnosis</td>
<td>Control</td>
<td>N =</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
<td>--------------</td>
<td>----------</td>
<td>--------</td>
<td>---------</td>
<td>-----------</td>
<td>---------</td>
<td>-----</td>
</tr>
<tr>
<td>Stubbs (2015)</td>
<td>Systematic review, mixed populations</td>
<td>145718</td>
<td>Mean age ranged from 22.5 to 54.4</td>
<td>% of male participants ranged from 42% to 89%</td>
<td>Australia, Canada, China, Finland, India, Japan, Singapore, Spain, Taiwan, UK, USA, Worldwide</td>
<td>Limited information</td>
<td>Schizophrenia, DM</td>
<td>35/44</td>
</tr>
<tr>
<td>Subramaniam (2014)</td>
<td>Mainly recruited from outpatients clinics following referrals from psychiatrist</td>
<td>973</td>
<td>M=41.7, SD=11.0</td>
<td>525/973 male (54.0%)</td>
<td>Singapore</td>
<td>419/917 atypical med, 332/917 typical, 159/917 atypical and typical</td>
<td>Schizophrenia, Obesity</td>
<td>5/6</td>
</tr>
<tr>
<td>Sugawara (2013)</td>
<td>Outpatients from four psychiatric hospitals</td>
<td>225</td>
<td>M=42.5, SD=12.8</td>
<td>106/225 male (47.1%)</td>
<td>Japan</td>
<td>Not stated</td>
<td>Schizophrenia, Obesity</td>
<td>5/6</td>
</tr>
<tr>
<td>Topic (2013)</td>
<td>Patients with recurrent depressive disorder</td>
<td>76</td>
<td>M=51.42, SD=8.5</td>
<td>Not stated</td>
<td>Croatia</td>
<td>Not stated</td>
<td>Depression, CVD, DM, asthma, dyslipidaemia</td>
<td>4/6</td>
</tr>
<tr>
<td>Vancampfort (2013)</td>
<td>Inpatients of a psychiatric centre</td>
<td>106</td>
<td>18-65</td>
<td>69/106 male (65.1%)</td>
<td>Belgium</td>
<td>1 (0.9%) no antipsychotic</td>
<td>Schizophrenia, DM</td>
<td>5/6</td>
</tr>
</tbody>
</table>
Pre-diabetic: M=38.0, SD=8.5  
Diabetic:  M=40.3, SD=10.9

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Description</th>
<th>Sample Size</th>
<th>Mean Age</th>
<th>SD</th>
<th>Treated with Antipsychotic Medications</th>
<th>Disease</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Winkel (2008)</td>
<td>Patients at psychiatric hospital and affiliate services</td>
<td>60</td>
<td>M=45.3, SD=13.0</td>
<td>26/60 (43.3%)</td>
<td>Belgium</td>
<td>Bipolar</td>
<td>DM, pre-diabetes</td>
</tr>
<tr>
<td>Vogelzangs (2010)</td>
<td>Recruited from community, general practice, and secondary mental health care</td>
<td>2315, of which 1959 depressive disorder (data on depression only used, where possible)</td>
<td>18-65, M=41.8, SD=13.0</td>
<td>778/2315 male (33.6%)</td>
<td>The Netherlands</td>
<td>Not stated</td>
<td>Depression, CVD</td>
</tr>
</tbody>
</table>
## Appendix 3- Effectiveness studies- data extraction and study characteristics

<table>
<thead>
<tr>
<th>Systematic Reviews</th>
<th>Author (year)</th>
<th>Aim of review</th>
<th>Intervention</th>
<th>Control</th>
<th>No. studies</th>
<th>No. participants</th>
<th>Outcome measures</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faulkner (2003)</td>
<td>To systematically review the literature on the effectiveness of interventions designed to control weight gain in schizophrenia</td>
<td>10 pharmacological interventions and 6 behavioural</td>
<td>9 studies included control group</td>
<td>16</td>
<td>453</td>
<td>Weight</td>
<td>30/44</td>
<td></td>
</tr>
<tr>
<td>Faulkner (2007)</td>
<td>To determine the effects of both pharmacological (excluding antipsychotic medication switching) and non-pharmacological strategies (diet/exercise) for reducing or preventing weight gain in people with schizophrenia</td>
<td>5 cognitive/behavioural intervention and 18 with pharmacological adjunct</td>
<td>All studies included control group</td>
<td>23</td>
<td>1037</td>
<td>Weight or another indicator of body mass</td>
<td>39/44</td>
<td></td>
</tr>
<tr>
<td>Firth (2015)</td>
<td>To establish the effectiveness of exercise for improving physical and mental health outcomes in schizophrenia patients</td>
<td>Various forms of exercise including yoga, aerobic-resistance training, gym access, soccer training, etc.,</td>
<td>All but 3 studies included control group</td>
<td>20 studies with data from 17 trials</td>
<td>659</td>
<td>Weight</td>
<td>36/44</td>
<td></td>
</tr>
<tr>
<td>Hjorth (2014)</td>
<td>To review controlled intervention studies on reducing overweight/obesity and/or reducing physical illness in patients with schizophrenia</td>
<td>Various: diet, exercise, cognitive behavioural therapy, or mixed combination of the three</td>
<td>All studies included control group</td>
<td>23</td>
<td>Not stated for 2 studies included so no total calculated</td>
<td>Weight</td>
<td>24/44</td>
<td></td>
</tr>
<tr>
<td>Tsoi (2013)</td>
<td>To examine efficacy of different interventions on smoking cessation and reduction, and assess any harmful effect of</td>
<td>Various: smoking cessation, smoking reduction, nicotine patch for relapse prevention, and trials</td>
<td>All studies included control group</td>
<td>34</td>
<td>2206</td>
<td>Smoking abstinence</td>
<td>42/44</td>
<td></td>
</tr>
<tr>
<td>Author (year)</td>
<td>Aim of study</td>
<td>Location/setting</td>
<td>Intervention</td>
<td>Control</td>
<td>No. participants</td>
<td>Outcome measures</td>
<td>Quality score</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>Chou (2004)</td>
<td>To evaluate the effectiveness of the nicotine-patch therapy for smoking cessation in patients with schizophrenia</td>
<td>Participants enrolled from day care ward of psychiatric hospital</td>
<td>8-week program of nicotine-patch therapy</td>
<td>Did not receive any other similar activity during study period</td>
<td>68</td>
<td>No. of cigarettes and carbon monoxide level</td>
<td>7/9</td>
<td></td>
</tr>
<tr>
<td>Heggelund (2011)</td>
<td>To investigate effects from high intensity training on peak oxygen uptake, net mechanical efficiency of walking, and risk factors for cardiovascular disease in patients with schizophrenia</td>
<td>Inpatients of University hospital</td>
<td>4x4-min interval training on a treadmill interspersed with 3 min of active resting periods. Training sessions 3 times per week for 8 weeks</td>
<td>Physical inactivity in the form of playing computer games</td>
<td>19</td>
<td>Weight, BMI, blood pressure, cholesterol, glucose</td>
<td>4/9</td>
<td></td>
</tr>
<tr>
<td>Kilbourne (2013)</td>
<td>To determine whether the Life Goals Collaborative Care (LGCC) intervention compared to enhanced usual care, reduced CVD risk factors and improved physical and mental health outcomes in patients with bipolar disorder</td>
<td>Recruited from mental health outpatient clinic and primary care outpatient clinic</td>
<td>Self-management sessions by health specialist (4 group sessions), care management by health specialist, clinical registry tracking, and guideline support</td>
<td>Received regular mailings regarding wellness topics in addition to standard mental health and medical treatment</td>
<td>116</td>
<td>BMI, blood pressure, cholesterol</td>
<td>7/9</td>
<td></td>
</tr>
<tr>
<td>McKibbin (2010)</td>
<td>To test the sustained impact of a 6-month diabetes management intervention in middle-aged and older adults with</td>
<td>Board-and-care and community clubhouse settings</td>
<td>24-week intervention with three modules: basic diabetes education; usual care and three brochures from the American Diabetes</td>
<td></td>
<td>52</td>
<td>Weight, BMI, glucose</td>
<td>8/9</td>
<td></td>
</tr>
<tr>
<td>Author (year)</td>
<td>Aim of study</td>
<td>Location/setting</td>
<td>Treatment</td>
<td>Comparator (if applicable)</td>
<td>No. participants</td>
<td>Outcome measures</td>
<td>Quality score</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>Centorrino (2006)</td>
<td>To study the impact of an intensive 24-week program of diet, exercise and counselling in 17 chronically psychotic patients who entered at average weight and BMI</td>
<td>Recruited using flyers on hospital grounds</td>
<td>24-week program of diet (1600 &amp; 2000 calorie diet for women &amp; men respectively), exercise (45 minute sessions of individualised fitness training) and nutritional counselling (45 minutes sessions), with sessions twice weekly</td>
<td>N/A</td>
<td>17</td>
<td>Weight, BMI, blood pressure, cholesterol, glucose</td>
<td>4/7</td>
<td></td>
</tr>
<tr>
<td>Weiner (2001)</td>
<td>To examine the efficacy, tolerability, and safety of supportive group psychotherapy and adjunctive sustained-release bupropion for nicotine addiction in patients with schizophrenia.</td>
<td>Outpatients from psychiatric research centre</td>
<td>14-week treatment phase: nine sessions of weekly group therapy led by clinic nurses trained in the educational model of the American Cancer Society Fresh Start Program, modified for patients with schizophrenia</td>
<td>N/A</td>
<td>8</td>
<td>Carbon monoxide level</td>
<td>6/7</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4 – Prevalence and risk factor studies: study references


### Appendix 5: Prevalence and risk factor studies - supplementary tables

#### Table 5.1: Pooled prevalence rates for physical ill-health conditions in people with schizophrenia

<table>
<thead>
<tr>
<th>Condition</th>
<th>PP (%)</th>
<th>Range (%)</th>
<th>95% CI (%)</th>
<th>Median value (%)</th>
<th>No. of Studies</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Disease</td>
<td>17.6</td>
<td>1.6-17.7</td>
<td>17.2-18.1</td>
<td>-</td>
<td>2</td>
<td>22540</td>
<td>129 - 22411</td>
</tr>
<tr>
<td>Hypertension/hypertensive disease</td>
<td>17.1</td>
<td>8.0-39.2</td>
<td>16.7-17.5</td>
<td>20.2</td>
<td>10</td>
<td>31005</td>
<td>32 - 22351</td>
</tr>
<tr>
<td>Ischemic Heart Disease (IHD)</td>
<td>9.3</td>
<td>2.3-11.8</td>
<td>8.4-10.2</td>
<td>-</td>
<td>2</td>
<td>4037</td>
<td>1074 - 2963</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.3</td>
<td>1.6-4.5</td>
<td>4.1-4.6</td>
<td>-</td>
<td>2</td>
<td>23425</td>
<td>1074 - 22351</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>9.2</td>
<td>-</td>
<td>8.2-10.2</td>
<td>-</td>
<td>1</td>
<td>2963</td>
<td>-</td>
</tr>
<tr>
<td>Myocardial Infarction (MI)</td>
<td>0.5</td>
<td>-</td>
<td>0.3-0.8</td>
<td>-</td>
<td>1</td>
<td>2963</td>
<td>-</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>3.2</td>
<td>1.5-3.8</td>
<td>2.7-3.7</td>
<td>-</td>
<td>2</td>
<td>4037</td>
<td>1074 - 2963</td>
</tr>
<tr>
<td>Cardiac Arrhythmia</td>
<td>3.6</td>
<td>-</td>
<td>2.5-4.7</td>
<td>-</td>
<td>1</td>
<td>1074</td>
<td>-</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0.9</td>
<td>-</td>
<td>0.4-1.5</td>
<td>-</td>
<td>1</td>
<td>1074</td>
<td>-</td>
</tr>
<tr>
<td>MI/IHD/Arrhythmia</td>
<td>13.5</td>
<td>-</td>
<td>13.1-14.0</td>
<td>-</td>
<td>1</td>
<td>22396</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9.2</td>
<td>0.8-20.0</td>
<td>9.1-9.3</td>
<td>10.5</td>
<td>20</td>
<td>190578</td>
<td>32 - 145718</td>
</tr>
<tr>
<td>Asthma</td>
<td>5.0</td>
<td>-</td>
<td>3.7-6.3</td>
<td>-</td>
<td>1</td>
<td>1074</td>
<td>-</td>
</tr>
<tr>
<td>Chronic Lung Disease (including COPD)</td>
<td>25.0</td>
<td>10.8-30.1</td>
<td>23.7-26.4</td>
<td>-</td>
<td>2</td>
<td>4037</td>
<td>1074 - 2963</td>
</tr>
<tr>
<td>Cancer</td>
<td>24.0</td>
<td>-</td>
<td>22.5-25.5</td>
<td>-</td>
<td>1</td>
<td>2963</td>
<td>-</td>
</tr>
<tr>
<td>Obesity</td>
<td>8.0</td>
<td>1.0-59.4</td>
<td>7.6-8.3</td>
<td>18.9</td>
<td>12</td>
<td>23095</td>
<td>32 - 11392</td>
</tr>
</tbody>
</table>

$PP =$ pooled prevalence rate; $95\% \text{ CI} = 95\%$ Confidence Interval
Table 5.2: Pooled prevalence rates for physical ill-health conditions in people with bipolar disorder

<table>
<thead>
<tr>
<th>Condition</th>
<th>PP (%)</th>
<th>Range (%)</th>
<th>95% CI (%)</th>
<th>Median value (%)</th>
<th>No. of Studies</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Disease</td>
<td>10.1</td>
<td>8.7-11.8</td>
<td>-</td>
<td>1</td>
<td>1441</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension/hypertensive disease</td>
<td>31.1</td>
<td>18.1-43.4</td>
<td>30.1-31.2</td>
<td>23.5</td>
<td>5</td>
<td>10950</td>
<td>159-5112</td>
</tr>
<tr>
<td>Ischemic Heart Disease (IHD)</td>
<td>18.5</td>
<td>3.8-28.7</td>
<td>17.7-19.3</td>
<td>-</td>
<td>2</td>
<td>8669</td>
<td>3557-5112</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.9</td>
<td>1.5-2.4</td>
<td>-</td>
<td>1</td>
<td>3557</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>21.9</td>
<td>20.8-23.0</td>
<td>-</td>
<td>1</td>
<td>5112</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction (MI)</td>
<td>0.9</td>
<td>0.9-0.9</td>
<td>0.7-0.12</td>
<td>-</td>
<td>2</td>
<td>7017</td>
<td>1905-5112</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>5.5</td>
<td>1.2-8.4</td>
<td>5.0-6.0</td>
<td>-</td>
<td>2</td>
<td>8669</td>
<td>3557-5112</td>
</tr>
<tr>
<td>Cardiac Arrhythmia</td>
<td>3.3</td>
<td>-</td>
<td>2.7-3.9</td>
<td>-</td>
<td>1</td>
<td>3557</td>
<td></td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>1.2</td>
<td>-</td>
<td>0.9-1.6</td>
<td>-</td>
<td>1</td>
<td>3557</td>
<td></td>
</tr>
<tr>
<td>Valvular disease</td>
<td>1.9</td>
<td>-</td>
<td>1.5-2.4</td>
<td>-</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>17.0</td>
<td>-</td>
<td>15.4-18.8</td>
<td>-</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artherosclerosis</td>
<td>2.6</td>
<td>-</td>
<td>1.9-3.4</td>
<td>-</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>16.6</td>
<td>-</td>
<td>15.0-18.3</td>
<td>-</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>11.3</td>
<td>3.7-26.1</td>
<td>10.9-11.8</td>
<td>6.7</td>
<td>9</td>
<td>17398</td>
<td>60-6490</td>
</tr>
<tr>
<td>Asthma</td>
<td>7.3</td>
<td>-</td>
<td>6.5-8.2</td>
<td>-</td>
<td>1</td>
<td>3557</td>
<td></td>
</tr>
<tr>
<td>Chronic Lung Disease (including COPD)</td>
<td>30.3</td>
<td>12.9-42.4</td>
<td>29.3-31.3</td>
<td>-</td>
<td>2</td>
<td>8669</td>
<td>3557-5112</td>
</tr>
<tr>
<td>Cancer</td>
<td>28.3</td>
<td>3.3-45.6</td>
<td>27.3-29.2</td>
<td>-</td>
<td>2</td>
<td>8669</td>
<td>3557-5112</td>
</tr>
<tr>
<td>Obesity</td>
<td>8.0</td>
<td>1.0-47.8</td>
<td>7.6-8.5</td>
<td>29.8</td>
<td>9</td>
<td>12613</td>
<td>50-6490</td>
</tr>
</tbody>
</table>

*PP = pooled prevalence rate; *95% CI = 95% Confidence Interval
Table 5.3: Pooled prevalence rates for physical ill-health conditions in people with depression

<table>
<thead>
<tr>
<th>Condition</th>
<th>PP(^{5}) (%)</th>
<th>Range (%)</th>
<th>95% CI(^{*}) (%)</th>
<th>Median value (%)</th>
<th>No. of Studies (n)</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Disease</td>
<td>7.9</td>
<td>6.1-46.1</td>
<td>7.4-8.5</td>
<td>-</td>
<td>3</td>
<td>8866</td>
<td>76 - 6831</td>
</tr>
<tr>
<td>Hypertension/hypertensive disease</td>
<td>21.5</td>
<td>11.5-23.8</td>
<td>20.7-22.5</td>
<td>-</td>
<td>3</td>
<td>8095</td>
<td>261 - 6831</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.3</td>
<td>-</td>
<td>3.2-5.7</td>
<td>-</td>
<td>1</td>
<td>1003</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6.8</td>
<td>2.7-9.2</td>
<td>6.2-7.6</td>
<td>6.7</td>
<td>4</td>
<td>4871</td>
<td>76 - 3531</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.3</td>
<td>-</td>
<td>0.2-7.1</td>
<td>-</td>
<td>1</td>
<td>76</td>
<td>-</td>
</tr>
<tr>
<td>Cancer</td>
<td>15.8</td>
<td>-</td>
<td>9.3-25.6</td>
<td>-</td>
<td>1</td>
<td>76</td>
<td>-</td>
</tr>
<tr>
<td>Obesity</td>
<td>28.9</td>
<td>20.1-30.1</td>
<td>28.0-29.7</td>
<td>-</td>
<td>3</td>
<td>11156</td>
<td>369 - 5695</td>
</tr>
</tbody>
</table>

\(^{5}\)PP = pooled prevalence rate; \(^{*}\)95% CI = 95% Confidence Interval
Appendix 6 – Effectiveness studies- study references


Faulkner, G., Cohn, T., & Remington, G. (2007). Interventions to reduce weight gain in schizophrenia (review). *Cochrane Database of Systematic Reviews, 1*.


Tsoi, D.T., Porwal, M., & Webster, A.C. (2013). Interventions for smoking cessation and reduction in individuals with schizophrenia (Review). *Cochrane Database of Systematic Reviews, 2*.

Appendix 7- Effectiveness studies- supplementary tables

Table 7.1: Pooled prevalence rates for risk factors in people with schizophrenia

<table>
<thead>
<tr>
<th></th>
<th>PP (%)</th>
<th>Range (%)</th>
<th>95% CI (%)</th>
<th>No. of Studies (n)</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia</td>
<td>14.9</td>
<td>4.0-69.8</td>
<td>14.6-15.3</td>
<td>8</td>
<td>38303</td>
<td>32 - 22434</td>
</tr>
<tr>
<td>Smoking</td>
<td>58.1</td>
<td>42.6-69.9</td>
<td>56.1-60.0</td>
<td>5</td>
<td>2508</td>
<td>32 - 1452</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>7.0</td>
<td>-</td>
<td>4.2-11.4</td>
<td>1</td>
<td>200</td>
<td>-</td>
</tr>
<tr>
<td>Impaired fasting glucose/glucose tolerance</td>
<td>16.1</td>
<td>15.3-17.4</td>
<td>14.1-18.3</td>
<td>3</td>
<td>1162</td>
<td>85 - 819</td>
</tr>
</tbody>
</table>

*PP = pooled prevalence rate; *95% CI = 95% Confidence Interval

Table 7.2: Pooled prevalence rates for risk factors in people with bipolar disorder

<table>
<thead>
<tr>
<th></th>
<th>PP (%)</th>
<th>Range (%)</th>
<th>95% CI (%)</th>
<th>No. of Studies (n)</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia</td>
<td>5.9</td>
<td>1.1-36.5</td>
<td>5.5-6.4</td>
<td>5</td>
<td>10527</td>
<td>104 - 6490</td>
</tr>
<tr>
<td>Smoking</td>
<td>48.5</td>
<td>27.0-50.1</td>
<td></td>
<td>3</td>
<td>2174</td>
<td>110 - 1905</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>43.5</td>
<td>-</td>
<td>36.5-50.1</td>
<td>1</td>
<td>184</td>
<td>-</td>
</tr>
<tr>
<td>Pre-diabetes</td>
<td>23.3</td>
<td>-</td>
<td>14.4-35.4</td>
<td>1</td>
<td>60</td>
<td>-</td>
</tr>
</tbody>
</table>

*PP = pooled prevalence rate; *95% CI = 95% Confidence Interval

Table 7.3: Pooled prevalence rates for risk factors in people with depression

<table>
<thead>
<tr>
<th></th>
<th>PP (%)</th>
<th>Range (%)</th>
<th>95% CI (%)</th>
<th>No. of Studies (n)</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia</td>
<td>13.8</td>
<td>14.0-14.3</td>
<td>11.9-16.0</td>
<td>2</td>
<td>1079</td>
<td>76 - 1003</td>
</tr>
<tr>
<td>Smoking</td>
<td>43.4</td>
<td>39.5-43.5</td>
<td>42.1-44.6</td>
<td>2</td>
<td>5956</td>
<td>261 - 5695</td>
</tr>
</tbody>
</table>

*PP = pooled prevalence rate; *95% CI = 95% Confidence Interval
Table 7.4: Pooled prevalence rates for risk factors in people with serious mental illness

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>PP (%)</th>
<th>Range (%)</th>
<th>95% CI (%)</th>
<th>No. of Studies (n)</th>
<th>Total Participants (n)</th>
<th>Participants (range across studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia</td>
<td>13.0</td>
<td>1.1-69.8</td>
<td>12.7-13.3</td>
<td>15</td>
<td>49909 (S, BP, D)</td>
<td>32 - 22434</td>
</tr>
<tr>
<td>Smoking</td>
<td>47.9</td>
<td>27.0-69.9</td>
<td>46.9-48.8</td>
<td>8*</td>
<td>(S, BP, D)</td>
<td>32 - 5695</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>24.5</td>
<td>7.0-43.5</td>
<td>20.5-29.0</td>
<td>2</td>
<td>384 (S, BP)</td>
<td>184 - 200</td>
</tr>
</tbody>
</table>

<sup>$PP = pooled prevalence rate; 95% CI = 95% Confidence Interval, *at least one study provided data on more than one population; S = schizophrenia, BP = bipolar disorder, D = Depression</sup>
Appendix 8- Physical co-morbidity in SMI: Research in Ireland

There has been some research in the area of physical health co-morbidity in SMI in an Irish context. This literature did not meet the criteria for inclusion in our review as we could not reliably stratify age and prevalence of physical conditions as these were reported for the whole sample in a general psychiatric population and/or with an age range exceeding 18-65 years. A chronological overview of the Irish literature is presented below.

Leonard, Browne and Halley (2002) conducted a study on patients prescribed clozapine within the Waterford Mental Health Service (catchment area population 106,529) to ascertain the prevalence of obesity, lipid and glucose abnormalities. The study had 21 participants (13 male, 8 female). They found that 6 patients (29%) met criteria for obesity (BMI>30), 11 patients (52%) were deemed to have hypertriglyceridaemia, 3 patients (14%) had hypercholesterolaemia, and 3 patients (14%) had a family history of Diabetes Mellitus. Although one patient (4.5%) met criteria for impaired fasting glucose (fasting blood glucose = 6.9 mmol/L), none of the cohort was found to be hyperglycaemic.

Morgan et al. (2003), in a prospective study in the South Monaghan catchment area of Cavan–Monaghan psychiatric service, followed up 72 patients with schizophrenia over 7.5 years. They found in the follow-up period that 25 patients out of 72 had died, giving a twofold increase in mortality (a relative risk of 2.06 (95% CI, 1.40 – 2.80; p=0.001)). The majority of deaths were from natural causes: 88% (n=22) (six circulatory; five neoplastic; four respiratory; two gastrointestinal; one endocrine; one genitourinary), 8% (n=2) were accidental deaths and 4% (n=1) was a death from suicide. Morgan et al. concluded that premature death in this cohort of schizophrenia endured despite investment in psychiatric care. This investment in psychiatric care may explain the reduced mortality from suicide, however, it may also indicate that the high mortality from natural causes requires either a similar level of investment or more awareness raising of the importance of managing co-morbidity in people with SMI.

Feeney et al. (2007) examined the point prevalence of diabetes, obesity, hyperlipidaemia and smoking in 50 outpatients taking clozapine in St Vincent’s Hospital, Fairview. They found that 36% of subjects were obese (n=18, BMI >30), 28.6% (n= 14) met the criteria for impaired fasting glucose, 61.2% (n=30) had hypercholesterolaemia (cholesterol levels greater than 5.0mmol/L), and 72% of subjects smoked. Feeney et al. (2007) questioned that while CHD mortality in Ireland is almost half what was in the 1980s whether similar levels of reductions are mirrored in people with schizophrenia.

O’Brien et al. (2007) examined the high prevalence of risk factors for physical illness in 27 patients on a long stay psychiatric unit in the west of Ireland. They found that 33.3% had pre-existing hypertension, 18.5% had hypercholesterolaemia and 11.1% (n=3) had diabetes mellitus. More than one tenth (11.1%, n=3) had pre-existing thyroid disorders and 29.6% (n=8) had blood dyscrasias. More than half (51.8%, n=14) were
obese (BMI>30) and 40.7% (n=11) met the criteria for metabolic syndrome and 70% of subjects smoked. O’Brien et al. (2007) concluded that an annual physical health assessment for long-term psychiatric inpatients would be of limited value because of the extent of existing co-morbidity. They suggested that primary care services should be considered in meeting the physical health needs of this client group.

Behan et al. (2008), in a cross-sectional survey of 92 people with schizophrenia/schizoaffective disorder in South County Dublin, found that 55% (n=51) of subjects smoked, the prevalence of established cardiovascular disease was 13% (n=12), and 4.3% (n=4) had type II diabetes. Less than half of the study population had a documented cholesterol test. Behan et al. (2008) suggested that the lack of blood tests in subject's clinical case notes may indicate a lack of standardised care.

Cahill and Jackson (2008) in a review of monitoring the physical health needs of individuals with SMI in Ireland found that documentation of co-morbidity and SMI within the daily psychiatric community was sparse. They suggested that the emphasis of government mental health policy, i.e. closer working with primary care, is more to facilitate improvements in mental health than physical health outcomes. Cahill and Jackson (2008) went on to suggest that mental health teams do have a role to play in the management of physical health issues but the primary responsibility for monitoring these should lie within primary care. They further suggested the development of local database or case-registers to identify individuals with SMI for physical health monitoring.

Payne and Essem (2008) conducted a prospective survey of psychiatric trainees over a 28 day period in an acute psychiatric unit attached to a teaching University Hospital in Cork. Following a physical examination, the psychiatric trainee was required to complete a form containing basic demographic data and document diagnosis, action taken and any further consultation or investigation undertaken. Any difficulties encountered were also documented. The results showed that trainees are required to draw on their previous medical and surgical experience on an almost daily basis in the management of primary care and acute conditions. Payne and Essem (2008, p130) noted that “while assessment of core competencies in psychiatry is addressed very well, currently there is no consensus on how to maintain competence in the area of medical or surgical expertise for trainees or consultants”, before going on to suggest that development of a course to up-skill psychiatrists in the management of medical problems and liaison with other physicians may be required.

Udo and Mooney (2011a) examined the physical assessment of 60 residents in long stay wards of a psychiatric hospital in Carlow/Kilkenny. Good practice was noted in the assessment of cardiovascular, respiratory, alimentary and central nervous systems. However, assessment of anthropometric measurements such as body mass index and waist circumference was very low, and lipid levels not assessed for any service user. Sensory examination e.g. eye tests and hearing examination, were completed in only 8% and 3% of residents respectively. Women did not have breast examinations
recorded. Another finding of this study was the lack of discussion with service users of their physical examination or of the results of any clinical tests that were required. Following this audit a new physical examination policy, examination form and laboratory investigation forms have come in to use.

Udo et al. (2011b) conducted a study to examine the prevalence of metabolic syndrome and obesity in a long-stay psychiatric unit in Kilkenny Mental Health Services, Ireland. They found 33% of residents were obese (n=10, BMI>30) and 66% (n=20) had metabolic syndrome. A significant proportion (15%, n=4) of residents had diabetes and 43% (n=13) were hypertensive. The majority (77%, n=23) had dyslipidaemia. Almost half (46%, n=14) smoked, which is lower than recorded in other Irish studies mentioned here. Udo et al. (2011b) noted that these outcomes were higher than those of the general Irish middle aged population and the accepted estimate of a general psychiatric population. It was also higher than that of a previous published study on an Irish long-stay psychiatric ward population. They concluded that there is a high prevalence of obesity and metabolic syndrome and recommended that people with SMI should have access to primary care and other health services on the same basis as any other citizen.

Gallagher et al. (2013) in a retrospective audit of clinical records of 85 patients, found limited physical health monitoring for patients taking anti-psychotic medications. At baseline audit of 40 subjects, only 2.5% (n=1) had a blood pressure measurement, 2.5% (n=1) had weight recorded, 52.5% (n=21) had cholesterol levels measured and 45% (n=18) had glucose measured. None had height or waist measured, so BMI could not be calculated. However, monitoring increased following the audit to 80% (n=32) for blood pressure measurement, 80% (n=32) for height, 78% (n=31) for waist measurement, 80% (n=32) for weight, 85% (n=34) for cholesterol levels and 85% (n=34) for glucose. Gallagher et al. (2013, p116) reported that the introduction of a screening clinic allowed “expeditious and efficient screening with minimal demand on constrained nursing or medical resources.”

Cullen and McCann (2015) in a small qualitative study of 10 outpatients attending a day centre in Ireland (location anonymous), interviewed service users with a diagnosis of schizophrenia, schizo-affective disorder or bipolar disorder to elicit their views and opinions relating to physical activity. Results showed that participants found physical activity beneficial in terms of physical, psychological and social well-being and that they perceived clear gains in relation to recovery and quality of life. However, participants reported that barriers to physical activity included lack of motivation, not being fit and being overweight, as well as support from qualified fitness instructors and medication side effects that made physical activity difficult e.g. stiffness. Cullen and McCann (2015) suggested that their findings supported the justification for the inclusion of physical activity in care plans and also in mental health policy directives.
References for Appendix 8


