# Cost and impact of non-treating severe mental illnesses (SMIs): The case study of schizophrenia

*Michela Tinelli, Panos Kanavos*
*LSE Enterprise*

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## *Authors:*

Michela Tinelli, Research Fellow, LSE Enterprise, London School of Economics and Political Science, UK, email: m.tinelli@lse.ac.uk

Panos Kanavos, Associate Professor in International Health Policy in the Department of Social Policy, Programme Director of the Medical Technology Research Group (MTRG) at LSE Health, London School of Economics and Political Science, UK

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## *Research team (in alphabetical order):*

Cyril HÖschl, Professor, Director, National Institute of Mental Health & Chairman, Dept. of Psychiatry, Charles, Czech Republic

Panos Kanavos, Associate Professor in International Health Policy in the Department of Social Policy, Programme Director of the Medical Technology Research Group (MTRG) at LSE Health, London School of Economics and Political Science, UK

Martin Knapp, Professor of Social Policy, Department of Social Policy, London School of Economics and Political Science UK; Director, Personal Social Services Research Unit (PSSRU), London School of Economics and Political Science UK; Director, NIHR School for Social Care Research UK

Maurizio Pompili, Professor and Director, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Italy

Michela Tinelli, Research Fellow, LSE Enterprise, London School of Economics and Political Science, UK

Petr Winkler, PhDr. Department of Social Psychiatry , National Institute of Mental Health, Czech Republic

## *Experts that contributed to the research (in alphabetical order):*

Celso Arango, Associate Professor of Psychiatry, University Complutense, and Head of Department, Hospital General Universitario Gregorio Marañón. Madrid, Spain

Per Bech, Clinical Professor, Institute of Clinical Medicine, University of Copenhagen & Head of Research, Dept. of Psychiatry Hillerød, The Capital Region of Denmark

Samantha Bellini, Psychologist, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Sara Beomonte Zobel, Medical Doctor, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Ginevra Berdini, Psychologist, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Miquel Bioque Alcázar, Dr, Unitat d'Esquizofrènia Clínic, Hospital Clínic de Barcelona, Spain

Ilaria Brandolese, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

John Cookson, Dr Consultant, Royal London Hospital (East London Foundation Trust), UK

Claudio Csillag, Consultant, Psychiatric Research Unit, Mental Health Centre North Zealand, Denmark

Martina Curto, Medical Doctor, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Giovanna De Sanctis, Psychologist, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Geert Dom, Professor and Head of Department, University of Antwerp, Advanced Research in Addiction Medicine & Psychiatry, PC Alexian Brothers, Belgium

Denise Erbuto, Medical Doctor, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Peter Falkai, Professor and Clinic Director, Ludwig-Maximilians-University Munich, Clinic for Psychiatry and Psychotherapy, Munich, Germany

Walter-Wolfgang Fleischhacker, Professor and Director, Department of Psychiatry and Psychotherapy, Medical University Innsbruck, Austria

Alberto Forte , Medical Doctor, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Kostas N. Fountoulakis, Associate Professor of Psychiatry, Department of Psychiatry, Division of Neurosciences School of Medicine, Aristotle University of Thessaloniki, Greece

Gloria Giordano, Medical Doctor, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Heinz Grunze, Professor of Clinical Psychiatry, Newcastle University, Institute of Neuroscience, Academic Psychiatry, UK

Martin Harrow, Professor Emeritus, Department of Psychiatry, University of Illinois at Chicago, USA

Paz Garcia-Portilla, Professor, Área de Psiquiatría, Universidad de Oviedo CIBERSAM, Spain

Cyril Höschl, Professor, Director, National Institute of Mental Health & Chairman, Dept. of Psychiatry, Charles , Czech Republic

Andreas Heinz, Professor of Psychiatry, Director and Chair, Department of Psychiatry and Psychotherapy at the Charité Campus Mitte, Universitätsmedizin Berlin, Germany

Arne Holte, Professor and Deputy Director-General, the Norwegian Institute of Public Health, Oslo, Norway

Luchezar G. Hranov, Head of the Second Psychiatric Clinic, Second Psychiatric Clinic of the University Hospital for Active Treatment in Neurology and Psychiatry “Sveti Naum”, Sofia, Bulgaria; Associate professor of psychiatry at the Department of Psychiatry and Medical Psychology of the Medical University, Sofia, Bulgaria

Georg Juckel, Professor for Psychiatry and Psychotherapy and specialist in psychiatry and psychotherapy, Department of Psychiatry, Psychotherapy and Preventive Medicine , Ruhr-Universität Bochum Germany

Kalman J. Kaplan, Professor of Clinical Psychology, Director of Program in Religion, Spirituality and Mental Health, Department of Psychiatry
University of Illinois at Chicago, USA

Martin Knapp , Professor of Social Policy, Department of Social Policy , London School of Economics and Political Science UK; Director, Personal Social Services Research Unit (PSSRU), London School of Economics and Political Science UK; Director, NIHR School for Social Care Research UK

Susanne Knappe, Dr Research Associate Department of Clinical Psychology and Psychotherapy, Technische Universität Dresden, Germany

Andreas Meyer-Lindenberg, Professor and Director, Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany

Christiane Montag, Dr Med, Department of Psychiatry and Psychotherapy at the Charité Campus Mitte, Universitätsmedizin Berlin, Germany

David Nutt, Edmond J Safra Professor of Neuropsychopharmacology and director of the Neuropsychopharmacology Unit in the Division of Brain Sciences.

Antonella Padovan Lang, Medical Director, Regione Veneto, Italy

Maurizio Pompili, Professor and Director, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Italy

Roger Pycha, Director Dr, Psychiatric Service, Azienda Sanitaria dell'Alto Adige, Italy

Michele Raja, PhD the Court of Rome, Italy

Elmars Rancans, Professor and Chair of the Department of psychiatry and narcology, Riga Stradins University, Latvia

Zoltán Rihmer, Professor of Psychiatry, Semmelweis University, Budapest, Hungary

Enrico Rosini, Professor and Director, Day Hospital Unit, Department of mental Health, San Giacomo Hospital, Sapienza University of Rome, Italy

Raimo Salokangas, Professor, Department of Psychiatry, University of Turku, Finland; Psychiatric Clinic, Turku University Central Hospital, Turku, Finland; Turku Psychiatric Clinic,

Turku Mental Health Centre, Turku, Finland.

Jerzy Samochowiec, Department of Psychiatry, Pomeranian Medical University, Poland

Livia Sanna, Medical doctor, Unit of Psychiatry, Neurosciences, Mental Health and Sensory Organs Department (NeSMOS), Faculty of Medicine and Psychology, Sant'Andrea Hospital, Sapienza University of Rome

Laura Sapienza, Medical Doctor, Unit of Psychiatry, Neurosciences, Mental Health and Sensory Organs Department (NeSMOS), Faculty of Medicine and Psychology, Sant'Andrea Hospital, Sapienza University of Rome

Andrea Schmitt, Professor, Clinic for Psychiatry and Psychotherapy, Ludwig-Maximilians-University Munich, Germany

Gianluca Serafini, Medical Doctor, Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, 00189 Rome, Italy

Eliot Sorel, Medical Doctor, George Washington University School of Medicine and Health Sciences & School of Public Health and Health Services, Washington

Dan Stein, Professor and Director, Research Unit on Anxiety and Stress Disorders, Cape Town, South Africa

Lidija Injac Stević, Professor (Associate), School of Medicine, University of Montenegro, Montenegro

Eduard Vieta, Professor of Psychiatry and the Director of the Bipolar Disorders Program of the Hospital Clinic at the University of Barcelona, in Barcelona, Spain

Danuta Wasserman, Professor in Psychiatry and Suicidology at Karolinska Institutet, Founding Head of the National Centre for Suicide Research and Prevention of Mental Ill-Health, Director of the WHO Collaborating Centre for Research, Methods Development and Training in Suicide Prevention, Stockholm, Sweden.

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# PREFACE

The socioeconomic impact of non-treatment of brain disorders, particularly when it comes to mental health illnesses, is shocking. A recent OECD report entitled “Making Mental Health Count” points out that health, social, and employment services should intervene earlier, involve key stakeholders and ensure they work together with the community in order to help people with mental health issues not only to tackle these but also be able to find work or stay in a job. The case study of schizophrenia provides a revealing example of a highly prevalent mental health condition that can still account for a large proportion of individuals that are not diagnosed, do not get any evidence-based treatment, or are likely to receive diagnosis and treatment with years of delay. Still, evidence shows that, if they are enrolled in appropriate treatment programmes, they can struggle to overcome non-adherence issues.

This report takes the forefront position to be used as important source of information for academic, as well as policy and practitioner stakeholders when looking into the multidimensional impact that non-treatment of schizophrenia has on the use of health and social care resources, criminal justice services, employment, education, violence and premature death, and homelessness. The voices emerging from the literature and the international community of experts that supported this work are in agreement to recommend urgent collaborative reform initiatives, which involve all parties. For example, stigma and negative perceptions about psychiatric care and schizophrenia, poor collaboration among the different types of providers, lack of continuity of care or appropriate clinician training are listed within the most common barriers to changes for patients/their caregivers, healthcare systems and providers, respectively.

Policy interventions that may respond to the growing urgency of the problem should target: engagement with, and empowerment of, people with schizophrenia, their families, and their communities; better use of integrated interventions; and ensuring that services are easily accessible by patients. Measuring unmet needs allows to have a better understanding of the scale of the problem, and what works in tackling it. Crucially, this report is a first step towards addressing a worrying lack of evidence of the impact of unmet needs in schizophrenia beyond local settings or country specific evaluations, as well as making us all aware of the challenges that need to be overcome to support future research.

What is more, this study is part of the broader investigation by the European Brain Council (EBC) of the cost of non-treatment of brain disorders in Europe. By providing an extensive review of the case for schizophrenia, it sheds light on the crucial issues to be looked at and provides for a robust methodology that can be translated to the other conditions to be considered in EBC’s broader study.

Frédéric Destrebecq

Executive Director, European Brain Council

# EXECUTIVE SUMMARY

- Unmet needs in schizophrenia arise from a discrepancy between the use of mental health services and the extent of need for those services.

- The impact of non-treatment is extensive and reveals a complex scenario with strong interrelationships between the individual, community, and providers of mental health services.

- There are still considerable gaps in our current knowledge about the impact of non-treatment in schizophrenia. The limited quality evidence reports on access to hospital facilities and emergency services, number of violent acts and loss of productivity at work (the USA as predominant setting). More evidence is needed to go beyond the clinical settings and cover the community overall as well as subgroups of people in stronger need (homelessness, prisoners and younger individuals).

- The economic data available are very limited, but still show a massive impact of unmet needs on healthcare and society overall. The overall number of cases of untreated schizophrenia is estimated to be about 8.5 million worldwide (3 million cases between Europe and the Americas). The overall economic burden would be about 56 billion US$ (20 billion US$ between Europe and the Americas).

- We found a broad agreement about the changes that need to be made to address unmet needs in schizophrenia, and they involve all parties: patients, caregivers, healthcare providers and healthcare systems.

# THE REPORT IN A NUTSHELL

**Unmet needs in schizophrenia arise from a discrepancy between the use of mental health services and the extent of need for those services.**

- The impact of non-treatment is extensive and involves strong interrelationships between the individual, community, and providers of mental health services.

- Non-treatment may occur at different levels of the patient pathway to include: missed (or delays in) diagnosis, lack of (or delays in) treatment, inappropriate treatment and non-adherence/non-compliance.

- The negative outcomes derived from unmet needs cover a cascade of interrelated factors including: unnecessary physical/mental disability and comorbidities that may require access to health and social care resources; experience of criminal justice system; reduced productivity in the workplace or employment; disrupted education; violence and premature death (suicides and homicides); and homelessness.

- Against this background, the impact of non-treatment in terms of indirect costs (community, education and workspace), direct healthcare costs (primary setting, hospital and community), direct non-medical costs (social services, special accommodation and informal care), social security and criminal justice costs is massive.

## From our evidence, we conclude that it is unacceptable that:

There are still considerable gaps in our current knowledge about the impact of non-treatment in schizophrenia. The limited quality evidence reports only on:

- A few outcomes (access to hospital facilities and emergency services; number of violent acts and loss of productivity at work). More evidence should be gathered on the economic impact of increased access to the criminal justice system, homelessness as well as of the burden of additional physical comorbidities and disabilities.

- Adult patients approaching clinical settings. More research is needed to address unmet needs across groups of population in needs (including the homeless, prisoners, and younger individuals) and settings (to collect also population level data).

- Delays in treatment or treatment discontinuation (non-adherence/compliance). More quality evidence is needed to cover earlier steps in the patient pathway (e.g. missed and delays in diagnosis at population level).

The limited economic evidence shows a massive impact of unmet needs on healthcare and society overall:

- In Canada the impact of undiagnosed psychosis (including schizophrenia) on the use of health resources (Lim et al., 2008) shows that the annual medical cost per capita is highest for the diagnosed mentally ill (C$2,515), lowest for the non-mentally ill (C$6430, with those in the undiagnosed category in the middle (C$1,442; Canada, 2003 figures).

- In the USA (Greater Kansas City) the annual cost of lack of treatment for severe mental illness (SMI) is about $6609 per case, 2010 figures (HSM Group, 2012). A high proportion (88%) of these costs is in the form of indirect costs to employers and individuals (about U$5785 per case of untreated SMI). About 10 % of the overall costs are estimated to be direct costs, or medical expenses associated with lack of sustained treatment (about US$696 per case of untreated SMI).

  When adapting the Greater Kansas City model to international estimates of the prevalence and treatment gap for schizophrenia, the overall number of cases of untreated schizophrenia would be around 8.5 million worldwide, with about 3 million cases between Europe and the Americas. The overall economic burden would

be about 56 billion US$ worldwide (20 billion US$ between Europe and the Americas only).

- In the USA the national re-hospitalization cost attributable to antipsychotic non-adherence is estimated at approximately US$1,500 million per year (2005 figures).

Patchy evidence across country settings highlights also the impact of non-adherence / non – compliance to psychotic treatment on: incarceration rates, unemployment rates and work loss, level of education achieved, or withdrawal from education, violence (self-harm or aggressive behaviour towards others) and death (suicides, homicides).

## Addressing the non-treatment of schizophrenia is an important goal to be met, with numerous challenges! The main barriers to be overcome involve us all:

### The patients and caregivers

- Stigma and negative perceptions about psychiatric care and schizophrenia; Suffering from psychotic symptoms or cognitive impairment; Lack of knowledge about side effects of medications; Lack of skills or management strategies to cope with side effects; Lack of illness awareness/not knowing what to do; Limited access to treatment; Previous history of non-adherence, substance abuse; Caregiver/patient personal beliefs of healthcare providers.

### Healthcare providers

- Lack of training in the interpersonal skills; Lack of continuity of care with a single clinician; Poor quality of communication and collaboration between the providers and the patients; Lack of appropriate training or education on schizophrenia; Lack of appropriate information on schizophrenia; Shift of the attention to other phenomena that have become “medicalised”; Attitude of all staff towards the patients; Lack of time for motivational interventions, trust building and establishment of a therapeutic relationship; Under-representation of psychotherapeutic approaches in treatment of patients with SMI.

### Healthcare system

- Poor collaboration among the different types of providers; Difficulties in providing the appropriate service; The system discourages the proper monitoring of patients once the treatment regimen is started; Lack of community services and integration between health and social care; Scarce attempt to make a patient feel welcome, empowered and valued.

### Researchers evaluating the impact of unmet needs

- Limited access to data on homelessness, prisoners, and younger individuals; Discrepancies in the information system that supports the management of care or in the methods used when assessing patient non-adherence/non-compliance as well as their self-reported outcomes (e.g. quality of life); Lack of comprehensive evaluation of the patient pathway of care from diagnosis, primary/hospital care to community services.

## We found also broad agreement about the changes that need to be made to transform the lives of those with unmet needs and of their families. Our recommendations include:

- Stigma and negative perception about schizophrenia are top priorities in all countries. Awareness campaigns aimed at the general public can be beneficial in increasing awareness of the nature of schizophrenia and its treatment.

- Promoting patient-centred care to ensure continuity of care, develop partnerships with caregivers and patients, support patient and stakeholder involvement in decision making, treat the patient as a person and not only "the symptoms".

- Assisting patients/their caregivers from diagnosis to their access to hospital and community care and ensuring that services are easily accessible by users.

- Promoting and implementing community care, with a focus on integrating health and social care.

- Supporting communication and collaboration across healthcare providers and co-ordination of mental health services across settings.

- Providing appropriate training and information to providers and patients.

- Using appropriate mechanisms for measurement of quality care.

- Overcoming discrepancies in electronic information system or in the assessment of non-adherence/non-compliance across settings.

- Drawing attention to hard-to-reach groups in need (e.g. prisoners, homeless or younger individuals).

# PART 1- DEFINING THE PROBLEM AND ITS SOCIAL AND ECONOMIC IMPACT

Schizophrenia is a highly burdensome condition in numerous countries. It is estimated that at least 26 million people worldwide have schizophrenia, and twice as many individuals (e.g. as caregivers) are indirectly affected by it (World Health Organisation, 2004). This has a substantial impact on everyday functioning, being one of the top ten causes of disability in individuals under the age of 25. In most cases, individuals who develop schizophrenia manifest behavioural and cognitive changes prior to the formal diagnosis of the condition (Cooke, 2014). Clinicians face various challenges in diagnosing this disorder, as well as in designing treatment plans that will reduce negative symptoms, maximize adherence and reduce side effects. Against this background, the impact of schizophrenia in terms of mortality, social disability, social stigma, impact on caregivers, and social costs is massive.

The protection and treatment of people with mental disorders is recognised by the United Nations as a fundamental human right (United Nations, 1991). All affected individuals should be helped to live a life free from prejudice, discrimination, and hostility. They have the right to: be protected from abuse and from behaviour, attitudes, and assumptions that lead to exclusion; and access health care and benefit from the best available treatment (Fleischhacker et al., 2014).

As well as the potential human cost, the burden of schizophrenia and other mental health disorders is very high on health care resources and on society as they contribute to increased hospitalisation and emergency care, physical comorbidities and premature death, school absence, access to criminal justice system for violent act, unemployment, sickness absence, and lost productivity at work (OECD, 2014).

The objectives of part 1 of the report are to define the problem of unmet needs in schizophrenia and define the key outcomes of the social and economic impact of untreated schizophrenia. A conceptual framework is presented to summarise the aspects involved when dealing with unmet needs of people with schizophrenia and their economic and social impact.

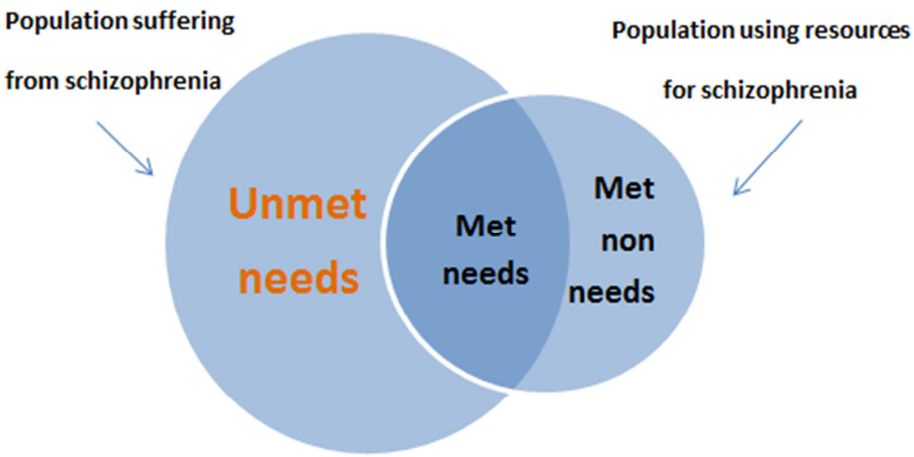
# The problem: untreated schizophrenia is due to a structural imbalance in the mental care sector

The core of the problem lies in a 'structural imbalance' where 'unmet needs' arise with a lack of correspondence between the use of mental health services and the extent of need for those services (Doessel, Williams, & Whiteford, 2010) (see figure 1).

## What 'unmet needs' are

Evidence shows that shortages in mental health services mean that some individuals experience missed (or delays in) diagnosis. Others that have been diagnosed and are in contact with mental health services may report lack of treatment; not receive appropriate treatment according to evidence; be non-adherence/non-compliance; or experience delays or insufficient treatment (Doessel et al., 2010) (OECD, 2014).

**Figure 1: 'Structural imbalance' between population with schizophrenia and population using health and social care resources for schizophrenia; adapted from** (Doessel et al., 2010)



## Identifying ‘unmet needs’

Several approaches are available to identify ‘unmet needs’, and they include both assessment in clinical setting (e.g. to measure delays in access to care, inappropriate treatment, or non-adherence to medication) as well as analysis of data collected at population/community level (e.g. to measure missed (or delays in) diagnosis), using epidemiological and perceived need for care surveys (Doessel et al., 2010) (Mojtabai et al., 2009).

There is a particular difficulty when determining the extent of ‘unmet needs’ for mental health services. Data sets on utilisation of resources (e.g. hospital administrative data or public/private insurance claims) can produce an incomplete picture of health status in the community because of several financial and social barriers to accessing health services that may prevent people to be diagnosed or result in delays in diagnosis. Complementary community data are therefore needed, looking not only at people who accessed but also at those who did not access the resources.

Another matter reported in the literature refers to 'met non-need'; people who use mental health services and do not have a diagnosis of schizophrenia. For example they can include: the ‘worried well’, where everyday stress and sadness are ‘medicalised’ as mental health illnesses; or individuals who want to improve sport and managerial performances may be supported by mental health professionals and receive mental health care (Doessel et al., 2010).

# The impact: negative outcomes derived from unmet needs

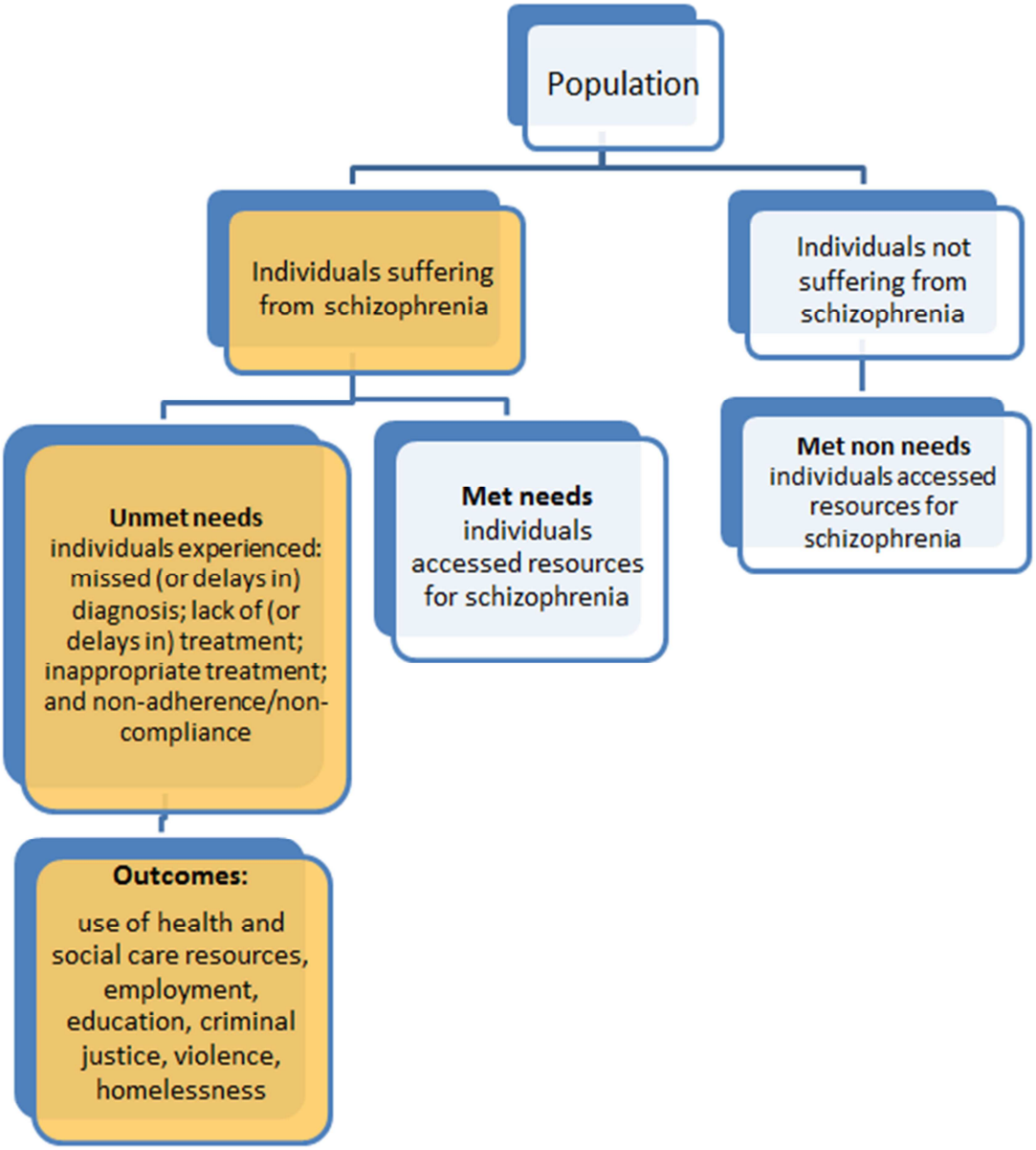
- Untreated or under-treated schizophrenia often sets in motion and perpetuates a cascade of increasing mental instability and other negative outcomes to include: unnecessary physical and mental disability; reduced productivity in the workplace or unemployment; divorce and family instability; disrupted education; violence and death (homicides, suicides); experience of criminal justice system for violent acts; homelessness.

- There is a significant association between schizophrenia and several somatic disorders such as nutritional/metabolic disorders, cardiovascular conditions, and sexual dysfunctions. Obesity, diabetes, and smoking are two times more frequently seen among patients with schizophrenia and other mental health disorders than in the general population (Torres-González et al., 2014). These conditions may compromise medication adherence and access to treatment as well as the quality of life of patients with schizophrenia (see figure 2).

All these negative outcomes are usually associated with increased costs of all resources used to include: indirect costs, direct healthcare costs, direct non-medical costs and other costs (OECD, 2012 and 2014).

**Indirect costs (community, education and workspace)** - Over 80 percent of these costs are related to morbidity, including the reduced or lost education/productivity due to illness (States, Project, & Metro, 2003). An even greater problem for employers is presenteeism, or lost productivity while at work. Research has shown that employees with untreated mental illness are far less productive compared to those who are successfully treated (Goetzel et al., 2004). They also include the school dropout and juvenile justice involvement with long term impact on adulthood productivity. Loss of productivity may also include premature deaths (mortality costs), homelessness of the individual with mental illness and the support costs of individuals providing care for family members with mental illness. These indirect cost estimates are conservative because they do not usually capture some measure of the pain, suffering, disruption and reduced productivity that are reflected in lost earnings.

## Figure 2 – Unmet needs in schizophrenia: a conceptual framework



**Direct health care costs (primary setting, hospital and community)** - Direct health care costs are costs for treatment and care services that fall on the government purse. These include medical resources used for care, treatment, and rehabilitation. Research has shown that untreated mental illness can lead to the need for much more resource-intensive care than if the patient were getting regular care and treatment (Wu et al., 2005). For example the schizophrenia patients may visit the emergency department in crisis mode and require hospitalisation until they are stable.

**Direct non-medical costs (institutionalisation and community)** - These include social services, special accommodation and informal care. Additionally, due to lack of treatment, the illness can progress to a point where patients need to be institutionalised (e.g. in nursing homes or long-term care facilities).

**Other costs (social security and criminal justice)** - Going without treatment can lead to more severe, more difficult-to-treat illness or even to permanent disability. Additional costs may include public expenditure related to the social security and the criminal justice systems. For example poor mental health can bring negative social consequences, such as higher expenditures on disability benefits, (OECD, 2012), as well as increased crime when patients with schizophrenia and other severe mental illnesses are 10 times more likely to become incarcerated compared to the general population (Prince, Akincigil, & Bromet, 2007).

# Key messages

- The issue of unmet needs in schizophrenia arises from a discrepancy between the use of mental health services and the extent of need for those services.

- The impact of non-treatment is extensive and reveals a complex scenario with strong interrelationships between the individual, community, and providers of mental health services.

- Unmet needs cover missed (or delays in) diagnosis, lack of (or delays in) treatment, inappropriate treatment and non-adherence/non-compliance.

- The key outcomes of the social and economic impact of untreated schizophrenia includes: health and social care resources, comorbidities; use of criminal justice resources; employment; education; violence and premature death; and homelessness.

# PART 2- EVIDENCE FROM THE INTERNATIONAL LITERATURE

Globally, the total costs – direct and indirect – of mental health (including moderate and severe mental illnesses such as schizophrenia) were estimated at USD 2 493 billion in 2010. In the EU, the cost was estimated to be equivalent to a loss of 3-4% of total GDP in 2004 (OECD, 2014). From a public health perspective, the unmet needs of persons with schizophrenia (who have not made contact with health services or if they have done so they received treatment with delay, they did not receive appropriate treatment or they were not adherent to their medications) are also a major problem. For example the treatment gap (percentage difference between number of people needing treatment and number of people receiving treatment) for schizophrenia worldwide is 32% (Kohn, Saxena, Levav, & Saraceno, 2004).

The indirect costs of mental health – the economic consequences attributable to disease, illness, or injury resulting in lost resources, but which do not involve direct payments related to the disease – are particularly high in both treated and non-treated groups. This includes the value of lost production due to unemployment, absences from work, presenteeism[1] or premature mortality (OECD, 2012). Across OECD countries, 88% of workers with schizophrenia or other severe mental illnesses stated that they accomplished less than they would like as a result of an emotional or physical problem, compared to 69% of those with moderate mental illness, and 26% of those with no mental illness. Unemployment is also a key issue for those individuals; they are typically six to seven times more likely to be unemployed than people with no such illnesses (OECD 2014).

An international survey aimed at exploring the opinions of the World Psychiatric Association (WPA) representatives regarding strategies to increase coverage of services, with a focus on areas where mental health specialists are scarce. Schizophrenia was defined as top priority for future health services redesign at international level (Patel et al., 2010). A series of policy actions, based on research evidence, stakeholder consultation, and examples of best practice worldwide, have been recently published to provide guidance to policy makers and all relevant stakeholders who influence care quality for schizophrenia, and supports their commitment to creating a better future (Fleischhacker et al., 2014).

According to the OECD reporting on the social and economic costs of neglecting mental health care (OECD 2014), a series of initiatives are suggested to respond better to the growing urgency of poor mental health. One of those covers measuring the burden of

[1] The loss in productivity that occurs when employees come to work even when unwell and consequently function at less than full capacity.

mental health to society (including also non-treatment) to better understand the scale of the problem and what works in tackling it. However, there is little information on almost all aspects of mental health in OECD countries, which means that policy makers cannot fully understand the scale of the challenge of mental health, or what works in tackling it. The challenge in collecting and mapping evidence is even greater when looking at the treatment gap, and their attached economic and social burden. Crucially, access to this information is required if policy makers are to commit greater resources to mental health care, to prioritise areas of greatest need, and make sensible decisions about effective and efficient care for mental ill-health. Part 2 aims to examine the current state of knowledge regarding the impact of unmet needs associated with non-treatment in schizophrenia in OECD countries. We explore also how complete is the evidence available and, in case it is not sufficient, propose how this problem can be studied further more concretely and robustly and what type of data would be needed for this purpose. Findings from a systematic literature research are reported to map current evidence of the impact of the problem available from the OECD countries literature. Following we comment on the evidence gathered and suggest future research to fill current gaps in the evidence and to inform policy.

# Methods

The search methodology was structured around the analytical framework pictured in figure 2.

- The focus of the search was on studies reporting on the following scenarios: missed or delays in diagnosis; no treatment or delays in treatment; inappropriate treatment (according to current care); and treatment discontinuation or drop out (non-adherence or non-compliance pending on the terminology used in the paper).

- Participants were individuals with schizophrenia (or psychosis).

- The type of studies screened were literature reviews, empirical studies of interventions irrespective of design and observational studies. Geography included OECD countries.

- Impact of unmet needs associated with non-treatment in schizophrenia was measured against the following outcomes: use of health and social care resources, comorbidities, use of criminal justice resources, employment, education, violence and premature death, and homelessness.

- A series of databases (MEDLINE, PsycINFO, ISI Web of Science, IBSS, and Social Care Online) and grey literature sources (OECD library, Open Grey library, Greylit library, and advanced Google search) were searched for outputs published in English (January 2004-September 2014).

- A series of experts checked the search methodology applied, commented on the results of the search and provided additional evidence. Mesh terms and corresponding text words are fully reported in appendix 1.

- The quality of the evidence was assessed against specific checklists: (Downs & Black, 1998) for observational/clinical studies; (Mogyorosy & Smith, 2005) for cost of illness studies; (Drummond & Jefferson, 1996) for cost effectiveness studies; PRISMA guidance (http://www.prisma-statement.org/statement.htm) for literature reviews.

# Results

### *Background results*

A total of 1017 papers were screened (811 from databases, 93 from grey literature and 43 from experts). Of these 47 were identified as relevant for the study, see figure 3.

- The majority of the papers reported on the impact of unmet needs on use of health care resources (27, 57%), violence/premature death (21, 45%) and employment (productivity, absenteeism; 13, 28%).

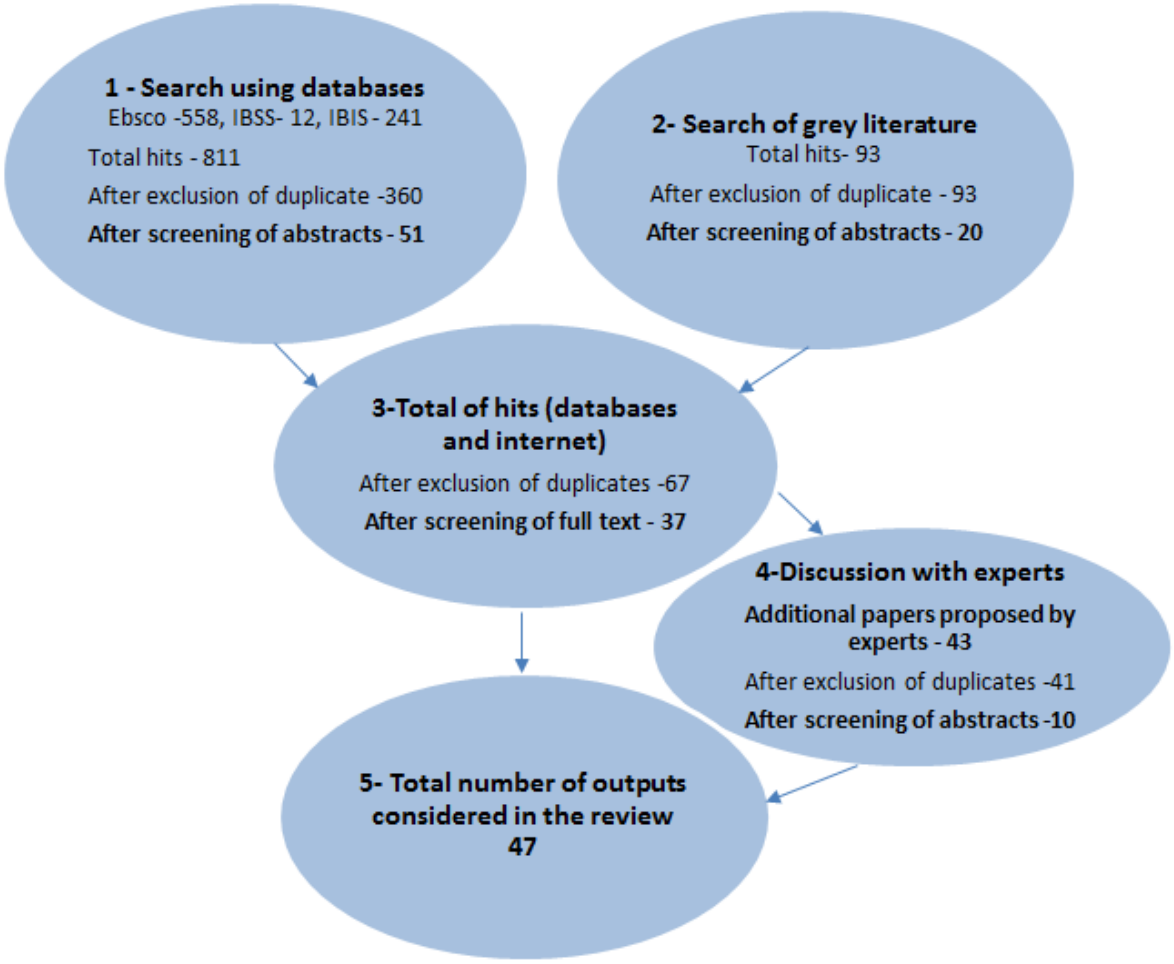
- A few papers commented on use of criminal justice resources (4, 9%), education (4, 9%), homelessness (3, 6%) or comorbidities (3, 6%).

Mapping of the evidence according to country settings is reported in table 1.

- The overall quality of the findings for observational studies in community (1) and clinical settings (24) as well as for RCT (2), cost-effectiveness models (4) and systematic reviews (7) was good.
- For the narrative reviews (7) and grey literature reporting (2) the quality of the findings used was difficult to assess as there was very limited information available on the sources of evidence accessed and the robustness of the modelling applied.

A detailed table reporting on findings according to each paper analysed is reported in appendix 2.

## Figure 3: Publications included in the review and selection process applied (numbers)



## Table 1 – Mapping of the evidence according to country settings

| | Outcomes | | | | | | |
|---|---|---|---|---|---|---|---|
| **Country setting (no. of papers)** | **Health care** | **Comorbidities** | **Criminal justice** | **Employment** | **Education** | **Violence Death** | **Homelessness** |
| **Australia (4)** | - | - | - | x | - | x | - |
| **Canada (2)** | x | - | - | x | - | - | - |
| **Croatia (1)** | - | - | - | - | - | x | - |
| **Denmark (2)** | x | - | - | - | - | x | - |
| **France (1)** | - | - | - | - | - | - | - |
| **Germany (3)** | x | - | - | x | - | x | - |
| **Greece (1)** | x | - | - | x | - | x | - |
| **Ireland (3)** | x | - | - | x | - | x | - |
| **Italy (3)** | x | - | - | x | - | x | - |
| **the Netherlands (2)** | x | - | - | x | - | x | - |
| **New Zeeland (1)** | x | - | - | - | - | - | - |
| **Norway (2)** | x | - | - | - | - | x | - |
| **Poland (1)** | x | - | - | x | - | - | - |
| **Portugal (2)** | x | - | - | - | - | x | - |
| **Slovenia (1)** | - | - | - | x | x | - | - |
| **Spain (3)** | x | - | - | x | - | x | - |
| **Sweden (4)** | x | - | - | - | - | x | - |
| **UK (8)** | x | - | - | x | - | x | - |
| **USA (11)** | x | - | x | x | x | x | x |
| **International (11)** | x | x | - | x | x | x | x |

## *Description of the evidence according to the outcomes*

### *Use of health care resources*

#### Impact of undiagnosed psychosis on the use of health resources

(Lim, Jacobs, Ohinmaa, Schopflocher, & Dewa, 2008).

- In a cross-sectional study looking at a population based measure of the economic burden of mental illness (including schizophrenia) in Canada, (Lim et al., 2008) reported that the utilisation of all health care services was highest for the diagnosed mentally ill, lowest for the non-mentally ill, with those in the undiagnosed category in the middle.

- The average annual medical cost per capita was C$643 for the non-mentally ill and C$2,515 for the diagnosed and C$1,442 for the undiagnosed (Canada, 2003 figures).

#### Impact of untreated psychosis on the use of health resources

(Cechnicki et al., 2014; HSM Group, 2012)(Mojtabai et al., 2009).

- (Mojtabai et al., 2009) found a substantial level of unmet need for care among individuals with schizophrenia both at community level and in clinical settings.
    - For example, in the United States, the Epidemiologic Catchment Area population study (conducted in the early 1980s) found that among individuals with symptoms in the past 6 months (6-month schizophrenia), only 57% had received some form of outpatient mental health care in this period: 40% from the specialty mental health sector (psychiatrists, psychologists, social worker, or other mental health professionals) and 17% from the general medical sector or the human services (such as the clergy or non-mental health social work) (Robins & Regier, 1991).
    - From the National Comorbidity population Surveys (NCS between 1990 and 1992; NCS-R between 2001 and 2003) it was found that at least 40% of individuals with actively symptomatic schizophrenia-spectrum disorders living in community settings in the United States have no consistent contact with needed services, and more than half have no contact with the specialty mental health treatment sector.
    - In a longitudinal study of first-contact patients with healthcare services (Jablensky, 2000) reported considerable variation across the industrialised and the developing countries in the patterns of service use and the unmet need for care.
    - As another example, in a clinical epidemiological study of first-admission psychotic disorders from the private and public inpatient facilities in the

USA (Mojtabai et al., 2002) only 54.6% of the 172 first-admission patients with a consensus diagnosis of schizophrenia had continuous medication visits in the 4 years following first admission (i.e., 3–6 visits per 6 months throughout the 4-year follow-up) and only 17.4% had continuous psychotherapy visits (i.e., 12–24 visits per 6 months).

- Patients with untreated schizophrenia can lead to the need for much more resource-intensive care (including increased inpatient care/hospitalisations, outpatient care, and long-term care/nursing homes) than schizophrenic patients who are getting regular care and treatment.

- In the USA (Greater Kansas City) the annual cost of untreated SMI was estimated to be $624 million (about $6609 per case of untreated SMI, 2010 estimates) (HSM Group, 2012). About 10 % of the overall costs were direct costs, or medical expenses associated with lack of sustained treatment (about $696 per case of untreated case of SMI). Direct costs included: increased inpatient care/hospitalisations, outpatient care, mental health organisations, and long-term care/nursing homes. For more details please see Part 4 - case studies.

- In Poland, (Cechnicki et al. 2014) found a lack of correlation between use of health resources (number of re-hospitalisations and duration of re-hospitalisations) and duration of untreated psychosis (DUP).

**Impact of non-adherence to treatment on the use of health resources** (H. Ascher-Svanum et al., 2006; Bodén, Brandt, Kieler, Andersen, & Reutfors, 2011; Higashi et al., 2013; Knapp, King, Pugner, & Lapuerta, 2004b; Llorca, 2008; Marcus & Olfson, 2008a; Novick et al., 2010; Offord, Lin, Mirski, & Wong, 2013; Sun, Liu, Christensen, & Fu, 2007) (Dilla, Ciudad, & Alvarez, 2013) (King et al., 2014) (Mojtabai et al., 2009) (Karve, Panish, Dirani, & Candrilli, 2012) (Hong, Windmeijer, Novick, Haro, & Brown, 2009) (Haddad, Brain, & Scott, 2014) (Sajatovic & Ross, 2009) (Weiden, Kozma, Grogg, & Locklear, 2004).

- Epidemiological studies find that many patients virtually drop out of treatment after their initial contact with services and receive little mental health care in subsequent years (Mojtabai et al., 2009).

- Clinical studies of patients in routine treatment settings indicate that the treatment patterns of these patients often does not meet the criteria set by evidence-based practice guidelines, while at least half of these patients continue to experience significant symptoms. The divergence from the guidelines is more pronounced with regard to psychosocial than medication treatments and in outpatient than in inpatient settings.

- We can identify a clear link between non-adherence and an increased risk of hospitalisation, use of emergency psychiatric services, longer length of hospital stay, and hospital costs (Higashi et al., 2013) (Dilla et al., 2013) (for examples see: Knapp et al., 2004; Marcus & Olfson, 2008; Ascher-Svanum et al., 2006; Bodén et al., 2011; Morken, Widen, & Grawe, 2008; Weiden et al., 2004).

- **Key evidence from Europe**
  - A multi-country observational study conducted in Denmark, Italy, Portugal, Spain, Ireland and the UK looking at the consequences of non-adherence with antipsychotic medication in the outpatient treatment of schizophrenia showed that non-adherence was significantly associated with an increased risk of relapse, hospitalisation and suicide attempts (Novick et al., 2010).
  - In a multi-country RCT based in UK, Italy, Germany and the Netherlands looking at the impact of non-adherence to medication in patients with schizophrenia (King et al., 2014) showed that the effect of non-adherence was not statistically significantly associated with health and social care costs, whereas patients who reported non-adherence had significantly lower societal costs than those reporting adherence.
  - Findings from an international European study (Germany, Italy, Spain, France Denmark, Greece, Ireland/the UK, the Netherlands, and Portugal); (Hong et al., 2009) demonstrate the significant economic burden of relapse (highly correlated to non-adherence to treatment), and show such costs were mainly due to hospital stay.

    Costs incurred by patients who ever relapsed during three years were almost double to those incurred by patients who never relapsed (£14055 vs. £7417). 61% of the cost difference was accounted for by hospital stay.

- **Key Evidence from USA**
  - (Sun et al., 2007) estimated that the national re-hospitalisation costs related to antipsychotic non-adherence was $1479 million, ranging from $1392 million to $1826 million in 2005.
  - (Offord et al., 2013) showed that early non-adherence is related to more hospitalisations (0.57 vs. 0.38; $P < 0.01$) with longer length of stay (5.0 vs. 3.0 days; $P < 0.01$) and higher yearly hospitalisation costs per person ($5,850 vs. $4,211; $P = 0.02$) compared with adherent patients.
  - (Karve et al., 2012) confirm that experiencing psychiatric-related relapse events almost doubles the direct costs of managing patients with schizophrenia. The mean schizophrenia-related total medical costs per patient were significantly higher among patients with 2 or more psychiatric-

related relapse events than among patients with <2 psychiatric-related relapse events (17,910 vs. 10,346; 2009 US$).

## Impact of non-compliance on the use of health resources

Four separate cost-effectiveness analyses (Damen, Thuresson, Heeg, & Lothgren, 2008; Treur, Heeg, Moeller, Schmeding, & van Hout, 2009) (Heeg et al., 2005) (Hensen, Heeg, Lo, & Hout, 2010) of compliance gains on antipsychotic treatments (based on discrete event simulation models) were conducted in Sweden (2), UK and Germany, respectively.

- In Sweden (Damen et al., 2008) considered two identical treatment arms except for percentage of compliant patients. The difference in compliance rates was varied from 0% to 15%, and incremental costs and effects were recorded and analysed. With a 5%, 10% and 15% difference in compliance rate, incremental effects increased to 0.021, 0.037 and 0.062, respectively, while generating cost savings of Swedish kronor (SEK) 31,500, SEK 62,000 and SEK 104,500, respectively (SEK9.25 = 1, Euro year 2007 values). On average, the model predicted that, with a 15% increase in compliance, 0.5 relapses were prevented, the average Positive And Negative Syndrome Scale (PANSS) score decreased by 3.3 points and patients spent 22 fewer days in hospital over 5 years. (Hensen et al., 2010) looked at the cost effectiveness of long-acting risperidone in Sweden and confirmed that compliance is the main driver of the cost effectiveness of the medicine. Similar results are reported in Germany (Treur et al., 2009).

- In the UK (Heeg et al., 2005) developed a model to incorporate social and environmental factors into the decision-making process for the prescription of new drugs to patients. The model was used to analyse the potential benefits of improving compliance with medication by 20% in patients in the UK. A 20% increase in compliance was estimated to save £16,147 and to avoid 0.55 psychotic episodes per patient over 5 years. Sensitivity analysis showed that the costs savings associated with increased compliance are robust over a range of variations in parameters.

### *Comorbidities*

The evidence gathered was limited to narrative reviews looking at the unmet needs in the management of schizophrenia (Fleischhacker et al., 2014) (Mojtabai et al., 2009) (Torres-González et al., 2014).

- Poor evidence is available and refers to narrative reviews commenting on the impact of unmet needs on comorbidities when managing schizophrenia.

- No economic estimates are available related to the impact of non-treating schizophrenia on its comorbidities.

- Evidence refers to international settings (not clearly specified).

- One of the most important issues is that people with schizophrenia die 15–20 years earlier than the general population. It is thus important not only to manage the symptoms of schizophrenia but also to treat coexisting physical illnesses. Under-diagnosis and under-treatment of schizophrenia (and related comorbidities) contribute to this high death rate. It should be a priority to develop and implement an evidence-based, integrated care package that addresses patients' mental and physical health needs (Fleischhacker et al., 2014).

- The high prevalence of medical problems in patients with schizophrenia calls for integration or better coordination of mental health and general medical services. (Mojtabai et al., 2009) reported that in the literature there has been a renewed interest in the medical care of these patients, including receipt of the needed preventive and treatment services for chronic medical conditions and dental care.

- In a more recent review (Torres-González et al., 2014) confirmed that, in schizophrenia, an increased likelihood risk for overweight, obesity, and abdominal obesity is present even in recently diagnosed and non-treated patients. However no economic estimates are available related to the impact of non-treating schizophrenia on its comorbidities.

### *Use of criminal justice resources*

- Only four papers were identified as suitable for analysis (H Ascher-Svanum et al., 2006; HSM Group, 2012; Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (Haddad et al., 2014); these studies included one observational study, one economic modelling and two narrative reviews/reports.
- The setting was limited to the USA. Comparison included: untreated psychosis (2), and non-adherence to treatment (2).

## Impact of untreated psychosis on the use of criminal justice resources

It is recognised that the costs of mental disorders are more indirect than direct, and they are primarily related to a lack of treatment.

- Two papers looking at the cost of non-treating mental illness in the USA (Greater Kansas City Area, Missouri (HSM Group, 2012) and Houston, Texas (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009)) reported on the indirect costs of mental health disorders, including the costs of lost productivity due not only to morbidity and premature deaths (mortality costs), but also other factors such as incarceration.
- In Greater Kansas City, the annual incarceration costs of individuals with severe mental illness resulted in $8.2 million to the criminal justice system (2010 estimates, (HSM Group, 2012)). For the Harris County, Texas, the 2008 costs of caring for the County's incarcerated people with mental illness exceeded $48 million (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).
- The annual costs for the criminal justice system per case of untreated severe mental illness are US$87 (2010; greater Kansas City Area, USA; HSM Group, 2012).

## Impact of non-adherence to psychotic treatment on the use of criminal justice resources

- In their literature review (Haddad et al., 2014) reported on the association between antipsychotic non-adherence and a significantly higher rate of psychiatric hospitalisation, use of emergency psychiatric services, arrest, violence, victimisation, and substance use plus poorer mental functioning, poorer life satisfaction, and more alcohol-related problems.

- Non-adherence is associated with poorer functional outcomes, including greater risks of psychiatric hospitalisations, use of emergency psychiatric services, as well as arrests, violence, victimisations, poorer mental functioning, poorer life satisfaction, greater substance use, and more alcohol-related problems (all $p < 0.01$; (H Ascher-Svanum et al., 2006)).

### *Employment (productivity, absenteeism)*

Thirteen publications were identified suitable for analysis (Cechnicki et al., 2014; Higashi et al., 2013; Hill et al., 2012; HSM Group, 2012; Lim et al., 2008; Llorca, 2008; Norman et al., 2012; OECD, 2014; Reininghaus et al., 2008; Šarotar, Pesek, Agius, Pregelj, & Kocmur, 2008; Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (Schimmelmann et al., 2008) (Hong et al., 2009).

- They included: observational studies (8), narrative reviews/reports (3), and systematic literature reviews (2).

- International settings covered: USA (2), Ireland (2), UK (2), Australia (1), Canada (1), Poland (1), Slovenia (1), Germany (1), Italy (1), Spain (1), Portugal (1), France (1), Denmark (1), Greece (1), the Netherlands (1), International literature (not specified, 2).

- Comparison included: undiagnosed psychosis (1), untreated psychosis (8), non-adherence to psychotic treatment (2), and non-compliance (1).

## Impact of undiagnosed psychosis on employment

- In a population based cross sectional study in Canada (Lim et al., 2008) reported that absenteeism (long-term work loss) is highest for the diagnosed mentally ill, lowest for the non-mentally ill, with those in the undiagnosed category in the middle. Unemployment rate is highest for the diagnosed 0.46%, but a smaller group of undiagnosed (0.26%) were unemployed compared with people with no mental illness (0.33%). The number of disability days per year (short-term work loss) were, respectively: 33 (diagnosed mentally ill), 27 (undiagnosed mentally ill), and 10 (non-mentally ill).

- The value of work loss from absenteeism was about 10% higher than the value of work loss from unemployment; and together they account for about 35% of the burden.

- The monetary value of work loss (due to both absenteeism and disability loss) was 14,110 C$ for the diagnosed compared with 3619 C$ for the undiagnosed (annual total burden of 17729 C$; (Canada, 2003 figures; Lim et al., 2008)).

## Impact of untreated psychosis on employment

(Cechnicki et al., 2014; HSM Group, 2012; Norman et al., 2012; OECD, 2014; Reininghaus et al., 2008; Šarotar et al., 2008; Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (Schimmelmann et al., 2008).

- Mental illnesses have a huge labour market cost: OECD data suggests that one in five working age people have had a mental problem at some point in time, reducing their employment prospects, productivity and wages (OECD, 2014).

- The high costs of mental illnesses (including untreated mental illnesses) for society suggest a strong need for better services. They have been shown to have a strong relationship with higher unemployment, higher absenteeism, lower productivity in

the workplace, and a rising burden of disability benefits claims across countries (OECD, 2014).

- Two studies looked at the cost of non-treating mental illness in the USA (Greater Kansas City Area, Missouri (HSM Group, 2012), and Houston, Texas (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009)) and reported on the impact of untreated psychosis on employment and productivity. When modelling the cost of non-treating mental illness in Greater Kansas City Area, USA (HSM Group, 2012) it is reported that overall about 24% of individuals with SMI are unemployed at any given time, and about half of those cases are due to lack of treatment. In Greater Kansas City, this can lead to more than 15,000 adults who are unemployed due to lack of treatment for SMI. A high proportion (88%) of the total burden of untreated SMI (including schizophrenia) was in the form of indirect costs to employers and individuals. The annual indirect costs (absenteeism, presenteeism, unemployment, premature death) per case of untreated SMI are US$5785 (2010).

- When looking at the consequences of untreated mental illness in Houston (Texas, USA) an insufficiently funded mental health service is reported to lead to societal productivity loss, homelessness, increased juvenile and adult criminal justice system involvement and decrease in life expectancy (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).

- Delay in treatment with antipsychotic medication (duration of untreated psychosis, DUP) was found to be allocated with unfavourable course of schizophrenia, including negative occupational functioning and disability benefit. In Poland (Cechnicki et al., 2014) analysed the relationship between the duration of DUP and the course of schizophrenia in a 20-year follow up study. In terms of employment, the relationship between longer DUP and worse employment outcome was statistically significant at 7 and 12 years from first hospitalisation. In Slovenia (Šarotar et al., 2008) showed that half of the patients with DUP longer than 1 year were on disability benefit as compared to 19% of patients who had received treatment with antipsychotic medication in the prodromal phase of the disease. In Canada (Norman et al., 2012) found that delay between onset of non-specific symptoms and treatment (duration of untreated illness, DUI) was a more robust predictor of occupational functioning and use of a disability pension compared with DUP. In Australia (Schimmelmann et al., 2008) in a longitudinal study involving 786 patients with first-episode psychosis (FEP) showed that duration of untreated psychosis is associated with a lower rate of employment/occupation ($p<0.01$). In the UK (Reininghaus et al., 2008) confirmed association between untreated psychosis and unemployment; unemployed subjects were more likely to experience longer periods of untreated psychosis when

reporting low (P < 0.01) or medium (P < 0.01) number of social contacts. No such difference could be observed for those with high social contacts (P = 0.60).

## Impact of non-adherence/non–compliance to psychotic treatment on employment

- Systematic review of the international literature showed that non-adherence, partial adherence and non-compliance can arise a downward spiral of events leading to inconsistent symptom control, relapse and re-hospitalisation, which in turn can lead to long-term functional disabilities, and loss of employment possibilities (Higashi et al., 2013) (Llorca, 2008).

- Findings from the large prospective pan-European Schizophrenia Outpatient Health Outcomes (SOHO) study show that relapsers had an earlier onset of schizophrenia and had a poorer level of social functioning at baseline (i.e. a lower frequency of paid employment and social contacts in previous 4 weeks) compared with individuals who never relapsed (Hong et al., 2009). (Hill et al., 2012) reported no association between DUP and gainful employment over 12 years.

### *Education*

Four papers were identified suitable for analysis (Šarotar et al., 2008; Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (Higashi et al., 2013; Llorca, 2008), including observational studies (2), systematic literature reviews (2), and one narrative review (1).

- International settings covered: USA (1), Ireland (1), Slovenia (1), International literature (not specified, 2).

- Comparison included: untreated psychosis (2), non-adherence to psychotic treatment (1), and non-compliance (1).

## Impact of untreated psychosis on education

(Šarotar et al., 2008; Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).

- Evidence from the USA showed that untreated subjects often have difficulty in school and have an increased likelihood of becoming involved with the juvenile justice system (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).

- In Slovenia (Šarotar et al., 2008) found that DUP longer than 1 year had a negative impact on the educational level achieved.

## Impact of non-adherence to psychotic treatment on education

There is evidence in the literature to say that non-adherence, partial adherence and non-compliance can lead to loss of education (systematic reviews conducted by (Higashi et al., 2013; Llorca, 2008).

### *Violence and premature death*

Twenty-one papers were identified suitable for analysis, including observational studies (11), literature reviews/meta-analysis (7), and one RCT, one model and one report. (Nielssen, Malhi, McGorry, & Large, 2012) (Challis, Nielssen, Harris, & Large, 2013) (OECD, 2014) (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (HSM Group, 2012) (Nielssen & Large, 2011) (Mork et al., 2013) (Nielssen & Large, 2009) (Yee, Large, Kemp, & Nielssen, 2011) (Arango, Bombín, González-Salvador, García-Cabeza, & Bobes, 2006) (Foley et al., 2007) (Higashi et al., 2013) (Novick et al., 2010) (Llorca, 2008) (Fazel, Buxrud, Ruchkin, & Grann, 2010) (H Ascher-Svanum et al., 2006) (Fazel, Zetterqvist, Larsson, Långström, & Lichtenstein, 2014; Hong et al., 2009; Kudumija Slijepcevic et al., 2014; Látalová, 2014; Mojtabai et al., 2009).

- International settings covered: USA (5), Australia (3), Ireland (2), Denmark (2), Sweden (2), Norway (1), Italy (2), Portugal (2), Spain (3), UK (2), Ireland (1), the Netherlands (1), Slovenia (1), Croatia (1), Germany (1), France (1), Greece (1), International literature (not specified, 6).

- Comparison included: untreated psychosis (10), non-adherence to psychotic treatment (9), and non-compliance (2).

- The majority of the evidence describes the social impact of unmet needs looking at prevalence of violent acts (self-harm or aggressive behaviour towards others), suicide attempt or criminal offences (due to violent acts and homicides).

- A recent OECD report (2014) described that psychiatric illness is a major risk factor for suicide and it has been estimated that 90% of suicide attempters and completers suffer from at least one, mostly unrecognised, untreated, or inadequately treated mental illness.

**Impact of untreated psychosis on violence and premature death** (Nielssen et al., 2012) (Challis, Nielssen, Harris, & Large, 2013) (OECD, 2014) (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (HSM Group, 2012) (Nielssen & Large, 2011) (Mork et al., 2013) (Nielssen & Large, 2009) (Kudumija Slijepcevic et al., 2014; Látalová, 2014).

- Violent behaviour frequently develops before the onset of a first episode. Available evidence suggests that the prevalence of violent behaviour in the first episode of psychosis, particularly schizophrenia, is greater than during the later stages of the illness. First-episode psychosis is associated with an increased risk of homicide. There is some limited evidence for an effect of DUP length on serious violence or aggression (Látalová, 2014).

- A review of the evidence on violence acts to self and others during the first episode of psychosis showed that a substantial proportion of first-episode patients commit an act of less serious violence or attempt suicide prior to initial treatment (Nielssen et al., 2012).

- In a systematic meta-analysis of the risk factors for deliberate self-harm before and after treatment for first-episode psychosis (Challis, Nielssen, Harris, & Large, 2013) reported that DUP is associated with an increased risk of deliberate self-harm.

- In Croatia (Kudumija Slijepcevic et al., 2014) reported that DUP before first contact with psychiatric services acts as one of the predictors of violence, together with older age and alcohol abuse.

- In the USA, over 15 percent of indirect costs of severe mental illness (treated and untreated cases) are related to mortality costs, or loss of productivity due to premature death (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).

- The annual cost burden of untreated SMI in the USA (Greater Kansas City) has been estimated to be $624 million (2010 estimates, (HSM Group, 2012)). A high proportion, 87.5%, of these costs is in the form of indirect costs to employers and individuals, including unrealised earnings due to permanent disability or premature death (suicides). The model estimated that 67 suicides in Greater Kansas City can be attributed to SMI annually (HSM Group, 2012).

- Psychosis is strongly associated with potentially lethal suicide attempts using sharp objects and patients who have never received treatment for psychosis appear to be at particular risk (Nielssen & Large, 2011).

- When compared with non-suicide attempters and those with suicide attempts without non-suicidal self-harm, patients with both suicide attempts and non-suicidal self-harm were more frequently women, younger at the onset of psychotic symptoms, had longer duration of untreated psychosis, and had higher levels of current impulsivity/aggression and depression (Norway, (Mork et al., 2013)).

- When looking at untreated psychotic illness in the survivors of violent suicide attempts, there appears to be a higher risk of violent suicide attempts during the first episode of psychosis than later in the illness (Nielssen & Large, 2009).

## Impact of non-adherence to psychotic treatment on violence and premature death

(H Ascher-Svanum et al., 2006) (Yee et al., 2011) (Arango et al., 2006) (Foley et al., 2007) (Higashi et al., 2013) (Novick et al., 2010) (Fazel et al., 2014; Hong et al., 2009) (Haddad et al., 2014).

- Good adherence to treatment appears to be associated with lower levels of aggressive behaviours and people with schizophrenia who adhere to their treatment and are clinically stable appear to be no more violent than the general population (Fleischhacker et al., 2014).
    - In the USA when observing medication adherence in the treatment of schizophrenia in usual care, lack of adherence was associated with poorer outcomes, including increased acts of violence (H Ascher-Svanum et al., 2006) (Haddad et al., 2014).

    - In Australia, when looking at severe non-lethal violence during psychotic illness, individuals who committed a severe violent offence were typically non-adherent to treatment, had co-morbid substance use and prior criminal convictions (Yee et al., 2011).

    - In Europe (Hong et al., 2009) showed that more relapsers (5.8%) had suicide attempts in the six months before baseline, compared to non-relapsers (3.3%). For other examples please refer to (Fazel et al., 2014) (Arango et al., 2006).

    - In contrast with the evidence reported above, (Foley et al., 2007) did not find an association between violence at presentation and DUP. They argued that the relationships between violence, DUP and psychopathology may be confounded by other methodological factors such as potential difficulties inherent in the completion of outcome measures used in the study (see the *Positive and Negative Syndrome Scale* PANSS).

- Suicide is one of the leading causes of premature death in patients with schizophrenia, but it is highly preventable. Evidence reported in a systematic review literature showed that non-adherence to antipsychotic medication is one of the risk factors for the development of suicidal behaviour in patients with schizophrenia (Higashi et al., 2013).
    - An international study conducted in Denmark, Italy, Portugal, Spain, Ireland and the UK showed how non-adherence is significantly associated with an increased risk of suicide attempts (Novick et al., 2010).

## Impact of non-compliance to psychotic treatment on violence and premature death

(Llorca, 2008) (Fazel et al., 2010).

- It is commonly recognised in the literature that non and partial compliance can lead to long-term negative outcomes (loss of autonomy, education or employment possibilities, homelessness, a likelihood of dropping out of care completely) and even suicide (Llorca, 2008).

- When looking at homicide in discharged patients with schizophrenia and other psychoses in Sweden, common factors associated with homicide were evidence of medication non-compliance and substance misuse (Fazel et al., 2010).

### *Homelessness*

Three reviews of the literature were suitable for analysis, two narratives on the USA (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (Mojtabai et al., 2009), and one systematic review on international settings (Llorca, 2008).

Limited evidence describes the economic impact of unmet needs looking at the use of healthcare resources (e.g. hospitalisation, emergency services) and housing costs.

## Impact of untreated psychosis on homelessness

- Many patients with schizophrenia are at increased risk of homelessness and associated adverse social and health outcomes, such as victimisation and sexually transmitted diseases (Mojtabai et al., 2009).

- People with schizophrenia and other severe mental illnesses who become homeless have difficulty accessing healthcare. The lack of a permanent address, complicated eligibility requirements and daily struggles with their untreated mental illness are

barriers to accessing primary care. This ultimately leads to use of higher-cost services such as emergency departments and inpatient care (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).

- The cost of providing permanent, supportive housing for people with severe mental illness may be offset by savings incurred by reductions in healthcare costs in public hospitals, and also in prisons, and shelter systems (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009).

**Impact of non-compliance to psychotic treatment on homelessness -** Non- and partial compliance can lead to long-term negative outcomes including homelessness (with a high likelihood of dropping out of care completely) (Llorca, 2008).

# KEY MESSAGES AND OPPORTUNITIES FOR FUTURE RESEARCH

- Results from the search of the literature reveal considerable gaps in our current knowledge on the extent of the unmet need for care.

- The majority of the evidence is limited to delays in or missed treatment in hospital settings, whilst very little is known on unmet needs at earlier (diagnosis) or later (community treatment) stages of the patient pathway.

- The majority of the evidence describes the impact on healthcare resource use, violence or employment whilst less attention is paid to homelessness and use of criminal justice resources outcomes.

    - **Limitations** due to the choice of sample - difficulties in reaching particular groups of the population in need – e.g. homelessness, prisoners or younger individuals.

    - **Future research** is needed to address unmet needs across settings. Retrospective data collection of patient level data from first-episode patients in contact with mental health services, primary care social care services could allow having broad-spectrum information on the impact of non-treatment on multiple outcome measures.

- The majority of the evidence identifies unmet needs in clinical setting.

    - **Limitations:** there is a lack of reliable data from population-based epidemiological studies on which to base the population estimates of treatment and the potential unmet need for treatment.

    - **Future research** could benefit from ongoing country specific national surveys to source information on the impact of non-treatment on multiple outcomes. For example one of the current English National surveys (such as LHA National Survey of Health and Development) could act as a useful source of

information on the impact of non-treatment on multiple outcomes (e.g. access and use of health and social care resources, employment, education).

This is a cohort of 5,362 births in 1946 followed up to the present day. It contains data on subjects' physical and mental health, including observational measures, diet and lifestyle, and family, employment and social circumstances. It would allow comparing people with a diagnosis of mental health illness vs individuals who self-reported a mental health problem but were not diagnosed/never received treatment for their mental health issue. Individuals could be followed longitudinally until their older life to capture the impact of childhood determinants (or delays in treatment) on access to resources in adulthood and older stages.

- Poor evidence on the impact of unmet needs on physical comorbidities.
    - **Limitations**: recognition and management of comorbidities in people with schizophrenia are made more difficult by barriers related to the patients, the attitudes of medical practitioners, and the structure of healthcare delivery services.
    - **Future research** should produce economic and social estimates related to the impact of non-treating schizophrenia on its comorbidities.
- Discrepancy of evidence across settings, few countries (e.g. USA, UK) present stronger evidence than others.
    - **Limitations**: discrepancies across settings in the information system that support the management of care and access to data on the diagnosis, care and treatment gap of schizophrenia.
    - **Future research**: the data base of evidence gathered here could be used to inform a future modelling exercise to predict the impact of non-treatment across multiple scenarios and settings.

# PART 3 - CHALLENGES AND FUTURE OPPORTUNITIES

Improving care for people with schizophrenia, their caregivers, and their families is an urgent health care priority across country settings (OECD, 2014).

Although schizophrenia is a disabling and severe mental disorder, people with the illness can, when supported by appropriate diagnosis, assessment, management, recognition and support of their needs, report a positive impact on their health which can lead to recovery (Fleischhacker et al., 2014).

Unfortunately the social and economic costs of neglecting mental healthcare are a major problem and three public health initiatives are suggested by OECD to respond better to the growing urgency of poor mental health (OECD, 2014). They include: Measuring mental health to better understand the scale of the problem, and what works in tackling it; Increasing provision of evidence-based services, especially through expanding the role of the primary care sector, with appropriate system-wide support; Securing better outcomes for mental disorders through greater use of incentives.

The objectives of part 3 of the report are to: discuss what the policy issues and policy gaps are in connection with non-treatment; and propose possible solutions on how to address those gaps identified.

Firstly, evidence from the literature is used to define possible issues and opportunities when dealing with the problem. Following that, comments from a group of leading experts (including researchers and practitioners) in the field of schizophrenia/psychoses are presented to shape recommendation to policy on the issues to be prioritised and their possible solutions.

# Source of the problem

Evidence from the literature report on the following reasons for unmet needs: patient/caregiver factors; provider factors; and health care system factors.

## *Patient/caregiver factors*

- **Lack of illness awareness** - Patients and their family members do not recognise that they/their relatives have symptoms. They may focus instead on various somatic concerns, such as gastrointestinal complaints, fatigability, and headaches. Others may recognise that there is a problem, but fail to identify it as schizophrenia. (Hirschfeld et al., 1997) (Statistics, 2012) (Cooke, 2014).

- **The direct impact of symptoms** – They cover depression, cognitive impairment, positive and negative symptoms. Few examples include: auditory hallucinations that may instruct the patient not to take the medication; withdrawal/lack of ability to begin and sustain planned activities such as taking the medication; or poor ability to understand information on their care and use it to make decisions (Haddad et al., 2014) (Statistics, 2012).

- **Lack of severity awareness** - Patients and their family members underestimate the severity of the problem, they do not see the psychotic episode as serious enough to seek treatment (Hirschfeld et al., 1997) (Statistics, 2012).

- **Limited access to treatment** - Patients and their family members who do recognise or acknowledge that they need help may face limited access to treatment (Hirschfeld et al., 1997) (Statistics, 2012).

- **Lack of awareness of the time course for symptom improvement** - Patients may not be aware of the time course for symptom improvement after starting antipsychotic medication and do not discuss switching to another antipsychotic, if they do not respond to an adequate trial of a medication (Haddad et al., 2014).

- **Lack of knowledge about side effects of medications -** It is important that patients are warned of side effects before starting medication. For example increasing the dose gradually and/or explaining to the patient that side effects should settle can reduce the likelihood of side effects impairing adherence. Managing side effects that emerge during treatment depends on their detection in liaison with the healthcare

providers. The use of a simple checklist can also aid the detection of side effects (Haddad et al., 2014).

- **Lack of skills or management strategies to cope with side effects –** The impact of side effects can sometimes be reduced in liaison with the healthcare provider, by altering the timing of medication-taking. For example, if clozapine is causing sedation, the greater part of the dose can be taken at night-time rather than splitting the dose equally between morning and night-time. Other strategies to manage side effects include dose reduction, recommending a specific treatment for a side effect (e.g. weight management program for antipsychotic-associated weight gain), prescribing another medication (e.g. an anticholinergic drug to treat antipsychotic-induced Parkinsonism), or switching to another antipsychotic (Haddad et al., 2014).

- **Stigma and negative perceptions about psychiatric care and schizophrenia** - Even when treatment for schizophrenia is readily available patients are sometimes reluctant to seek psychiatric care because they fear prejudice and discrimination (Statistics, 2012) (Fleischhacker et al., 2014).

- **Monetary costs to the patients and their families** - They have to bear the financial expenses associated with mental health treatment and care (Doessel et al., 2010) (Statistics, 2012).

- **Lack of support from family/caregivers to remind patients to take the medications** - Although professional support can be helpful, often the most important source of help and support in the management of the disease is the network of relationships: friends, family and community (Cooke, 2014). For example, they can offer to accompany the friend or relative to appointments, or help them when taking medications. One aspect of non-adherence to medication can be viewed as lack of capacities within the family to remind patients to take their medication (Haddad et al., 2014).

### *Provider factors*

- **Lack of appropriate information, training and education on schizophrenia** - Reasons that rest with the primary care providers include the failure of medical schools in providing appropriate education about psychiatric diagnosis, psychopharmacology, or psychotherapy for schizophrenia (Fleischhacker et al., 2014) (Haddad et al., 2014).

- **The believe that schizophrenia is not a "real" illness** - Primary care providers may believe that psychiatric disorders are not "real" illnesses compared with other

physical illnesses with tangible biomarkers that can assist in the assessment of risk, diagnosis and monitoring of their progression (Doessel et al., 2010) (Cooke A, 2014).

- **Lack of training in interpersonal skills** - Primary care providers may have limited training in the interpersonal skills that enable them to manage emotional distress people and therefore they prefer to avoid dealing with these patients (Haddad et al., 2014). Emotional support and help with practical issues is often as important as help targeted directly at 'symptoms' (Cooke, 2014).

- **Poor quality of communication and collaboration between the providers and the patients in care management** - There is a lack of alliance with patients and their families to ensure that recommendations on treatment goals and strategies are met (Fleischhacker et al., 2014) (Statistics, 2012). A useful role for professionals is helping friends, family and self-help groups to support people in needs (Cooke, 2014).

- **Care plan limitations** - Managed care plans can make it difficult for physicians to prescribe newer medications, even though they are now widely regarded as safer first-line treatments. Managed care procedures can also inhibit appropriate referral to a psychiatrist (Hirschfeld et al., 1997).

- **Lack of continuity of care with a single clinician** - Extensive evidence exists that initiatives designed to improve continuity of care can produce a favourable outcome in schizophrenia care (Haddad et al., 2014) (Fleischhacker et al., 2014).

- **The attention is on other phenomena** - that have become medicalised - see sadness and general stress of everyday life as commented by (Doessel et al., 2010).

- **Social and cultural factors** - (Fleischhacker et al., 2014) (Statistics, 2012) report that social and cultural factors can either increase or decrease adherence. There is also huge diversity in the way that experiences are understood (and treated) in different cultures. In some cultures, experiences such as hearing voices are highly valued as spiritual gifts (Cooke, 2014).

### *Health care system factors*

- **Difficulties in providing the appropriate service** – e.g. providers who have been trained specifically in these modalities are not readily found in some communities/primary care premises (Hirschfeld et al., 1997) (Fleischhacker et al., 2014).

- **Poor collaboration among the different parties** - Lack of integrated team approach, involving psychiatrists, a range of health care professionals, social care providers, and other external agencies. It also involves collaboration with people with schizophrenia, their families, and other sources of support (Fleischhacker et al., 2014).

- **Lack of adequate insurance reimbursement for services** - For private health care systems, such a team approach will require careful alignment of reimbursement mechanisms to support high-quality care (Statistics, 2012) (Fleischhacker et al., 2014).

- **Lack of monitoring of patients** - The system discourages the proper monitoring of patients once the treatment regimen is started. For example, see patients who need to be re-evaluated at frequent intervals, to assess whether the treatment is working in a reasonable amount of time and to give the provider the opportunity to make adjustments in the treatment regimen (Haddad et al., 2014).

# Challenges in the evaluation of the impact

Multiple challenges have been identified in the literature when dealing with the social and economic impact of untreated schizophrenia. The most recurrent include:

- **Discrepancies in the information system that supports the management of care –** There is evidence that shows how electronic records have potential to improve medication management for patients in mental health centres over traditional records. However, medication documentation for patients diagnosed with schizophrenia can be deficient in many areas, regardless of documentation format (Tsai & Bond, 2008) (OECD, 2014).

- **Discrepancies between different criteria used for the assessment and diagnosis of schizophrenia** - There are diagnostic discrepancies due to cultural differences and they refer to different characteristics of patients and clinical presentation of the illness in different countries, as well as to different interpretation of the psychiatrists due to their personal and professional experience, their personal training and the environment where they work (Rezvyy, Oiesvold, Parniakov, & Olstad, 2005). Over time, the list of psychiatric diagnoses has expanded to a point that some have argued that the list is now so exhaustive that we would all fit one category or another. The newest version of the diagnostic manual, DSM 5, has been so controversial (Cooke, 2014).

- **Discrepancies in methods used when assessing non-adherence/ non-compliance** - Multiple methods have been used in research studies to quantify adherence, and the choice of method greatly impacts the finding (Haddad et al., 2014)(Sajatovic & Ross, 2009).

- **Choice of sample** – researchers may experience difficulties in reaching particular groups of the population in need – e.g. homeless people, prisoners, or younger groups (Mojtabai et al., 2009).

# What can be done to address the problem

- **Providing educational programs to increase provider knowledge and understanding about schizophrenia** - Ensure that enough medical professionals are expertly trained to perform detailed assessment and diagnosis in patients with suspected schizophrenia. Train junior doctors in thorough clinical assessment, accurate diagnosis, and good prescribing practice (Fleischhacker et al., 2014). Professionals need to shift from seeing themselves as treating disease to seeing themselves as providing skilled help and support to people who are experiencing understandable distress (Cooke, 2014).

- **Increasing patient, caregivers/family and society knowledge and understanding about schizophrenia** - (Fleischhacker et al., 2014) highlight the needs of concrete support, information, and educational programs to families and caregivers on how to enhance care for an individual living with schizophrenia in a manner that entails minimal disruption to their lives. Campaigns to increase awareness and tackle prejudice and discrimination toward people with schizophrenia can be effective in diminishing negative attitude.

- **Enhancing the role of patients and their families in decision making for patient care** - WHO Global Mental Health Action Plan (World Health Organization, 2013), which emphasizes the use of evidence-based therapies and the empowerment of people with mental disorders. (Fleischhacker et al., 2014) report how patient empowerment constitutes a significant factor in achieving recovery. The British Psychological Society says that it should be standard practice for service users to be involved at all levels, from planning the service as a whole to providing feedback to individual teams and, perhaps most importantly, in planning their own care (Cooke, 2014).

- **Developing performance standards for behavioural health care** -The limitations of current care are such that the UK Schizophrenia Commission has labelled schizophrenia "the abandoned illness" (The Schizophrenia Commission, 2012). It is therefore imperative that our existing (and effective) tools are available to all those with schizophrenia who need them; our best practices should become standard and monitored using appropriate performance indicators. There is good evidence that high-quality, early intervention services increase the likelihood of a good outcome and are cost-effective (Fleischhacker et al., 2014).

- **Providing care treatment guidelines and protocols accessible to patients and providers** - (Fleischhacker et al., 2014) invite practitioners and policy makers to provide an evidence-based, integrated care guidance for people with schizophrenia that addresses their mental and physical health needs. Such recommendations should be agreed jointly by health care providers and people with schizophrenia (or their representative if appropriate). National and international psychiatric organizations should work together to develop and implement consistent guidance for good prescribing practice (Hirschfeld et al., 1997).

- **Supporting more effective collaboration among primary care providers, psychiatrists, and other mental health professionals** - (Fleischhacker et al., 2014) say that all stakeholders, including organisations that support people living with schizophrenia, should be consulted to regularly revise, update, and improve policy on the management of schizophrenia. An integrated approach, delivered by a multidisciplinary team working with the patients and their families, can significantly improve the outcome of schizophrenia treatment and coexisting physical illness.

- **Promoting the use of tools to remember daily medication doses** - There is increasing interest in electronic reminders and monitoring systems to enhance adherence (e.g. see "Short Message Service" text messaging and real-time medication monitoring linked to smart pill containers or an electronic ingestible event marker; Haddad, Brain, & Scott, 2014).

- **Ensuring that services are easily accessible by patients** - The provision of adequate measures to decrease the burden of illness requires effective coordination of services, their accessibility and continuity of health and social care (Fleischhacker et al., 2014). Service structures need to allow providers the flexibility to tailor help to the particular needs of each person rather than offering standardised packages of care (Cooke, 2014).

# Challenges and opportunities in addressing the problem: the experts' view

## *Objectives and methods*

The data reported here were collected through a web-based survey designed to assess international experts' perceptions of unmet needs in schizophrenia. In particular we aimed at collecting their feedback on what the policy issues and policy gaps are in connection with non-treatment; and possible solutions on how to address those gaps. The survey was conducted by the London School of Economics in collaboration with a team of international experts in schizophrenia who supported its dissemination to international colleagues. A snowball sampling approach was used and replies were collected between December 2014 and January 2015. Subjects were contacted by email in a two-step process, including initial contact and one reminder at two-week intervals. Given the limited resources and time constraints the goal of the project was to get opinions from a series of high-profile international experts rather than a representative sample of mental health professionals/researchers based in particular country settings.

A series of 5-point Likert questions (strongly disagree, disagree, unsure, agree, strongly agree) were used to examine the above objectives and they are detailed in each relevant findings section. In brief, however, we relied upon two relevant question sets:

- Challenges in addressing the non-treatment of schizophrenia (including patient/caregiver, provider health care system and evaluation of the impact factors);
- Opportunities in addressing the non-treatment of schizophrenia.
- Additional information was collected on the country of residence and on the personal academic and professional experience of the expert (number of years and field of research/practice).

Responses were anonymised and the frequency of responses to questions was analysed using SPSS software. Data were analysed for the whole study population.

## *Results: survey responses*

Responses in time for analysis for this reporting arrived from 25 experts (13.7%; 25/183) from Germany (5), USA (4), Spain (3), Italy (2), Austria (1), England (1), Finland (1), Greece (1), Hungary (1), Denmark (1), Poland (1), South Africa (1), Latvia (1), Bulgaria (1), Montenegro (1).

Almost all of them (96%; 24/25) reported research experience (average of 20 years) in the field of schizophrenia, suicide, psychiatry, social neuroscience, clinical psychology, depression/anxiety. 88% (22/25) had also clinical experience (average of 23 years) in clinical psychology and psychiatry/psychotherapy.

## *Results: expert feedback on the source of the problem*

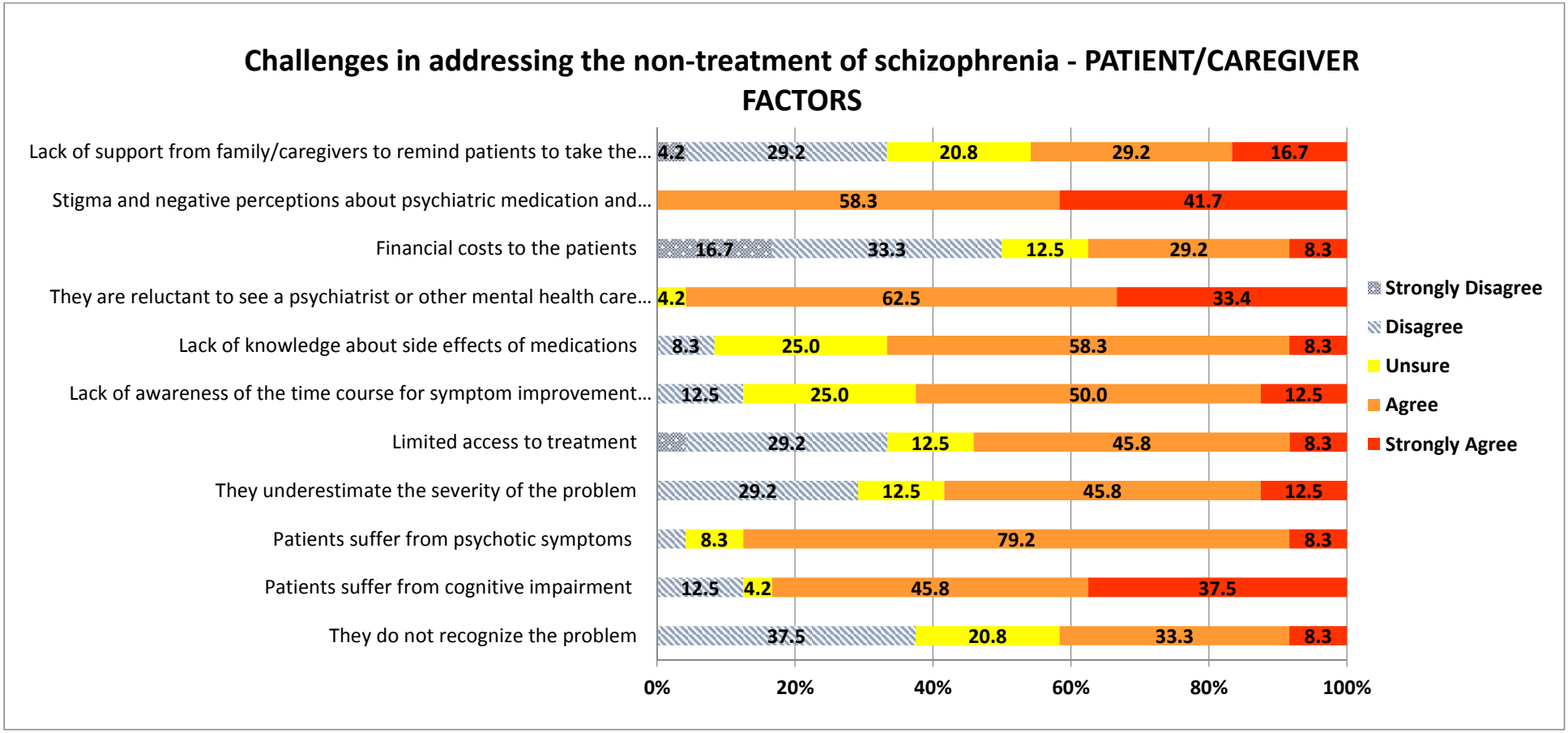
## *Barriers to change: patient and caregiver factors*

The majority of the experts stated they *strongly agreed/agreed (%)* with the following:

- Stigma and negative perceptions about psychiatric care and schizophrenia (Stigma and negative perceptions about psychiatric treatment (100%); being reluctant to see a psychiatrist or other mental health care specialist (95.9%);
- The direct impact of symptoms (suffering from psychotic symptoms (87.5%) or cognitive impairment (83.3%);
- Lack of knowledge about side effects of medications (66.7% );
- Lack of skills or management strategies to cope with side effects (62.5%);
- Lack of illness awareness/not knowing what to do (58.3%);
- Limited access to treatment (54.1%).

Additional factors suggested by the experts included: previous history of non-adherence, sustance abuse or caregiver/patient personal beliefs of healthcare providers. Details are reported in table 2.

## Table 2 - Challenges in addressing the non-treatment of schizophrenia - PATIENT/CAREGIVER FACTORS



## Barriers to change: provider factors

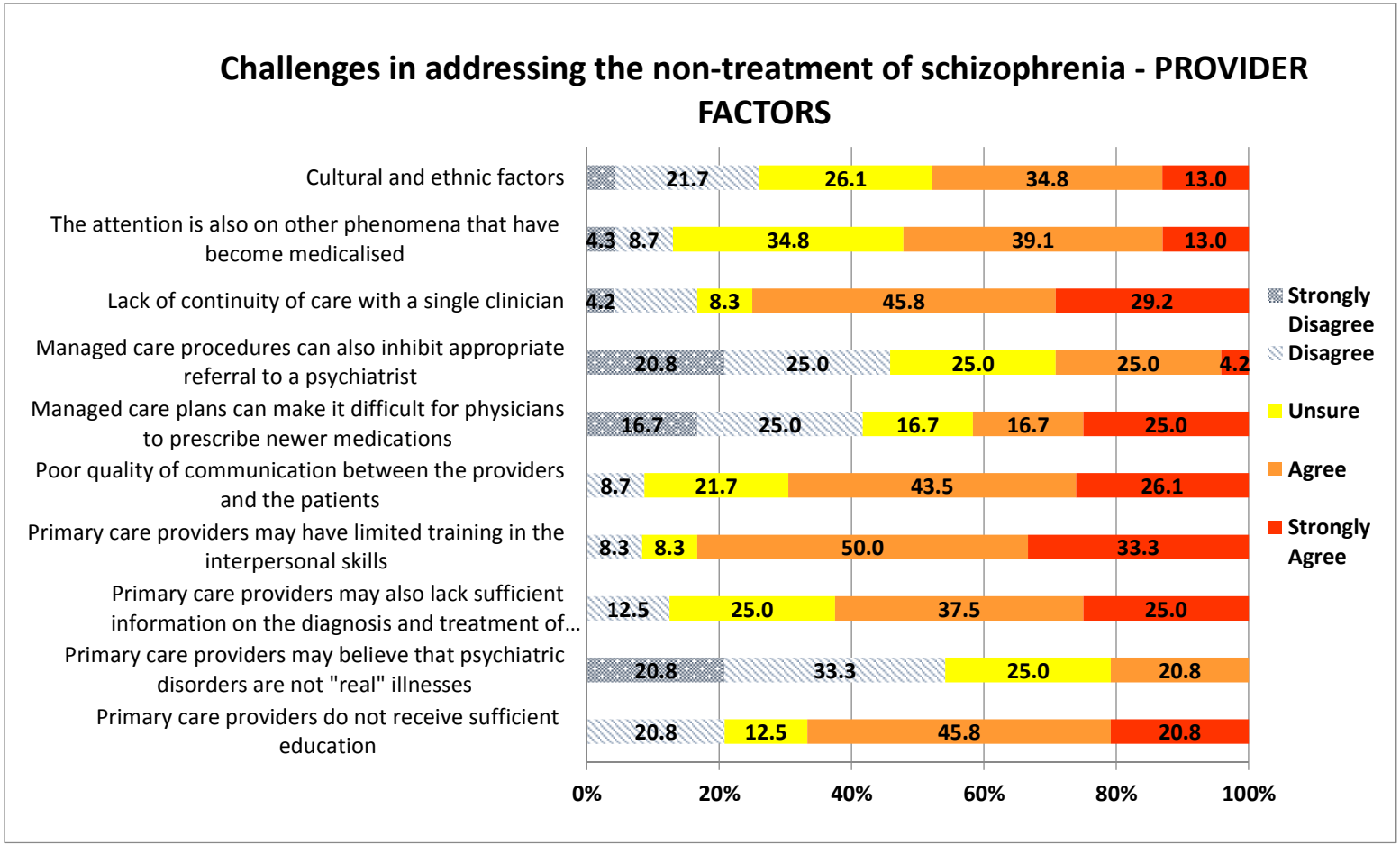
The majority of the experts stated they *strongly agreed/agreed (%)* with the following:

- Lack of training in the interpersonal skills (83.3%);
- Lack of continuity of care with a single clinician (75.0%);
- Poor quality of communication and collaboration between the providers and the patients (69.6%);
- Lack of appropriate training or education on schizophrenia (66.7%);
- Lack of appropriate information on schizophrenia (62.5%);
- The attention is on other phenomena that have become medicalised (52.1%).

Almost half of the experts reported *cultural and ethnic factors (47.8%).*

Additional factors suggested by the experts included: attitude of all staff towards the patients; lack of time for motivational interventions, trust building and establishment of a therapeutic relationship; under-representation of psychotherapeutic approaches in treatment of patients with SMI. Details are reported in table 3.

## Table 3 – Challenges in addressing the non-treatment of schizophrenia - PROVIDER FACTORS



## Barriers to change: healthcare system factors

The majority of the experts stated they *strongly agreed/agreed (%)* with the following:

- Poor collaboration among the different types of providers (86.4%);
- Difficulties in providing the appropriate service (62.5%);
- The system discourages the proper monitoring of patients once the treatment regimen is started (58.3%).

Only 29.6% strongly agreed/agreed the *lack of adequate insurance reimbursement* can be an issue.

Additional factors suggested by the experts included: poor community services, including long waiting lists in community centres, lack of non-pharmacological treatments and social support, scarce attempt to make a patient feel welcome and valued. Full details are in table 4.

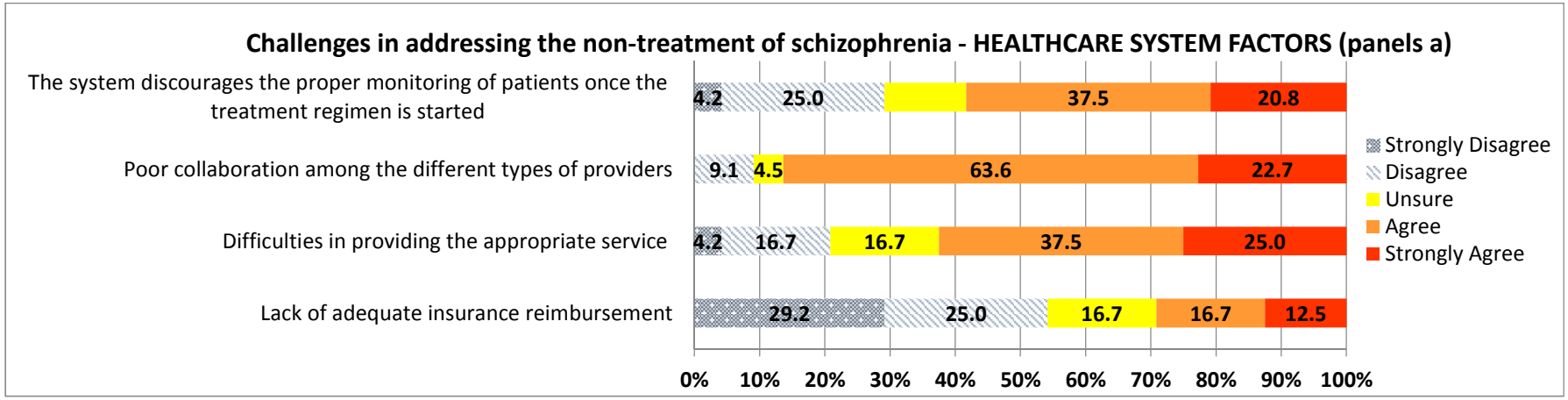
## *Expert feedback on the challenges in the evaluation of the impact*

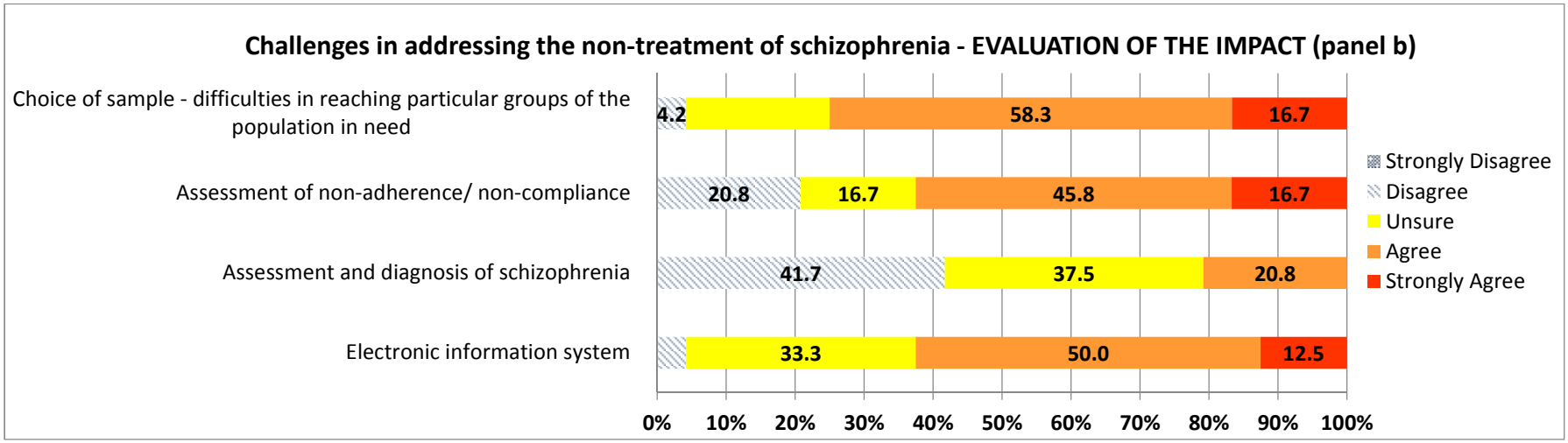
The majority of the experts stated they *strongly agreed/agreed (%)* with the following issues:

- Choice of sample to include homeless people, prisoners or minors (75%);
- Discrepancies in the information system that supports the management of care or in the methods used when assessing patient non-adherence/non-compliance (both 62.5%).

Additional factors suggested by the experts included: discrepancy in quality care measures (eg self-reported outcome and quality of life); comprehensive evaluation of the patient pathway of care from hospital to community; and the role of new long acting injectable antipsychotics. Assessment and diagnosis of schizophrenia only by 20.8% strongly agreed/agreed. Full details are in table 4.

# Table 4 - Challenges in addressing the non-treatment of schizophrenia - HEALTHCARE SYSTEM FACTORS (panel a) and EVALUATION OF THE IMPACT (panel b)



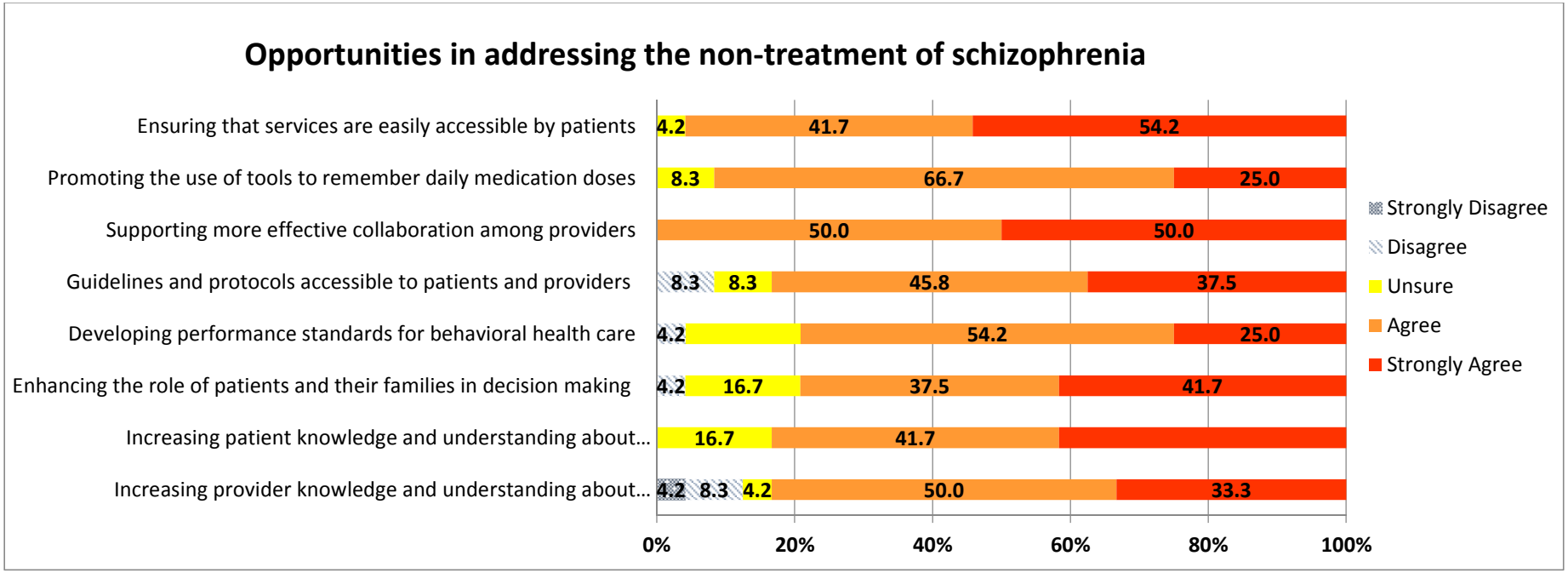
## *Expert feedback on the opportunities in addressing the non-treatment of schizophrenia*

The experts were supportive of all the opportunities reported in the literature (see "what can be done" above). They stated they *strongly agreed/agreed (%)* with the following initiatives:

- Supporting more effective collaboration among providers (100%).
- Ensuring that services are easily accessible by patients (95.8%).
- Promoting the use of tools to remember daily medication doses (91.7%).
- Increasing provider and patient knowledge and understanding about schizophrenia or guidelines and protocols accessible to patients and providers (83.3-83.4%).
- Developing performance standards for behavioural health care or enhancing the role of patients and their families in decision making (79.2%).

Additional factors suggested by the experts included: promoting and implementing community care; decreasing waiting times and ensuring that the services are welcoming. Full details are in table 5.

## Table 5 – Opportunities in addressing the non-treatment of schizophrenia



# KEY MESSAGES FOR POLICY AND PRACTICE

Addressing the non-treatment of schizophrenia is an important goal to be met with numerous challenges. The care of people with schizophrenia can be vastly improved through changes in health service organization and better use of integrated psychological, medical, and social interventions. This approach, combined with active engagement on the part of people with schizophrenia, their families, and their communities, could lead to better lives for all those affected.

Public health initiatives that may respond better to the growing urgency of the problem should target the following aspects:

- **Measuring unmet needs to better understand the scale of the problem, and what works in tackling it** - Key barriers to be overcome may include the limited access to information on particular groups of individuals in great needs (e.g. prisoners, homeless people, minors); discrepancies in the information system that supports the management of care and in methods used when assessing non-adherence/ non-compliance or patient self-reported outcomes.

- **Engagement on the part of people with schizophrenia, their families, and their communities** - Increasing patient knowledge and understanding about schizophrenia and enhancing the role of patients and their families in decision making.

- **Better use of integrated psychological, medical, and social interventions** - Supporting more effective collaboration among providers; increasing provider knowledge and understanding about schizophrenia or guidelines and protocols accessible to patients and providers; overcoming current lack of non-pharmacological treatment and social interventions.

- **Changes in health service organization** - Ensuring that services are easily accessible by patients; promoting the use of tools to remember daily medication doses; increasing access to evidence-based services; developing performance standards for behavioural health care; promoting and implementing community care; decreasing waiting times and ensuring that the services are welcoming.

Successful initiatives able to improve the outcome of schizophrenia treatment comprise:

- Expanding the role of the primary care sector with appropriate training and system-wide support; promoting interdisciplinary collaboration among the different types of

providers; promoting integrated care across settings; and empowering the patient/caregiver with effective information, education and participating into the decision making process. Awareness campaigns aimed at the general public can be beneficial in increasing awareness of the nature of schizophrenia and its treatment.

Key barriers to be overcome would include patients/caregivers (e.g. stigma and negative perceptions about psychiatric care and schizophrenia), providers (e.g. primary care providers lack of training in the interpersonal skills or education on schizophrenia), healthcare system factors (e.g. poor collaboration among the different types of providers and settings, difficulties in providing the appropriate service) and researchers (e.g. accessing subgroups in greater needs, discrepancies in the assessment of non-adherence).

# PART 4 – CASE STUDIES

According to the quality of the evidence gathered in both parts 2 (literature review) and 3 (survey with experts), three different case studies were extrapolated to present evidence on the impact of untreated psychosis across different country settings. They include: the United States, Germany and Spain.

## National health plans, universal coverage, and funding mechanisms

The three case studies present different models of health systems:

- **USA** - the health care system is **based on the private insurance model**. This model is characterised by employment-based or individual purchase of private health insurance financed by individual and employer contributions. Service delivery and financing are owned and managed by the private entities operating in an open market economy.

- **Germany** - The German health care system is **based on the social insurance or Bismarck model**. Statutory sickness funds and private insurance cover the entire population. Payment from employers and employees finance these sickness funds and participation is compulsory. Private insurance exists for self-employed individuals. The provider network consists of independent private entities.

- **Spain** - With the introduction of the NHS, financing of health services in Spain shifted from the Bismarck model towards **the Beveridge model**. To date, 80% of funding is provided by the **state through the generation of taxes**, 18% is funded throughout work-related contributions to insurance funds shared between the employer and the employee and the remainder is financed by other insurance schemes. Co-payments apply to drugs and some medical devices (6.1% of all health care expenditure).

They are summarised in table 6. For more details please refer to the literature (European Parliament, 1998) (Kulesher & Elizabeth Forrestal, 2014).

### Table 6: Case studies: comparing health care systems

| | USA | Germany | Spain |
|---|---|---|---|
| **Universal coverage** | No | Yes | Yes |
| **National Health Insurance** | No | No | Yes |
| **Social Insurance** | No | Yes - | No |
| **Private Insurance** | Yes | Yes | No |
| **Methods of Financing Health Care** | **Predominant system of finance**: Private Insurance **Main supplementary system of finance**: Public System Financing: Medicare: payroll tax, premiums, federal tax revenue; Medicaid: federal, state tax revenue. | **Predominant system of finance**: public: compulsory social insurance. Multi-payer system in which health care is funded by private and public contributions **Main supplementary system of finance**: private voluntary insurance, direct payments, public taxation. | **Predominant system of finance**: public: taxation **Main supplementary system of finance**: private voluntary insurance, direct payments. |

# Evidence from the literature

Evidence available revolves around the impact of untreated (i.e. lack of treatment for the USA only) and non-adherence/compliance to treatment in schizophrenia (and other SMI; see table 7). Evidence from the USA publications included: use of health care and criminal justice resources, employment, education, violence and homelessness. Findings for Germany and Spain were limited to healthcare resources, employment and violence.

## Table 7: Case studies: evidence on the impact of unmet needs

| | USA (11 papers) | Germany (3 papers) | Spain (3 papers) |
|---|---|---|---|
| **Use of health resources** (hospitalisation, emergency services, medications, visits with specialists, long-term care/nursing homes) | Impact of **untreated psychosis** , **non-adherence / non –compliance** to psychotic treatment | Impact of **non-adherence / non-compliance** to psychotic treatment | Impact of **non-adherence / non-compliance** to psychotic treatment |
| **Use of criminal justice resources** (incarceration) | Impact of **untreated psychosis**, **non-adherence / non –compliance** to psychotic treatment | - | - |
| **Employment** (unemployment rates, work loss) | Impact of **untreated psychosis** , **non-adherence / non –compliance** to psychotic treatment | Impact of **non-adherence / non-compliance** to psychotic treatment | Impact of **non-adherence / non-compliance** to psychotic treatment |
| **Education** (level of education achieved, or withdrawal from education) | Impact of **untreated psychosis** | - | - |
| **Violence** (self-harm or aggressive behaviour towards others) and Death (suicides, homicides) | Impact of **untreated psychosis**, **non-adherence / non-compliance** to psychotic treatment | Impact of **non-adherence / non-compliance** to psychotic treatment | Impact of **non-adherence / non-compliance** to psychotic treatment |
| **Homelessness** (use of healthcare resources (e.g. hospitalisation, emergency services) and housing costs | Impact of **untreated** psychosis, **non-adherence / non –compliance** to psychotic treatment | - | - |

# Key findings on the impact of untreated psychosis

Key findings on the impact of untreated psychosis are limited to the USA case study (see table 8). An economic model was developed by The HSM Group, Ltd. to quantify the costs of untreated SMI (major depression, bipolar disorder, schizophrenia, anxiety disorders) among adults in Greater Kansas City (HSM Group, 2012).

**The prevalence of SMI and percentage of untreated cases** - Census data (U.S. Census Bureau, 2010) was combined with mental illness prevalence rates (see details presented elsewhere: http://hcfgkc.org/costs-untreated-mental-illness) to estimate about 94,500 cases of untreated SMI in Greater Kansas City. Either individually or in combination, serious mental illnesses were reported to affect between 10% and 15% of the population annually (schizophrenia accounted for 0.5%). The percentage of untreated cases was near 40% for each SMI category (schizophrenia 35.7%).

**The annual costs** (Figure 4) - The costs associated with SMI were estimated using peer-reviewed publications and public datasets. Overall, the annual cost of untreated SMI to Greater Kansas City was estimated to be US$624 million (about $6609 per case of untreated case of SMI). A high proportion (88%) of these costs was in the form of indirect costs to employers and individuals (about US$5785 per case of untreated case of SMI). Indirect costs included unrealised earnings due to higher unemployment rates, the cost of lost productive time at work due to untreated SMI (presenteeism), time missed from work (absenteeism), and unrealised earnings due to permanent disability or premature death (suicides).

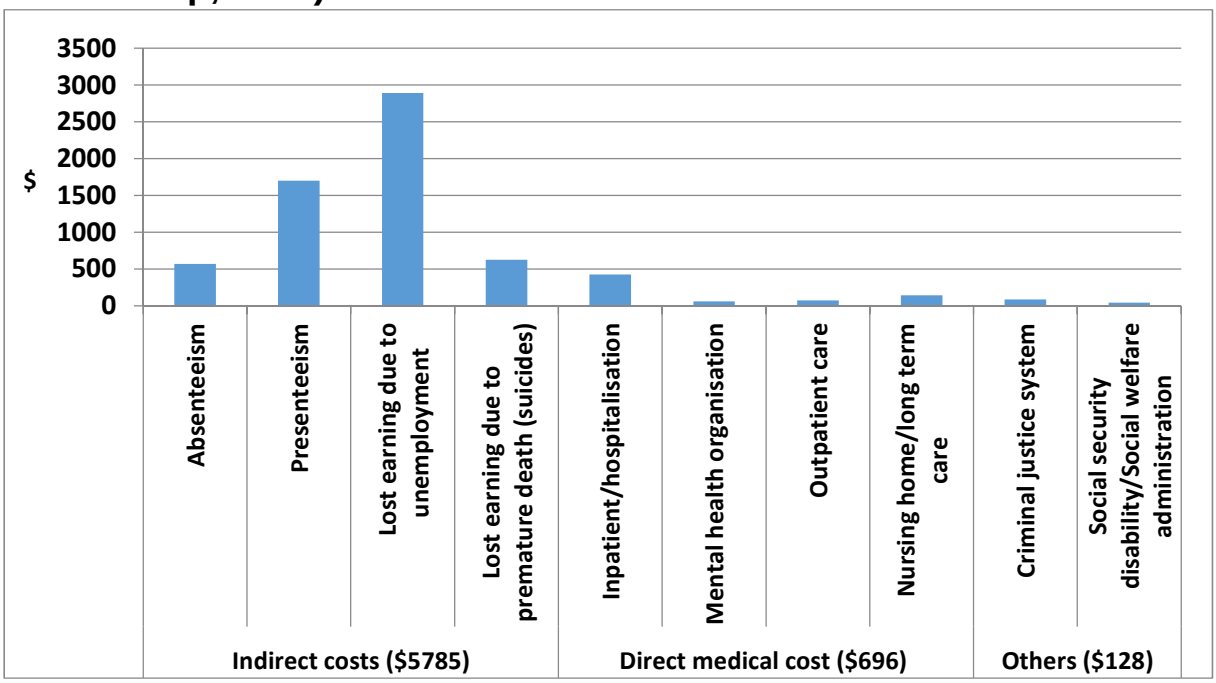
About 10% of the overall costs are estimated to be direct costs, or medical expenses associated with lack of sustained treatment (about US$696 per case of untreated case of SMI). Direct costs include increased inpatient care/hospitalisations, outpatient care, mental health organisation, and long-term care/nursing homes. The remaining costs (2%; $128 per case of untreated case of SMI) are due to criminal activity, social security disability, and social welfare administration costs. Untreated SMI is associated with an estimated 67 suicides per year in Greater Kansas City, more than 11,000 incarcerations, and more than 15,000 unemployed adults.

## Table 8: The impact of untreated schizophrenia (the evidence is limited to the USA case study)

| Outcomes | Evidence |
|---|---|
| **All outcomes** (direct medical costs; indirect costs for unemployment, absenteeism, presenteeism and premature death; criminal justice system, social security disability, social welfare administration) | *(HSM Group, 2012)* Annual total costs per case of untreated severe mental illness (major depression, bipolar disorder, schizophrenia, anxiety disorders) US$6609 (2010; greater Kansas City Area, USA) For more information see Figure 4. |
| **Use of health resources** (hospitalisation, emergency services, medications, visits with specialists, long-term care/nursing homes) | *(HSM Group, 2012)* Annual total costs per case of untreated severe mental illness (Inpatient/hospitalisation, mental health organisation, outpatient care, nursing home/long term care) US$696 (2010; greater Kansas City Area, USA). |
| **Use of criminal justice resources** (incarceration) | *(HSM Group, 2012)* Annual total costs of criminal justice system per case of untreated severe mental illness US$87 (2010; greater Kansas City Area, USA). |
| **Employment** (unemployment rates, work loss) | *(Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009)* The workplace bears a significant burden of costs of illness due to untreated and under-treated problems. *(HSM Group, 2012)* Annual total indirect costs (absenteeism, presenteeism, unemployment, premature death) per case of untreated severe mental illness US$87 (2010; greater Kansas City Area, USA). |
| **Education** | Evidence from the USA showed that untreated subjects often have difficulty in school and have an increased likelihood of becoming involved with the juvenile justice system (Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009). |
| **Violence** (self-harm or aggressive behaviour towards others) and death (suicides, homicides) | *(HSM Group, 2012)* Untreated SMI is associated with an estimated 67 suicides per year in Greater Kansas City (2010; greater Kansas City Area, USA).<br><br>*(Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009) (Friedman, 2006)* untreated people with severe mental illnesses (schizophrenia, depressive and bipolar disorder) are two to three times as likely as people without such illnesses |

| | |
|---|---|
| | to be aggressive and tending to commit an assault. |
| **Homelessness** (use of healthcare resources (e.g. hospitalisation, emergency services) and housing costs) | *(Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009)* People with SMI who become homeless have difficulty accessing healthcare. The lack of a permanent address, complicated eligibility requirements and daily struggles with their lack of (adherence to) treatments are barriers to accessing primary care. This ultimately leads to use of higher-cost services such as emergency departments and inpatient care. (Culhane, Metraux, & Hadley, 2001) have estimated that these costs are in excess of US$28,000 per homeless person per year. |

## Figure 4: Annual cost untreated SMI (US$, per case; adapted from HSM Group, 2012)

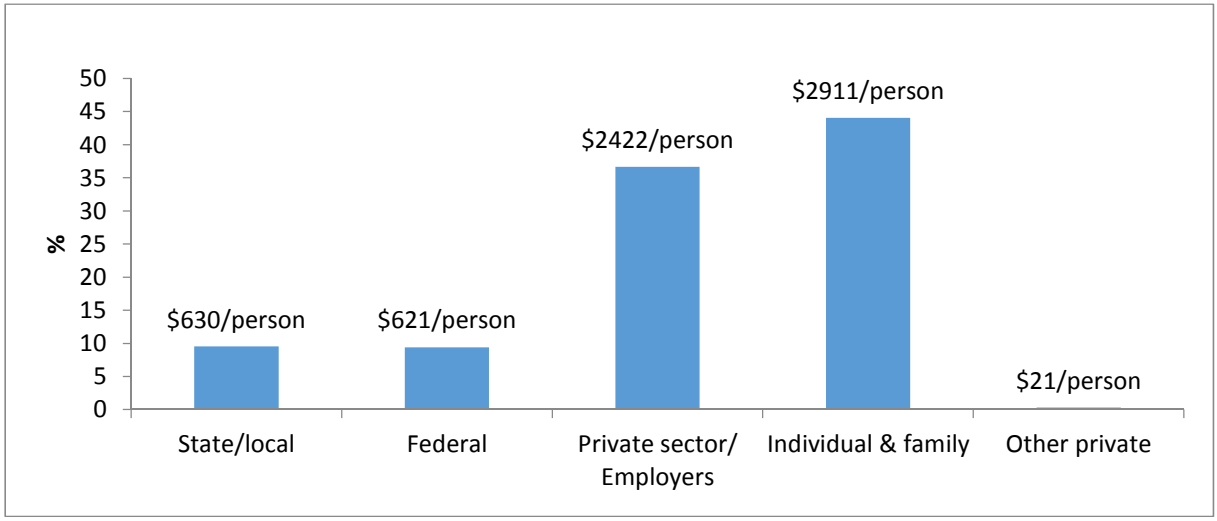



**Who pays for the costs** (Figure 5) - Preventable hospitalisations, outpatient visits, and nursing home stays cost state, federal, and private payers millions of dollars. The estimated burden to state and local governments in Greater Kansas City is US$59.6 million annually (about US$630 per case of untreated SMI). The burden to the federal government is U$58.7 million annually (about US$621 per case of untreated SMI).

Employers would also benefit from a more productive workforce and avoid medical and disability costs. Absenteeism and presenteeism cost employers US$228.9 million annually (about US$2422 per case of untreated SMI).

Burden to individuals and families (due to unrealised earnings at work) equals to US$275.2 million annually (about US$2911 per case of untreated SMI).

## Figure 5: Annual cost per untreated person with SMI (adpated from HSM Group, 2012)




**Adapting the Greater Kansas City model to Europe and beyond** (Table 9) – the annual average (direct and indirect) costs per case of untreated SMI in Greater Kansas City (HSM Group, 2012) were combined with international estimates of the prevalence (WHO, 2004) and treatment gap (Kohn et al., 2004) for schizophrenia to calculate indicative figure of the burden of untreated schizophrenia in Europe, Americas and worldwide.

Raw estimates show that the overall number of cases of untreated schizophrenia would be around 8.5 million worldwide, with about 3 million cases between Europe and the Americas. The overall economic burden would be about 56 billion US$ worldwide (20 billion US$ between Europe and the Americas only). As with any population-based measurement of prevalence, caution should be exercised in basing broad conclusions on the present findings. The rates presented here may be an underestimation of the real impact of unmet needs in schizophrenia (Kohn et al., 2004). Further limitations involve the fact that the economic data are based on raw figures from one small study in the USA with limited evidence of the quality of data source used and they have been further applied to an international setting.

## Table 9: The burden of untreated schizophrenia on Europe, Americas and worldwide

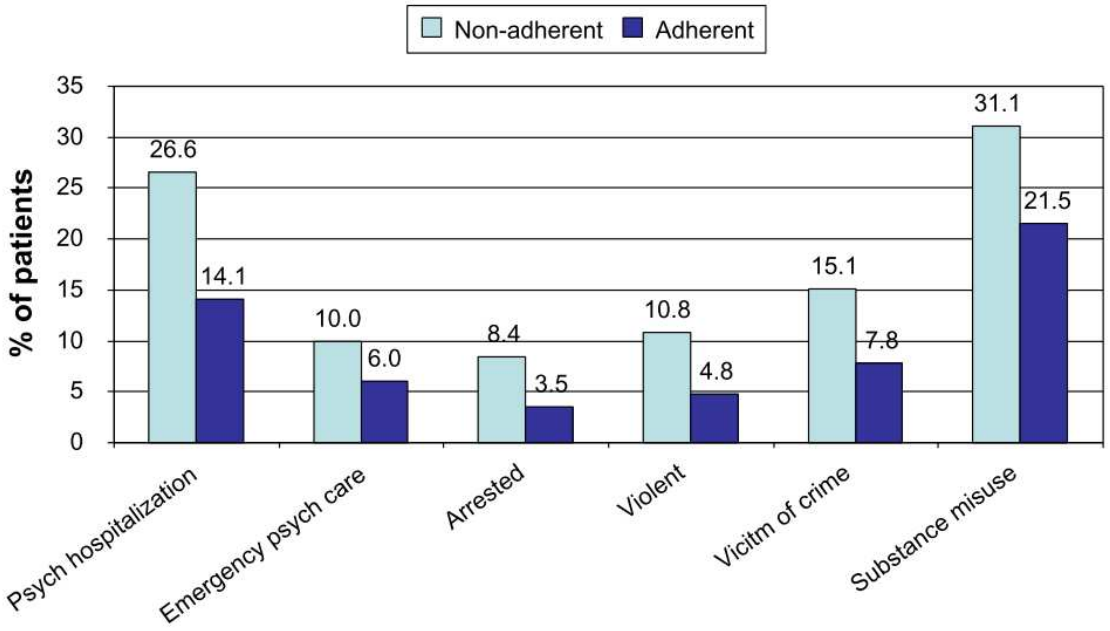
| | World | Americas | Europe | Sources |
|---|---|---|---|---|
| Prevalence Schizophrenia (millions) | 26.3 | 3.9 | 4.4 | WHO, 2004 |
| Treatment gap (%) | 2.2 | 56.8 | 17.8 | Kohn et al., 2004 |
| Cost of untreated schizophrenia (annual costs US$, per case) | 6,609 | 6,609 | 6609 | HSM Group, 2012 |
| *Cost of untreated schizophrenia (indirect annual costs US$, per case)* | *5,785* | *5,785* | *5,785* | |
| *Cost of untreated schizophrenia (direct medical annual costs US$, per case)* | *696* | *696* | *696* | |
| *Cost of untreated schizophrenia (other annual costs US$, per case)* | *128* | *128* | *128* | |
| **Untreated individuals with schizophrenia (million)** | **8.5** | **2.2** | **0.8** | |
| **Cost of untreated schizophrenia (total annual costs US$, million)** | **55,968** | **14,640** | **5,176** | |
| ***Cost of untreated schizophrenia (indirect annual costs US$, million)*** | ***48,992*** | ***12,815*** | ***4,531*** | |
| ***Cost of untreated schizophrenia (direct medical annual costs US$, million)*** | ***5,890*** | ***1,541*** | ***545*** | |
| ***Cost of untreated schizophrenia (other annual costs US$, million)*** | ***1,086*** | ***284*** | ***100*** | |

# Key findings on the impact of non-adherence/compliance to treatment

A few studies across the USA, Spain and Germany consistently showed that non-adherence is significantly associated with poorer outcomes, including use of health resources (i.e. greater risk of hospitalization, greater use of emergency services, longer length of hospital stay and greater mean costs) , violence, and greater risk of suicide (see table 10).

Evidence on the use of criminal justice resources, homelessness and unemployment is less conclusive and inconsistent across settings. Findings from one of the few studies commenting on the association between antipsychotic non-adherence and multiple outcome measures are summarised below (see Figure 6).

**Figure 6: Association between antipsychotic non- adherence and outcomes in a 3-year prospective observational USA study (adapted from (H Ascher-Svanum et al., 2006) (Haddad et al. 2014)).**



## Table 10: Case studies: Key findings on the impact of non-adherence to treatment

| | USA | Germany and Spain |
|---|---|---|
| **Use of health resources** (hospitalisation, emergency services, medications, visits with specialists, long-term care/nursing homes) | Compared with adherent patients, those who were not adherent during the first year were more likely to be hospitalised in the following 2 years (OR 1.55; 95% CI 1.21–1.98) and more likely to use emergency psychiatric services in the following 2 years (OR 1.49; 95% CI 1.12–1.98) *(Ascher-Svanum et al., 2006) see figure 6*.<br><br>The risk of hospitalisation is correlated with the degree of non-adherence, with a gap of 1–10 days in antipsychotic medication being associated with an odds ratio for admission of 1.98, a gap of 11–30 days with an odds ratio of 2.81, and a gap of more than 30 days with an odds ratio of 3.96 *(Haddad et al. 2014) (Weiden et al., 2004).*<br><br>**The national re-hospitalisation cost in the USA attributable to antipsychotic non-adherence was estimated at approximately US$1,500 million per year in 2005** *(Sun et al, 2007).* | Non-adherence is associated with a range of poorer long-term outcomes, with clinical and economic implications.<br><br>For example: Non-adherence was significantly associated with an increased risk of relapse (OR 0.58; 95% CI 0.49–0.69), hospitalisation (OR 0.61; 95% CI 0.53–0.70) and suicide attempts (OR 0.60; 0.43–0.85) *(Novick et al., 2010)*.<br><br>**Annual costs incurred by EU patients (Germany, Italy, Spain, France, Denmark, Greece, Ireland/the UK, the Netherlands, Portugal) who ever relapsed (as consequence of their non-adherence; £14,055 total cost per patient in 2005) during three years were almost double to those incurred by patients who never relapsed (£7417).** 61% of the cost difference was accounted for by hospital stay. The impact of relapse was even greater in the 1-year cost *(Hong et al., 2009)*. |

| | | |
|---|---|---|
| **Use of criminal justice resources** (incarceration) | (H Ascher-Svanum et al., 2006) **Non-adherence was associated with** poorer functional outcomes, including **greater risks of arrests compared with adherent patients (8.4% versus 3.5%; p < 0.001)** (Figure 6). | - |
| **Employment** (unemployment rates, work loss) | - | Relapsers had an earlier onset of schizophrenia and had a poorer level of social functioning at baseline (i.e. a **lower frequency of paid employment and social contacts in previous 4 weeks;** *(Hong et al., 2009)).* |
| **Violence** (self-harm or aggressive behaviour towards others) and death (suicides, homicides) | **Non-adherence is associated with a significantly higher rate of violence, victimisation, and substance use** (Figure 6) *(H Ascher-Svanum et al., 2006) (Haddad et al., 2014)*.<br>(Higashi et al., 2013) reported that non-adherence to schizophrenia medication increases the risk of suicide fourfold (relative risk adjusted for age and gender 4.2, 95% CI 1.7– 10.1) while another review (Llorca, 2008) reported that non-adherent patients (documented refusal of oral or depot injection) were at seven times greater risk of suicide. In a large prospective multisite study which included 1906 patients, non-adherent patients were more than twice as likely to be violent than adherent patients (10.8% versus 4.8%; p < | **Non-adherence was significantly associated with an increased risk of suicide attempts** (OR 0.60; 0.43–0.85) *(Novick et al., 2010)*.<br><br>More relapsers (5.8%) had suicide attempts in the six months before baseline, compared to non-relapsers (3.3%; p<0.01; *Hong et al., 2009)*.<br><br>Spain only: Arango 2006 - Treatment non-adherence is predictor of violence.<br>Violent patients presented fewer months of adherence to medication and a lower rate of adherence during follow-up compared with non-violent patients (P<0.01). |

| | | |
|---|---|---|
| | 0.001). | |
| **Homelessness** (use of healthcare resources (e.g. hospitalisation, emergency services) and housing costs) | *(Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009)* People with SMI who become homeless have difficulty accessing healthcare. The lack of a permanent address, complicated eligibility requirements and daily struggles with their lack of (adherence to) treatments are barriers to accessing primary care. **This ultimately leads to use of higher-cost services such as emergency departments and inpatient care.** (Culhane et al., 2001) **have estimated that these costs are in excess of US$28,000 per homeless person per year.** | - |

## *Challenges and future opportunities*

The expert survey data (see part 3) were reanalysed to compare evidence gathered from experts based in the USA (4), Germany (5) and Spain (3). Please note that the small sample size did not allow testing the significance of the difference between groups.

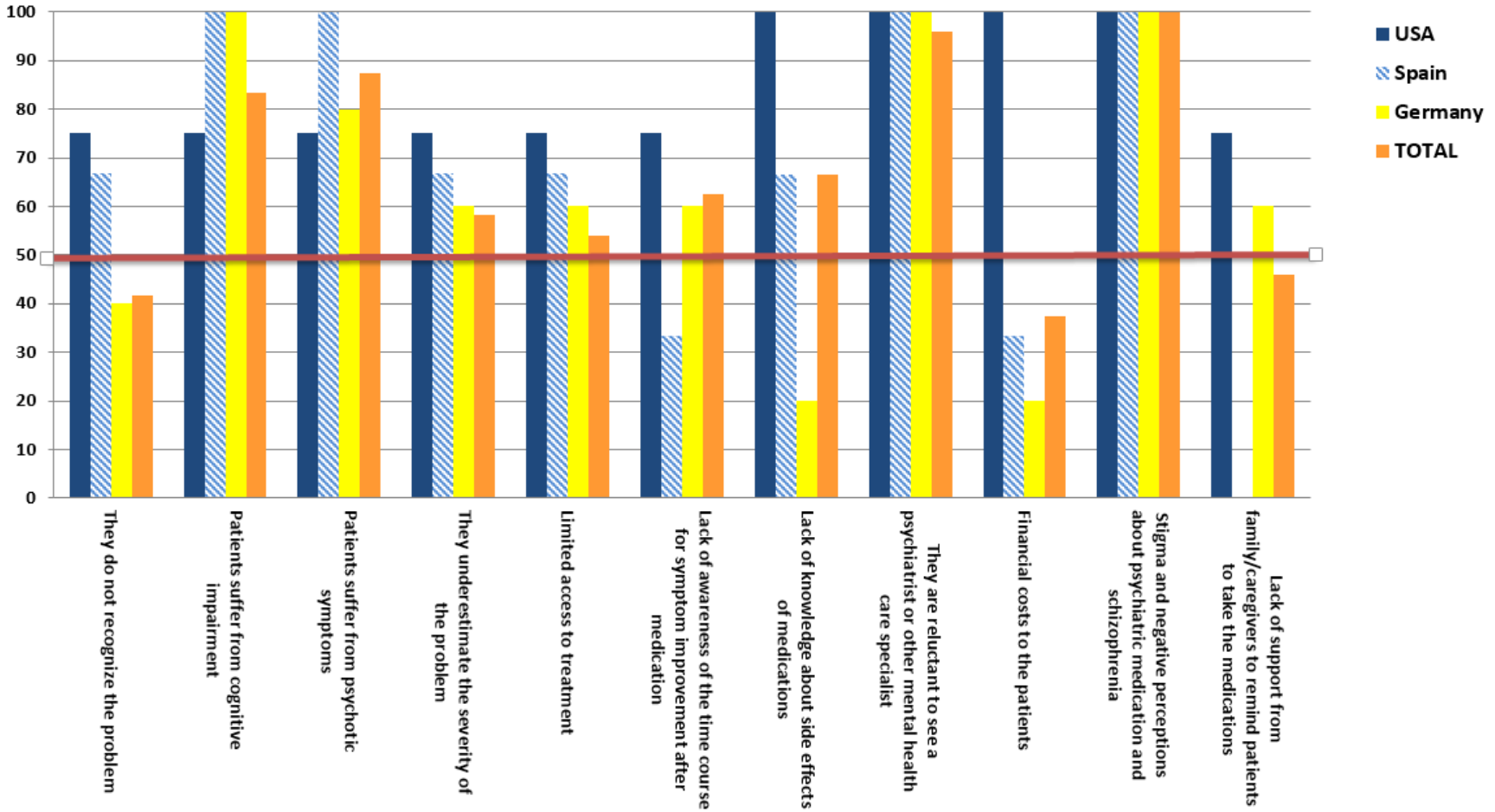
### Challenges in addressing the non-treatment of schizophrenia - PATIENT/CAREGIVER FACTORS

The majority of the experts stated they *strongly agreed/agreed (%)* with the following:

| USA | Germany | Spain |
|---|---|---|
| • **Stigma and negative perceptions about schizophrenia (100%)**<br>• **Lack of knowledge about side effects of medications (100%)**<br>• **Financial costs to the patients (100%)**<br>• Lack of illness awareness (75%)<br>• Lack of severity awareness (75%)<br>• Lack of awareness of the time course for symptom improvement (75%)<br>• The direct impact of symptoms (75%)<br>• Limited access to treatment (75%)<br>• Lack of support from family/caregivers (75%) | • **Stigma and negative perceptions about schizophrenia (100%)**<br>• **The direct impact of symptoms (100%)**<br>• Lack of severity awareness (60%)<br>• Lack of awareness of the time course for symptom improvement (60%)<br>• Limited access to treatment (60%)<br>• Lack of support from family/caregivers (60%) | • **Stigma and negative perceptions about schizophrenia (100%)**<br>• **The direct impact of symptoms (100%)**<br>• Lack of illness awareness (67%)<br>• Lack of severity awareness (67%)<br>• Lack of knowledge about side effects of medications (67%)<br>• Limited access to treatment (67%) |

More details are in table 11.

## Table 11 – Case studies: Challenges in addressing the non-treatment of schizophrenia - PATIENT/CAREGIVER FACTORS (agreed/strongly agreed %)



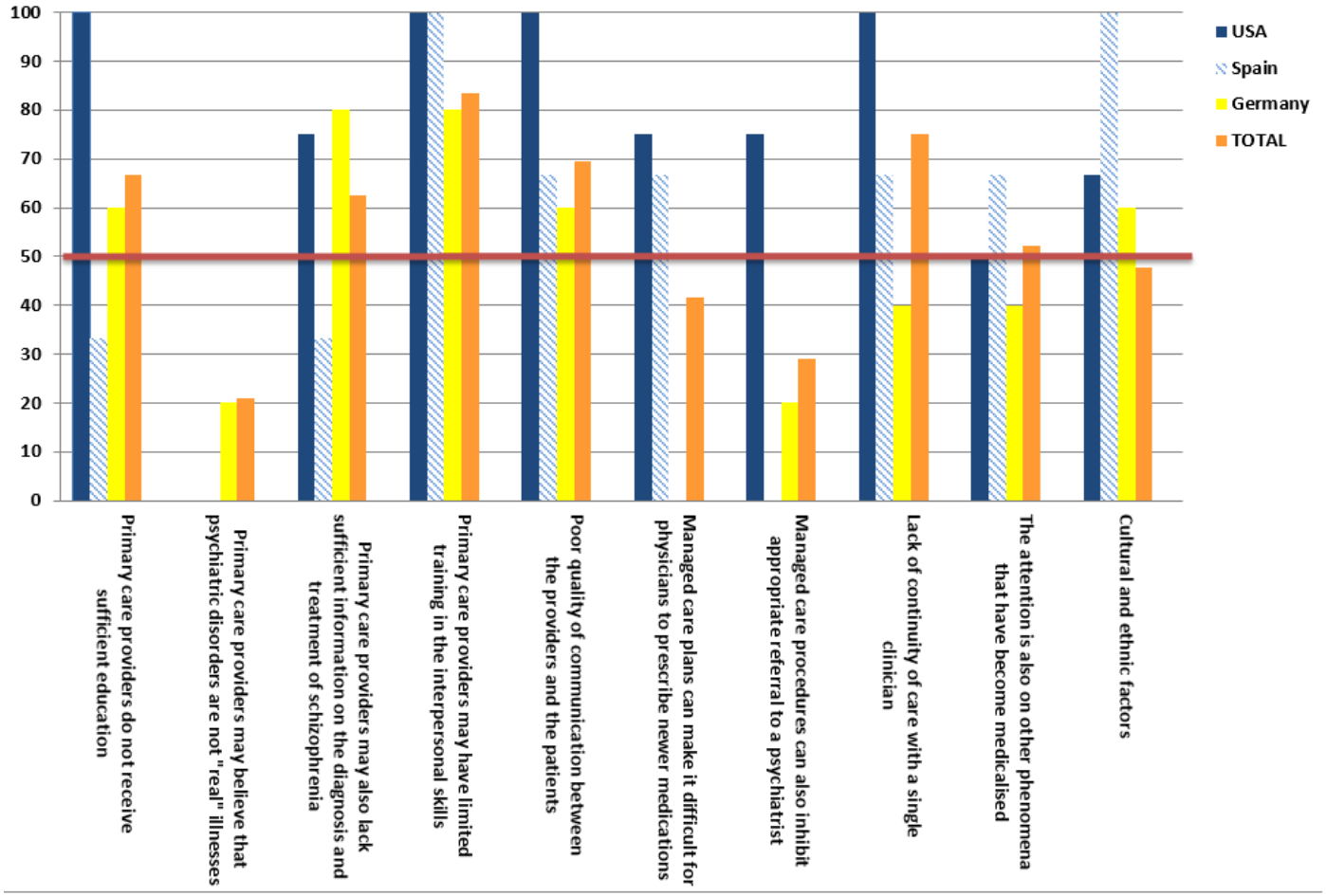
## Challenges in addressing the non-treatment of schizophrenia - PROVIDER FACTORS

The majority of the experts stated they *strongly agreed/agreed (%)*with the following:

| USA | Germany | Spain |
|---|---|---|
| • **Lack of training and education on schizophrenia (100%)**<br>• **Lack of training in the interpersonal skills (100%)**<br>• **Poor quality of communication between the providers and the patients (100%)**<br>• **Lack of continuity of care (100%)**<br>• Lack of appropriate information on diagnosis and treatment (75%)<br>• Care plan limitations (75%)<br>• Cultural and ethnic factors (67%)<br>• The attention is also on other phenomena that have become medicalised (50%) | • **Lack of training in the interpersonal skills (80%)**<br>• **Lack of appropriate information on diagnosis and treatment (80%)**<br>• Lack of training and education on schizophrenia (60%)<br>• Poor quality of communication between the providers and the patients (60%)<br>• Cultural and ethnic factors (60%) | • **Lack of training in the interpersonal skills (100%)**<br>• **Cultural and ethnic factors (100%)**<br>• Poor quality of communication between the providers and the patients (67%)<br>• Care plan limitations (67%)<br>• Lack of continuity of care (67%)<br>• The attention is also on other phenomena that have become medicalised (67%) |

More details are in table 12.

## Table 12 – Case studies: Challenges in addressing the non-treatment of schizophrenia - PROVIDER FACTORS (agreed/strongly agreed %)



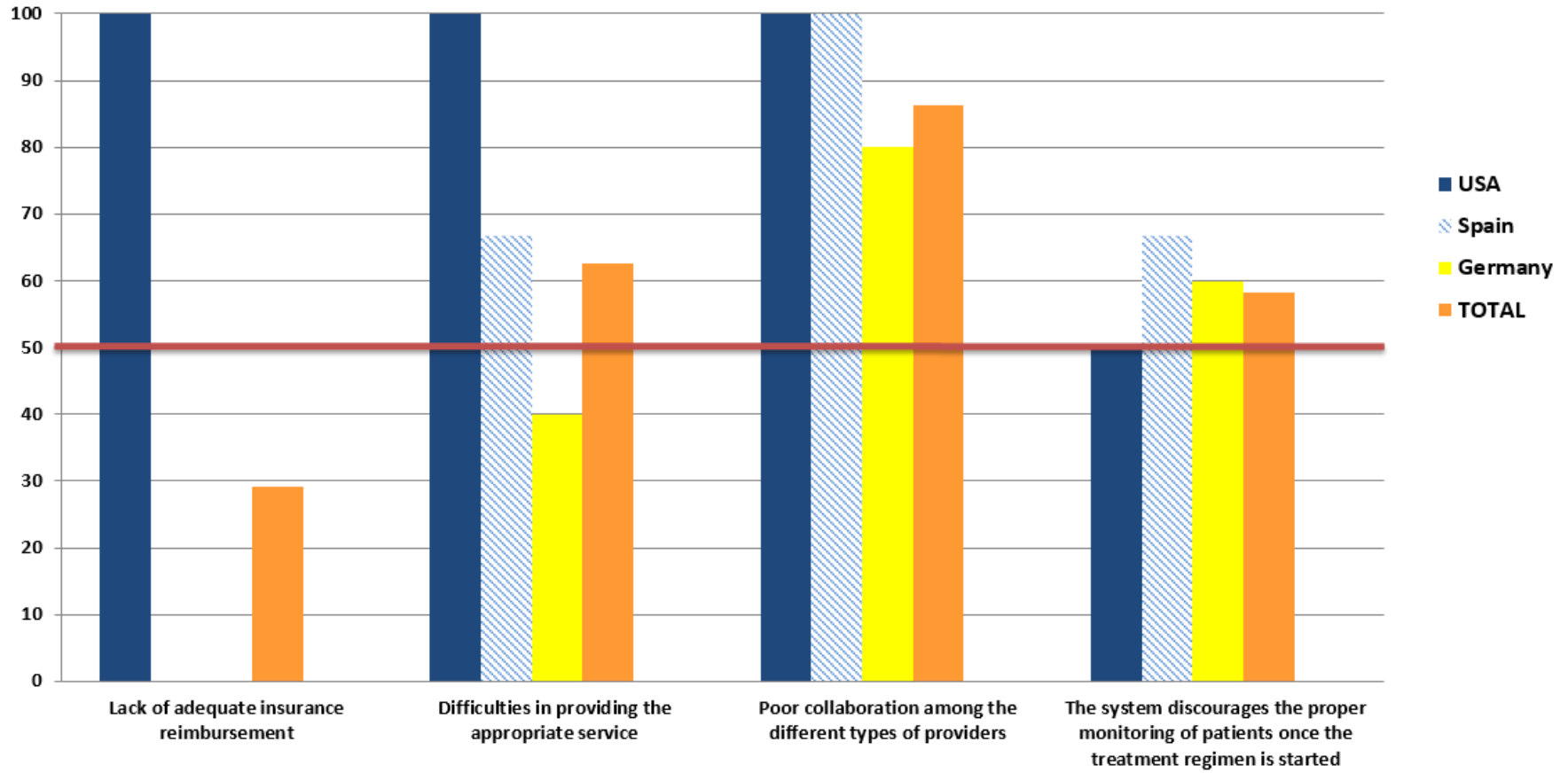
## Challenges in addressing the non-treatment of schizophrenia - HEALTHCARE SYSTEM FACTORS

The majority of the experts stated they *strongly agreed/agreed (%)*with the following:

| USA | Germany | Spain |
|---|---|---|
| • **Lack of adequate insurance reimbursement (100%)**<br>• **Difficulties in providing the appropriate service (100%)**<br>• **Poor collaboration among the different types of providers (100%)**<br>• The system discourages the proper monitoring of patients (50%) | • **Poor collaboration among the different types of providers (80%)**<br>• The system discourages the proper monitoring of patients (60%) | • **Poor collaboration among the different types of providers (100%)**<br>• Difficulties in providing the appropriate service (67%)<br>• The system discourages the proper monitoring of patients (67%) |

More details are in table 13.

## Table 13 – Case studies: Challenges in addressing the non-treatment of schizophrenia - HEALTHCARE SYSTEM FACTORS (agreed/strongly agreed %)



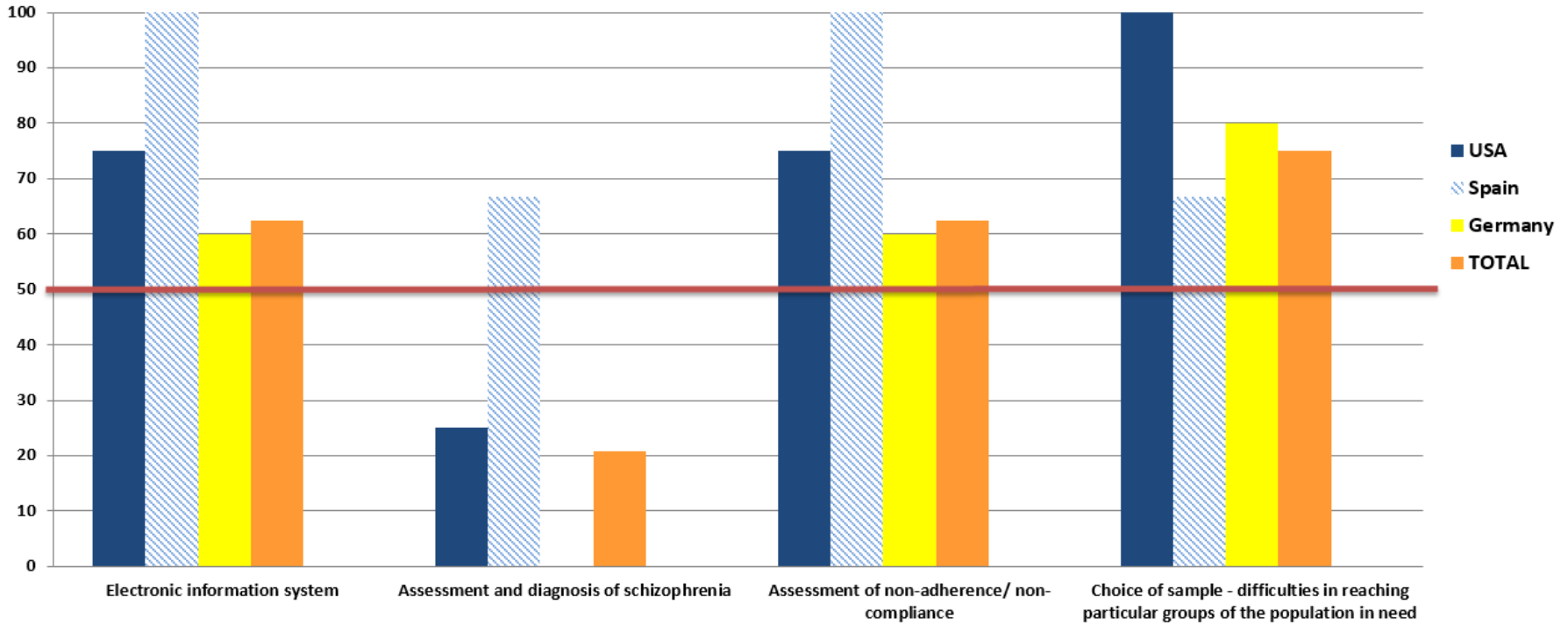
## Challenges in addressing the non-treatment of schizophrenia - EVALUATION OF THE IMPACT

The majority of the experts stated they *strongly agreed/agreed (%)*with the following:

| USA | Germany | Spain |
|---|---|---|
| • **Choice of sample (100%)**<br>• Discrepancies in the information system that supports the managment of care (75%)<br>• Discrepancies between the different criteria used for the assessment of non-adherence/ non-compliance (75%) | • **Choice of sample (80%)**<br>• Discrepancies in the information system that supports the management of care (60%)<br>• Discrepancies between the different criteria used for the assessment of non-adherence/ non-compliance (60%) | • **Discrepancies in the information system that supports the management of care (100%)**<br>• **Discrepancies between the different criteria used for the assessment of non-adherence/ non-compliance (100%)**<br>• Choice of sample (100%)<br>• Discrepancies between the different criteria used for the diagnosis (67%) |

More details are in table 14.

## Table 14- Case studies: Challenges in addressing the non-treatment of schizophrenia - EVALUATION OF THE IMPACT (agreed/strongly agreed %)



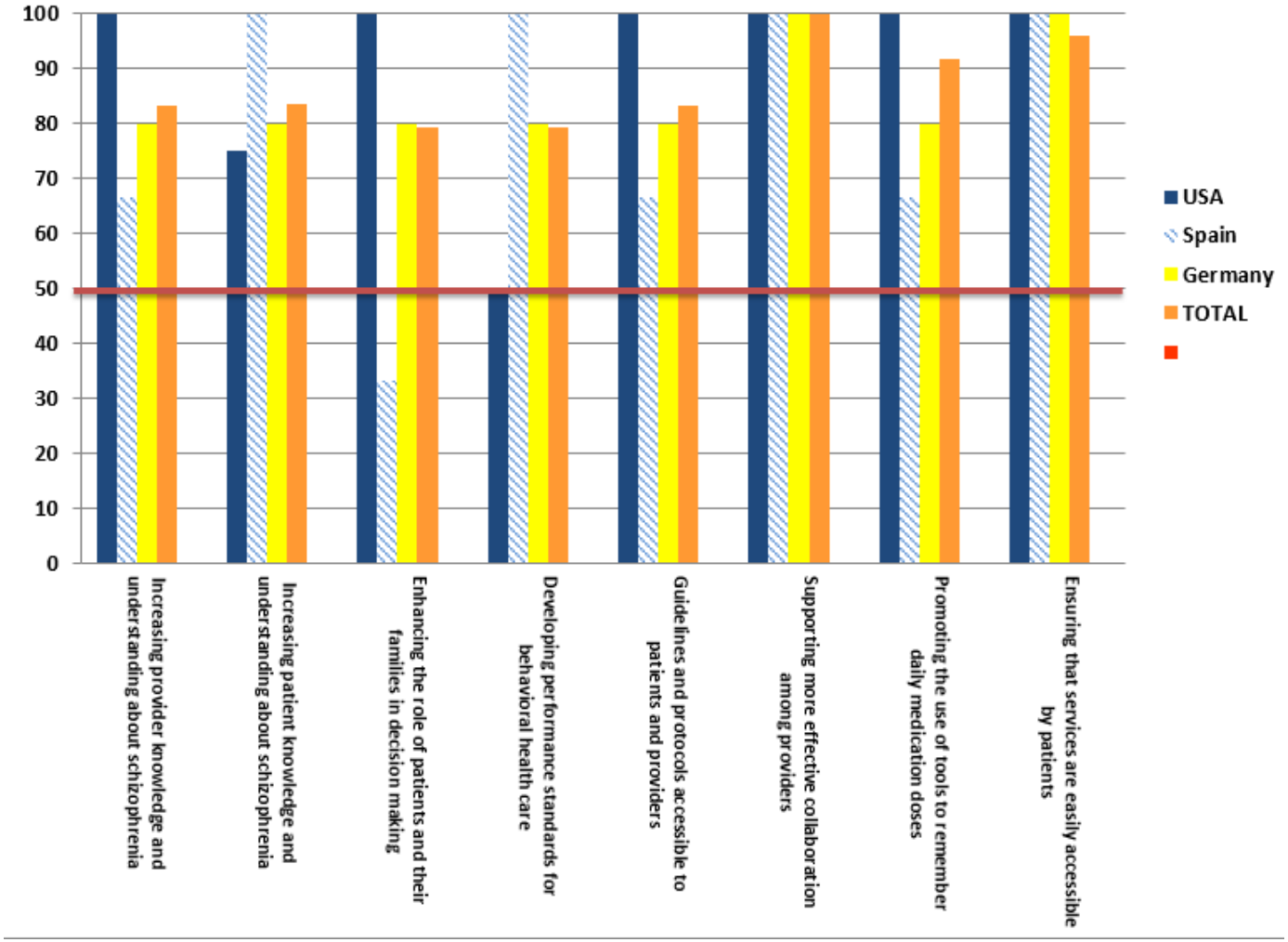
## Opportunities in addressing the non-treatment of schizophrenia

The majority of the experts stated they *strongly agreed/agreed (*%)with the following:

| USA | Germany | Spain |
|---|---|---|
| • **Supporting more effective collaboration among providers (100%)**<br>• **Ensuring that services are easily accessible by patients (100%)**<br>• **Increasing provider knowledge and understanding about schizophrenia (100%)**<br>• **Enhancing the role of patients and their families in decision making (100%)**<br>• **Providing care treatment guidelines and protocols accessible to patients and providers (100%)**<br>• **Promoting the use of tools to remember daily medication doses (100%)**<br>• Increasing patient knowledge and understanding about schizophrenia (75%)<br>• Developing performance standards for behavioural health care (50%) | • **Supporting more effective collaboration among providers (100%)**<br>• **Ensuring that services are easily accessible by patients (100%)**<br>• Increasing patient knowledge and understanding about schizophrenia (80%)<br>• Increasing provider knowledge and understanding about schizophrenia (80%)<br>• Enhancing the role of patients and their families in decision making (80%)<br>• Providing care treatment guidelines and protocols accessible to patients and providers (80%)<br>• Promoting the use of tools to remember daily medication doses (80%)<br>• Developing performance standards for behavioural health care (80%) | • **Supporting more effective collaboration among providers (100%)**<br>• **Ensuring that services are easily accessible by patients (100%)**<br>• **Increasing patient knowledge and understanding about schizophrenia (100%)**<br>• **Developing performance standards for behavioural health care (100%)**<br>• Increasing provider knowledge and understanding about schizophrenia (67%)<br>• Providing care treatment guidelines and protocols accessible to patients and providers (67%)<br>• Promoting the use of tools to remember daily medication doses (67%) |

More details are in table 15.

## Table 15 – Case studies: Opportunities in addressing the non-treatment of schizophrenia (agreed/strongly agreed %)



# KEY MESSAGES

## Discrepancy of evidence across settings: the USA present stronger evidence than others

Access to data on the diagnosis, care and treatment gap of schizophrenia may vary according to country setting.

The economic evidence available is very limited (mainly on the USA); however it shows a massive impact of unmet needs on healthcare and society overall:

- In the USA (Greater Kansas City) the annual cost of lack of treatment for severe mental illness is about $6609 per case, 2010 figures (HSM Group, 2012). A high proportion (88%) of these costs is in the form of indirect costs to employers and individuals (about U$5785 per case of untreated SMI). About 10 % of the overall costs are estimated to be direct costs, or medical expenses associated with lack of sustained treatment (about US$696 per case of untreated SMI).

  When adapting the Greater Kansas City model to international estimates of the prevalence and treatment gap for schizophrenia the overall number of cases of untreated schizophrenia would be around 8.5 million worldwide, with about 3 million cases between Europe and the Americas. The overall economic burden would be about 56 billion US$ worldwide.

- In the USA the national re-hospitalisation cost attributable to antipsychotic non-adherence is estimated at approximately US$1,500 million per year (2005 figures).

Data available from the literature review could be used to model unmet needs across multiple scenarios and settings where there is lack of quality evidence.

## Common challenges and opportunities in the three case studies: the expert views

**Patient factors** - Due to stigma and a lack of awareness and understanding of mental illness, a substantial proportion of mental disorders in OECD countries is undiagnosed, untreated or undertreated (OECD, 2014).

- Stigma and negative perception about schizophrenia are top priories in all countries. People suffering from mental health have to cope not only with symptoms associated with mental disorders, but also with stigma and prejudice – a "second illness" that frequently inhibits recovery from the first. Not only mental health-related stigma results in social isolation, low self-esteem, and more limited chances in areas such as employment, education and housing, but it also exacerbates unmet needs, reducing early interventions and increasing the treatment gap for mental illness (OECD, 2014). OECD countries have used legislation to protect the rights of people with mental disorders both in the community and in inpatient settings, although people with mental disorders still face discrimination, stigma, and marginalisation from society, which in turn increases the risk of violation of their rights (OECD, 2014).

- In all case studies it also recognised that symptoms of schizophrenia itself (such as depression, cognitive impairment, positive and negative symptoms) can reduce awareness of physical problems, reduce capacity to take action to seek help and use health care services, leading to untreated or poorly managed schizophrenia.

- Person-centred care, a model of care that takes into account patient's preferences and needs, ensures continuity of care, develops partnerships with caregivers and patients, and treats the patient as a person and not only the symptoms, is commonly recognised as a crucial element to overcome the challenge of unmet needs in schizophrenia (OECD, 2014).

**Provider and health system factors** - All the experts from the three countries reported that communication and collaboration across healthcare providers, training, patient and stakeholder involvement, and use of mechanisms for measurement of quality care are all essential to successful implementation of new and changing work practices to address unmet needs (OECD, 2014).

- Lack of communication and interpersonal skills. It is commonly recognised that there is a lack of alliance between the providers and the patients/their families to ensure that recommendations on treatment goals and strategies are met.

- Clear communication and co-ordination between primary care, specialist mental health care and the patient are vital to promote adequate coordination of mental health services, follow-up and care management once the physical health problem has been identified. Co-ordination of mental health services is crucial in order to guarantee the continuity of care for people with mental disorders who are often lost to follow up (OECD, 2014). Professional experts across country case studies recognise that when the system discourages such cooperation between parties in

the monitoring of patient there is an increased risk of under treatment or non-adherence to treatment.

- The majority of the experts recognised that health care providers do believe that psychiatric disorders are real illnesses, regardless of their country of residence.

- In all case studies it is recognised that discrepancies in electronic information system, in the assessment of non-adherence/non-compliance and in reaching particular groups of the population in needs are common challenges in the evaluation of the unmet needs.

## *Discrepancies in challenges and opportunities across the three case studies: the expert views*

Different experience of healthcare systems, health service delivery and culture may influence possible challenges and opportunities to tackle unmet needs.

### Patient factors

- **Lack of support from family and caregivers**. Experts from USA and Germany may confirm that there is a lack of support from family and caregivers in the management of the medication as possible cause of poor adherence (Fleischhacker et al., 2014). This is not so evident in different cultural contexts (see Spain) where the family plays a stronger role in supporting its members when they are in need of care.

- **Financial costs to the patients.** In the USA, where the health care system is based on the private insurance model, financial costs are considered strong challenges for the patients, whereas in other countries (based on national health insurance – Spain - and social health insurance – Germany) this factor is of less relevance.

- Other discrepancies in findings across case studies include lack of awareness of the problem, or the course of the symptoms as well as poor knowledge of the side effects.

### Provider and health system factors

- **Primary care providers do not receive sufficient education and information.** In the USA it is recognised that few medical schools do not provide sufficient education about psychiatric diagnosis, psychopharmacology, or psychotherapy for depression (Hirschfeld et al., 1997). Postgraduate education of primary care providers may also lack sufficient information on the diagnosis and treatment of psychosis. The

physician may be inadequately prepared to use the most modern methods. In addition, many providers have limited training in the interpersonal skills that enable them to manage emotional distress. This may lead to their avoidance of addressing schizophrenia and other mood disorders (Hirschfeld et al., 1997). In other countries, such Germany or Spain this lack of training and education may not be so evident. OECD data on the frequency of new graduate mental health professionals per 100,000 in population (OECD, 2014) confirmed discrepancies between the USA and other countries. For example Germany presented a higher level of newly educated professionals who can attend more advanced postgraduate degree courses in "psychiatry and psychotherapy" compared with the USA. In Germany the professional group of psychiatrists has had a relatively constant net increase of 4.5% over the last few years making it the fastest growing medical speciality. A similar development is observed for psychological psychotherapists (OECD, 2014).

- **Lack of adequate insurance reimbursement.** In the USA (where the predominant system of finance is private insurance) many insurance and managed care companies actively discourage patients from seeing mental health care professionals. Furthermore, when care for psychosis is rendered directly by a primary care physician, there may still be difficulties in obtaining reimbursement (Hirschfeld et al., 1997). Such issues are not currently present in other countries (e.g. Germany or Spain) with different methods of financing care.

- **Management of care procedure can also inhibit appropriate referral in place.** In the USA, the difficulties in providing the appropriate service are more evident than in other countries and this may be due to a more evident lack of collaboration between healthcare providers (Hirschfeld et al., 1997). For example, physicians may restrict their approach to medication and fail to refer patients to other providers for psychotherapy when it might be useful in addition to antipsychotic drugs. Psychotherapists may similarly fail to refer patients to a physician for evaluation of the possible benefits from taking medication. Cost-saving plans in the managed care system often discourage providers from "sharing" patients or providing psychotherapy (Hirschfeld et al., 1997).

- **Performance indicators.** Mental health care outcomes are too rarely measured and monitored, often due to a lack of good outcomes indicators, or a framework establishing desirable and undesirable outcomes. Developing performance standard for behavioural healthcare constitutes a clear opportunity to tackle unmet needs across countries. A lack of agreement over which key measures can capture good treatment outcomes for mental health has limited any progress in driving towards better outcomes. However, despite the challenge of coming up with such a framework, countries such as the USA, do have already in place a system to measure outcomes in mental health (OECD, 2014) and may value more other initiatives

compared with developing performance standards (see responses from experts: Spain 100%, Germany 80%, USA 50%).

- **Other discrepancies include difference in cultural and ethical factors and in management of care plan** that may limit the prescription of new medications (e.g. USA) more than in other countries (e.g. Germany). Countries such as Spain, where patients and stakeholders are less experienced about patients centred-decision making, may value less enhancing the role of patients and their families in decision making compared with other countries (such as USA and Germany where such practices has been in use in healthcare for longer time and there is already evidence of their benefit) (Perestelo-Perez, Gonzalez-Lorenzo, Perez-Ramos, Rivero-Santana, & Serrano-Aguilar, 2011).

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# APPENDICES

## *Appendix 1 - Mesh terms and search strategy*

| | Operator | # | MeSH term (explode all trees) | Operator | # | Corresponding text words |
|---|---|---|---|---|---|---|
| Population: Severe mental illness | ( | 1 | [mh "Mental disorder"] | ( | 25 | "severe mental illness" OR "severe mental illnesses" OR "severe mental disorders" OR Psychosis OR "severe mental disorder" OR "major mental illnesses" OR "major mental disorders" OR "major mental illness" OR "major mental disorder" |
| Population: Schizophrenia | OR) | 2 | [mh "Schizophrenia"] | OR) | 26 | "Schizophrenia" OR "Schizophrenic Disorders" OR "Schizophrenic Disorder" |
| Outcome: Cost/burden/unmet needs/impact on health and social care resources | AND ( | 3 | [mh "Costs and Cost Analysis"] OR<br><br>[mh Health Care Costs] | AND ( | 27 | Costs or cost OR Costing OR Expenditure OR (Financial (cost OR benefit OR burden)) OR Saving OR Economic OR "Health Care Costs" OR<br><br>"Service use" OR "resource use" OR "Service utilisation" OR "resource utilisation" OR "Service utilization" OR "resource utilization" OR "Service contact" OR "resource contact" OR "economic consequences" OR "social and economic consequences" |
| | OR | 4 | [mh "Cost of Illness"] | OR | 28 | "Cost of illness" OR "burden of illness" OR "Cost of Disease" OR "Cost of Sickness" OR "Costs of Disease" OR "Disease Cost?" OR "Sickness Cost" |

| | | | | | | |
|---|---|---|---|---|---|---|
| | OR | 5 | [mh "Cost-Benefit Analysis"] | OR | 29 | Cost-Benefit OR "Cost Benefit" OR "Costs and Benefits" OR "Benefits and Costs" OR "Cost-Benefit Analyses" OR "Cost Benefit Analysis" OR "Cost Effectiveness" OR "Cost-Benefit Data" OR "Cost Benefit Data" |
| | OR | 6 | [mh "Health Services Misuse"] | OR | 30 | "Health Service Misuse" OR "Health Service underuse" OR "Health Services Misuse" OR "Health Services underuse" OR "misuse of services" OR "misuse of health services" OR "misuse of healthcare services" |
| | OR | 7 | [mh"Social Work/utilization"] [mh "Social Work, Psychiatric/utilization"] [mh "Social Welfare/utilization"] | OR | 31 | "Social care misuse" OR "social care underuse" |
| | OR | 8 | [mh "Social Change] | OR | 32 | "Social impact" OR "social change" |
| Outcome: Intangible costs | | | | | | "Intangible costs" OR "Intangible cost" OR Disability adjusted life years lost" OR DALY OR "morbidity outcomes" |
| Outcome: Criminal justice resources | OR | 9 | [mh Criminal Law], [mh prison] | OR | 33 | "Criminal justice" OR prison OR crime |

| | | | | | | |
|---|---|---|---|---|---|---|
| Outcome: Violence and death (suicides, homicides) | OR | 10 | [mh Violence], [mh death], [mh Suicide], [mh homicide] | OR | 34 | Violence OR death OR "premature death" OR Suicide, homicide, killing OR Murder OR killings OR Murders Or "self-harm" OR "premature mortality" |
| Outcome: Education | OR | 11 | [mh "Educational Status"], [mh education] | OR | 35 | "Educational Status" OR education OR schooling |
| Outcome: Employment | OR | 12 | [mh Career], [mh employment], [mh Absenteeism] | OR | 36 | Career OR employment OR Absenteeism OR productivity OR "missed work" OR "sickness absence" OR presenteeism OR unemployment OR underemployment OR "disability claims" OR "benefit claims" OR "disability claim" OR "benefit claim" OR "value of lost production" |
| Outcome: Homelessness | OR | 13 | [mh "Homeless Persons"] | OR | 37 | "Homeless Person" OR "Homeless Persons" OR Homeless OR Homelessness OR "Street People" |
| Outcome: Comorbidities | OR) | 14 | [mh "Comorbidity"] | OR) | 38 | Comorbidity OR comorbidities |
| Comparison: Missed diagnosis | AND ( | 15 | [mh "Delayed Diagnosis"] | AND ( | 39 | "Missed diagnosis" OR "misdiagnosis" OR "under-diagnosed" OR "underrecognised" OR unrecognised OR under recorded OR "Unmet Needs in Diagnosis" OR "Delayed Diagnosis" OR "lack of diagnosis" |
| Comparison: Missed treatment/delayed treatment | OR | 16 | | OR | 40 | "treatment gap" OR "non-treatment" OR "non-treating" OR "under-treated" OR untreated OR "never treated" OR "duration of untreated" OR untreated OR "Inaccessible treatment" OR<br><br>"Failure in Initial Treatment" OR "Delay in Initial Treatment" OR "delayed treatment" OR "non-seeking treatment" OR "Unmet Needs in Treatment" OR "Unmet Need in Treatment" OR "inadequately treated" OR "lack of |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | | treatment" OR "insufficiently treated" |
| Comparison: Inappropriate therapy | OR | 17 | | OR | 41 | "Non-efficacious therapy" OR "Non-efficacious treatment" OR "Non-efficacious care" OR mistreated OR mistreatment OR "inappropriate treatment" OR "inappropriate therapy" OR "inappropriate care" |
| Comparison: Patient lack of adherence/ compliance | OR | 18 | [mh "Patient Compliance"] | OR | 42 | "lack of compliance" OR "non-compliance" OR "non-compliant" OR "non-adherence" OR "lack of adherence" OR "Patient Non-Adherence" OR "Patient Non-Compliance" OR "Patient Nonadherence" OR "Patient Noncompliance" OR "lack of Patient Cooperation" |
| Comparison: Patient refusal | OR) | 19 | [mh "Treatment Refusal"] | OR) | 43 | "Refusal of Treatment" OR "Patient Refusal of Treatment" |
| Geography | AND ( | 20 | [mh "North America"] | AND | 44 | "North America" OR USA OR "United States" OR UK OR "Great Britain" OR "United Kingdom" OR England OR Wales OR Scotland OR "Northern Ireland" OR Australia OR Oceania OR "New Zealand" OR Austria OR Belgium OR Canada OR "Czech Republic" OR Denmark OR Estonia OR Finland OR France OR Germany OR Greece OR Hungary OR Iceland OR Ireland OR Israel OR Italy OR Luxembourg OR Netherlands OR Norway OR Poland |
| | OR | 21 | [mh "Europe"] | | | |
| | OR | 22 | [mh "Australia"] | | | |
| | OR | 23 | [mh "Oceania"] | | | |
| | OR) | 24 | [mh "Developed countries"] | | | OR Portugal OR "Slovak Republic" OR Slovenia OR Spain OR Sweden OR Switzerland OR Chile OR Japan Or Korea Or Mexico OR ((developed OR OECD OR (high NEXT income) OR industrialised) NEXT (country OR nation?)) |

## *Appendix 2- Summary of the evidence according to publications*

| Reference | Nationality | Date | Population | Study design | Comparison | Outcomes | Results |
|---|---|---|---|---|---|---|---|
| **(Arango et al., 2006)** | Spain | 2006 | Patients treated for schizophrenia | RCT | Non adherence | Violence | **Violence** - In a randomised clinical trial comparing different formulations of zuclopenthixol in patients with schizophrenia and previous violence, violent acts during the follow-up year were inversely proportional to treatment adherence, better compliance, and greater reduction of positive symptoms. |
| **(Haya Ascher-Svanum, Zhu, Faries, Lacro, & Dolder, 2006)** | USA | 2006 | Patients treated for schizophrenia | Prospective, observational | Non adherence | Health Care Utilisation, Use Of Criminal Justice Resources, Violence | **Utilization health care** -antipsychotic non adherence was related to an increase in hospitalisation rate, hospital days or hospital costs. **Use of criminal justice resources –** Non-adherence was associated with poorer functional outcomes, including greater risks not only of psychiatric hospitalisations, use of emergency psychiatric services, but also of arrests, violence, victimisations, poorer mental functioning, poorer life satisfaction, greater substance use, and more alcohol-related problems (all $p < 0.01$). **Violence** - lack of adherence was associated with poorer outcomes, including increased act of violence. |
| **(Bodén et al., 2011)** | Sweden | 2011 | Patients with schizophrenia | Prospective, observational | Non adherence | Health Care Utilisation | **Utilization health care** -antipsychotic non-adherence was related to an increase in hospitalisation rate, hospital days or hospital costs. |
| **(Cechnicki et** | Poland | 2014 | Participants with | Prospective, | Untreated | Health Care Utilisation, | **Use of health care resources** They found a lack of correlation between use of health resources |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **al., 2014)** | | | schizophrenia | observational | psychosis | Employment | (number of re-hospitalisations and duration of re-hospitalisations) and duration of untreated psychosis DUP. **In terms of employment**, the relationship between longer DUP and worse employment outcome was statistically significant at 7 and 12 years from first hospitalization. |
| **(Challis, Nielssen, Harris, & Large, 2013)** | International literature, unspecified | 2013 | Patients with schizophrenia | Systematic review and meta-analysis | Untreated psychosis | Violence | **Violence** - DUP was associated with an increased risk of deliberate self-harm |
| **(Damen et al., 2008)** | Sweden | 2008 | Patients with schizophrenia | Discrete event simulation model | Non-compliance | Utilisation Healthcare | **Utilization health care** The authors compared staying on branded risperidone with generic substitution; differences between treatments included the probability of non-compliance and medication costs. The model predicted that it was cost-effective to keep a patient with schizophrenia in Germany on branded risperidone instead of switching them to generic risperidone (with a 40% reduction in medication costs and an incremental probability of becoming non-compliant after generic substitution greater than 5.2%). |
| **(Dilla et al., 2013)** | USA, UK and New Zeeland | 2013 | patients with schizophrenia | Systematic review | Non-adherence to,<br><br>anti-psychotic medication | Utilisation Healthcare | **Utilization health care** This systematic review of the economic aspects of non-adherence to antipsychotic medication in patients with schizophrenia showed that poor adherence to antipsychotic treatment is linked to increased hospitalisation rates and resource utilisation which resulted in increased direct health care costs. |

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| **(Fazel et al., 2010)** | Sweden | 2010 | Patients with psychosis patients with schizophrenia and other psychoses | Prospective case control | Non-compliance | Death | **Death** - When looking at homicide in discharged patients with schizophrenia and other psychoses in Sweden, common factors associated with homicide were evidence of medication non-compliance and substance misuse. |
| **(Foley et al., 2007)** | Ireland | 2007 | With a diagnosis of psychotic illness | Retro-spective, observa-tional | Non-adherence | Violence | **Violence** - In contrast with other evidence, (Foley et al., 2007) did not find an association between violence at presentation and DUP. The relationships between violence, DUP and psychopathology may be confounded by potential difficulties inherent in the PANSS. |
| **(Heeg et al., 2005)** | UK | 2005 | Patients with schizophrenia | discrete event simulation (DES) model | Non-compliance | utilisation healthcare | **Use of health care resources -** (Heeg et al., 2005) developed a model to incorporate social and environmental factors into the decision-making process for the prescription of new drugs to patients. The model was used to analyse the potential benefits of improving compliance with medication by 20% in patients in the UK. A 20% increase in compliance was estimated to save £16 147 and to avoid 0.55 psychotic episodes per patient over 5 years. Sensitivity analysis showed that the costs savings associated with increased compliance are robust over a range of variations in parameters. |
| **(Hensen et al., 2010)** | Sweden | 2010 | Patients with schizophrenia | discrete event simulation (DES) model | Non-compliance | utilisation healthcare | (Hensen et al., 2010) looked at the cost effectiveness of long-acting risperidone in Sweden and confirmed that compliance is the main driver of the cost effectiveness of the medicine. |
| **(Higashi et al.,** | International | 2013 | Details are | Systematic | Non- | Health Care | **Use of health care resources -** we can identify a |

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| **2013)** | literature, unspecified | | missing | literature review | adherence | Utilisation, Employment, Education, Death | clear link between non adherence and an increased risk of hospitalisation , use of emergency psychiatric services, longer length of hospital stay. **Employment, Education -** Non-adherence, partial adherence can create a downward spiral of events leading to inconsistent symptom control, relapse and rehospitalisation, which in turn can lead to long-term functional disabilities, loss of employment and education possibilities.<br><br>**Death** – non-adherence to antipsychotic medication is one of the risk factors for the development of suicidal behaviour in patients with schizophrenia. |
| **(Hill et al., 2012)** | Ireland | 2012 | Patients with psychosis | Prospective, observational | Non-adherence | Employment | **Employment** - the authors reported no association between DUP and gainful employment over 12 years. |
| **HSM Group. (2012)** | USA | 2012 | Patients with schizophrenia and other psychoses | Model's estimates | Untreated psychosis | Use Of Health Care Resources, Use Of Criminal Justice Resources, Employment, Death | **Use of health care resources -** In Greater Kansas City the annual inpatient hospitalizations costs for untreated schizophrenia was estimated as $39.9 million higher compared with patients receiving regular care (modelling based on 2011 estimates). The annual outpatient care costs for untreated schizophrenia were $6.7 million higher compared with patients receiving regular care.<br><br>**Use of criminal justice resources -** In Greater Kansas City, the annual incarceration costs of individuals with severe mental illness resulted in $8.2 million to the criminal justice system (2011 estimates). **Employment** - overall about |

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| | | | | | | | 24% of individuals with severe mental illness are unemployed at any given time, and about half of those cases are due to lack of treatment. In Greater Kansas City, this can lead to more than 15,000 adults who are unemployed due to lack of treatment for SMI. **Death** - The model estimated 67 suicides in Greater Kansas City can be attributed to SMI annually |
| **(King et al., 2014)** | the Netherlands, Germany, UK and Italy | 2014 | patients with schizophrenia | RCT | Non-adherence | Health and social care utilization | **Utilization health and social care** - In a multicountry RCT based in UK, Italy, Germany and the Netherlands looking at the impact of non-adherence to medication in patients with schizophrenia (King et al., 2014) showed that the effect of non-adherence was not statistically significantly associated with health and social care costs, whereas patients who reported non-adherence had significantly lower societal costs than those reporting adherence. |
| **(Knapp, King, Pugner, & Lapuerta, 2004a)** | UK | 2004 | Patients living in institutions ions that they had been prescribed anti-psychotic medication | Cross-sectional | Non-adherence | Utilization Health Care | **Utilization health care** -antipsychotic non-adherence was related to an increase in hospitalisation rate, hospital days or hospital costs. |
| **(Lim et al., 2008)** | Canada | 2008 | Adult population aged 20 and above | Cross-sectional | Undiagnosed mental illness | Health Care Utilisation, Employment | **The utilisation of all health care services** was highest for the diagnosed mentally ill, lowest for the non-mentally ill, with those in the undiagnosed category in the middle. The average medical cost per capita was C$643 for the non-mentally ill and C$2,515 for the diagnosed and C$1,442 for the undiagnosed |

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| | | | | | | | (2003 figures).<br><br>**Employment** - The authors reported that absenteeism (long-term work loss) is highest for the diagnosed mentally ill, lowest for the non-mentally ill, with those in the undiagnosed category in the middle. Unemployment rate is highest for the diagnosed 0.46%, but a smaller group of undiagnosed (0.26%) were unemployed compared with people with no mental illness (0.33%). The number of disability days per year (short- term work loss) were, respectively: 33 (diagnosed mentally ill), 27 (undiagnosed mentally ill), and 10 (non-mentally ill). |
| **(Llorca, 2008)** | International literature, unspecified | 2008 | Patients with schizophrenia | Systematic literature review | Non-compliance | Utilisation Healthcare, Employment, Violence/Death, Education, Homelessness | **Utilisation health care, Employment, Violence/Death, Education, Homelessness** - non-adherence, partial adherence and non-compliance can arise a downward spiral of events leading to inconsistent symptom control, relapse and rehospitalisation, which in turn can lead to long-term functional disabilities, long-term negative outcomes (loss of autonomy, education or employment possibilities, homelessness, a likelihood of dropping out of care completely) and even suicide. |
| **(Marcus & Olfson, 2008b)** | USA | 2008 | Patients with schizophrenia | Prospective, observa-tional | Non-adherence | Utilization Health Care | **Utilization health care** - antipsychotic non-adherence was related to an increase in hospitalisation rate, hospital days or hospital costs. |
| **(Mork et al., 2013)** | Norway | 2013 | Patients with schizophrenia | Cross-sectional | Untreated psychosis | Violence | **Violence** - When compared with non-suicide attempters and those with suicide attempts |

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| | | | | | | | without non-suicidal self-harm, patients with both suicide attempts and non-suicidal self-harm were more frequently women, younger at the onset of psychotic symptoms, had longer duration of untreated psychosis, and had higher levels of current impulsivity/aggression and depression |
| **(Nielssen & Large, 2009)** | Australia | 2009 | Patients with psychosis | Cross-sectional | Untreated psychosis | Death | **Death**- When looking at untreated psychotic illness in the survivors of violent suicide attempts, there appears to be a higher risk of violent suicide attempts during the first episode of psychosis than later in the illness. |
| **(Nielssen & Large, 2011)** | Australia | 2011 | Patients with schizophrenia and other psychoses | Cross-sectional | Untreated psychosis | Death | **Death**- Psychosis is strongly associated with potentially lethal suicide attempts using sharp objects and patients who have never received treatment for psychosis appear to be at particular risk |
| **(Nielssen et al., 2012)** | International literature, unspecified | 2012 | Patients with schizophrenia and other psychoses | Literature review | Untreated psychosis | Death | **Death**- This overview of violence to self and others during the first episode of psychosis showed that a substantial proportion of first-episode patients commit an act of less serious violence or attempt suicide prior to initial treatment. |
| **(Norman et al., 2012)** | Canada | 2012 | | Prospective, observational | Duration untreated psychosis, duration untreated illness (DUI) | Employment | **Employment -** Delay between onset of non-specific symptoms and treatment (duration of untreated illness, DUI) was a more robust predictor of occupational functioning and use of a disability pension compared with DUP. |

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| **(Novick et al., 2010)** | Denmark, Italy, Portugal, Spain, Ireland and the UK | 2010 | Patients with psychosis | Prospective, observational | Non adherence | Health Care Utilisation, Death | **Utilization health care and death** - Non-adherence was significantly associated with an increased risk of relapse, hospitalisation and suicide attempts. |
| **OECD (2014)** | International literature, unspecified | 2014 | Patients with schizophrenia and other psychoses | Report | Untreated | Employment, Death | **Employment** - Mental illnesses have a huge labour market cost: OECD data suggests that one in five working age people have had a mental problem at some point in time, reducing their employment prospects, productivity and wages. The high costs of mental ill-health for society suggest a strong need for better services. Untreated mental illnesses can have a detrimental impact on wider society. Mild-to-moderate mental illness has been shown to have a strong relationship with higher unemployment, higher absenteeism, lower productivity in the workplace, and a rising burden of disability benefits claims across countries. **Death**- psychiatric illness is a major risk factor for suicide and it has been estimated that 90% of suicide attempters and completers suffer from at least one, mostly unrecognised, untreated, or inadequately treated mental illness. |
| **(Offord et al., 2013)** | USA | 2013 | Patients with schizophrenia | Prospective, observa-tional | Non-adherence | Utilisation Healthcare | **Utilization health care** - Early non- adherence is related to more hospitalizations (0.57 vs. 0.38; $P < 0.01$) with longer length of stay (5.0 vs. 3.0 days; $P < 0.01$) and higher costs ($5,850 vs. $4,211; $P = 0.02$) compared with adherent patients. |
| **(Reininghaus** | UK | 2008 | Patients with | Prospective, observa- | Duration untreated | Employment | **Employment** - The authors confirmed association between untreated psychosis and |

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| **et al., 2008)** | | | psychosis | tional | psychosis | | unemployment; unemployed subjects were more likely to experience longer periods of untreated psychosis when reporting low (P < 0.01) or medium (P <0.01) number of social contacts. No such difference could be observed for those with high social contacts (P = 0.60). |
| **(Šarotar et al., 2008)** | Slovenia | 2008 | Patients with schizophrenia | Retro-spective, observ-ational | Duration untreated psychosis | Employment, Education | **Employment** - half of the patients with DUP longer than 1 year were on disability benefit as compared to 19% of patients who had received treatment with antipsychotic medication in the prodromal phase of the disease. **Education** - DUP longer than 1 year had a negative impact on the educational level achieved. |
| **(Schnapp WB, Burruss JW, Hickey S, Mortesen K, 2009)** | USA | 2009 | Patients with schizophrenia and other psychoses | Narrative review | Untreated psychosis | Use Of Criminal Justice Resources, Employment, Education, Death, Homelessness | **Use of criminal justice resources** - For the Harris County, Texas, the 2008 costs of caring for the County's incarcerated people with mental illness exceeded $48 million. **Employment, Education/schooling, violence/death, Homelessness**<br><br>An insufficiently funded mental health service is reported to lead to societal productivity loss, homelessness, increased juvenile and adult criminal justice system involvement and decrease in life expectancy. More than 5.6 billion dollars are lost every year in productivity and annual earnings as a result of severe mental illness. **Education** - untreated subjects often have difficulty in school and have an increased likelihood of becoming involved with the juvenile justice system. **Death**- In the USA over 15 percent of indirect costs of severe mental illness (treated and untreated cases) are related to mortality costs, or loss of |

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| | | | | | | | productivity due to premature death |
| **(Schimmelmann et al., 2008)** | Australia | 2008 | Patients with first-episode psychosis | Prospective, observational | untreated psychosis | Employment | **Employment** - longitudinal study involving 786 patients with first-episode psychosis (FEP). This study showed that duration of untreated psychosis is associated with a lower rate of employment/occupation ($p<0.01$). |
| **(Sun et al., 2007)** | USA | 2007 | Patients with schizophrenia | Modelling | Non-adherence | Utilisation Healthcare | **Utilization health care** - When modelling hospitalization costs associated with antipsychotic non adherence in the treatment of schizophrenia in the United States (Sun et al., 2007) estimated that the national re-hospitalization costs related to antipsychotic non adherence was $1479 million, ranging from $1392 million to $1826 million in 2005. |
| **(Treur et al., 2009)** | Germany | 2009 | Patients with schizophrenia | Discrete event simulation model | Non-compliance | Utilisation Healthcare | **Utilization health care** - The authors considered two identical treatment arms except for percentage of compliant patients. The difference in compliance rates was varied from 0% to 15%, and incremental costs and effects were recorded and analysed. With a 5%, 10% and 15% difference in compliance rate, incremental effects increased to 0.021, 0.037 and 0.062, respectively, while generating cost savings of Swedish kronor (SEK)31 500, SEK62 000 and SEK104 500, respectively (SEK9.25 = 1, Euro year 2007 values). On average, the model predicted that, with a 15% increase in compliance, 0.5 relapses were prevented, the average Positive And Negative Syndrome Scale (PANSS) score decreased by 3.3 points and patients spent 22 fewer days in hospital over 5 years. |

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| **(Yee et al., 2011)** | Australia | 2011 | Patients with schizophrenia and other psychoses | Cross-sectional | Non-adherence | Violence | **Violence -** When looking at severe non-lethal violence during psychotic illness, individuals who committed a severe violent offence were typically non-adherent to treatment, had co-morbid substance use and prior criminal convictions. |
| **(Torres-González et al., 2014)** | International literature, unspecified | 2014 | Details are missing | Narrative review | Missed treatment | Comorbidities | **Comorbidities** - In schizophrenia, an increased likelihood risk for overweight, obesity, and abdominal obesity is present even in recently diagnosed and non-treated patients; however no economic estimates were available related to the impact of non-treating schizophrenia on its comorbidities. |
| **(Hong et al., 2009)** | Germany, Italy, Spain, France, Denmark Greece Ireland/the UK the Netherlands and Portugal | 2009 | Patients with schizophrenia | Prospective, observational | Non-adherence | Utilisation Healthcare, Employment, violence suicide | **Use of health and social care resources** - Our findings confirm the significant economic burden of relapse, and show such costs were mainly due to hospital stay. Costs incurred by patients who ever relapsed (£14,055) during three years were almost double to those incurred by patients who never relapsed (£7417). 61% of the cost difference was accounted for by hospital stay. The impact of relapse was even greater in the 1-year cost comparison.<br><br>**Employment -** relapsers had an earlier onset of schizophrenia and had a poorer level of social functioning at baseline (i.e. a lower frequency of paid employment and social contacts in previous 4 weeks).<br><br>**Violence suicide** - more relapsers (5.8%) had suicide attempts in the six months before baseline, compared to non- relapsers (3.3%). |

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| **(Karve et al., 2012)** | USA | 2012 | Patients with schizophrenia and other psychosis | Prospective, observational | Non-adherence | Utilisation Healthcare | **Use of health and social care resources**- Patients with psychiatric-related relapse events had all-cause and schizophrenia-related total medical costs approximately 2 times higher. Costs associated with schizophrenia-related inpatient service utilisation accounted for over 69% of total schizophrenia-related total medical costs among patients with psychiatric-related relapse events. Overall, these cost estimates are important in determining the additional direct economic burden exerted on the Medicaid system by such patients |
| **(Fazel et al., 2014)** | Sweden | 2014 | Patients with schizophrenia and other psychosis | Observational , Longitudinal | Non-adherence | Violence | **Violence** - Compared with periods when participants were not on medication, violent crime fell by 45% in patients receiving antipsychotics (hazard ratio [HR] 0·55, 95% CI 0·47–0·64) and by 24% in patients prescribed mood stabilisers (0·76, 0·62–0·93) |
| **(Kudumija Slijepcevic et al., 2014)** | Croatia | 2014 | male in-patients with paranoid schizophrenia | Cross-sectional study | Untreated psychosis | Violence | **Violence** - DUP before first contact with psychiatric services was a Predictor of violent offending together with older age, and alcohol abuse. |
| **(Látalová, 2014)** | International | 2014 | Patients with psychosis | Systematic literature review | Untreated psychosis | Violence and risk of homicide | **Violence** - Available evidence suggests that the prevalence of violent behaviour in the first episode of psychosis, particularly schizophrenia, is greater than during the later stages of the illness. First-episode psychosis is associated with an increased risk of homicide. There is some limited support for an effect of DUP length on serious violence or aggression. Violent behaviour frequently develops before the onset of a first episode. |

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| **(Mojtabai et al., 2009)** | USA | 2009 | Patients with schizophrenia | Narrative literature review and observational study | Untreated psychosis, non-adherence | Utilisation Healthcare, co-morbidities and homelessness | **Utilisation Healthcare** – In epidemiological surveys, approximately 40% of the respondents with schizophrenia report that they have not received any mental health treatments in the preceding 6-12 months. Clinical epidemiological studies also find that many patients virtually drop out of treatment after their index contact with services and receive little mental health care in subsequent years. Clinical studies of patients in routine treatment settings indicate that the treatment patterns of these patients often fall short of the benchmarks set by evidence-based practice guidelines, while at least half of these patients continue to experience significant symptoms. The divergence from the guidelines is more pronounced with regard to psychosocial than medication treatments and in outpatient than in inpatient settings. The expansion of managed care has led to further reduction in the use of psychosocial treatments and, in some settings, continuity of care. In conclusion, we found a substantial level of unmet need for care among individuals with schizophrenia both at community level and in treatment settings.<br><br>**Comorbidities -** The high prevalence of medical problems in patients with schizophrenia also calls for integration or better coordination of mental health and general medical services. There has been a renewed interest in the medical care of these patients, including receipt of the needed preventive and treatment services for chronic medical conditions and dental care. |

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| | | | | | | | **Homelessness** - Many patients with schizophrenia are at increased risk of homelessness and associated adverse social and health outcomes, such as victimisation and sexually transmitted diseases. |
| **(Haddad et al., 2014)** | International including UK and USA | 2014 | Patients with schizophrenia | Narrative review | Non-adherence | Healthcare resources, criminal justice resources, violence | **Healthcare resources, criminal justice** - In their literature review (Haddad et al., 2014) reported on the association between antipsychotic non-adherence and outcome. Non-adherence was associated with a significantly higher rate of psychiatric hospitalisation, use of emergency psychiatric services, arrest, violence, victimization, and substance use plus poorer mental functioning, poorer life satisfaction, and more alcohol-related problems. |
| **(Fleischhacker et al., 2014)** | International | 2014 | Patients with schizophrenia | Narrative review | Non-adherence | Healthcare resources, co-morbidities, criminal justice resources, violence | **Healthcare resources** – Long-term (maintenance) antipsychotic medication significantly reduces the number of relapses (at 7–12 months) and the number of hospitalisations in patients with schizophrenia, compared with placebo (data from a combined analysis of 65 clinical trials)<br><br>**Comorbidities** – Under-diagnosis and under-treatment contribute to this high death rate. It should be a priority to develop and implement an evidence-based, integrated care package that addresses patients' mental and physical health needs.<br><br>**Violence** - good adherence to treatment appears to be associated with lower levels of aggression and people with schizophrenia who adhere to their treatment and are clinically |

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| | | | | | | | stable appear to be no more violent than the general population. Non-adherent individuals are more likely to have poor long-term function, to be violent and be arrested. |
| **(Sajatovic et al., 2009)** | International | 2009 | Patients with schizophrenia | Narrative review | Non-adherence | Healthcare resources | **Healthcare resources** - Based on data from patients with schizophrenia in the Medicaid program, there is evidence that the national re-hospitalisation cost related to antipsychotic non-adherence was $1479 million in the United States in 2005 (Sun et al). Based on data from a large sample of patients treated for schizophrenia in the United States between 1997 and 2003, Ascher-Svanum et al. reported that adherence to antipsychotics was associated with lower utilisation of acute care services and greater engagement in outpatient mental health treatment. |
| **(Barnes, 2011)** | International | 2011 | Patients with schizophrenia | Narrative review | Non-adherence | Healthcare resources, criminal justice resources, violence | **Healthcare resources** - Hospitalisation rates, which are a proxy marker for more severe relapse, are increased in non-adherent patients, with rates quoted of 150% (Knapp et al., 2004) 200% (Ascher-Svanum et al., 2006; Ward et al., 2006) and 400% (Morken et al., 2008) over those found in adherent patients.<br><br>**Criminal justice resources, violence** - Non-adherent patients are more likely to use substances, be violent, be arrested (Ascher-Svanum et al., 2006), attempt suicide (Leucht et al., 2006; Tiihonen et al. 2006; Ward et al., 2006), and have poorer long-term functioning (Ascher-Svanum et al., 2006). |
| **(Morken et** | Norway | 2008 | Patients with | Observational | Non- | Healthcare | **Healthcare resources** - Odds Ratio of being |

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| **al., 2008)** | | | schizophrenia | study | adherence | resources | admitted to hospital was 4.00 among non-adherent patients compared to adherent group. |
| **(Weiden et al., 2004)** | USA | 2004 | Patients with schizophrenia | Observational study | Non-compliance/adherence | Healthcare resources | **Healthcare resources** - Risk of hospitalisation was significantly correlated with compliance. Lower compliance was associated with a greater risk of hospitalisation over and above any other risk factors for hospitalisation. For example, the presence of any gap in medication coverage was associated with increased risk of hospitalisation, including gaps as small as one to ten days (odds ratio [OR]=1.98). A gap of 11 to 30 days was associated with an OR of 2.81, and a gap of more than 30 days was associated with an OR of 3.96. |

# LSE Enterprise contact details

LSE Enterprise Limited
London School of Economics and Political Science

Eighth Floor, Tower Three
Houghton Street
London
WC2A 2AZ

Tel: +44 (0)20 7955 7128
Fax: +44 (0)20 7955 7980
Email: enterprise@lse.ac.uk
Web: lse.ac.uk/enterprise

LSE Enterprise