Department of Statistics and Quantitative Methods

Division of Biostatistics, Epidemiology and Public Health

Laboratory of Healthcare Research and Pharmacoepidemiology

PhD program in Public Health

Cycle XXXII

Curriculum in Epidemiology and Research on the Systems of Prevention, Diagnosis and Treatment

The quality of clinical pathways delivered to patients with severe mental disorders. A multi-regional Italian investigation based on healthcare utilization databases.
The QUADIM project

Surname: MONZIO COMPAGNONI

Name: MATTEO

Registration number: 738700

Supervisor: Prof. GIOVANNI CORRAO

Coordinator: Prof. GUIDO GRASSI

ACADEMIC YEAR 2018/2019

Contents

List of abbreviations

ADT   Antipsychotic Drug Therapy

AMI   Any Mental Illness

ATC   Anatomical Therapeutic Chemical

CCM   National Center for Disease Prevention and Control

CI   Confidence Interval

CMHC   Community Mental Health Centers

CP   Clinical Pathway

DCC   Day Care Centers

DMH   Department of Mental Health

GHPW   General Hospital Psychiatric Wards

HCU   Healthcare Utilization

ICD-10   International Classification of Diseases, 10th revision

ICD-9-CM   International Classification of Diseases, 9th revision, Clinical Modifications

MCS   Multisource Comorbidity Score

MHIS   Mental Health Information System

MHS   Mental Health Service

NHS   National Health Service

OECD   Organization for Economic Cooperation and Development

OR   Odds ratio

QUADIM   Clinical pathways in patients with severe mental disorders in Italy

RCT   Randomized Clinical Trial

RF   Residential Facilities

RR   Relative Rate

SAS   Statistical Analysis System

SISM   Italian Mental Health Information System

SMI   Serious Mental Illness

WHO   World Health Organization

Abstract

Improving the quality of care is a leading priority for national health systems, consistent with the aim of improving population health, while maintaining the sustainability of the whole health system, especially for the mental health system, since it is composed by a complex network of community mental health teams of professionals and a wide range of community-based treatment, rehabilitation, day-care and residential care facilities.

The quality of routine mental healthcare is still far from optimal, worldwide and in Italy, because it is not always delivered in accordance with evidence-based mental health standards and it can vary greatly among providers. Indeed, the construct of process indicators in the field of mental health is often not completely consistent with recommendations in evidence-based guidelines, where existing. To date, only few studies have analyzed this issue in Italy, despite the quality of mental health care has become a frequent subject of international evaluations.

Given these premises, the QUADIM Project ("Clinical pathways in patients with severe mental disorders in Italy"), an Italian multi-regional project funded in 2016 by the Italian Health Ministry, was conducted with the aim to assess the quality of healthcare pathways provided to patients with serious mental illnesses (SMI) assisted by regional Departments of Mental Health (DMHs) in a real-world setting, using a set of process indicators developed by a panel of experts starting from a document approved by the italian Unified State-Regions Conference (2014).

The main aim of this thesis was the conduction and the management of this project, which constituted my thesis project during the PhD.

For each of the four SMI investigated (i.e., schizophrenic, depressive, bipolar and personality disorders), from the regional Healthcare Utilization (HCU) databases were identified the cohorts of adult patients affected by this specific mental disorder and taken in care by regional DMHs during the years 2015-2016. The adherence of these patients to the defined process indicators was evaluated during the first 12 months of follow-up, assessing strengths and weaknesses of the four regional mental health systems.

As far as the process indicators were designed and developed taking inspiration from clinical recommendations that should be followed for improving the quality of mental healthcare, and by considering that a better process profile, as measured by these indicators, not necessarily lead to better outcomes, a secondary aim of the QUADIM project was the conduction of a validation study for evaluating their relationship with measurable clinical outcomes. Thus, among patients affected by an incident schizophrenic spectrum disorder, case-crossover study was conducted in order to validate some process indicators, relating them, as a proxy of the quality of delivered care, with some clinical outcomes, such as admission to hospital psychiatric wards (GHPWs).

The layout of the thesis has been divided into different sections. I will proceed in the first instance by giving an overview of the QUADIM project and the methods used to identify the cohorts of patients affected by SMI, to design and develop the process indicators and to conduct the validation study among patients with incident schizophrenic spectrum disorder; proceeding with a detailed description of the results and reporting the main findings of the validation study. Finally, the implications of monitoring the process of care of patients with incident schizophrenic disorder and, more in general, of the proposed approach, were discussed.

Chapter 1

Introduction

1.1 Severe mental illnesses

Mental illnesses are common and globally widespread. Only in the United States, nearly one in five U.S. adults live with a mental illness condition (46.6 million in 2017) [1]. Mental illnesses include many different conditions that vary in degree of severity, ranging from mild to moderate to severe. Two broad categories can be used to describe these conditions: Any Mental Illness (AMI) and Serious Mental Illness (SMI), with the AMI condition that encompasses all recognized mental illnesses [2].

Any mental illness is defined as a mental, behavioural, or emotional disorder. AMI can vary in severity, ranging from no impairment to mild, moderate, and even severe impairment, e.g., individuals with serious mental illness. Instead, there is still no agreement at international level on a shared definition of serious mental illness [3].

During the years, the various definitions proposed for defining mental illnesses appear to be either hyper- or hypo-inclusive, depending not only on the width of the chosen criteria, but also on the goals of the definition itself, e.g., whether the intention is to estimate the prevalence of individuals with severe mental illness in the general population or the prevalence of patients with severe mental disorders attending mental health services. In the former case it is likely that the intention is to plan mental health policies in accordance with current population real needs, whereas in the latter the aim is at evaluating the conformity of mental health services with the mission entrusted to them.

In setting out operative criteria for SMI definition, the National Advisory Mental Health Council (NAMHC, 1993) utilized not only the diagnosis, but also considered criteria related to the severity, that were defined in the domains of recent treatments, symptoms, and social/occupational functioning. For instance, severity criteria included any recent inpatient psychiatric hospitalization or nursing home placement, any outpatient treatment in a speciality mental health setting, the use

1

of antipsychotic medication or the presence of psychotic symptoms. The US Substance Abuse and Mental Health Services Administration (SAMHSA) defined a patient affected by SMI as an individual suffering from one of the disorders included in the "Diagnostic and statistical manual of mental disorders", other than a substance use disorder, and having a serious impairment [4].

Despite there is no internationally agreed definition of severe mental illnesses, as a general rule, criteria for the definition of SMI are based on diagnosis, disability and service utilization [3]. Thus, SMI is generally defined as a mental, behavioural, or emotional disorder resulting in serious functional impairment, which substantially interferes with or limits one or more major life activities. Psychotic disorders like schizophrenic and bipolar disorders, and some forms of non-psychotic disorders like major depression, obsessive-compulsive disorders and panic disorders are generally included in the SMI [5].

In Italy, during the year 2017, the standardized prevalence rate of patients affected by AMI was about 170 individuals every 10,000 adult inhabitants. Whereas, standardized prevalence rates of patients affected by schizophrenic, bipolar, depressive and personality disorders were, respectively, of 36, 14, 39 and 12 patients every 10,000 adult inhabitants. Analyzing the prevalence rates of users treated by diagnostic group, there are important gender differences, e.g., rates related to schizophrenic and personality disorders are greater in men than women, while the opposite occurs for affective and depressive [6].

In the United States, in 2017, were estimated 46.6 million adults aged 18 or older with AMI, representing the 18.9% of all US adults. The proportion of prevalent cases of AMI was higher among women (22.3%) than men (15.1%), and young adults aged 18-25 years had the highest prevalence of AMI (25.8%) compared to adults aged 26-49 years (22.2%) or 50 and older (13.8%). Instead, for what concerns SMI were estimated 11.2 million US adults aged 18 or older with SMI, representing 4.5% of all US adult population. Prevalence proportion of SMI was higher among women (5.7%) than men (3.3%), whereas young adults aged 18-25 years had the highest prevalence of SMI (7.5%) compared to adults aged 26-49 years (5.6%) or 50 and older (2.7%) [1].

Despite lower prevalence, the burden of mental illnesses is particularly concentrated among those patients who experience disability due to SMI. Indeed, Narrow et al. [7], re-analyzing the Epidemiological Catchment Area (ECA) study data, showed that persons affected by SMI differed in mental health service utilization from those affected by AMI, i.e., patients with SMI required more outpatients services and experienced more psychiatric hospital admissions, thus consuming a greater amount of resources than non-SMI patients.

Thus, in recent years a consensus has emerged in many countries, including the UK, that the activities of mental health services should be targeted especially towards patients suffering from SMI [8]. In Italy, this policy was provided for by a project of the italian Ministry of Health in 1999 ("Progetto obiettivo per la salute mentale"), in UK by the National Service Framework for Mental Health (Department of Health, 1999) and in US by the National Advisory Mental Health Council (NAMHC, 1993). Several reports on mental health services have indicated deficiencies in this topic in UK [9]. In other countries, such as Italy, there is no clear guidance on targeting specific groups among those with mental illness; nevertheless, there is an increasing awareness that those with SMI should be given higher priority [10].

Finally, SMI, including schizophrenia spectrum and affective disorders, is the main focus of mental health systems, particularly in community-based mental health systems. As Leff [11] asserted, the success or failure of community care is judged by the results achieved with these patients and their families. Furthermore, community care is not simply a network of community mental health facilities; more important, it involves the delivery of appropriate and evidence-based treatments [12].

1.2 Clinical Pathways

In public health, in addition to assessing the burden of a disease or condition, the evaluation of the impact of health interventions is also important to measure both the appropriateness of care provided and the performance of healthcare system. This aspect is implemented in the analysis of the process following the taking charge of the patient with an illness, especially a chronic condition, conducted with specific indicators that evaluate the diagnostic, therapeutic and care procedures to which the patients are subjected during their care process. This framework makes possible the evaluation of the adherence to guidelines, measuring the gap between the standard expected process and the therapeutic path observed in the current clinical practice.

The identification of process indicators can be facilitated by the scientific literature, which, especially for the main diseases, e.g., the chronic and non-chronic ones, offers a large variety of evidence-based guidelines. The implementation of such guidelines at patient level defines the clinical pathway (CP) of a patient.

Clinical pathways represent the application of evidence-based guidelines related to a clinical condition, in a specific organizational framework of a health authority, considering the resources available. CPs are local models that, based on the more recent guidelines and in relation to the available resources, allow the analysis of differences between an ideal expected situation and the one observed in a real-world context, in order to improve quality. They are also tools that allow healthcare agencies to outline the best care pathway that is possible to provide, within their own organizations, for a specific clinical condition [13].

Therefore, in the last decades, the identification and development of CPs is becoming an important instrument aimed at assessing the continuity of care and at implementing guidelines, to ensure a stable and complete taken in charge of the patient.

CPs have been implemented in a wide spectrum of healthcare systems, mainly in order to improve the efficiency of hospital care while maintaining or improving quality. CPs, or "integrated care pathways" as they are called in the UK, are considered to be useful tools for designing care processes, improving both the clinical governance and the quality of provided clinical care, and ensuring that the delivered care is based on the latest research [14–16]. From the 1990's, clinical pathways have been spread all over the world [17] and today are utilized worldwide as a tool to design and improve care processes within the patient-centred care concept [18,19].

Although they have been utilized for more than 3 decades, there is still uncertainty about the issue of CPs, particularly concerning their definition, their actual use, the methods used for their implementation and their effects on clinical outcomes [20]. About this last concern, some evidence exists to support the use of CPs in order to change behaviour and improve healthcare quality [21–24].

In Italy, is widely adopted the definition of CPs contained in the "Piano Nazionale per il Governo delle Liste d'Attesa" 2012-2014, which characterizes the CP as: "A pre-defined, articulated and coordinated sequence of services provided to patients, at in/out-hospital/territorial level, which involves the integrated participation of various specialists and professionals (in addition to the patient himself), in order to achieve the most appropriate diagnosis and therapy for a specific pathological situation" [25,26].

Therefore, CPs consist in the set of activities provided by different healthcare professionals to answer the patient's demand, from the diagnosis to the healing or to the end of life. For some conditions, the network of services to be activated is limited to a single hospital structure requiring little interdependence with other operating units or hospitals, since that hospital unit most of the needed diagnostic and therapeutic services. On the other hand, other clinical conditions, as oncological diseases, refer to many services among those provided at hospital, territory and community-based level.

Finally, CPs are a useful and powerful tool to constantly monitor the quality of care provided and the impact of health interventions, and must be quantitatively evaluated with the aim of analyzing the benefits associated with their implementation.

1.3 The mental health system in Italy

The 1978 reform legislation

Under the WHO perspective, a mental health system is defined as the structure and all those activities whose primary purpose is to promote, restore or maintain mental health. The mental health system includes organizations and resources focused on improving mental health [27]. The building blocks of the mental health system are governance (including mental health plans and legislation), financing, mental health services, primary care, human resources, links with other sectors and an information system [27,28].

As regards the mental health's framework, the twentieth century has been characterized by the gradual shift of the mental health care from large isolated institutions towards a community level. In the last decades, the move of psychiatric care from mental hospitals towards community-based services has been a common feature, to a greater or lesser extent, of the national health service of the majority of Western countries, although some observers can argue that this deinstitutionalization process might have gone too far [29]. However, the clinical and management assumptions underlying this trend have been different and their translation into community-based service delivery models followed different paths [30,31].

In Italy, the reform of the mental health care began about forty years ago with the 1978 reform legislation. This italian psychiatric reform law, also called "Law 180", made radical changes to the whole concept of italian mental health care, which, until then, had combined some components of community care with a prevalent mental hospital care. The Law 180 stated that community care must stand alone; this led to the closing of the psychiatric hospitals and to the promotion of a community-based framework for the psychiatric care. All the new admissions to public psychiatric hospital were stopped and Community Psychiatric Services were established to provide comprehensive care to populations in defined geographical areas [32]. Therefore, acute psychiatric units in general hospitals, to which all patients requiring compulsory or voluntary hospitalization had to be admitted, were integrated with the network of community-based mental health services. Thus, Italy became the first developed country to base its mental health care solely on a community-based network of mental health facilities. This process was neither linear nor uniform, and the effective closing down of the psychiatric hospitals ended only twenty years later, at the end of the 1990s [28].

The 1978 italian psychiatric reform law stated a general guideline and did not provide specific directions on its implementation, charging italian Regions with the responsibility of managing this transition towards community-based psychiatric care. Recent legislation emphasizes the role of the Regions in planning, coordination and delivery of healthcare services; therefore, there is a wide variation across the 20 italian Regions in the amount of resources devoted to community-based psychiatric care and in the range of services provided.

This regional implementation process caused relevant differences between macro-geographical areas and, even though over 40 years have passed since the 1978 psychiatric reform, some inequalities still remain in terms of resources allocation and services delivery patterns[28]. Thus, in the following decades, each italian Region set up its own mental health system [33,34], and, from an evaluative point of view, each regional mental health system represents a single evaluation unit, relatively homogeneous in terms of policies, resources and service delivery [34].

The mental health system

Despite the differences in terms of policies, resources allocation and services delivery patterns, the italian Regions provide mental health care through a similar set of territorial structure at a community level.

In the Italian National Health Service (NHS), the Department of Mental Health (DMH) is the organization responsible for specialist mental health care in the community, as stated by the Progetto Obiettivo "Tutela Salute Mentale 1998-2000" [35]. The DMH is the organization providing community mental health care, i.e., the DMH is in charge of the planning and management of all medical and social resources related to prevention, treatment, and rehabilitation in mental health to the population of a defined catchment area, through a network of community services, including outreach teams, hospitals, day care and residential facilities.

Since the early 1980s, the majority of italian Regions adopted, to a greater or lesser extent, an organization model for DMHs centered on multi-disciplinary teams led by consultant psychiatrists, including psychiatrists, psychologists, nurses, social workers, occupational therapists, rehabilitation counsellors and auxiliary staff. Each DMH should be able to provide the full range of mental health care, from acute emergency treatment to long-term rehabilitation. Therefore, within each DMH there should be various of the following facilities: Community Mental Health Centers (CMHC), General Hospital Psychiatric Wards/units (GHPW), Day Care Centers (DCC) and Community Residential Facilities (RF). Patients can access directly specialist mental health

services, although they are often referred by their primary care practitioner. CMHCs are the entry point of the system for the overwhelming majority of cases [28,34].

The PROG-CSM survey showed that, in 2005, Departments of Mental Health were widespread in all Italian Regions, though the DMH level of complexity varied. More than half of the DMHs included not only Mental Health Services for adults, but also services for substance abuse, child and adolescent psychiatry, and clinical psychology services. Concerning the availability of the whole network of mental health facilities, about eight DMHs out of ten included RFs or DCFs and almost all had GHPWs, while day hospitals were less frequent (they were present in about half the DMHs). The level of complexity in terms of mental health facility availability is high in six DMHs of the ten, intermediate in a quarter and low in one of the ten [28,36].

Nowadays, the network of mental health services in Italy is composed by 183 DMHs, with a total of 1,114 CMHCs, 849 DCCs (with 2.9 places/10,000 adult patients, ap.), 1,998 RFs (with 5.2 beds/10,000 ap.) and 318 GHPWs (with 10.1 beds/10,000 ap.), as shown in the third "Annual Report on Mental Health in Italy, year 2017" [6].

In Italy, during the year 2017, 851,189 patients had at least one contact with a mental health service (169.4/10,000 adult patients, ap.). The information system recorded 11,474,311 outpatient and home contacts (with a mean of 15.3 contacts for patient), 1,582,966 day care attendances (325.9/10,000 ap.), 109,622 admissions to general hospital psychiatric wards (with a mean length of hospital stay of 13 days) and 11,549,682 days of recovery to residential facilities (with a mean length of recovery stay equal to 816 days for patient) [6].

1.4 Evaluating quality of mental health care

Improving the quality of care is a leading priority for national health systems, consistent with the aim of improving population health, while maintaining the sustainability of the whole health system [37], especially for the mental health system, being composed by a complex network of different types of community mental health teams and a wide range of treatment, rehabilitation, employment and residential care facilities, currently operating in the community.

Information is needed in the mental health system by all stakeholders. Clinicians are interested in evaluating treatment outcomes, managers are interested in analyzing the effectiveness of the services they lead, while policymakers want to learn the outcomes of their healthcare policies. Also other stakeholders, such as users, patients' families and advocacy non-governmental organisations, that are keen to monitor the quality of care and respect for human rights, have an interest in information. Furthermore, information is needed also to verify the system infrastructure and the responsible and transparent management of the scarce resources allocated for the mental health care. There is a consensus that rational planning aimed at achieving a well-functioning mental health system is hardly possible in the absence of valid monitoring and evaluation, both based on good quality information [38,39]. Reliable and timely health information is the foundation for effective health services management and public health action [40].

Persuaded that what "gets measured gets done", World Health Organization (WHO) included "monitoring community mental health" through strengthening information systems, as one of the ten recommendations that can make a difference in mental health care [41].

CPs development and use is more common in other areas of medical practice than in psychiatry, where their use has been rather limited to date [42]. Some of the barriers to the implementation of mental health CPs include: (i) defining the start and end of an episode of care, as this is clearly problematic with some long-term or intermittently relapsing and remitting mental health conditions; (ii) standardizing packages of care for complex disorders; and (iii) having high levels of individual variation within designated clinical case-mix groups [43,44]. Thus, only few studies have assessed the impact of CPs in mental health [42–49], with inconsistent results that were debated. Therefore, to date, little is known about the practice and patient characteristics that predict effectiveness of community-based care pathways.

Quality of mental health care

The quality of routine mental health care is still far from optimal, worldwide and in Italy, because it is not always delivered in accordance with evidence-based mental health standards and it can vary greatly among providers [37,50–52]. Thus, patients with severe mental disorders are frequently treated with care pathways that are not consistent with the recommendations based on scientific evidence in this area [50,53–55] and that do not fulfil the expected quality standards. To date, only few studies have analyzed this issue in Italy, despite the quality of mental health care has become a frequent subject of international evaluations [56], and these studies have shown in their results serious gaps in the treatment of patients with severe mental disorders. For instance, in Lombardy, northern Italy, the internationally validated criterion of "minimally adequate treatment" [50] revealed that, in 2007, approximately half of the patients treated for schizophrenic and affective disorders in public DMHs did not receive adequate care [50]. Furthermore, always in Lombardy, Lora et al. [53], using a set of clinical indicators on almost 28,000 patients with schizophrenic disorder, highlighted critical issues regarding the treatment of cases at onset and the delivery of psychosocial interventions, while the hospital treatment of the acute episodes was characterized by better quality.

1.5 The QUADIM project

As outlined by Saraceno [57], there is an urgent need to assess the development of community care at system level, because in order to deliver a high standard of community care an integrated system of service delivery has to be adopted and needs to be conceived in a rational way. So, the assessment of the quality of care pathways plays a key role in improving and optimizing the organization of healthcare systems. Indeed, not surprisingly, the OECD recently stated that the quality of care of mental health disorders "will continue to trail behind that of other diseases until appropriate indicators are used to measure quality, and appropriate data are collected" [58].

Thus, measuring the quality of mental health care by performance indicators (i.e., measurable elements of practice performance for which exist evidence or consensus of their ability to assess the quality of care provided [51]) fits into this issue and explains why, in the last few decades, policymakers, researchers and clinician focused on designing evidence-based indicators able to routinely monitor the quality of mental healthcare.

Such a line also affected Italy, where the closing down process of psychiatric hospitals, subsequent the 1978 psychiatric reform, led to difficulties in providing effective care to people with severe mental illness and where the subsequent development of a widespread network of community mental health care facilities needs to be evaluated [59].

Despite their widespread use [53,60–62], however, the construct of process indicators in the field of mental health is often not completely consistent with recommendations in evidence-based guidelines, where existing. In fact, their ability in appreciating the component of quality of healthcare causally associated with clinical outcomes that treatments would like to avoid, that is the component here defined validity of process indicator, is largely untested [53], making its evaluation in the real-life setting essential.

In Italy, the development and validation of indicators for assessing and evaluating integrated healthcare pathways for specific clinical conditions are the main objective of a specific national working group of the Italian Health Ministry, Health Planning Dept. [63], that has been dealing with this issue for over three years. As far as mental health is concerned, the working group took advantage from the so-called **QUADIM Project**.

Funded in 2016 by the Italian Health Ministry through the research programs of the National Center for Disease Prevention and Control (CCM), the QUADIM Project ("Clinical pathways in

patients with severe mental disorders in Italy") is an italian multi-regional project aimed to evaluate the quality of healthcare pathways provided to patients with severe mental illness (schizophrenic, depressive, bipolar and personality disorders) treated in the Departments of Mental Health of four Italian Regions (Lombardy, Emilia-Romagna, Lazio and the province of Palermo for Sicily).

The care packages provided by the DMHs of the four Regions involved were analyzed using a methodology previously used in the Lombardy Region [50,53–55], thus, the assessment of the quality of care was based on process indicators for clinical pathways in SMI identified from the document approved by the italian Unified State-Regions Conference (2014) [64].

For designing process indicators, the QUADIM project took inspiration by the clinical evidence-based recommendations that should be followed for improving the quality of mental healthcare. For example, the constant contact with mental health services, as well as the persistence with drug treatment, are expected to improve mental health. However, by considering that a better process profile, as measured by these indicators, not necessarily lead to better outcomes, a validation study for evaluating their relationship with measurable clinical outcomes was designed by the mixed interdepartmental working group of the Health Ministry.

The designed process indicators were properly processed and adapted to the needs of the project and, mainly, to the different SMI under investigation.

1.6 Objectives

The <u>main aim</u> of this thesis was the conduction and the management (with the collaboration of the scientific coordination group) of an Italian multi-regional project in order to assess the quality of healthcare pathways provided to patients with severe mental illness (i.e., schizophrenic, depressive, bipolar and personality disorders) assisted by regional DMHs in a real-world setting, using a set of process indicators developed by a panel of experts starting from a document approved by the italian Unified State-Regions Conference (2014) [64].

For each of the 4 SMI investigated, from the regional Healthcare Utilization (HCU) databases were identified the cohorts of adult patients affected by this specific mental disorder and taken in care by regional DMHs during the years 2015-2016. The adherence of these patients to the designed process indicators was evaluated during the first 12 months of follow-up, assessing strengths and weaknesses of the 4 regional mental health systems.

As far as the process indicators were designed and developed taking inspiration from clinical recommendations that should be followed for improving the quality of mental healthcare, and considering that a better process profile, as measured by these indicators, not necessarily lead to better outcomes, a <u>secondary aim</u> of the QUADIM project was the conduction of a validation study for evaluating their relationship with measurable clinical outcomes. Thus, another objective of the project was the validation of some process indicators, relating them, as a proxy of the quality of delivered care, with some clinical outcomes, such as admission to hospital psychiatric wards (GHPWs).

One validation study was conducted among patients affected by an incident schizophrenic spectrum disorder.

The activities planned for this project included the writing of a research protocol, the presentation of the protocol to an ethical committee, the design of process indicators, the coordination of the centres included in the project about the selection of the patients with SMI and the linkage with the HCU databases, the performance of all the statistical analyses, the preparation of a final report and the writing of a manuscript to be submitted to a peer-reviewed scientific journal.

Regular meetings were planned with the scientific staff involved in the project.

Chapter 2

Methods

2.1 Data sources

Data for the QUADIM project were retrieved retrospectively from the computerized Healthcare Utilization (HCU) databases of the four Italian Regions involved in the project and localized in North West (Lombardy), North East (Emilia-Romagna), Centre (Lazio) and South (Palermo province, for Sicily region).

Overall, these data covered almost 22 million of beneficiaries of the Italian National Health Service, that is nearly the 37% of the entire Italian population.

Healthcare Utilization databases

In Italy, the National Health Service (NHS), established by the law n. 833 on December 23rd, 1978, and progressively submitted to various reforms, the latest in the year 2012, guarantees health care to all the citizens and have a Regional structure. Therefore, each region has its own Regional Health Service which is managed with large degrees of independence.

An automated system of HCU databases allows each Italian region to locally manage the healthcare provided by NHS; indeed, the NHS covers the entire Italian population (i.e., all Italian citizens have equal access to healthcare services) and since the 1990s its management has produced the implementation of health information systems, common to all Italian regions. In this framework were introduced the HCU databases, used by health agencies to record all the services provided to citizens.

Thus, HCU databases refer to the collection of data regarding health services dispensed to the whole population of a specific geographic area. In Italy, they were primarily instituted for administrative purposes, with the aim of monitoring costs and planning and managing healthcare services. They are also used for reimbursement of health services from Regions to local health

authorities [65]. Nevertheless, they actually represent a powerful tool in the field of pharmacoepidemiology.

Indeed, although these databases were created to respond to purely administrative needs, their use is becoming increasingly common in the conduction of studies in the field of pharmacoepidemiology, both at a national [66–68] and international level [69–72], as well as for evaluating the effectiveness and the safety of drugs used for the treatment of several diseases [73]. In the process of approval of drugs, HCU databases represent a valid tool for the conduction of post-marketing studies. For this reasons, HCU databases are an important tool for integrating the results coming from RCTs, and for evaluating their external validity.

The information stored in the HCU databases include the distribution of all drugs reimbursed by the NHS, diagnosis at discharge from public or private hospitals, the outpatient health services, specialist visits and diagnostic exams reimbursable by the NHS, the emergency room service, the certificates of delivery assistance, the exemptions for a specific disease and demographical information on residents who receive NHS assistance.

Motivations that lead researchers to use these data sources are, mainly, (i) the fact that they guarantee broad coverage at the population level (almost all citizens beneficiaries of NHS) and (ii) their ability to track accurately all the contacts that the citizens have with the regional services of the NHS. Furthermore, they often contain health information referred to many years, allowing to study uncommon adverse events, or those who required a long latency period; and the use of these databases are associated to low costs and relatively rapid time of execution. Indeed, all the information are directly available for a specific population in a specific period of time, avoiding long time for collecting data [66].

These aspects make HCU databases highly appreciated, as they allow to reflect current clinical practice for large and non-selected populations, producing real-world evidence [74], based on results that can be widely generalized.

In the Italian regions, the permission to access to the HCU databases is regulated by the Regional directorate and is permitted to the scientific institutions that own specific requirements, guaranteeing the ability and the expertise to handle such data and the intention to use them for scientific purposes [75].

To perform this study, the following regional databases were used:

- The Assisted Registry database, which contains the list of all the resident citizens beneficiaries of the NHS, with associated anagraphical data (such as date of birth, gender, municipality of residence, prescribing physician, etc.).

- The Hospital Discharge Forms database, which contains information on all the hospitalizations, both ordinary and in day-hospital, of all subjects accepted by both public and private hospitals. The information included in this database cover the dates of admission and discharge, the main and five secondary diagnosis of discharge (coded according to the 9th International Classification of Diseases, ICD-9-CM), the main and five secondary interventions to which patients underwent (coded according to the 9th International Classification of Diseases, ICD-9-CM), the date of the main intervention, etc.

- The databases of drugs dispensed from Territorial and Hospital Pharmacies, in which all outpatient prescriptions of drugs reimbursed by the NHS are collected at the dispensation time. They both include the date of administration, the ATC code of the drug and the quantity of packages dispensed.

- The Outpatient's Service database, which collects all the health services dispensed in the outpatient setting, including laboratory tests, imaging diagnostic procedures, radiotherapy and chemotherapy. Were available information about the description and the date of the health service dispensed. Interventions or procedures dispensed were coded according to the ICD-9-CM codes.

- The Italian Mental Health Information System (SISM) database, i.e., a specific automated system concerning psychiatric care provided by the regional DMHs accredited by the NHS. This database collects demographic information and the ICD-10, or ICD-9-CM, diagnoses of all patients attending mental health services and records all treatments provided to them (outpatient and home visits, day treatment attendance, admissions to general hospital and residential facilities). Further information about the Italian Mental Health Information System, and its history, are available in **Appendix I**.

As a unique identification code is used for all the previous databases within each region, it was possible to interconnect HCU databases through a record-linkage procedure, allowing to search out the complete care pathway of beneficiaries of NHS. In order to protect privacy, individual

identification codes are automatically converted into anonymous codes and the inverse process is avoided erasing the conversion table.

Details of HCU databases use in the field of mental health have been reported in more details elsewhere [76].

Harmonization and data processing

Although databases did not substantially differ across all regions for several aspects, a between-region data harmonization was performed, thus allowing data extraction processes to be targeted the same semantic concepts (e.g., information were uniformly encoded by using for each variable the same names, values and formats). For each administrative unit, anonymized data were extracted and processed locally by using Statistical Analysis System (SAS) programs, which were developed by the author of this thesis, according to a protocol previously approved by the Italian Health Ministry working group [63]. Therefore, a coordination activity of the standardization and harmonization procedures of the data extracted from HCU databases of the 4 regions was carried out.

2.2 Study design

A retrospective cohort study, based on the use of regional HCU databases, was conducted to describe and assess the quality of healthcare pathways provided to patients with SMI assisted by the regional DMHs.

2.3 Cohort(s) selection

The target population consisted of all beneficiaries of the NHS resident in the four territorial units aged over 18 years old. According to the Italian Institute of Statistics, this population amounts for almost 18 million individuals [http://demo.istat.it/index.html]. Of these, from the SISM database were identified patients who during the recruitment period had at least a contact with a local Mental Health Service (MHS) accredited by the NHS and received in that occasion diagnosis of at least one of the 4 SMI investigated (i.e., schizophrenic, bipolar, depressive or personality disorder).

Since administrative and bureaucratic issues have limited the time availability of the requested data in some regions (i.e., Lazio), the available recruitment period varied according to the considered territorial unit, i.e., from January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo, and from January to December 2015 for Lazio. This decision regarding Lazio region was taken because if the recruitment period had lasted longer, i.e., including also the year 2016, not all the identified patients would have had at least one year of follow-up, needed to assess the quality of care delivered, as will be explained in the next chapter.

For each of the 4 SMI considered, 4 distinct cohorts were identified, composed by patients, respectively: (A) with prevalent disorder; (B) with incident disorder; (C) with incident disorder at the onset (incident disorder on patients aged 18-25 years); and (D) discharged from GHPWs.

Inclusion and exclusion criteria for each of the identified cohorts of patients are described below.

Schizophrenic disorder

Prevalent Cohort (A)

The prevalent cohort consisted of all beneficiaries of the NHS resident in the four territorial units who, during the recruitment period, had at least a contact with a local DMHs and had diagnosis of schizophrenia spectrum disorder.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the prevalent cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of schizophrenia spectrum disorder

Exclusion criteria

None.

Incident Cohort (B)

The incident cohort consisted in the portion of the identified prevalent cohort (A) that, in the 2 years preceding the recruitment period, has not experienced any contact suggestive of the presence schizophrenia spectrum disorder with a structure accredited by NHS.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-65 years
- who experienced a contact with local DMHs with diagnosis of schizophrenia spectrum disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of schizophrenia spectrum disorder
- experienced at least one hospital admission with a main or secondary diagnosis of schizophrenia spectrum disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of antipsychotic drugs (having an interval between the two dispensations inferior to one year)

Incident Cohort at the onset (C)

The incident cohort at the onset consisted in the portion of the incident cohort's (B) patients who were aged 18-25 years during the recruitment period.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort at the onset were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-25 years
- who experienced a contact with local DMHs with diagnosis of schizophrenia spectrum disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of schizophrenia spectrum disorder
- experienced at least one hospital admission with a main or secondary diagnosis of schizophrenia spectrum disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of antipsychotic drugs (having an interval between the two dispensations inferior to one year)

GHPW discharged cohort (D)

The GHPW discharged cohort consisted in the portion of the identified prevalent cohort (A) that, during the recruitment period, experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the GHPW discharged cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of schizophrenia spectrum disorder
- who experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events

Exclusion criteria

None.

Bipolar disorder

The prevalent cohort consisted of all beneficiaries of the NHS resident in the four territorial units who, during the recruitment period, had at least a contact with a local DMHs and had diagnosis of bipolar disorder.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the prevalent cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of bipolar disorder

Exclusion criteria

None.

Incident Cohort (B)

The incident cohort consisted in the portion of the identified prevalent cohort (A) that, in the 2 years preceding the recruitment period, has not experienced any contact suggestive of the presence of bipolar disorder with a structure accredited by NHS.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-65 years
- who experienced a contact with local DMHs with diagnosis of bipolar disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of bipolar disorder
- experienced at least one hospital admission with a main or secondary diagnosis of bipolar disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of mood stabilizers (having an interval between the two dispensations inferior to one year)

Incident Cohort at the onset (C)

The incident cohort at the onset consisted in the portion of the incident cohort's (B) patients who were aged 18-25 years during the recruitment period.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort at the onset were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-25 years
- who experienced a contact with local DMHs with diagnosis of bipolar disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of bipolar disorder
- experienced at least one hospital admission with a main or secondary diagnosis of bipolar disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of mood stabilizers (having an interval between the two dispensations inferior to one year)

GHPW discharged cohort (D)

The GHPW discharged cohort consisted in the portion of the identified prevalent cohort (A) that, during the recruitment period, experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the GHPW discharged cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of bipolar disorder
- who experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events

Exclusion criteria

None.

Depressive disorder

The prevalent cohort consisted of all beneficiaries of the NHS resident in the four territorial units who, during the recruitment period, had at least a contact with a local DMHs and had diagnosis of major depressive disorder.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the prevalent cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of major depressive disorder

Exclusion criteria

None.

Incident Cohort (B)

The incident cohort consisted in the portion of the identified prevalent cohort (A) that, in the 2 years preceding the recruitment period, has not experienced any contact suggestive of the presence of major depressive disorder with a structure accredited by NHS.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-65 years
- who experienced a contact with local DMHs with diagnosis of major depressive disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of major depressive disorder
- experienced at least one hospital admission with a main or secondary diagnosis of major depressive disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of antidepressants (having an interval between the two dispensations inferior to one year)

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

Incident Cohort at the onset (C)

The incident cohort at the onset consisted in the portion of the incident cohort's (B) patients who were aged 18-25 years during the recruitment period.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort at the onset were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-25 years
- who experienced a contact with local DMHs with diagnosis of major depressive disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of major depressive disorder
- experienced at least one hospital admission with a main or secondary diagnosis of major depressive disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of antidepressants (having an interval between the two dispensations inferior to one year)

GHPW discharged cohort (D)

The GHPW discharged cohort consisted in the portion of the identified prevalent cohort (A) that, during the recruitment period, experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the GHPW discharged cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of schizophrenia spectrum disorder
- who experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events

Exclusion criteria

None.

Personality disorder

The prevalent cohort consisted of all beneficiaries of the NHS resident in the four territorial units who, during the recruitment period, had at least a contact with a local DMHs and had diagnosis of personality disorder.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the prevalent cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of personality disorder

Exclusion criteria

None.

Incident Cohort (B)

The incident cohort consisted in the portion of the identified prevalent cohort (A) that, in the 2 years preceding the recruitment period, has not experienced any contact suggestive of the presence of personality disorder with a structure accredited by NHS.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-65 years
- who experienced a contact with local DMHs with diagnosis of personality disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of personality disorder
- experienced at least one hospital admission with a main or secondary diagnosis of personality disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of mood stabilizers (having an interval between the two dispensations inferior to one year)

Incident Cohort at the onset (C)

The incident cohort at the onset consisted in the portion of the incident cohort's (B) patients who were aged 18-25 years during the recruitment period.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the incident cohort at the onset were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18-25 years
- who experienced a contact with local DMHs with diagnosis of personality disorder

Exclusion criteria

From the patients identified with the inclusion criteria were excluded those who, in the 2 years preceding the recruitment period:

- experienced at least one contact with local DMHs with diagnosis of personality disorder
- experienced at least one hospital admission with a main or secondary diagnosis of personality disorder
- experienced at least one hospital admission in a GHPW
- received at least two prescriptions of mood stabilizers (having an interval between the two dispensations inferior to one year)

GHPW discharged cohort (D)

The GHPW discharged cohort consisted in the portion of the identified prevalent cohort (A) that, during the recruitment period, experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events.

Recruitment period

From January 2015 to December 2016 for Lombardy, Emilia-Romagna and Palermo and from January to December 2015 for Lazio.

Inclusion criteria

In the GHPW discharged cohort were included patients:

- who were NHS beneficiaries for more than 2 years before the index date
- aged 18 years or older
- who experienced a contact with local DMHs with diagnosis of personality disorder
- who experienced at least one hospital discharge from a GHPW or from other psychiatric facilities for acute events

Exclusion criteria

None.

For each of the 4 SMI investigated (i.e., schizophrenia spectrum, bipolar, major depressive and personality disorder), members of each described cohort were linked to the HCU database, in order to retrieve the health services provided to them from two years before the recruitment period to the end of follow-up. In this way, it was possible to build up the entire diagnostic and therapeutic pathways of cohorts' subjects.

For all the members of incident (B) and incident at the onset (C) cohorts, the date of the first visit or contact during the recruitment period was recorded as the cohort entry. For prevalent cohorts' (A) members, the cohort entry was fixed at the 1st January 2015. Whereas, for each GHPW discharged cohorts' (D) member, the date of the first discharge from GHPW during the recruitment period was recorded as the cohort entry.

Cohorts members accumulated person-years of follow-up starting from the date of cohort entry until the occurrence of one of the following events, whichever came first: death, emigration, or end-point of follow-up, i.e. 365 days after the cohort entry date.

For each considered SMI, the prevalence and incidence rates, both raw and age-standardized, were calculated; for the latter, the direct method of standardization was adopted, using the 2016 Italian standard population as the reference one, available on the website of the Italian Institute of Statistics.

For all diagnostic (ICD 10 or ICD-9-CM) and therapeutic codes used, please see **Appendix II**.

2.4 Process indicators

Once identified and implemented the algorithms for the inclusion of patients with SMI, the designing, development and validation of process indicators for assessing and evaluating the health care pathways provided to these patients were carried out.

Designing

For designing process indicators, the QUADIM project took inspiration from the clinical evidence-based recommendations that should be followed for improving the quality of mental healthcare. After a wide research in the literature, and with the continuous collaboration of the scientific coordination group and the clinicians involved in the project, the clinical indicators that were identified in the document of the State-Regions Unified Conference (2014) [64] on the treatment pathways in SMI were updated and modified.

The work of revision and updating of these clinical indicators has ended with the drafting of a manual, for each of the SMI investigated, in which (i) the specific algorithms for the cohorts' selection, (ii) the definition of the process indicators and their (iii) statistical implementation (e.g., specific codes, health services and methods used) were defined in details.

The target population consisted in the members of each cohort described above, referring to patients with schizophrenia spectrum, bipolar, major depressive and personality disorders. For each of these SMI was drafted a specific manual consisting in a set of the more appropriated process indicators that were identified and described in detail, in order to standardize their implementation to assess the quality of the healthcare delivered to patients affected from that disease.

Implementation

In the manuals drafted, the ordering and classification of the forms concerning each single designed process indicator were a function of the **(i)** observation unit (Patient, Family, Patient and Family); **(ii)** healthcare service type (outpatient territorial assistance, residential or semi-residential care facilities, hospital care and any other contact with DMHs); **(iii)** content of the provided service (pharmacological, psychoeducational or psychotherapeutic treatment); **(iv)** cohort to which the indicator must be applied (prevalent, incident, incident at onset or GHPW discharged), and also according to the **(v)** calculation method of the indicator itself. In particular, the indicators were implemented and calculated based on one of the 3 following methods:

1) **Intensity**

For process indicators defined as a measure of the intensity with which a specific healthcare service is delivered to the patients and/or their families, statistical methods for calculating rates were adopted.

Therefore, the indicator consists of the ratio between a numerator (total count of the times in which the analyzed specific healthcare service was provided) and a denominator (total number of temporal units accumulated by the considered cohort during the follow-up period). More precisely, the numerator calculation method varies according to the healthcare service to which researchers are interested, whereas the denominator is always calculated as the total number of person-months of follow-up accumulated by the cohort during the observation period.

Still with the regards to the denominator calculation, with the exception for the indicators assessing the intensity of residential or hospital care, when one or more admissions to hospitals or residential facilities occur for any reason, the months spent in these facilities must not be counted, i.e., being so excluded from the denominator calculation.

2) **Persistence**

For process indicators defined as an instrument to measure and assess the persistence of patients and/or their families with a specific delivered healthcare service, i.e., the continue contact of patients with a service without any episode of discontinuation, the actuarial life-table method was used.

Using the actuarial life-table method, it was possible to calculate the cumulative monthly probability, over the first 12 months of follow-up, of not experiencing the event under examination (failure event, which varies according to the service that the indicator aims to evaluate, e.g., discontinuation of attending territorial mental health services). Thus, it was possible to evaluate monthly the cumulative proportions of patients who have not yet experienced the failure event in that month, until the 12th month of follow-up.

When one or more admissions to hospitals or residential facilities occur for any reason, the period of follow-up must be interrupted at the admission date e must restart from the date of discharge, thus the months spent in these facilities are not considered for the indicator calculation. This, because we had no information on various mental

healthcare services (e.g., mental health outpatient services) in hospitalized patients, and thus we reasoned that the estimates of the process indicators could be affected by the so-called immeasurable time bias [77].

3) **Proportion**

For process indicators defined as an instrument to assess the proportion of patients to which a specific healthcare service or visit or treatment was delivered, a simple calculation method for proportion was adopted.

This method estimates the percentage of patients, belonging to the considered cohort, to which a specific healthcare service or visit or treatment was delivered by calculating the ratio between a numerator (i.e., the number of patients to which the specific healthcare service was provided during the follow-up period) and a denominator consisting in the total number of patients belonging to the cohort.

2.5 Validation study

The process indicators were designed and developed taking inspiration from clinical recommendations that should be followed for improving the quality of mental healthcare; however, a better process profile, as measured by these indicators, not necessarily lead to better outcomes. Indeed, in the field of mental health, process indicators' ability in appreciating the component of quality of healthcare causally associated with clinical outcomes that treatments would like to avoid, that is the component here defined validity of process indicators, is largely untested. To date, little is known about the practice and patient characteristics that predict effectiveness of community-based care patients affected by SMI.

Thus, a validation study needed to be conducted to evaluate in a real-life setting the association between a set of process indicators (i.e., the most clinically relevant, such as persistence with the pharmacological treatment or the territorial outpatient assistance) as a proxy of the quality of delivered care, and measurable clinical outcomes (e.g., admission to hospital psychiatric wards, GHPWs).

A validation study was conducted among patients having an incident schizophrenic disorder, with the aim of validating a set of indicators for quality of mental healthcare through their relationship with a measurable clinical outcome, i.e., admissions to GHPWs.

A case-crossover study design (i.e., a within-patient case-only design) was adopted. Thus, the validation study was performed on patients with an incident disorder who have experienced hospitalization in the psychiatric ward [78].

It was investigated whether each of those patients experiencing the outcome experienced the exposure (i.e., attended at least once the territorial mental health services or was covered by an high adherence to antipsychotic drug therapy) during one period just before outcome onset (current period) and two delayed reference periods. The effect of the current versus the reference exposure on the risk of admission to GHPWs was estimated by the conditional logistic regression model for estimating the case-crossover odds ratio, and corresponding 95% confidence intervals. As comparisons were made within each cohort member experiencing the outcome, the case-control design implicitly avoid confounding by subject-specific time-invariant attributes [79].

In addition, was also addressed the potential presence of protopathic bias, occurring when the outcome is associated with an exposure that actually results from early symptoms of the outcome

[80]. Increased territorial mental health services attendance and antipsychotic drug therapy use before occurrence of emergency hospitalization in GHPW is expected because of symptoms worsening. Thus, a paradoxical positive exposure-outcome association might be observed. For this reason, a delayed time-window between current exposure and outcome occurrence was introduced [81].

The width of current, referent and delayed time-widows was fixed at 45 days in the main analysis. However, due to arbitrariness in the choice, secondary analyses were also performed by expanding the breadth at 90 days.

A schematic representation of within-person case-crossover design used in the validation study and widths of delayed, current and reference time-windows used for in the analyses are reported in **Figure 3.3.1**.

In each participating Region data were extracted and analyzed locally from the local epidemiological observatory, or similar regional structure (Emilia-Romagna, Lazio and Sicily Region). Concerning Lombardy Region, data were extracted and analyzed locally in the regional infrastructure by the researchers of University of Milan-Bicocca by means of a remote connection (the "Data-as-a-Service platform (DaaS)") [82].

Thus, the above calculations were separately performed within each Region and the region-specific estimates were, summarized by using a random-effect model. The approach proposed by DerSimonian and Laird was used for estimating such effects [83]. The heterogeneity of estimates between regions was tested by Cochran's Q test and measured with the I^2 statistics (the proportion of between-region variability due to heterogeneity) [84].

For all diagnostic (ICD 10 or ICD-9-CM) and therapeutic codes used, please see **Appendix II**.

Further details regarding the design and the statistical methodology used in the validation study are described extensively in the Results section (please see "3.3 Validation study" paragraph).

All analyses were performed using the Statistical Analysis System Software (version 9.4; SAS Institute, Cary, NC, USA). Statistical significance was set at the 0.05 level. All p-values were two-sided.

Chapter 3

Results

3.1 Process indicators

Once identified and implemented the algorithms for the inclusion of patients with the 4 SMI investigated, process indicators for assessing and evaluating the health care pathways provided to these patients were calculated. Their estimates are given below.

3.1.1 Schizophrenic spectrum disorder

Cohorts' size

For each previously described cohort, the number of patients identified by the algorithms previously described and enrolled in the cohort is reported in the following table.

Table 3.1.1 Number of patients with schizophrenic spectrum disorder who met the inclusion and exclusion criteria in three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and in the whole Italian sample. Italy, QUADIM Project, 2015-2016

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Recruitment period	2015	2015-2016	2015-2016	2015-2016	2015-2016
Size of the resident adult population at 01/01/2016	4,922,315	1,043,939	3,735,638	8,323,030	18,024,922
PREVALENT COHORT (A)					
Cohort's size	**11,939**	**6,600**	**18,393**	**37,968**	**74,900**
Raw prevalence rate (x10'000)	24.3	63.2	49.2	45.6	41.6
Age-standardized prevalence rate (x10'000)	**18.5**	**49.5**	**37.7**	**34.8**	**35.1**
Mean age (SD)	50.0 (13.9)	49.2 (14.6)	51.9 (15.0)	50.9 (14.6)	50.9 (14.5)
INCIDENT COHORT (B)					
Cohort's size	**1,904**	**1,154**	**2,486**	**2,425**	**7,969**
Raw incidence rate (x10'000)	3.9	5.5	3.3	1.5	4.4
Age-standardized incidence rate (x10'000 PY)	**3.1**	**4.5**	**2.9**	**1.3**	**2.9**
Mean age (SD)	45.0 (12.1)	43.0 (12.2)	42.8 (12.5)	40.1 (13.2)	42.5 (12.5)
INCIDENT COHORT AT THE ONSET (C)					
Cohort's size	**165**	**127**	**300**	**444**	**1,036**
Mean age (SD)	22.2 (2.1)	22.4 (2.1)	22.0 (2.0)	21.7 (2.1)	21.9 (2.1)
GHPW DISCHARGED COHORT (D)					
Cohort's size	**1,107**	**1,234**	**2,992**	**6,611**	**11,944**
Mean age (SD)	44.8 (12.8)	45.7 (13.4)	45.1 (14.5)	45.8 (13.8)	45.5 (13.6)

3.1.1.1 Intensity of outpatient visits

This process indicator assesses the intensity of outpatient visits delivered to patients during the follow-up period. For each person-year (PY) accumulated by the cohort patients, the average number of outpatient visits delivered by territorial and day-care facilities of the regional DMHs was calculated.

Table 3.1.1.1.A Estimates of the intensity of outpatient visits delivered to patients affected by schizophrenic spectrum disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	10,748	5,228	17,537	34,883	68,396
%	90.0	79.2	95.3	91.9	91.3
No. of outpatient visits / PY	**21.6**	**10.8**	**41.0**	**23.9**	**26.6**
Cohort B					
Patients with at least 1 outpatient visit	1,606	895	2,245	2,100	6,846
%	84.3	77.6	90.3	86.6	85.9
No. of outpatient visits / PY	**15.2**	**11.4**	**29.4**	**17.8**	**19.9**
Cohort C					
Patients with at least 1 outpatient visit	141	94	284	398	917
%	85.5	74.0	94.7	89.6	88.5
No. of outpatient visits / PY	**19.8**	**15.3**	**30.7**	**25.0**	**24.7**
Cohort D					
Patients with at least 1 outpatient visit	1,008	1,051	2,779	6,147	10,985
%	91.1	85.2	92.9	93.0	92.0
No. of outpatient visits / PY	**35.3**	**16.9**	**45.8**	**36.6**	**36.8**

A modified version of this process indicator has been calculated, in order to assess the intensity of psychiatric outpatient visits delivered during the follow-up period. For each person-year (PY) accumulated by cohort patients, the average number of psychiatric visits delivered by territorial and day-care facilities of the regional DMHs was calculated

Table 3.1.1.1.B Estimates of the intensity of psychiatric visits delivered to patients affected by schizophrenic spectrum disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 psychiatric visit	9,548	4,897	14,040	32,750	61,235
%	80.0	74.2	76.3	86.3	81.8
No. of psychiatric visits / PY	**7.3**	**5.2**	**4.9**	**10.7**	**8.2**
Cohort B					
Patients with at least 1 psychiatric visit	1,405	852	1,927	2,031	6,215
%	73.8	73.8	77.5	83.8	78.0
No. of psychiatric visits / PY	**5.9**	**5.2**	**4.8**	**9.7**	**6.6**
Cohort C					
Patients with at least 1 psychiatric visit	129	91	265	385	870
%	78.2	71.7	88.3	86.7	84.0
No. of psychiatric visits / PY	**10.9**	**7.1**	**9.1**	**12.9**	**10.7**
Cohort D					
Patients with at least 1 psychiatric visit	956	1,013	2,428	5,772	10,169
%	86.4	82.1	81.1	87.3	85.1
No. of psychiatric visits / PY	**10.6**	**7.2**	**5.9**	**15.7**	**11.9**

3.1.1.2 Persistence with outpatient MHS assistance

This indicator assesses the persistence with the outpatient assistance delivered by the territorial mental healthcare services (MHS), i.e., territorial and day-care facilities, during the follow-up period. The proportion of cohort patients who experienced the discontinuation of attending territorial MHS in the first 12 months of follow-up was calculated. Attendance of territorial MHS was considered regular if the time-span between two consecutive outpatient visits was 90 days or shorter, or discontinuing otherwise.

Table 3.1.1.2 Estimates of the proportion of patients affected by schizophrenic spectrum disorder who experienced an episode of discontinuation of attending territorial MHS in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	10,748	5,228	17,537	34,883	68,396
%	90.0	79.2	95.3	91.9	91.3
No. of patients discontinuing MHS attendance	**3,219**	**2,884**	**5,116**	**9,143**	**20,362**
%	29.9	55.2	29.2	26.2	27.2
Cohort B					
Patients with at least 1 outpatient visit	1,606	895	2,245	2,100	6,846
%	84.3	77.6	90.3	86.6	85.9
No. of patients discontinuing MHS attendance	**785**	**528**	**1,426**	**804**	**3,543**
%	48.9	59.0	63.5	38.3	44.5
Cohort C					
Patients with at least 1 outpatient visit	141	94	284	398	917
%	85.5	74.0	94.7	89.6	88.5
No. of patients discontinuing MHS attendance	**63**	**57**	**173**	**154**	**447**
%	44.7	60.6	60.9	38.7	43.1
Cohort D					
Patients with at least 1 outpatient visit	1,008	1,051	2,779	6,147	10,985
%	91.1	85.2	92.9	93.0	92.0
No. of patients discontinuing MHS attendance	**201**	**433**	**1,220**	**1,337**	**3,191**
%	19.9	41.2	43.9	21.8	26.7

3.1.1.3 Timeliness of the first outpatient visit after discharge from GHPW

This process indicator assesses the timeliness of the first outpatient visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first outpatient visit (i.e., delivered by territorial and day-care facilities of the regional DMHs) within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.1.3 Estimates of the proportion of patients affected by schizophrenic spectrum disorder who received the first outpatient visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	1,107	1,234	2,992	6,611	11,944
Patients with at least 1 outpatient visit	1,008	1,051	2,779	6,147	10,985
%	91.1	85.2	92.9	93.0	92.0
Patients with the first outpatient visit within the first 14 days after the discharge	653	622	1,726	3,905	6,906
%	59.0	50.4	57.7	59.1	57.8

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.1.4 Timeliness of the first psychiatric visit after discharge from GHPW

This indicator assesses the timeliness of the first outpatient psychiatric visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first psychiatric visit, delivered by territorial and day-care facilities of the regional DMHs, within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.1.4 Estimates of the proportion of patients affected by schizophrenic spectrum disorder who received the first psychiatric visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	1,107	1,234	2,992	6,611	11,944
Patients with at least 1 psychiatric visit	956	1,013	2,428	5,772	10,169
%	86.4	82.1	81.1	87.3	85.1
Patients with the first psychiatric visit within the first 14 days after the discharge	414	477	742	2,458	4,091
%	37.4	38.7	24.8	37.2	34.3

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.1.5 Patients receiving home assistance
(after the cohort entry)

This process indicator evaluates the timeliness of the first home visit delivered after the cohort entry to the patients affected by the schizophrenic spectrum disorder. The proportion of patients who experienced at least one home visit by the DMHs' professionals in the year following the index visit was calculated.

Table 3.1.1.5 Estimates of the proportion of patients affected by schizophrenic spectrum disorder to whom at least one home visit was delivered by the DMHs' professionals in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort A					
Cohort's size	11,939	6,600	18,393	37,968	56,507
Patients who received at least 1 home visit	2,356	666	NA	7,045	10,067
%	19.7	10.1	-	18.6	17.8
Cohort B					
Cohort's size	1,904	1,154	2,486	2,425	5,483
Patients who received at least 1 home visit	267	86	NA	227	580
%	14.0	7.5	-	9.4	10.6
Cohort C					
Cohort's size	165	127	300	444	736
Patients who received at least 1 home visit	18	6	NA	47	71
%	10.9	4.7	-	10.6	9.6

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.
B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

3.1.1.6 Timeliness of home assistance after discharge from GHPW

This process indicator assesses the timeliness of the first home visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who experienced at least one home visit by the DMHs' professionals after the index discharge from GHPW was calculated.

Table 3.1.1.6 Estimates of the proportion of patients affected by schizophrenic spectrum disorder to whom at least one home visit was delivered by the professionals of regional DMHs within the 365 days following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort D					
Cohort's size	1,107	1,234	2,992	6,611	8,952
Patients who received at least 1 home visit	309	201	NA	1,860	2,370
%	27.9	16.3	-	28.1	26.5

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.

B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

3.1.1.7 Intensity of recovery to residential facilities

This process indicator measures the intensity of the use of the residential facilities. The proportion of cohort patients experiencing at least one admission to residential facilities during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to residential facilities, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in regional residential facilities was calculated.

Table 3.1.1.7 Estimates of the (i) proportion of patients affected by schizophrenic spectrum disorder who experienced at least one admission to residential facilities in the year following the index visit; and of the (ii) average number of days spent in residential facilities by those patients, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 admission to residential facilities	1,308	149	3,651	6,752	11,860
%	11.0	2.3	19.8	17.8	15.8
No. of days of recovery in residential facilities / PY	**186.0**	**281.2**	**177.7**	**142.7**	**159.9**
Cohort B					
Patients with at least 1 admission to residential facilities	214	45	807	811	1,877
%	11.2	3.9	32.5	33.4	23.6
No. of days of recovery in residential facilities / PY	**141.7**	**300.8**	**107.3**	**45.6**	**88.9**
Cohort C					
Patients with at least 1 admission to residential facilities	26	7	121	192	346
%	15.8	5.5	40.3	43.2	33.4
No. of days of recovery in residential facilities / PY	**99.2**	**313.2**	**42.6**	**48.2**	**55.4**

3.1.1.8 Intensity of recovery to hospital facilities (in GHPW)

This process indicator measures the intensity of the utilization of the hospital facilities. The proportion of cohort patients experiencing at least one admission to GHPWs during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to GHPWs, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in hospital facilities was calculated.

Table 3.1.1.8 Estimates of the (i) proportion of patients affected by schizophrenic spectrum disorder who experienced at least one hospital admission in a psychiatric ward in the year following the index visit; and of the (ii) average number of days spent in hospital facilities by those patients, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients with at least 1 hospital admission to hospital facilities	1,335	1,081	2,409	4,794	9,619
	%	11.2	16.4	13.1	12.6	12.8
	No. of days of recovery in hospital facilities / PY	**37.2**	**18.5**	**19.2**	**25.0**	**24.5**
Cohort B						
	Patients with at least 1 hospital admission to hospital facilities	261	307	849	776	2,193
	%	13.7	26.6	34.2	32.0	27.5
	No. of days of recovery in hospital facilities / PY	**19.6**	**13.1**	**13.3**	**15.4**	**14.7**
Cohort C						
	Patients with at least 1 hospital admission to hospital facilities	48	51	161	191	451
	%	29.1	40.2	53.7	43.0	43.5
	No. of days of recovery in hospital facilities / PY	**13.5**	**13.6**	**17.0**	**19.3**	**17.2**

3.1.1.9 Antipsychotic drug treatment

This process indicator measures the proportion of patients affected by a schizophrenic spectrum disorder that were in, or started, an antipsychotic drug treatment during the follow-up period. For the cohorts A and D, the proportion of patients in treatment with antipsychotic drugs was calculated. For the cohort B and C the proportion of patients who started a pharmacological treatment with antipsychotics during the follow-up period was calculated.

Table 3.1.1.9 Estimates of the proportion of patients with a schizophrenic spectrum disorder who were in treatment with (cohorts A and D), or started a treatment with (cohorts B and C), antipsychotic drugs in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with antipsychotics	9,228	4,647	16,398	30,047	60,320
	%	77.3	70.4	89.2	79.1	80.5
Cohort B						
	Patients who started a treatment with antipsychotics	921	649	2,032	1,676	5,278
	%	48.4	56.2	81.7	69.1	66.2
Cohort C						
	Patients who started a treatment with antipsychotics	99	82	266	344	791
	%	60.0	64.6	88.7	77.5	76.4
Cohort D						
	Patients who were in treatment with antipsychotics	1,013	1,076	2,704	5,453	10,246
	%	91.5	87.2	90.4	82.5	85.8

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.1.10 Persistence with Antipsychotic drug treatment

This indicator assesses the persistence with the antipsychotic drug treatment of the patients affected by a schizophrenic spectrum disorder that were in, or started, a treatment with antipsychotics during the follow-up period. The proportion of cohort patients who were not persistent with the pharmacological treatment with antipsychotics in the first 12 months of treatment was calculated. Starting from the index prescription of antipsychotics, consecutively refilled prescriptions were considered uninterrupted if the time-span between the end of one prescription and the beginning of the following one (or of censoring) was 30 days or shorter, since gaps less than 30 days being considered permissible. Conversely, if the between-prescription time-span was longer than 30 days, treatment discontinuation was assumed.

Table 3.1.1.10 Estimates of the proportion of patients affected by schizophrenic spectrum disorder who discontinued antipsychotic drug therapy in the year following the index prescription, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with antipsychotics	9,228	4,647	16,398	30,047	60,320
	%	77.3	70.4	89.2	79.1	80.5
	Patients who discontinued antipsychotic drug therapy	**6,794**	**2,534**	**11,514**	**22,729**	**43,581**
	%	73.6	54.5	70.2	75.7	72.2
Cohort B						
	Patients who started a treatment with antipsychotics	921	649	2,032	1,676	5,278
	%	48.4	56.2	81.7	69.1	66.2
	Patients who discontinued antipsychotic drug therapy	**671**	**428**	**1,459**	**1,350**	**3,908**
	%	72.9	65.9	71.8	80.5	74.0
Cohort C						
	Patients who started a treatment with antipsychotics	99	82	266	344	791
	%	60.0	64.6	88.7	77.5	76.4
	Patients who discontinued antipsychotic drug therapy	**81**	**61**	**206**	**275**	**623**
	%	81.8	74.4	77.4	79.9	78.8
Cohort D						
	Patients who were in treatment with antipsychotics	1,013	1,076	2,704	5,453	10,246
	%	91.5	87.2	90.4	82.5	85.8
	Patients who discontinued antipsychotic drug therapy	**829**	**682**	**2,152**	**4,579**	**8,242**
	%	81.8	63.4	79.6	84.0	80.4

3.1.1.11 Assessments of glycated haemoglobin and lipid profile in patients treated with antipsychotics

The side effects of a drug treatment must be monitored. This process indicator assesses the level of clinical monitoring of the safety of antipsychotic drug therapy. This clinical monitoring of the antipsychotic treatment consists in the clinical evaluations of glycaemic and lipid profiles. A patient treated with antipsychotic drugs was considered adherent to this recommendation whether he/she every year was submitted to at least 2 glycated haemoglobin assays and at least one lipid profile assessment (i.e., total and HDL cholesterol and triglycerides). The proportion of patients treated with antipsychotics who were adherent with this recommendation during the year following the index antipsychotic prescription was calculated.

Table 3.1.1.11 Estimates of the proportion of schizophrenic patients who were adherent with the recommendations to keep monitored the side effects of the antipsychotic drug therapy, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with antipsychotics	9,228	4,647	16,398	30,047	60,320
Patients who received a set of 2 glycated haemoglobins and 1 lipid profile assessment	**1,691**	**1,253**	**4,915**	**8,493**	**16,352**
%	18.3	27.0	30.0	28.3	27.1
Cohort B					
Patients who started a treatment with antipsychotics	921	649	2,032	1,676	5,278
Patients who received a set of 2 glycated haemoglobins and 1 lipid profile assessment	**104**	**100**	**353**	**257**	**814**
%	11.3	15.4	17.4	15.3	15.4
Cohort C					
Patients who started a treatment with antipsychotics	99	82	266	344	791
Patients who received a set of 2 glycated haemoglobins and 1 lipid profile assessment	**8**	**3**	**34**	**35**	**80**
%	8.1	3.7	12.8	10.2	10.1
Cohort D					
Patients who were in treatment with antipsychotics	1,013	1,076	2,704	5,453	10,246
Patients who received a set of 2 glycated haemoglobins and 1 lipid profile assessment	**133**	**221**	**502**	**977**	**1,833**
%	13.1	20.5	18.6	17.9	17.9

3.1.1.12 Intensity of interventions for patients' families

This process indicator assesses the intensity of outpatient visits and interventions delivered to the patients affected by schizophrenic spectrum disorder and their families. The proportion of cohort patients whose families received at least one intervention delivered by territorial and day-care facilities of regional DMHs was calculated.

Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychological interventions delivered by DMHs professionals to patients and their families was calculated.

Among all the interventions delivered by territorial and day-care facilities of the regional DMHs, those aimed at the families of the schizophrenic patients were: (i) meeting with family members; (ii) family psychotherapy sessions, (iii) family groups and (iv) psychoeducational interventions aimed at the family.

Table 3.1.1.12 Estimates of the intensity of psychological interventions delivered by DMHs professionals to patients affected by schizophrenic spectrum disorder and their families, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least one territorial intervention aimed at their families	3,228	3,706	7,115	13,161	27,210
%	27.0	56.2	38.7	34.7	36.3
No. of interventions aimed at patients' families / PY	**0.9**	**2.8**	**2.0**	**1.4**	**1.6**
Cohort B					
Patients with at least one territorial intervention aimed at their families	466	623	986	952	3,027
%	24.5	54.0	39.7	39.3	38.0
No. of interventions aimed at patients' families / PY	**0.8**	**2.9**	**1.9**	**1.9**	**1.8**
Cohort C					
Patients with at least one territorial intervention aimed at their families	74	76	177	267	594
%	44.8	59.8	59.0	60.1	57.3
No. of interventions aimed at patients' families / PY	**1.8**	**4.6**	**4.1**	**3.9**	**3.7**
Cohort D					
Patients with at least one territorial intervention aimed at their families	509	798	1,578	3,461	6,346
%	46.0	64.7	52.7	52.4	53.1
No. of interventions aimed at patients' families / PY	**2.0**	**4.0**	**2.9**	**2.8**	**2.9**

3.1.1.13 Intensity of psychoeducational interventions

This process indicator assesses the intensity of psychoeducational sessions or meetings delivered by territorial and day-care facilities to the patients affected by schizophrenic spectrum disorder during the follow-up period. The proportion of cohort patients who experienced at least one psychoeducational intervention by the DMHs' professionals in the year following the index visit was calculated. Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychoeducational sessions delivered by DMHs professionals to patients and their families was calculated.

Table 3.1.1.13 Estimates of the intensity of psychoeducational interventions delivered by territorial and day-care facilities to schizophrenic patients, in the year following the index visit, by cohort and Region.

	Lazio [A]	Palermo	Emilia-Romagna	Lombardy	All regions together [B]
Cohort A					
Cohort's size	11,939	6,600	18,393	37,968	62,961
Patients who received at least 1 psychoeducational intervention	NA	446	1,101	1,156	2,703
%	-	6.8	6.0	3.0	4.3
No. of psychoeducational interventions / PY	**-**	**2.5**	**6.2**	**4.6**	**4.9**
Cohort B					
Cohort's size	1,904	1,154	2,486	2,425	6,065
Patients who received at least 1 psychoeducational intervention	NA	106	193	103	402
%	-	9.2	7.8	4.2	6.6
No. of psychoeducational interventions / PY	**-**	**3.3**	**5.3**	**5.1**	**4.7**
Cohort C					
Cohort's size	165	127	300	444	871
Patients who received at least 1 psychoeducational intervention	NA	10	66	56	132
%	-	7.9	22.0	12.6	15.2
No. of psychoeducational interventions / PY	**-**	**4.4**	**4.9**	**6.2**	**5.4**
Cohort D					
Cohort's size	1,107	1,234	2,992	6,611	10,837
Patients who received at least 1 psychoeducational intervention	NA	134	289	268	691
%	-	10.9	9.7	4.1	6.4
No. of psychoeducational interventions / PY	**-**	**3.3**	**4.5**	**4.8**	**4.4**

Note

A. This indicator wasn't calculated in the Lazio Region since the information regarding the psychoeducational intervention delivered by territorial and day-care facilities was missing.

B. The size of Lazio Region's cohort was excluded from the calculation of the whole sample size

3.1.1.14 Intensity of psychotherapeutic interventions

This indicator measures the intensity of psychotherapy sessions and meetings delivered to patients with schizophrenic spectrum disorder. The proportion of patients who received at least one psychotherapeutic intervention by the territorial and day-care facilities' professionals in the year following the index visit was calculated.

For each person-year (PY) accumulated by the cohort patients, the average number of psychotherapy sessions delivered to patients and/or their families was calculated. Psychotherapeutic interventions delivered to patients, but also to their families were considered.

Table 3.1.1.14 Estimates of the intensity of psychotherapeutic interventions delivered by DMHs professionals to patients affected by schizophrenic spectrum disorder and their families, in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who received at least 1 psychotherapy session	1,587	621	834	3,065	6,107
	%	13.3	9.4	4.5	8.1	8.2
	No. of psychotherapeutic interventions / PY	**9.6**	**6.0**	**8.0**	**8.1**	**8.3**
Cohort B						
	Patients who received at least 1 psychotherapy session	242	149	200	402	993
	%	12.7	12.9	8.0	16.6	12.5
	No. of psychotherapeutic interventions / PY	**7.7**	**5.0**	**7.8**	**8.2**	**7.5**
Cohort C						
	Patients who received at least 1 psychotherapy session	48	32	77	154	311
	%	29.1	25.2	25.7	34.7	30.0
	No. of psychotherapeutic interventions / PY	**13.1**	**6.4**	**10.0**	**9.2**	**9.7**
Cohort D						
	Patients who received at least 1 psychotherapy session	218	147	230	714	1,309
	%	19.7	11.9	7.7	10.8	11.0
	No. of psychotherapeutic interventions / PY	**9.7**	**4.0**	**6.9**	**8.1**	**7.7**

In the recruitment period, a cohort of around 75,000 prevalent patients affected by a schizophrenic spectrum disorder was identified, with an age-standardized prevalence rate of 35.1 prevalent cases per 10,000 adult persons. Instead, with regard to the incident cohort, were enrolled almost 8,000 patients with an incident schizophrenic disorder, exhibiting an age-standardized incident rate of 2.9 cases per 10,000 person-years.

Regarding the intensity of MHS assistance, on average, the number of outpatients visits delivered by the territorial and day-care facilities of the regional DMHs varies from a minimum of 19 (cohort B) to a maximum of 37 (cohort D) outpatients interventions every person-years of observation; while the average number of psychiatric visits ranged from 7 (cohort B) to 12 (cohort D) interventions per person-year.

The patients of the cohort A and D were more persistent with the outpatient assistance delivered by the territorial MHS, with a percentage of patients persistent with MHS assistance near to 73%. Whereas, around the 55% of patients with an incident schizophrenic disorder experienced a discontinuation episode of the MHS territorial assistance. Furthermore, the percentages of patients discontinuing the outpatient assistance delivered by the territorial MHS were very heterogeneous among the regions.

For what concerns the cohort of patients discharged from an admission to GHPWs, they received the first outpatient visit after the index discharge with a discrete timeliness.

Home visits were more frequently delivered to patients belonging to cohorts A; also cohort D members received an adequate home assistance by the DMHs' professionals.

Regarding the intensity of the use of the residential facilities, patients with an incident disorder (both cohort B and C) experienced a greater number of admissions to residential facilities, however showing a shorter time of recovery (i.e., on average prevalent patients spent a greater number of days in residential facilities).

Particular is the situation of the district of Palermo, where the proportion of patients admitted to residential facilities was smaller than that of the other regions, while those patients experienced longer recovery stays in residential facilities.

Overall, in all the cohorts of patients with schizophrenic disorder the number who were in, or started a, treatment with antipsychotics was adequate; however, a higher number of patients experienced an episode of discontinuation of this recommended drug therapy.

Around 3 out of 10 patients belonging to the cohort A were adherent with the recommendations to keep monitored the side effects of the antipsychotic drug therapy, whereas patients with an incident disorder (cohorts B and c) were less adherent with the clinical monitoring of the treatment with antipsychotics.

On average, the patients with an incident schizophrenic spectrum disorder at the onset (cohort C) received a greater number of psychological interventions aimed at their families, symptom of greater attention in taking in charge of such patients. Also with regard to psychoeducational and psychotherapeutic sessions, the cohort C's patients received a more intense territorial MHS assistance. This was observed also for patients discharged from a GHPW admission.

3.1.2 Bipolar disorder

Cohorts' size

For each previously described cohort, the number of patients identified by the algorithms previously described and enrolled in the cohort is reported in the following table.

Table 3.1.2 Number of patients with bipolar disorder who met the inclusion and exclusion criteria in three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and in the whole Italian sample. Italy, QUADIM Project, 2015-2016

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Recruitment period	2015	2015-2016	2015-2016	2015-2016	2015-2016
Size of the resident adult population at 01/01/2016	4,922,315	1,043,939	3,735,638	8,323,030	18,024,922
PREVALENT COHORT (A)					
Cohort's size	**5,748**	**2,039**	**11,104**	**14,636**	**33,527**
Raw prevalence rate (x10'000)	11.7	19.5	29.7	17.6	18.6
Age-standardized prevalence rate (x10'000)	**8.7**	**14.9**	**21.8**	**13.1**	**14.6**
Mean age (SD)	53.0 (14.2)	52.9 (14.3)	55.6 (14.7)	53.2 (14.6)	53.7 (14.4)
INCIDENT COHORT (B)					
Cohort's size	**1,082**	**432**	**1,376**	**1,210**	**4,100**
Raw incidence rate (x10'000)	1.1	2.1	1.8	0.7	2.3
Age-standardized incidence rate (x10'000 PY)	**1.7**	**1.6**	**1.5**	**0.6**	**1.4**
Mean age (SD)	47.4 (11.7)	46.7 (12.3)	46.2 (11.8)	43.1 (12.9)	45.8 (12.2)
INCIDENT COHORT AT THE ONSET (C)					
Cohort's size	**68**	**29**	**85**	**152**	**334**
Mean age (SD)	21.9 (2.2)	22.5 (2.0)	22.3 (1.9)	21.7 (2.3)	22.1 (2.1)
GHPW DISCHARGED COHORT (D)					
Cohort's size	**656**	**460**	**1,741**	**2,691**	**5,548**
Mean age (SD)	47.5 (13.6)	48.9 (13.7)	50.1 (14.0)	49.3 (14.3)	49.0 (13.9)

3.1.2.1 Intensity of outpatient visits

This process indicator assesses the intensity of outpatient visits delivered to patients during the follow-up period. For each person-year (PY) accumulated by the cohort patients, the average number of outpatient visits delivered by territorial and day-care facilities of the regional DMHs was calculated.

Table 3.1.2.1.A Estimates of the intensity of outpatient visits delivered to patients affected by bipolar disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	5,149	1,515	10,448	13,204	30,316
%	89.6	74.3	94.1	90.2	90.4
No. of outpatient visits / PY	**15.3**	**9.4**	**24.3**	**14.7**	**17.6**
Cohort B					
Patients with at least 1 outpatient visit	894	307	1,221	1,036	3,458
%	82.6	71.1	88.7	85.6	84.3
No. of outpatient visits / PY	**10.6**	**9.2**	**16.4**	**12.1**	**12.9**
Cohort C					
Patients with at least 1 outpatient visit	57	17	78	133	285
%	83.8	58.6	91.8	87.5	85.3
No. of outpatient visits / PY	**15.9**	**13.1**	**24.5**	**17.7**	**18.7**
Cohort D					
Patients with at least 1 outpatient visit	592	358	1,595	2,484	5,029
%	90.2	77.8	91.6	92.3	90.6
No. of outpatient visits / PY	**26.0**	**14.4**	**35.2**	**28.4**	**29.1**

A modified version of this process indicator has been calculated, in order to assess the intensity of psychiatric outpatient visits delivered during the follow-up period. For each person-year (PY) accumulated by cohort patients, the average number of psychiatric visits delivered by territorial and day-care facilities of the regional DMHs was calculated

Table 3.1.2.1.B Estimates of the intensity of psychiatric visits delivered to patients affected by bipolar disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 psychiatric visit	4,804	1,458	9,081	12,763	28,106
%	83.6	71.5	81.8	87.2	83.8
No. of psychiatric visits / PY	**7.8**	**5.0**	**5.1**	**8.0**	**6.8**
Cohort B					
Patients with at least 1 psychiatric visit	819	297	1,105	1,016	3,237
%	75.7	68.8	80.3	84.0	79.0
No. of psychiatric visits / PY	**6.1**	**4.9**	**4.7**	**7.7**	**6.0**
Cohort C					
Patients with at least 1 psychiatric visit	52	17	75	131	275
%	76.5	58.6	88.2	86.2	82.3
No. of psychiatric visits / PY	**10.4**	**6.2**	**8.2**	**10.5**	**9.5**
Cohort D					
Patients with at least 1 psychiatric visit	558	343	1,448	2,413	4,762
%	85.1	74.6	83.2	89.7	85.8
No. of psychiatric visits / PY	**11.1**	**6.8**	**6.4**	**13.8**	**10.6**

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.2.2 Persistence with outpatient MHS assistance

This indicator assesses the persistence with the outpatient assistance delivered by the territorial mental healthcare services (MHS), i.e., territorial and day-care facilities, during the follow-up period. The proportion of cohort patients who experienced the discontinuation of attending territorial MHS in the first 12 months of follow-up was calculated. Attendance of territorial MHS was considered regular if the time-span between two consecutive outpatient visits was 90 days or shorter, or discontinuing otherwise.

Table 3.1.2.2 Estimates of the proportion of patients affected by bipolar disorder who experienced an episode of discontinuation of attending territorial MHS in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	5,149	1,515	10,448	13,204	30,316
%	89.6	74.3	94.1	90.2	90.4
No. of patients discontinuing MHS attendance	**1,928**	**956**	**4,415**	**4,422**	**11,721**
%	37.4	63.1	42.3	33.5	38.7
Cohort B					
Patients with at least 1 outpatient visit	894	307	1,221	1,036	3,458
%	82.6	71.1	88.7	85.6	84.3
No. of patients discontinuing MHS attendance	**497**	**280**	**763**	**458**	**1,998**
%	55.6	91.2	62.5	44.2	57.8
Cohort C					
Patients with at least 1 outpatient visit	57	17	78	133	285
%	83.8	58.6	91.8	87.5	85.3
No. of patients discontinuing MHS attendance	**31**	**15**	**57**	**68**	**171**
%	54.4	88.2	73.1	51.1	60.0
Cohort D					
Patients with at least 1 outpatient visit	592	358	1,595	2,484	5,029
%	90.2	77.8	91.6	92.3	90.6
No. of patients discontinuing MHS attendance	**150**	**258**	**955**	**664**	**2,027**
%	25.3	72.1	59.9	26.7	40.3

3.1.2.3 Timeliness of the first outpatient visit after discharge from GHPW

This process indicator assesses the timeliness of the first outpatient visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first outpatient visit (i.e., delivered by territorial and day-care facilities of the regional DMHs) within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.2.3 Estimates of the proportion of patients affected by bipolar disorder who received the first outpatient visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	656	460	1,741	2,691	5,548
Patients with at least 1 outpatient visit	592	358	1,595	2,484	5,029
%	90.2	77.8	91.6	92.3	90.6
Patients with the first outpatient visit within the first 14 days after the discharge	353	212	911	1,583	3,059
%	53.8	46.1	52.3	58.8	55.1

3.1.2.4 Timeliness of the first psychiatric visit after discharge from GHPW

This indicator assesses the timeliness of the first outpatient psychiatric visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first psychiatric visit, delivered by territorial and day-care facilities of the regional DMHs, within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.2.4 Estimates of the proportion of patients affected by bipolar disorder who received the first psychiatric visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	656	460	1,741	2,691	5,548
Patients with at least 1 psychiatric visit	558	343	1,448	2,413	4,762
%	85.1	74.6	83.2	89.7	85.8
Patients with the first psychiatric visit within the first 14 days after the discharge	236	167	451	1,097	1,951
%	36.0	36.3	25.9	40.8	35.2

3.1.2.5 Patients receiving home assistance
(after the cohort entry)

This process indicator evaluates the timeliness of the first home visit delivered after the cohort entry to the patients affected by the bipolar disorder. The proportion of patients who experienced at least one home visit by the DMHs' professionals in the year following the index visit was calculated.

Table 3.1.2.5 Estimates of the proportion of patients affected by bipolar disorder to whom at least one home visit was delivered by the DMHs' professionals in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort A					
Cohort's size	5,748	2,039	11,104	14,636	22,423
Patients who received at least 1 home visit	631	134	NA	1,474	2,239
%	11.0	6.6	-	10.1	10.0
Cohort B					
Cohort's size	1,082	432	1,376	1,210	2,724
Patients who received at least 1 home visit	79	26	NA	56	161
%	7.3	6.0	-	4.6	5.9
Cohort C					
Cohort's size	68	29	85	152	249
Patients who received at least 1 home visit	5	1	NA	9	15
%	7.4	3.4	-	5.9	6.0

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.
B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

3.1.2.6 Timeliness of home assistance after discharge from GHPW

This process indicator assesses the timeliness of the first home visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who experienced at least one home visit by the DMHs' professionals after the index discharge from GHPW was calculated.

Table 3.1.2.6 Estimates of the proportion of patients affected by bipolar disorder to whom at least one home visit was delivered by the professionals of regional DMHs within the 365 days following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort D					
Cohort's size	656	460	1,741	2,691	3,807
Patients who received at least 1 home visit	128	43	NA	574	745
%	19.5	9.3	-	21.3	19.6

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.
B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.2.7 Intensity of recovery to residential facilities

This process indicator measures the intensity of the use of the residential facilities. The proportion of cohort patients experiencing at least one admission to residential facilities during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to residential facilities, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in regional residential facilities was calculated.

Table 3.1.2.7 Estimates of the (i) proportion of patients affected by bipolar disorder who experienced at least one admission to residential facilities in the year following the index visit; and of the (ii) average number of days spent in residential facilities by those patients, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 admission to residential facilities	703	18	1,551	2,212	4,484
%	12.2	0.9	14.0	15.1	13.4
No. of days of recovery in residential facilities / PY	**102.8**	**235.8**	**92.9**	**92.2**	**94.7**
Cohort B					
Patients with at least 1 admission to residential facilities	134	4	322	235	695
%	12.4	0.9	23.4	19.4	17.0
No. of days of recovery in residential facilities / PY	**73.7**	**222.2**	**55.2**	**7.7**	**22.6**
Cohort C					
Patients with at least 1 admission to residential facilities	14	0	28	45	87
%	20.6	0.0	32.9	29.6	26.0
No. of days of recovery in residential facilities / PY	**81.9**	**0.0**	**22.7**	**15.6**	**21.1**

3.1.2.8 Intensity of recovery to hospital facilities (in GHPW)

This process indicator measures the intensity of the utilization of the hospital facilities. The proportion of cohort patients experiencing at least one admission to GHPWs during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to GHPWs, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in hospital facilities was calculated.

Table 3.1.2.8 Estimates of the (i) proportion of patients affected by bipolar disorder who experienced at least one hospital admission in a psychiatric ward in the year following the index visit; and of the (ii) average number of days spent in hospital facilities by those patients, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 hospital admission to hospital facilities	812	424	1,381	1,944	4,561
%	14.1	20.8	12.4	13.3	13.6
No. of days of recovery in hospital facilities / PY	**37.2**	**17.8**	**16.3**	**25.4**	**24.0**
Cohort B					
Patients with at least 1 hospital admission to hospital facilities	151	132	387	235	905
%	14.0	30.6	28.1	19.4	22.1
No. of days of recovery in hospital facilities / PY	**17.2**	**13.5**	**11.8**	**17.6**	**14.4**
Cohort C					
Patients with at least 1 hospital admission to hospital facilities	16	14	31	44	105
%	23.5	48.3	36.5	28.9	31.4
No. of days of recovery in hospital facilities / PY	**75.5**	**24.0**	**20.1**	**34.2**	**34.7**

3.1.2.9 Drug treatment with mood stabilizers

This process indicator measures the proportion of patients affected by a bipolar disorder that were in, or started, a mood stabilizers drug treatment during the follow-up period. For the cohorts A and D, the proportion of patients in treatment with mood stabilizers was calculated. For the cohort B and C the proportion of patients who started a pharmacological treatment with mood stabilizers during the follow-up period was calculated.

Table 3.1.2.9 Estimates of the proportion of patients with a bipolar disorder who were in treatment with (cohorts A and D), or started a treatment with (cohorts B and C), mood stabilizer drugs in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with mood stabilizers	3,541	1,374	8,014	10,642	23,571
	%	61.6	67.4	72.2	72.7	70.3
Cohort B						
	Patients who started a treatment with mood stabilizers	358	211	954	752	2,275
	%	33.1	48.8	69.3	62.1	55.5
Cohort C						
	Patients who started a treatment with mood stabilizers	34	13	61	102	210
	%	50.0	44.8	71.8	67.1	62.9
Cohort D						
	Patients who were in treatment with mood stabilizers	543	376	1,429	2,179	4,527
	%	82.8	81.7	82.1	81.0	81.6

3.1.2.10 Persistence with mood stabilizers treatment

This indicator assesses the persistence with the mood stabilizer drug treatment of the patients affected by a bipolar disorder that were in, or started, a treatment with mood stabilizers during the follow-up period. The proportion of cohort patients who were not persistent with the pharmacological treatment with mood stabilizers in the first 12 months of treatment was calculated. Starting from the index prescription of mood stabilizers, consecutively refilled prescriptions were considered uninterrupted if the time-span between the end of one prescription and the beginning of the following one (or of censoring) was 30 days or shorter, since gaps less than 30 days being considered permissible. Conversely, if the between-prescription time-span was longer than 30 days, treatment discontinuation was assumed.

Table 3.1.2.10 Estimates of the proportion of patients affected by bipolar disorder who discontinued the therapy with mood stabilizers in the year following the index prescription, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with mood stabilizers	3,541	1,374	8,014	10,642	23,571
%	61.6	67.4	72.2	72.7	70.3
Patients who discontinued therapy with mood stabilizers	**2,207**	**565**	**3,603**	**7,441**	**13,816**
%	62.3	41.1	45.0	69.9	58.6
Cohort B					
Patients who started a treatment with mood stabilizers	358	211	954	752	2,275
%	33.1	48.8	69.3	62.1	55.5
Patients who discontinued therapy with mood stabilizers	**251**	**118**	**539**	**551**	**1,459**
%	70.1	55.9	56.5	73.3	64.1
Cohort C					
Patients who started a treatment with mood stabilizers	34	13	61	102	210
%	50.0	44.8	71.8	67.1	62.9
Patients who discontinued therapy with mood stabilizers	**27**	**6**	**37**	**80**	**150**
%	79.4	46.2	60.7	78.4	71.4
Cohort D					
Patients who were in treatment with mood stabilizers	543	376	1,429	2,179	4,527
%	82.8	81.7	82.1	81.0	81.6
Patients who discontinued therapy with mood stabilizers	**384**	**187**	**749**	**1,718**	**3,038**
%	70.7	49.7	52.4	78.8	67.1

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.2.11 Assessment of clinical monitoring in patients treated with Mood stabilizers

The side effects of a drug treatment must be monitored. This process indicator assesses the level of clinical monitoring of the safety of the drug therapy with mood stabilizer agents.

Different drug classes are usually prescribed to patients affected by bipolar disorder and the main drug classes included in the ensemble of mood stabilizer agents are: Antipsychotics, Lithium, Valproate, Carbamazepine and Lamotrigine. For each of these classes, the clinical controls needed to monitor the side effects of the pharmacological treatment are different.

The clinical monitoring of the antipsychotic treatment consists in the clinical evaluations of glycaemic and lipid profiles. A patient treated with **Antipsychotic agents (Table 3.1.2.11.A)** was considered adherent to this recommendation whether he/she every year was submitted to at least 1 glycated haemoglobin assay and at least one lipid profile assessment (i.e., total and HDL cholesterol and triglycerides). The proportion of bipolar patients treated with antipsychotics who were adherent with this recommendation during the year following the index antipsychotic prescription was calculated.

Table 3.1.2.11.A Estimates of the proportion of bipolar patients who were adherent with the recommendations to keep monitored the side effects of the antipsychotic drug therapy, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with antipsychotics	2,569	899	5,400	6,555	15,423
Patients who were adherent with the recommendation	**565**	**260**	**1,669**	**1,806**	**4,300**
%	22.0	28.9	30.9	27.6	27.9
Cohort B					
Patients who started a treatment with antipsychotics	254	129	617	481	1,481
Patients who were adherent with the recommendation	**37**	**22**	**124**	**74**	**257**
%	14.6	17.1	20.1	15.4	17.4
Cohort C					
Patients who started a treatment with antipsychotics	19	8	42	67	136
Patients who were adherent with the recommendation	**0**	**0**	**2**	**3**	**5**
%	0.0	0.0	4.8	4.5	3.7
Cohort D					
Patients who were in treatment with antipsychotics	399	267	1,016	1,579	3,261
Patients who were adherent with the recommendation	**62**	**60**	**209**	**301**	**632**
%	15.5	22.5	20.6	19.1	19.4

The clinical monitoring of the treatment with lithium consists in the clinical evaluations of lithaemia and of electrolytes. A patient treated with **Lithium (Table 3.1.2.11.B)** was considered adherent to this recommendation whether he/she every year was submitted to at least 1 lithaemia evaluation and 1 electrolytes exam. The proportion of bipolar patients treated with lithium who were adherent with this recommendation during the year following the index lithium prescription was calculated.

Table 3.1.2.11.B Estimates of the proportion of bipolar patients who were adherent with the recommendations to keep monitored the side effects of the lithium drug therapy, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with Lithium	812	290	2,256	3,790	7,148
Patients who were adherent with the recommendation	**402**	**173**	**1,599**	**2,908**	**5,082**
%	49.5	59.7	70.9	76.7	71.1
Cohort B					
Patients who started a treatment with Lithium	63	27	249	256	595
Patients who were adherent with the recommendation	**29**	**11**	**162**	**194**	**396**
%	46.0	40.7	65.1	75.8	66.6
Cohort C					
Patients who started a treatment with Lithium	7	2	24	42	75
Patients who were adherent with the recommendation	**2**	**1**	**15**	**32**	**50**
%	28.6	50.0	62.5	76.2	66.7
Cohort D					
Patients who were in treatment with Lithium	185	112	501	847	1,645
Patients who were adherent with the recommendation	**83**	**67**	**331**	**623**	**1,104**
%	44.9	59.8	66.1	73.6	67.1

The clinical monitoring of the treatment with valproate/carbamazepine consists in the clinical evaluations of liver function and haemachrome. A patient treated with **Valproate/Carbamazepine (Table 3.1.2.11.C)** was considered adherent to this recommendation whether he/she every year was submitted to at least 1 liver function evaluation and 1 haemachrome exam. The proportion of bipolar patients treated with valproate/carbamazepine who were adherent with this recommendation during the year following the index valproate/carbamazepine prescription was calculated.

Table 3.1.2.11.C Estimates of the proportion of bipolar patients who were adherent with the recommendations to keep monitored the side effects of the valproate/carbamazepine drug therapy, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with Valproate/Carbamazepine	2,051	838	3,541	4,645	11,075
	Patients who were adherent with the recommendation	**861**	**372**	**1,904**	**2,621**	**5,758**
	%	42.0	44.4	53.8	56.4	52.0
Cohort B						
	Patients who started a treatment with Valproate/Carbamazepine	222	146	469	325	1,162
	Patients who were adherent with the recommendation	**68**	**56**	**215**	**159**	**498**
	%	30.6	38.4	45.8	48.9	42.9
Cohort C						
	Patients who started a treatment with Valproate/Carbamazepine	22	8	33	38	101
	Patients who were adherent with the recommendation	**2**	**4**	**11**	**18**	**35**
	%	9.1	50.0	33.3	47.4	34.7
Cohort D						
	Patients who were in treatment with Valproate/Carbamazepine	369	255	798	1,030	2,452
	Patients who were adherent with the recommendation	**132**	**115**	**369**	**531**	**1,147**
	%	35.8	45.1	46.2	51.6	46.8

The clinical monitoring of the treatment with lamotrigine consists in the clinical evaluations of liver function, haemachrome and electrolytes. A patient treated with **Lamotrigine (Table 3.1.2.11.D)** was considered adherent to this recommendation whether he/she every year was submitted to at least 1 evaluation of liver function, haemachrome and electrolytes. The proportion of bipolar patients treated with lamotrigine who were adherent with this recommendation during the year following the index lamotrigine prescription was calculated.

Table 3.1.2.11.D Estimates of the proportion of bipolar patients who were adherent with the recommendations to keep monitored the side effects of the lamotrigine drug therapy, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with Lamotrigine	220	210	798	953	2,181
Patients who were adherent with the recommendation	**88**	**83**	**373**	**447**	**991**
%	40.0	39.5	46.7	46.9	45.4
Cohort B					
Patients who started a treatment with Lamotrigine	16	23	82	74	195
Patients who were adherent with the recommendation	**2**	**3**	**30**	**24**	**59**
%	12.5	13.0	36.6	32.4	30.3
Cohort C					
Patients who started a treatment with Lamotrigine	1	1	4	11	17
Patients who were adherent with the recommendation	**0**	**0**	**0**	**2**	**2**
%	0.0	0.0	0.0	18.2	11.8
Cohort D					
Patients who were in treatment with Lamotrigine	28	66	130	221	445
Patients who were adherent with the recommendation	**11**	**23**	**54**	**95**	**183**
%	39.3	34.8	41.5	43.0	41.1

3.1.2.12 Intensity of interventions for patients' families

This process indicator assesses the intensity of outpatient visits and interventions delivered to the patients affected by bipolar disorder and their families. The proportion of cohort patients whose families received at least one intervention delivered by territorial and day-care facilities of regional DMHs was calculated.

Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychological interventions delivered by DMHs professionals to patients and their families was calculated.

Among all the interventions delivered by territorial and day-care facilities of the regional DMHs, those aimed at the families of the bipolar patients were: (i) meeting with family members; (ii) family psychotherapy sessions, (iii) family groups and (iv) psychoeducational interventions aimed at the family.

Table 3.1.2.12 Estimates of the intensity of psychological interventions delivered by DMHs professionals to patients affected by bipolar disorder and their families, in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients with at least one territorial intervention aimed at their families	1,216	949	3,489	4,177	9,831
	%	21.2	46.5	31.4	28.5	29.3
	No. of interventions aimed at patients' families / PY	**0.7**	**2.2**	**1.3**	**1.0**	**1.1**
Cohort B						
	Patients with at least one territorial intervention aimed at their families	191	181	377	328	1,077
	%	17.7	41.9	27.4	27.1	26.3
	No. of interventions aimed at patients' families / PY	**0.6**	**1.9**	**1.1**	**1.0**	**1.0**
Cohort C						
	Patients with at least one territorial intervention aimed at their families	28	13	36	65	142
	%	41.2	44.8	42.4	42.8	42.5
	No. of interventions aimed at patients' families / PY	**1.3**	**4.2**	**3.2**	**1.9**	**2.3**
Cohort D						
	Patients with at least one territorial intervention aimed at their families	210	262	804	1,327	2,603
	%	32.0	57.0	46.2	49.3	46.9
	No. of interventions aimed at patients' families / PY	**1.2**	**3.2**	**2.1**	**2.3**	**2.2**

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.2.13 Intensity of psychoeducational interventions

This process indicator assesses the intensity of psychoeducational sessions or meetings delivered by territorial and day-care facilities to the patients affected by bipolar disorder during the follow-up period. The proportion of cohort patients who experienced at least one psychoeducational intervention by the DMHs' professionals in the year following the index visit was calculated. Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychoeducational sessions delivered by DMHs professionals to patients and their families was calculated.

Table 3.1.2.13 Estimates of the intensity of psychoeducational interventions delivered by territorial and day-care facilities to bipolar patients, in the year following the index visit, by cohort and Region.

	Lazio [A]	Palermo	Emilia-Romagna	Lombardy	All regions together [B]
Cohort A					
Cohort's size	5,748	2,039	11,104	14,636	27,779
Patients who received at least 1 psychoeducational intervention	NA	145	388	325	858
%	-	7.1	3.5	2.2	3.1
No. of psychoeducational interventions / PY	**-**	**2.7**	**5.8**	**3.9**	**4.5**
Cohort B					
Cohort's size	1,082	432	1,376	1,210	3,018
Patients who received at least 1 psychoeducational intervention	NA	41	51	26	118
%	-	9.5	3.7	2.1	3.9
No. of psychoeducational interventions / PY	**-**	**3.6**	**3.9**	**4.2**	**3.9**
Cohort C					
Cohort's size	68	29	85	152	266
Patients who received at least 1 psychoeducational intervention	NA	5	7	11	23
%	-	17.2	8.2	7.2	8.6
No. of psychoeducational interventions / PY	**-**	**7.4**	**2.9**	**2.4**	**3.6**
Cohort D					
Cohort's size	656	460	1,741	2,691	4,892
Patients who received at least 1 psychoeducational intervention	NA	53	118	112	283
%	-	11.5	6.8	4.2	5.8
No. of psychoeducational interventions / PY	**-**	**3.5**	**4.1**	**4.8**	**4.2**

Note

A. This indicator wasn't calculated in the Lazio Region since the information regarding the psychoeducational intervention delivered by territorial and day-care facilities was missing.

B. The size of Lazio Region's cohort was excluded from the calculation of the whole sample size

3.1.2.14 Intensity of psychotherapeutic interventions

This indicator measures the intensity of psychotherapy sessions and meetings delivered to patients with bipolar disorder. The proportion of patients who received at least one psychotherapeutic intervention by the territorial and day-care facilities' professionals in the year following the index visit was calculated.

For each person-year (PY) accumulated by the cohort patients, the average number of psychotherapy sessions delivered to patients and/or their families was calculated. Psychotherapeutic interventions delivered to patients, but also to their families were considered.

Table 3.1.2.14 Estimates of the intensity of psychotherapeutic interventions delivered by DMHs professionals to patients affected by bipolar disorder and their families, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who received at least 1 psychotherapy session	909	220	604	1,780	3,513
%	15.8	10.8	5.4	12.2	10.5
No. of psychotherapeutic interventions / PY	**9.7**	**6.9**	**7.4**	**8.2**	**8.4**
Cohort B					
Patients who received at least 1 psychotherapy session	145	55	99	239	538
%	13.4	12.7	7.2	19.8	13.1
No. of psychotherapeutic interventions / PY	**8.4**	**5.8**	**5.8**	**7.5**	**7.2**
Cohort C					
Patients who received at least 1 psychotherapy session	20	5	20	65	110
%	29.4	17.2	23.5	42.8	32.9
No. of psychotherapeutic interventions / PY	**10.9**	**6.0**	**9.9**	**8.7**	**9.2**
Cohort D					
Patients who received at least 1 psychotherapy session	138	53	147	423	761
%	21.0	11.5	8.4	15.7	13.7
No. of psychotherapeutic interventions / PY	**10.2**	**5.3**	**6.1**	**8.9**	**8.3**

In the recruitment period, a cohort of around 34,000 prevalent patients affected by bipolar disorder was identified, with an age-standardized prevalence rate of almost 15 prevalent cases per 10,000 adult persons. Instead, with regard to the incident cohort, were enrolled about 4,000 patients with an incident bipolar disorder, exhibiting an age-standardized incident rate of 1.4 cases per 10,000 person-years.

Regarding the intensity of MHS assistance, the average number (for every person-years of observation) of outpatients visits delivered by the territorial and day-care facilities of the regional DMHs varies from a minimum of 13 (cohort B) to a maximum of 29 (cohort D); while the average number of psychiatric visits ranged from 6 (cohort B) to 11 (cohort D) interventions per person-year. Around 6 out of 10 patients belonging to the cohorts B and C experienced an episode of discontinuation with the outpatient assistance delivered by the territorial MHS, whereas only the 40% of patients with prevalent bipolar disorder interrupted their attending with MHS assistance. The percentages of patients discontinuing the outpatient assistance delivered by the territorial MHS were very heterogeneous among the regions, e.g., considering the cohort A, in Lombardy about one out of three patients experienced a discontinuation episode, whereas in the Palermo's district more than the 60% of patients interrupted the territorial outpatient assistance.

Regarding the intensity of the use of the residential facilities, a greater proportion of patients with an incident disorder at the onset (cohort B) were admitted to residential facilities, however showing a shorter time of recovery. Indeed, on average prevalent patients spent a greater number of days in residential facilities, i.e., 94 days of recovery spent in residential facilities for person-year.

Overall, in all the cohorts of patients with bipolar disorder the number who were in, or started a, treatment with mood stabilizers was adequate. For example, about the 50% of cohorts B and C patients started a treatment with mood stabilizers, but the 65% of these patients were not persistent with this drug therapy during the first year of treatment.

Only 3 out of 10 patients belonging to the cohort A were adherent with the clinical monitoring recommendations for the antipsychotic drug therapy, whereas in the cohort B patients this percentage was lower (17%). Instead, regarding the pharmacological treatment with lithium, the majority of patients were adherent with the recommendations to receive at least 1 lithaemia evaluation and 1 electrolytes exam every year (from a minimum of 66% in cohort B, to a maximum of 71% in the cohort A). Patients with an incident bipolar disorder at the onset (cohort C) received a greater number of psychological interventions aimed at their families and a greater number of psychotherapeutic interventions.

3.1.3 Major depressive disorder

Cohorts' size

For each previously described cohort, the number of patients identified by the algorithms previously described and enrolled in the cohort is reported in the following table.

Table 3.1.3 Number of patients with major depressive disorder who met the inclusion and exclusion criteria in three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and in the whole Italian sample. Italy, QUADIM Project, 2015-2016

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Recruitment period	2015	2015-2016	2015-2016	2015-2016	2015-2016
Size of the resident adult population at 01/01/2016	4,922,315	1,043,939	3,735,638	8,323,030	18,024,922
PREVALENT COHORT (A)					
Cohort's size	**17,259**	**9,106**	**26,402**	**47,327**	**100,094**
Raw prevalence rate (x10'000)	35.1	87.2	70.7	56.9	55.5
Age-standardized prevalence rate (x10'000)	**26.0**	**65.4**	**51.3**	**42.1**	**46.2**
Mean age (SD)	54.2 (14.7)	55.5 (14.1)	56.7 (15.5)	54.5 (15.3)	55.2 (14.9)
INCIDENT COHORT (B)					
Cohort's size	**7,789**	**3,963**	**7,657**	**11,313**	**30,722**
Raw incidence rate (x10'000)	15.8	19.0	10.2	6.8	17.0
Age-standardized incidence rate (x10'000 PY)	**11.9**	**14.4**	**7.9**	**5.3**	**9.9**
Mean age (SD)	52.6 (15.2)	54.1 (14.2)	52.5 (16.0)	50.4 (16.1)	52.4 (15.4)
INCIDENT COHORT AT THE ONSET (C)					
Cohort's size	**373**	**149**	**361**	**753**	**1,636**
Mean age (SD)	21.8 (2.1)	22.3 (2.2)	22.1 (2.0)	21.7 (2.2)	22.0 (2.1)
GHPW DISCHARGED COHORT (D)					
Cohort's size	**672**	**538**	**1,972**	**4,097**	**7,279**
Mean age (SD)	50.3 (14.0)	51.7 (13.6)	52.5 (14.9)	51.5 (14.4)	51.5 (14.2)

3.1.3.1 Intensity of outpatient visits

This process indicator assesses the intensity of outpatient visits delivered to patients during the follow-up period. For each person-year (PY) accumulated by the cohort patients, the average number of outpatient visits delivered by territorial and day-care facilities of the regional DMHs was calculated.

Table 3.1.3.1.A Estimates of the intensity of outpatient visits delivered to patients affected by major depressive disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	14,257	5,393	22,025	39,093	80,768
%	82.6	59.2	83.4	82.6	80.7
No. of outpatient visits / PY	**8.8**	**4.4**	**11.8**	**7.6**	**8.6**
Cohort B					
Patients with at least 1 outpatient visit	5,676	2,529	5,515	8,317	22,037
%	72.9	63.8	72.0	73.5	71.7
No. of outpatient visits / PY	**5.8**	**4.5**	**6.0**	**5.8**	**5.7**
Cohort C					
Patients with at least 1 outpatient visit	296	97	295	594	1,282
%	79.4	65.1	81.7	78.9	78.4
No. of outpatient visits / PY	**10.5**	**8.3**	**8.6**	**12.3**	**10.7**
Cohort D					
Patients with at least 1 outpatient visit	592	401	1,708	3,603	6,324
%	88.1	74.5	86.6	87.9	86.9
No. of outpatient visits / PY	**20.5**	**10.8**	**25.4**	**18.6**	**20.0**

A modified version of this process indicator has been calculated, in order to assess the intensity of psychiatric outpatient visits delivered during the follow-up period. For each person-year (PY) accumulated by cohort patients, the average number of psychiatric visits delivered by territorial and day-care facilities of the regional DMHs was calculated

Table 3.1.3.1.B Estimates of the intensity of psychiatric visits delivered to patients affected by major depressive disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 psychiatric visit	13,041	5,172	19,268	37,761	75,242
%	75.6	56.8	73.0	79.8	75.2
No. of psychiatric visits / PY	**5.6**	**2.7**	**3.7**	**5.1**	**4.6**
Cohort B					
Patients with at least 1 psychiatric visit	5,118	2,425	4,951	8,051	20,545
%	65.7	61.2	64.7	71.2	66.9
No. of psychiatric visits / PY	**4.0**	**2.8**	**2.8**	**4.6**	**3.7**
Cohort C					
Patients with at least 1 psychiatric visit	271	94	271	576	1,212
%	72.7	63.1	75.1	76.5	74.1
No. of psychiatric visits / PY	**7.9**	**5.1**	**4.1**	**8.2**	**7.0**
Cohort D					
Patients with at least 1 psychiatric visit	556	392	1,555	3,511	6,032
%	82.7	72.9	78.9	85.7	82.9
No. of psychiatric visits / PY	**9.4**	**5.7**	**5.5**	**10.3**	**8.6**

3.1.3.2 Persistence with outpatient MHS assistance

This indicator assesses the persistence with the outpatient assistance delivered by the territorial mental healthcare services (MHS), i.e., territorial and day-care facilities, during the follow-up period. The proportion of cohort patients who experienced the discontinuation of attending territorial MHS in the first 12 months of follow-up was calculated. Attendance of territorial MHS was considered regular if the time-span between two consecutive outpatient visits was 90 days or shorter, or discontinuing otherwise.

Table 3.1.3.2 Estimates of the proportion of patients affected by major depressive disorder who experienced an episode of discontinuation of attending territorial MHS in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients with at least 1 outpatient visit	14,257	5,393	22,025	39,093	80,768
	%	82.6	59.2	83.4	82.6	80.7
	No. of patients discontinuing MHS attendance	**8,248**	**4,309**	**13,502**	**15,257**	**41,316**
	%	**57.9**	**79.9**	**61.3**	**39.0**	**41.3**
Cohort B						
	Patients with at least 1 outpatient visit	5,676	2,529	5,515	8,317	22,037
	%	72.9	63.8	72.0	73.5	71.7
	No. of patients discontinuing MHS attendance	**4,087**	**2,434**	**5,182**	**4,208**	**15,911**
	%	**72.0**	**96.2**	**94.0**	**50.6**	**51.8**
Cohort C						
	Patients with at least 1 outpatient visit	296	97	295	594	1,282
	%	79.4	65.1	81.7	78.9	78.4
	No. of patients discontinuing MHS attendance	**211**	**96**	**283**	**296**	**886**
	%	**71.3**	**99.0**	**95.9**	**49.8**	**54.2**
Cohort D						
	Patients with at least 1 outpatient visit	592	401	1,708	3,603	6,324
	%	88.1	74.5	86.6	87.9	86.9
	No. of patients discontinuing MHS attendance	**194**	**263**	**1,059**	**1,205**	**2,821**
	%	**32.8**	**65.6**	**62.0**	**33.4**	**38.8**

3.1.3.3 Timeliness of the first outpatient visit after discharge from GHPW

This process indicator assesses the timeliness of the first outpatient visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first outpatient visit (i.e., delivered by territorial and day-care facilities of the regional DMHs) within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.3.3 Estimates of the proportion of patients affected by major depressive disorder who received the first outpatient visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	672	538	1,972	4,097	7,279
Patients with at least 1 outpatient visit	592	401	1,708	3,603	6,324
%	88.1	74.5	86.6	87.9	86.9
Patients with the first outpatient visit within the first 14 days after the discharge	351	214	852	2,112	3,516
%	**52.2**	**39.8**	**43.2**	**51.5**	**48.3**

3.1.3.4 Timeliness of the first psychiatric visit after discharge from GHPW

This indicator assesses the timeliness of the first outpatient psychiatric visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first psychiatric visit, delivered by territorial and day-care facilities of the regional DMHs, within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.3.4 Estimates of the proportion of patients affected by major depressive disorder who received the first psychiatric visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	672	538	1,972	4,097	7,279
Patients with at least 1 psychiatric visit	556	392	1,555	3,511	6,032
%	82.7	72.9	78.9	85.7	82.9
Patients with the first psychiatric visit within the first 14 days after the discharge	242	180	463	1,534	2,375
%	36.0	33.5	23.5	37.4	32.6

3.1.3.5 Patients receiving home assistance
(after the cohort entry)

This process indicator evaluates the timeliness of the first home visit delivered after the cohort entry to the patients affected by major depressive disorder. The proportion of patients who experienced at least one home visit by the DMHs' professionals in the year following the index visit was calculated.

Table 3.1.3.5 Estimates of the proportion of patients affected by major depressive disorder to whom at least one home visit was delivered by the DMHs' professionals in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort A					
Cohort's size	17,259	9,106	26,402	47,327	73,692
Patients who received at least 1 home visit	881	187	NA	1,803	2,871
%	5.1	2.1	-	3.8	3.9
Cohort B					
Cohort's size	7,789	3,963	7,657	11,313	23,065
Patients who received at least 1 home visit	209	52	NA	148	409
%	2.7	1.3	-	1.3	1.8
Cohort C					
Cohort's size	373	149	361	753	1,275
Patients who received at least 1 home visit	9	2	NA	17	28
%	2.4	1.3	-	2.3	2.2

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.

B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

3.1.3.6 Timeliness of home assistance after discharge from GHPW

This process indicator assesses the timeliness of the first home visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who experienced at least one home visit by the DMHs' professionals after the index discharge from GHPW was calculated.

Table 3.1.3.6 Estimates of the proportion of patients affected by major depressive disorder to whom at least one home visit was delivered by the professionals of regional DMHs within the 365 days following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort D					
Cohort's size	672	538	1,972	4,097	5,307
Patients who received at least 1 home visit	117	30	NA	492	645
%	17.4	5.6	-	12.0	12.2

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.
B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

3.1.3.7 Intensity of recovery to residential facilities

This process indicator measures the intensity of the use of the residential facilities. The proportion of cohort patients experiencing at least one admission to residential facilities during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to residential facilities, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in regional residential facilities was calculated.

Table 3.1.3.7 Estimates of the (i) proportion of patients affected by major depressive disorder who experienced at least one admission to residential facilities in the year following the index visit; and of the (ii) average number of days spent in residential facilities by those patients, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 admission to residential facilities	818	16	1,785	3,229	5,848
%	4.7	0.2	6.8	6.8	5.8
No. of days of recovery in residential facilities / PY	**83.2**	**252.4**	**65.5**	**60.9**	**65.9**
Cohort B					
Patients with at least 1 admission to residential facilities	215	5	482	737	1,439
%	2.8	0.1	6.3	6.5	4.7
No. of days of recovery in residential facilities / PY	**82.2**	**310.4**	**38.1**	**20.2**	**36.4**
Cohort C					
Patients with at least 1 admission to residential facilities	17	1	28	73	119
%	4.6	0.7	7.8	9.7	7.3
No. of days of recovery in residential facilities / PY	**139.1**	**103.1**	**21.4**	**25.8**	**41.7**

3.1.3.8 Intensity of recovery to hospital facilities (in GHPW)

This process indicator measures the intensity of the utilization of the hospital facilities. The proportion of cohort patients experiencing at least one admission to GHPWs during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to GHPWs, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in hospital facilities was calculated.

Table 3.1.3.8 Estimates of the (i) proportion of patients affected by major depressive disorder who experienced at least one hospital admission in a psychiatric ward in the year following the index visit; and of the (ii) average number of days spent in hospital facilities by those patients, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients with at least 1 hospital admission to hospital facilities	817	501	1,640	3,076	6,034
	%	4.7	5.5	6.2	6.5	6.0
	No. of days of recovery in hospital facilities / PY	**29.9**	**15.8**	**13.9**	**19.8**	**19.2**
Cohort B						
	Patients with at least 1 hospital admission to hospital facilities	230	227	556	770	1,783
	%	3.0	5.7	7.3	6.8	5.8
	No. of days of recovery in hospital facilities / PY	**22.7**	**11.4**	**9.5**	**12.8**	**12.9**
Cohort C						
	Patients with at least 1 hospital admission to hospital facilities	17	14	34	75	140
	%	4.6	9.4	9.4	10.0	8.6
	No. of days of recovery in hospital facilities / PY	**49.5**	**7.4**	**8.9**	**15.2**	**17.1**

3.1.3.9 Antidepressant drug treatment

This process indicator measures the proportion of patients affected by a major depressive disorder that were in, or started, an antidepressant drug treatment during the follow-up period. For the cohorts A and D, the proportion of patients in treatment with antidepressant drugs was calculated. For the cohort B and C the proportion of patients who started a pharmacological treatment with antidepressants during the follow-up period was calculated.

Table 3.1.3.9 Estimates of the proportion of patients with a major depressive disorder who were in treatment with (cohorts A and D), or started a treatment with (cohorts B and C), antidepressant drugs in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with antidepressants	7,425	4,648	20,373	31,896	64,342
%	43.0	51.0	77.2	67.4	64.3
Cohort B					
Patients who started a treatment with antidepressants	1,743	1,728	4,982	6,346	14,799
%	22.4	43.6	65.1	56.1	48.2
Cohort C					
Patients who started a treatment with antidepressants	62	51	178	354	645
%	16.6	34.2	49.3	47.0	39.4
Cohort D					
Patients who were in treatment with antidepressants	382	352	1,479	2,932	5,165
%	56.8	65.4	75.0	71.6	71.0

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.3.10 Persistence with Antidepressant drug treatment

This indicator assesses the persistence with the antidepressant drug treatment of the patients affected by a major depressive disorder that were in, or started, a treatment with antidepressants during the follow-up period. The proportion of cohort patients who were not persistent with the pharmacological treatment with antidepressants in the first 12 months of treatment was calculated. Starting from the index prescription of antidepressant agents, consecutively refilled prescriptions were considered uninterrupted if the time-span between the end of one prescription and the beginning of the following one (or of censoring) was 30 days or shorter, since gaps less than 30 days being considered permissible. Conversely, if the between-prescription time-span was longer than 30 days, treatment discontinuation was assumed.

Table 3.1.2.10 Estimates of the proportion of patients affected by major depressive disorder who discontinued antidepressant drug therapy in the year following the index prescription, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with antidepressants	7,425	4,648	20,373	31,896	64,342
	%	43.0	51.0	77.2	67.4	64.3
	Patients who discontinued therapy with antidepressants	**5,631**	**2,652**	**14,919**	**24,655**	**47,857**
	%	75.8	57.1	73.2	77.3	74.4
Cohort B						
	Patients who started a treatment with antidepressants	1,743	1,728	4,982	6,346	14,799
	%	22.4	43.6	65.1	56.1	48.2
	Patients who discontinued therapy with antidepressants	**1,362**	**1,207**	**3,855**	**5,190**	**11,614**
	%	78.1	69.8	77.4	81.8	78.5
Cohort C						
	Patients who started a treatment with antidepressants	62	51	178	354	645
	%	16.6	34.2	49.3	47.0	39.4
	Patients who discontinued therapy with antidepressants	**54**	**37**	**148**	**294**	**533**
	%	87.1	72.5	83.1	83.1	82.6
Cohort D						
	Patients who were in treatment with antidepressants	382	352	1,479	2,932	5,165
	%	56.8	65.4	75.0	71.6	71.0
	Patients who discontinued therapy with antidepressants	**301**	**199**	**1,118**	**2,409**	**4,054**
	%	78.8	56.5	75.6	82.2	78.5

3.1.3.11 Assessment of clinical monitoring in patients treated with Antidepressant agents

The side effects of a drug treatment must be monitored. This process indicator assesses the level of clinical monitoring of the safety of antidepressant drug therapy. This clinical monitoring of the antidepressant treatment consists in the clinical examination of electrolytes and in the administration of an electrocardiogram (ECG). A patient treated with antidepressant drugs was considered adherent to this recommendation whether he/she every year was submitted to at least 1 electrolytes exam and at least one ECG. The proportion of patients treated with antidepressant agents who were adherent with this recommendation during the year following the index antidepressant prescription was calculated.

Table 3.1.3.11 Estimates of the proportion of depressive patients who were adherent with the recommendations to keep monitored the side effects of antidepressant drug therapy, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who were in treatment with antidepressants	7,425	4,648	20,373	31,896	64,342
Patients who received a set of 1 electrolytes exam and 1 ECG	**1,323**	**977**	**3,575**	**6,950**	**12,825**
%	17.8	21.0	17.5	21.8	19.9
Cohort B					
Patients who started a treatment with antidepressants	1,743	1,728	4,982	6,346	14,799
Patients who received a set of 1 electrolytes exam and 1 ECG	**248**	**347**	**741**	**1,158**	**2,494**
%	14.2	20.1	14.9	18.2	16.9
Cohort C					
Patients who started a treatment with antidepressants	62	51	178	354	645
Patients who received a set of 1 electrolytes exam and 1 ECG	**5**	**2**	**14**	**44**	**65**
%	8.1	3.9	7.9	12.4	10.1
Cohort D					
Patients who were in treatment with antidepressants	382	372	1,479	2,932	5,165
Patients who received a set of 1 electrolytes exam and 1 ECG	**48**	**73**	**218**	**686**	**1,025**
%	12.6	19.6	14.7	23.4	19.8

3.1.3.12 Intensity of interventions for patients' families

This process indicator assesses the intensity of outpatient visits and interventions delivered to the patients affected by major depressive disorder and their families. The proportion of cohort patients whose families received at least one intervention delivered by territorial and day-care facilities of regional DMHs was calculated.

Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychological interventions delivered by DMHs professionals to patients and their families was calculated.

Among all the interventions delivered by territorial and day-care facilities of the regional DMHs, those aimed at the families of the depressive patients were: (i) meeting with family members; (ii) family psychotherapy sessions, (iii) family groups and (iv) psychoeducational interventions aimed at the family.

Table 3.1.3.12 Estimates of the intensity of psychological interventions delivered by DMHs professionals to patients affected by major depressive disorder and their families, in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients with at least one territorial intervention aimed at their families	2,441	2,582	4,615	8,042	17,680
	%	14.1	28.4	17.5	17.0	17.7
	No. of interventions aimed at patients' families / PY	**0.51**	**0.82**	**0.61**	**0.54**	**0.58**
Cohort B						
	Patients with at least one territorial intervention aimed at their families	787	1,198	910	1,610	4,505
	%	10.1	30.2	11.9	14.2	14.7
	No. of interventions aimed at patients' families / PY	**0.32**	**0.84**	**0.36**	**0.45**	**0.44**
Cohort C						
	Patients with at least one territorial intervention aimed at their families	88	56	70	217	431
	%	23.6	37.6	19.4	28.8	26.3
	No. of interventions aimed at patients' families / PY	**0.94**	**1.68**	**0.86**	**1.52**	**1.26**
Cohort D						
	Patients with at least one territorial intervention aimed at their families	208	291	703	1,564	2,766
	%	31.0	54.1	35.6	38.2	38.0
	No. of interventions aimed at patients' families / PY	**1.13**	**2.27**	**1.47**	**1.63**	**1.59**

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.3.13 Intensity of psychoeducational interventions

This process indicator assesses the intensity of psychoeducational sessions or meetings delivered by territorial and day-care facilities to the patients affected by major depressive disorder during the follow-up period. The proportion of cohort patients who experienced at least one psychoeducational intervention by the DMHs' professionals in the year following the index visit was calculated. Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychoeducational sessions delivered by DMHs professionals to patients and their families was calculated.

Table 3.1.3.13 Estimates of the intensity of psychoeducational interventions delivered by territorial and day-care facilities to depressive patients, in the year following the index visit, by cohort and Region.

	Lazio [A]	Palermo	Emilia-Romagna	Lombardy	All regions together [B]
Cohort A					
Cohort's size	17,259	9,106	26,402	47,327	82,835
Patients who received at least 1 psychoeducational intervention	NA	365	378	631	1,374
%	-	4.0	1.4	1.3	1.7
No. of psychoeducational interventions / PY	**-**	**2.2**	**5.1**	**4.0**	**3.8**
Cohort B					
Cohort's size	7,789	3,963	7,657	11,313	22,933
Patients who received at least 1 psychoeducational intervention	NA	195	49	134	378
%	-	4.9	0.6	1.2	1.6
No. of psychoeducational interventions / PY	**-**	**2.5**	**4.4**	**4.2**	**3.3**
Cohort C					
Cohort's size	373	149	361	753	1,263
Patients who received at least 1 psychoeducational intervention	NA	12	8	36	56
%	-	8.1	2.2	4.8	4.4
No. of psychoeducational interventions / PY	**-**	**2.2**	**2.1**	**10.1**	**7.3**
Cohort D					
Cohort's size	672	538	1,972	4,097	6,607
Patients who received at least 1 psychoeducational intervention	NA	38	81	127	246
%	-	7.1	4.1	3.1	3.7
No. of psychoeducational interventions / PY	**-**	**3.5**	**4.9**	**5.1**	**4.8**

Note

A. This indicator wasn't calculated in the Lazio Region since the information regarding the psychoeducational intervention delivered by territorial and day-care facilities was missing.

B. The size of Lazio Region's cohort was excluded from the calculation of the whole sample size

3.1.3.14 Intensity of psychotherapeutic interventions

This indicator measures the intensity of psychotherapy sessions and meetings delivered to patients with major depressive disorder. The proportion of patients who received at least one psychotherapeutic intervention by the territorial and day-care facilities' professionals in the year following the index visit was calculated.

For each person-year (PY) accumulated by the cohort patients, the average number of psychotherapy sessions delivered to patients and/or their families was calculated. Psychotherapeutic interventions delivered to patients, but also to their families were considered.

Table 3.1.3.14 Estimates of the intensity of psychotherapeutic interventions delivered by DMHs professionals to patients affected by major depressive disorder and their families, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who received at least 1 psychotherapy session	3,626	1,000	1,864	8,602	15,092
%	21.0	11.0	7.1	18.2	15.1
No. of psychotherapeutic interventions / PY	**9.4**	**6.0**	**6.3**	**7.4**	**7.7**
Cohort B					
Patients who received at least 1 psychotherapy session	1,543	514	681	2,600	5,338
%	19.8	13.0	8.9	23.0	17.4
No. of psychotherapeutic interventions / PY	**7.8**	**5.8**	**5.5**	**7.4**	**7.1**
Cohort C					
Patients who received at least 1 psychotherapy session	189	54	75	321	639
%	50.7	36.2	20.8	42.6	39.1
No. of psychotherapeutic interventions / PY	**11.0**	**7.9**	**6.7**	**10.0**	**9.8**
Cohort D					
Patients who received at least 1 psychotherapy session	139	77	171	765	1,152
%	20.7	14.3	8.7	18.7	15.8
No. of psychotherapeutic interventions / PY	**9.8**	**5.8**	**5.7**	**8.9**	**8.4**

3.1.3.15 Combined pharmacological and psychotherapeutic treatment

Patients affected by major depressive disorder should be treated with both pharmacological treatment with antidepressants and psychotherapeutic sessions. This indicator assesses the proportion of patients who received a combined treatment of both pharmacological antidepressant therapy and psychotherapeutic sessions.

Table 3.1.3.15 Estimates of the intensity of combined pharmacological and psychotherapeutic treatment delivered to depressive and their families, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients who received at least 1 psychotherapy session	3,626	1,000	1,864	8,602	15,092
Patients who were in treatment with antidepressants	7,425	4,648	20,373	31,896	64,342
Patients who received combined pharmacological/psychotherapeutic treatment	**1,401**	**572**	**1,226**	**5,268**	**8,467**
%	8.1	6.3	4.6	11.1	8.5
Cohort B					
Patients who received at least 1 psychotherapy session	1,543	514	681	2,600	5,338
Patients who started a treatment with antidepressants	1,743	1,728	4,982	6,346	14,799
Patients who received combined pharmacological/psychotherapeutic treatment	**370**	**253**	**349**	**1,332**	**2,304**
%	4.8	6.4	4.6	11.8	7.5
Cohort C					
Patients who received at least 1 psychotherapy session	189	54	75	321	639
Patients who started a treatment with antidepressants	62	51	178	354	645
Patients who received combined pharmacological/psychotherapeutic treatment	**33**	**21**	**30**	**163**	**247**
%	8.8	14.1	8.3	21.6	15.1
Cohort D					
Patients who received at least 1 psychotherapy session	139	77	171	765	1,152
Patients who were in treatment with antidepressants	382	372	1,479	2,932	5,165
Patients who received combined pharmacological/psychotherapeutic treatment	**79**	**61**	**136**	**621**	**897**
%	11.8	11.3	6.9	15.2	12.3

In the recruitment period, a cohort of around 100,000 prevalent patients affected by major depressive disorder was identified, with an age-standardized prevalence rate of 46.2 prevalent cases per 10,000 adults. Instead, with regard to the incident cohort, were enrolled about 31,000 patients with an incident bipolar disorder, exhibiting an age-standardized incident rate of 9.9 cases per 10,000 person-years.

Regarding the intensity of MHS assistance, the average number (for every person-years of observation) of outpatients visits delivered by the territorial and day-care facilities of the regional DMHs varies from a minimum of 5.7 (cohort B) to a maximum of 20 (cohort D); while the average number of psychiatric visits ranged from 3.7 (cohort B) to 8.6 (cohort D) interventions per person-year.

About half of the patients belonging to the cohorts B and C experienced an episode of discontinuation with the outpatient assistance delivered by the territorial MHS.

For what concern the recommended pharmacological treatment for patients affected by major depressive disorder, the 50% of patients with an incident disorder (cohort B) started a drug therapy with antidepressant agents, but only the 20% of them were persistent to the treatment. Furthermore, only 1 out of 5 cohort B patients who were treated with antidepressants were adherent with the clinical monitoring recommendations for the antidepressant drug therapy. Instead, regarding the cohort A patients, the 65% of them were treated with antidepressants, and the 75% of them experienced an episode of discontinuation of the drug therapy during the year following the index visit.

Patients with an incident bipolar disorder at the onset (cohort C) received a greater number of psychoeducational and psychotherapeutic interventions; furthermore, the 15% of cohort C patients received a combined treatment of both pharmacological antidepressant therapy and psychotherapeutic sessions.

Cohorts' size

For each previously described cohort, the number of patients identified by the algorithms previously described and enrolled in the cohort is reported in the following table.

Table 3.1.4 Number of patients with personality disorder who met the inclusion and exclusion criteria in three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and in the whole Italian sample. Italy, QUADIM Project, 2015-2016

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Recruitment period	2015	2015-2016	2015-2016	2015-2016	2015-2016
Size of the resident adult population at 01/01/2016	4,922,315	1,043,939	3,735,638	8,323,030	18,024,922
PREVALENT COHORT (A)					
Cohort's size	**5,098**	**1,254**	**10,779**	**19,768**	**36,899**
Raw prevalence rate (x10'000)	10.4	12.0	28.9	23.8	20.5
Age-standardized prevalence rate (x10'000)	**8.4**	**9.6**	**23.5**	**19.3**	**15.2**
Mean age (SD)	44.5 (13.9)	44.8 (15.2)	47.0 (14.2)	44.8 (13.8)	45.3 (14.3)
INCIDENT COHORT (B)					
Cohort's size	**1,666**	**465**	**2,598**	**3,202**	**7,931**
Raw incidence rate (x10'000)	1.7	2.2	3.5	1.9	4.4
Age-standardized incidence rate (x10'000 PY)	**2.8**	**1.8**	**3.1**	**1.7**	**2.4**
Mean age (SD)	41.9 (12.6)	40.7 (13.3)	40.7 (12.6)	37.8 (13.2)	40.3 (12.9)
INCIDENT COHORT AT THE ONSET (C)					
Cohort's size	**243**	**78**	**403**	**821**	**1,545**
Mean age (SD)	22.0 (2.2)	21.7 (2.2)	21.5 (2.2)	21.2 (2.2)	21.6 (2.2)
GHPW DISCHARGED COHORT (D)					
Cohort's size	**415**	**197**	**1,814**	**3,505**	**5,931**
Mean age (SD)	41.2 (12.9)	42.8 (13.9)	43.1 (13.0)	42.1 (12.7)	42.3 (13.1)

3.1.4.1 Intensity of outpatient visits

This process indicator assesses the intensity of outpatient visits delivered to patients during the follow-up period. For each person-year (PY) accumulated by the cohort patients, the average number of outpatient visits delivered by territorial and day-care facilities of the regional DMHs was calculated.

Table 3.1.4.1.A Estimates of the intensity of outpatient visits delivered to patients affected by personality disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	4,494	842	9,850	17,168	32,354
%	88.2	67.1	91.4	86.8	87.7
No. of outpatient visits / PY	**16.2**	**7.6**	**27.7**	**17.3**	**19.8**
Cohort B					
Patients with at least 1 outpatient visit	1,339	318	2,167	2,495	6,319
%	80.4	68.4	83.4	77.9	79.7
No. of outpatient visits / PY	**9.7**	**6.9**	**13.6**	**11.6**	**11.6**
Cohort C					
Patients with at least 1 outpatient visit	201	54	347	663	1,265
%	82.7	69.2	86.1	80.8	81.9
No. of outpatient visits / PY	**13.2**	**10.1**	**16.9**	**18.2**	**16.7**
Cohort D					
Patients with at least 1 outpatient visit	364	158	1,626	3,228	5,376
%	87.7	80.2	89.6	92.1	90.6
No. of outpatient visits / PY	**27.9**	**12.7**	**43.7**	**30.7**	**33.9**

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

A modified version of this process indicator has been calculated, in order to assess the intensity of psychiatric outpatient visits delivered during the follow-up period. For each person-year (PY) accumulated by cohort patients, the average number of psychiatric visits delivered by territorial and day-care facilities of the regional DMHs was calculated

Table 3.1.4.1.B Estimates of the intensity of psychiatric visits delivered to patients affected by personality disorder, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 psychiatric visit	4,067	801	8,574	16,286	29,728
%	79.8	63.9	79.5	82.4	80.6
No. of psychiatric visits / PY	**8.2**	**4.3**	**5.4**	**8.5**	**7.4**
Cohort B					
Patients with at least 1 psychiatric visit	1,170	302	1,916	2,410	5,798
%	70.2	64.9	73.7	75.3	73.1
No. of psychiatric visits / PY	**5.8**	**4.1**	**4.3**	**7.2**	**5.8**
Cohort C					
Patients with at least 1 psychiatric visit	180	51	313	633	1,177
%	74.1	65.4	77.7	77.1	76.2
No. of psychiatric visits / PY	**7.8**	**6.2**	**6.2**	**9.7**	**8.3**
Cohort D					
Patients with at least 1 psychiatric visit	348	151	1,456	3,096	5,051
%	83.9	76.6	80.3	88.3	85.2
No. of psychiatric visits / PY	**10.8**	**5.9**	**6.7**	**14.0**	**11.3**

3.1.4.2 Persistence with outpatient MHS assistance

This indicator assesses the persistence with the outpatient assistance delivered by the territorial mental healthcare services (MHS), i.e., territorial and day-care facilities, during the follow-up period. The proportion of cohort patients who experienced the discontinuation of attending territorial MHS in the first 12 months of follow-up was calculated. Attendance of territorial MHS was considered regular if the time-span between two consecutive outpatient visits was 90 days or shorter, or discontinuing otherwise.

Table 3.1.4.2 Estimates of the proportion of patients affected by personality disorder who experienced an episode of discontinuation of attending territorial MHS in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 outpatient visit	4,494	842	9,850	17,168	32,354
%	88.2	67.1	91.4	86.8	87.7
No. of patients discontinuing MHS attendance	**1,986**	**542**	**4,412**	**5,625**	**12,565**
%	**44.2**	**64.4**	**44.8**	**32.8**	**38.8**
Cohort B					
Patients with at least 1 outpatient visit	4,494	842	9,850	17,168	32,354
%	88.2	67.1	91.4	86.8	87.7
No. of patients discontinuing MHS attendance	**1,986**	**542**	**4,412**	**5,625**	**12,565**
%	**44.2**	**64.4**	**44.8**	**32.8**	**38.8**
Cohort C					
Patients with at least 1 outpatient visit	201	54	347	663	1,265
%	82.7	69.2	86.1	80.8	81.9
No. of patients discontinuing MHS attendance	**132**	**43**	**250**	**304**	**729**
%	**65.7**	**79.6**	**72.0**	**45.9**	**57.6**
Cohort D					
Patients with at least 1 outpatient visit	364	158	1,626	3,228	5,376
%	87.7	80.2	89.6	92.1	90.6
No. of patients discontinuing MHS attendance	**103**	**102**	**921**	**837**	**1,963**
%	**28.3**	**64.6**	**56.6**	**25.9**	**36.5**

3.1.4.3 Timeliness of the first outpatient visit after discharge from GHPW

This process indicator assesses the timeliness of the first outpatient visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first outpatient visit (i.e., delivered by territorial and day-care facilities of the regional DMHs) within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.4.3 Estimates of the proportion of patients affected by personality disorder who received the first outpatient visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	415	197	1,814	3,505	5,931
Patients with at least 1 outpatient visit	364	158	1,626	3,228	5,376
%	87.7	80.2	89.6	92.1	90.6
Patients with the first outpatient visit within the first 14 days after the discharge	239	83	1,011	2,010	3,343
%	57.6	42.1	55.7	57.3	56.4

3.1.4.4 Timeliness of the first psychiatric visit
after discharge from GHPW

This indicator assesses the timeliness of the first outpatient psychiatric visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who received the first psychiatric visit, delivered by territorial and day-care facilities of the regional DMHs, within the 14 days immediately following the index discharge from GHPW was calculated.

Table 3.1.4.4 Estimates of the proportion of patients affected by personality disorder who received the first psychiatric visit within the 14 days immediately following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort D					
Cohort's size	415	197	1,814	3,505	5,931
Patients with at least 1 psychiatric visit	348	151	1,456	3,096	5,051
%	83.9	76.6	80.3	88.3	85.2
Patients with the first psychiatric visit within the first 14 days after the discharge	146	66	466	1,297	1,975
%	35.2	33.5	25.7	37.0	33.3

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.4.5 Patients receiving home assistance
(after the cohort entry)

This process indicator evaluates the timeliness of the first home visit delivered after the cohort entry to the patients affected by the personality disorder. The proportion of patients who experienced at least one home visit by the DMHs' professionals in the year following the index visit was calculated.

Table 3.1.4.5 Estimates of the proportion of patients affected by personality disorder to whom at least one home visit was delivered by the DMHs' professionals in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort A					
Cohort's size	5,098	1,254	10,779	19,768	26,120
Patients who received at least 1 home visit	467	60	NA	2,084	2,611
%	9.2	4.8	-	10.5	10.0
Cohort B					
Cohort's size	1,666	465	2,598	3,202	5,333
Patients who received at least 1 home visit	76	17	NA	120	213
%	4.6	3.7	-	3.7	4.0
Cohort C					
Cohort's size	243	78	403	821	1,142
Patients who received at least 1 home visit	12	5	NA	40	57
%	4.9	6.4	-	4.9	5.0

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.

B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.4.6 Timeliness of home assistance after discharge from GHPW

This process indicator assesses the timeliness of the first home visit delivered to cohort D patients after the index discharge from GHPW. The proportion of cohort D patients who experienced at least one home visit by the DMHs' professionals after the index discharge from GHPW was calculated.

Table 3.1.4.6 Estimates of the proportion of patients affected by personality disorder to whom at least one home visit was delivered by the professionals of regional DMHs within the 365 days following the index discharge from GHPW. GHPW discharged cohort, by Region.

	Lazio	Palermo	Emilia-Romagna [A]	Lombardy	All regions together [B]
Cohort D					
Cohort's size	415	197	1,814	3,505	4.117
Patients who received at least 1 home visit	71	15	NA	707	793
%	17.1	7.6	-	20.2	19.3

Note

A. This indicator wasn't calculated in the Emilia-Romagna Region since the information regarding the home visits delivered by the professionals of the regional DMHs was missing.
B. The size of Emilia-Romagna Regions' cohort was excluded from the calculation of the whole sample size

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.4.7 Intensity of recovery to residential facilities

This process indicator measures the intensity of the use of the residential facilities. The proportion of cohort patients experiencing at least one admission to residential facilities during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to residential facilities, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in regional residential facilities was calculated.

Table 3.1.4.7 Estimates of the (i) proportion of patients affected by personality disorder who experienced at least one admission to residential facilities in the year following the index visit; and of the (ii) average number of days spent in residential facilities by those patients, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least 1 admission to residential facilities	546	24	1,813	3,177	5,560
%	10.7	1.9	16.8	16.1	15.1
No. of days of recovery in residential facilities / PY	**135.1**	**206.6**	**116.9**	**110.4**	**115.3**
Cohort B					
Patients with at least 1 admission to residential facilities	95	6	437	399	937
%	5.7	1.3	16.8	12.5	11.8
No. of days of recovery in residential facilities / PY	**94.4**	**301.0**	**75.2**	**50.8**	**68.1**
Cohort C					
Patients with at least 1 admission to residential facilities	25	1	78	137	241
%	10.3	1.3	19.4	16.7	15.6
No. of days of recovery in residential facilities / PY	**128.0**	**73.0**	**63.0**	**51.8**	**63.2**

3.1.4.8 Intensity of recovery to hospital facilities (in GHPW)

This process indicator measures the intensity of the utilization of the hospital facilities. The proportion of cohort patients experiencing at least one admission to GHPWs during the follow-up period was calculated.

Furthermore, only considering those patients who experienced at least one admission to GHPWs, for each person-year (PY) accumulated by this restricted cohort the average number of days spent in hospital facilities was calculated.

Table 3.1.4.8 Estimates of the (i) proportion of patients affected by personality disorder who experienced at least one hospital admission in a psychiatric ward in the year following the index visit; and of the (ii) average number of days spent in hospital facilities by those patients, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients with at least 1 hospital admission to hospital facilities	507	190	1,481	2,659	4,837
	%	9.9	15.2	13.7	13.5	13.1
	No. of days of recovery in hospital facilities / PY	**32.4**	**20.3**	**19.1**	**24.6**	**23.6**
Cohort B						
	Patients with at least 1 hospital admission to hospital facilities	91	71	459	379	1,000
	%	5.5	15.3	17.7	11.8	12.6
	No. of days of recovery in hospital facilities / PY	**17.9**	**17.1**	**16.7**	**16.5**	**16.8**
Cohort C						
	Patients with at least 1 hospital admission to hospital facilities	19	10	85	131	245
	%	7.8	12.8	21.1	16.0	15.9
	No. of days of recovery in hospital facilities / PY	**6.5**	**6.7**	**26.5**	**19.5**	**20.4**

3.1.4.9 Drug treatment with mood stabilizers

This process indicator measures the proportion of patients affected by a personality disorder that were in, or started, a mood stabilizers drug treatment during the follow-up period. For the cohorts A and D, the proportion of patients in treatment with mood stabilizers was calculated. For the cohort B and C the proportion of patients who started a pharmacological treatment with mood stabilizers during the follow-up period was calculated.

Table 3.1.4.9 Estimates of the proportion of patients with a personality disorder who were in treatment with (cohorts A and D), or started a treatment with (cohorts B and C), mood stabilizer drugs in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with mood stabilizers	2,308	550	6,603	10,291	19,752
	%	45.3	43.9	61.3	52.1	53.5
Cohort B						
	Patients who started a treatment with mood stabilizers	334	160	1,141	1,029	2,664
	%	20.0	34.4	43.9	32.1	33.6
Cohort C						
	Patients who started a treatment with mood stabilizers	50	25	173	279	527
	%	20.6	32.1	42.9	34.0	34.1
Cohort D						
	Patients who were in treatment with mood stabilizers	350	158	1,446	2,635	4,589
	%	84.3	80.2	79.7	75.2	77.4

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.4.10 Persistence with mood stabilizers treatment

This indicator assesses the persistence with the mood stabilizer drug treatment of the patients affected by a personality disorder that were in, or started, a treatment with mood stabilizers during the follow-up period. The proportion of cohort patients who were not persistent with the pharmacological treatment with mood stabilizers in the first 12 months of treatment was calculated. Starting from the index prescription of mood stabilizers, consecutively refilled prescriptions were considered uninterrupted if the time-span between the end of one prescription and the beginning of the following one (or of censoring) was 30 days or shorter, since gaps less than 30 days being considered permissible. Conversely, if the between-prescription time-span was longer than 30 days, treatment discontinuation was assumed.

Table 3.1.4.10 Estimates of the proportion of patients affected by personality disorder who discontinued the therapy with mood stabilizers in the year following the index prescription, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who were in treatment with mood stabilizers	2,308	550	6,603	10,291	19,752
	%	45.3	43.9	61.3	52.1	53.5
	Patients who discontinued therapy with mood stabilizers	**1,535**	**312**	**3,421**	**6,740**	**12,008**
	%	66,5	56,7	51,8	65,5	60,8
Cohort B						
	Patients who started a treatment with mood stabilizers	334	160	1,141	1,029	2,664
	%	20.0	34.4	43.9	32.1	33.6
	Patients who discontinued therapy with mood stabilizers	**228**	**115**	**703**	**686**	**1,732**
	%	68,3	71,9	61,6	66,7	65,0
Cohort C						
	Patients who started a treatment with mood stabilizers	50	25	173	279	527
	%	20.6	32.1	42.9	34.0	34.1
	Patients who discontinued therapy with mood stabilizers	**34**	**21**	**122**	**196**	**373**
	%	68,0	84,0	70,5	70,3	70,8
Cohort D						
	Patients who were in treatment with mood stabilizers	350	158	1,446	2,635	4,589
	%	84.3	80.2	79.7	75.2	77.4
	Patients who discontinued therapy with mood stabilizers	**271**	**106**	**892**	**1,941**	**3,210**
	%	77,4	67,1	61,7	73,7	69,9

3.1.4.12 Intensity of interventions for patients' families

This process indicator assesses the intensity of outpatient visits and interventions delivered to the patients affected by personality disorder and their families. The proportion of cohort patients whose families received at least one intervention delivered by territorial and day-care facilities of regional DMHs was calculated.

Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychological interventions delivered by DMHs professionals to patients and their families was calculated.

Among all the interventions delivered by territorial and day-care facilities of the regional DMHs, those aimed at the families of the personality patients were: (i) meeting with family members; (ii) family psychotherapy sessions, (iii) family groups and (iv) psychoeducational interventions aimed at the family.

Table 3.1.4.12 Estimates of the intensity of psychological interventions delivered by DMHs professionals to patients affected by personality disorder and their families, in the year following the index visit, by cohort and Region.

	Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A					
Patients with at least one territorial intervention aimed at their families	1,131	491	2,961	5,122	9,705
%	22.2	39.2	27.5	25.9	26.3
No. of interventions aimed at patients' families / PY	**1.0**	**1.6**	**1.3**	**1.0**	**1.1**
Cohort B					
Patients with at least one territorial intervention aimed at their families	255	175	544	696	1,670
%	15.3	37.6	20.9	21.7	21.1
No. of interventions aimed at patients' families / PY	**0.6**	**1.3**	**0.9**	**0.9**	**0.8**
Cohort C					
Patients with at least one territorial intervention aimed at their families	67	32	156	308	563
%	27.6	41.0	38.7	37.5	36.4
No. of interventions aimed at patients' families / PY	**1.0**	**2.1**	**1.9**	**1.9**	**1.8**
Cohort D					
Patients with at least one territorial intervention aimed at their families	164	96	785	1,586	2,631
%	39.5	48.7	43.3	45.2	44.4
No. of interventions aimed at patients' families / PY	**1.7**	**2.6**	**2.3**	**2.2**	**2.2**

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

3.1.4.13 Intensity of psychoeducational interventions

This process indicator assesses the intensity of psychoeducational sessions or meetings delivered by territorial and day-care facilities to the patients affected by personality disorder during the follow-up period. The proportion of cohort patients who experienced at least one psychoeducational intervention by the DMHs' professionals in the year following the index visit was calculated. Furthermore, for each person-year (PY) accumulated by the cohort patients, the average number of psychoeducational sessions delivered by DMHs professionals to patients and their families was calculated.

Table 3.1.4.13 Estimates of the intensity of psychoeducational interventions delivered by territorial and day-care facilities to personality patients, in the year following the index visit, by cohort and Region.

	Lazio [A]	Palermo	Emilia-Romagna	Lombardy	All regions together [B]
Cohort A					
Cohort's size	5,098	1,254	10,779	19,768	31,801
Patients who received at least 1 psychoeducational intervention	NA	79	480	482	1,041
%	-	6.3	4.5	2.4	3.3
No. of psychoeducational interventions / PY	**-**	**2.1**	**6.6**	**4.6**	**5.3**
Cohort B					
Cohort's size	1,666	465	2,598	3,202	6,265
Patients who received at least 1 psychoeducational intervention	NA	79	480	482	1,041
%	-	6.3	4.5	2.4	3.0
No. of psychoeducational interventions / PY	**-**	**2.1**	**6.6**	**4.6**	**5.2**
Cohort C					
Cohort's size	243	78	403	821	1,302
Patients who received at least 1 psychoeducational intervention	NA	5	22	49	76
%	-	6.4	5.5	6.0	5.8
No. of psychoeducational interventions / PY	**-**	**5.2**	**4.6**	**6.3**	**5.7**
Cohort D					
Cohort's size	415	197	1,814	3,505	5,516
Patients who received at least 1 psychoeducational intervention	NA	10	166	168	344
%	-	5.1	9.2	4.8	6.2
No. of psychoeducational interventions / PY	**-**	**3.3**	**5.0**	**4.4**	**4.6**

Note

A. This indicator wasn't calculated in the Lazio Region since the information regarding the psychoeducational intervention delivered by territorial and day-care facilities was missing.

B. The size of Lazio Region's cohort was excluded from the calculation of the whole sample size

3.1.4.14 Intensity of psychotherapeutic interventions

This indicator measures the intensity of psychotherapy sessions and meetings delivered to patients with personality disorder. The proportion of patients who received at least one psychotherapeutic intervention by the territorial and day-care facilities' professionals in the year following the index visit was calculated.

For each person-year (PY) accumulated by the cohort patients, the average number of psychotherapy sessions delivered to patients and/or their families was calculated. Psychotherapeutic interventions delivered to patients, but also to their families were considered.

Table 3.1.4.14 Estimates of the intensity of psychotherapeutic interventions delivered by DMHs professionals to patients affected by personality disorder and their families, in the year following the index visit, by cohort and Region.

		Lazio	Palermo	Emilia-Romagna	Lombardy	All regions together
Cohort A						
	Patients who received at least 1 psychotherapy session	1,583	232	1,036	4,080	6,931
	%	31.1	18.5	9.6	20.6	18.8
	No. of psychotherapeutic interventions / PY	**11.5**	**7.1**	**7.9**	**8.9**	**9.3**
Cohort B						
	Patients who received at least 1 psychotherapy session	515	105	349	1,038	2,007
	%	30.9	22.6	13.4	32.4	25.3
	No. of psychotherapeutic interventions / PY	**9.6**	**6.3**	**7.6**	**8.9**	**8.7**
Cohort C						
	Patients who received at least 1 psychotherapy session	120	30	94	359	603
	%	49.4	38.5	23.3	43.7	39.0
	No. of psychotherapeutic interventions / PY	**9.7**	**9.8**	**9.4**	**10.8**	**10.3**
Cohort D						
	Patients who received at least 1 psychotherapy session	108	23	192	686	1,009
	%	26.0	11.7	10.6	19.6	17.0
	No. of psychotherapeutic interventions / PY	**11.4**	**3.5**	**6.6**	**9.2**	**8.8**

In the recruitment period, 37,000 patients affected by prevalent personality disorder were identified, with an age-standardized prevalence rate of almost 15.2 prevalent cases per 10,000 adults. Instead, regarding the incident cohort, about 8,000 patients with an incident personality disorder were enrolled, exhibiting an age-standardized incident rate of 2.4 cases per 10,000 person-years.

Regarding the intensity of MHS assistance, the average number (for every person-years of observation) of outpatient visits delivered by the territorial and day-care facilities of the regional DMHs was equal to 12 and to 20, respectively, for cohort B and cohort A members. Considering the outpatient psychiatric visits, patients with the prevalent disorder (cohort A) experienced 7 visits every person-year. The patients with an incident personality disorder at the onset were less persistent with MHS attendance than the other cohorts' members; only the 42% of cohort C patients were persistent with attending territorial MHS assistance, whereas in cohorts A, B and D the proportion of persistent patients was around the 60%.

Regarding the intensity of the use of the residential facilities, patients of cohort A exhibited an average number of days spent in residential facilities almost double than the patients of cohort B.

For what regards the recommended pharmacological treatment for patients affected by personality disorder, in the cohorts A, B and D respectively the 53%, 34% and 80% of the patients started a treatment with mood stabilizers. Of those, the proportion of patients discontinuing the mood stabilizers drug therapy ranged from 60% to 70% in the various cohorts.

Patients with an incident bipolar disorder at the onset (cohort C) and those discharged from an admission to GHPW (cohort D) received a greater number of psychological interventions aimed at their families. Regarding the intensity of psychoeducational sessions, all the cohorts exhibited similar values. Cohort C received more frequently sessions pf psychotherapy.

3.2 Validation study

After the having designed, developed and calculated process indicators for the SMI considered in the QUADIM project, a validation study was conducted to evaluate, in a real-life setting, the association between a set of process indicators for quality of mental healthcare and measurable clinical outcomes (i.e., admission to hospital psychiatric wards, GHPWs), among patients with an incident schizophrenic disorder.

The results of this validation study are reported below, following the structure of a scientific article.

Incident Schizophrenic spectrum disorder validation study

Aim

By considering that a better process profile, as measured by process indicators for quality of mental healthcare, not necessarily lead to better outcomes, a validation study for evaluating their relationship with measurable clinical outcomes was designed.

The current paper reports methods and main findings of the validation study and discusses the implications of monitoring the process of care of patients with incident schizophrenic disorder and, more in general, of the proposed approach.

Methods

Data sources

The QUADIM project is based on computerized Healthcare Utilization (HCU) databases from four Italian administrative units localized in North West (Lombardy region), North East (Emilia-Romagna region), Centre (Lazio region) and South (Palermo district). Overall, these data covered almost 22 million beneficiaries of the Italian National Health Service (NHS), nearly 37% of the entire Italian population.

All Italian citizens have equal access to health care services as part of the NHS. An automated system of HCU databases allows each Italian region to locally manage the healthcare provided by NHS. HCU data include a variety of information on residents who receive NHS assistance, diagnosis at discharge from public or private hospitals, outpatient drug prescriptions, specialist visits and diagnostic exams reimbursable by the NHS. In addition, a specific automated system concerning psychiatric care is provided by the regional Departments of Mental Health (DMHs) accredited by the NHS. The system provides demographic information and the ICD-10, or ICD-9-CM, diagnoses of all patients attending Mental Health outpatient Services (MHS) and records all treatments provided to them (outpatient and home visits, day treatment attendance, and residential facilities). As a unique identification code is used for all databases within each region, their record-linkage allows searching out the complete care pathway of beneficiaries of NHS. In order to protect privacy, individual identification codes are automatically converted into anonymous codes and the inverse process is avoided erasing the conversion table. Details of HCU databases use in the field of mental health have been reported elsewhere [76].

Harmonization and data processing

Although databases did not substantially differ across all regions for several aspects, a between-region data harmonization was performed, thus allowing data extraction processes to be targeted the same semantic concepts (e.g., information were uniformly encoded by using for each variable the same names, values and formats). Anonymized data were extracted and processed locally by using a Statistical Analysis System (SAS) programs which was developed by a researcher of the University of Milano-Bicocca (Author: the author of this thesis) according to a protocol previously approved by the scientific coordination group of the project.

Diagnostic and therapeutic codes used in the current study for drawing records and fields from databases are reported in **Appendix II**.

Cohort selection

The target population consisted of all beneficiaries of the NHS resident in the four territorial units aged 18-65 years old. According to the Italian Institute of Statistics, this population amounts for 13.5 million individuals [http://demo.istat.it/index.html]. Of these, we identified patients who during the recruitment period (from January 2015 to June 2016 for Lombardy, Emilia-Romagna and Palermo, and from January to December 2015 for Lazio), had at least a contact with a local MHS accredited by the NHS and received in that occasion diagnosis of schizophrenia spectrum disorder (ICD-10 codes F2x.*, or ICD-9-CM codes 295.*, 297.*, 298.2, 298.3, 298.4, 298.8, 298.9). These patients were labelled as prevalent cases, and the date of their first visit during the considered period was recorded as that of the index visit.

With the aim of including only newly diagnosed individuals, the prevalent cases who had already received diagnosis of schizophrenia any time prior 2015, and those who experienced at least a hospital admission in a psychiatric ward (GHPW, ward code "40") and/or received at least two prescriptions of antipsychotic drugs within two year prior the index visit, were excluded. Finally, patients who did not reach at least 1 year of follow-up were excluded, to ensure at least one year of potential exposure to the considered care pathways. The remaining patients represented the study cohort.

Each member of the cohort accumulated person-years of follow-up from one year after the index date until the earliest among the dates of outcome onset (i.e., emergency hospital admission to GHPWs) or censoring (i.e., death from any cause, migration, or end of study period, December 31st , 2016 for Lazio region, or December 31st , 2017 for the other regions).

Measuring adherence with recommendations

Starting with the first month after receiving diagnosis of schizophrenic spectrum disorder, the following month-by-month contacts with MHS, as well as all antipsychotic drug prescriptions of each cohort member were monitored. Persistence with attending MHS was defined as the continue contact during follow-up without any episode of discontinuation, the latter occurring when for the first time a patient did not show up to any territorial service for an entire month or longer.

The duration of each antipsychotic prescription was calculated by dividing the total amount of the drug prescribed by the defined daily dose. Starting from the index date, consecutively refilled prescriptions were considered uninterrupted if the time-span between the end of one prescription and the beginning of the following one (or of censoring) was 30 days or shorter, since gaps less than 30 days being considered permissible. Conversely, if the between-prescription time-span was longer than 30 days, treatment discontinuation was assumed. So, antipsychotic drug therapy (ADT) was defined persistent if during follow-up no episode of treatment discontinuation occurred.

Using the actuarial life-table method, we calculated the probability of not experiencing discontinuation of attending territorial MHS and ADT over the first 12 months of follow-up.

Assessing the association between adherence with recommendations and mental health-related admissions

Two approaches were used for assessing the exposure (to clinical recommendations) - outcome (admission to GHPW) association. One, Poisson regression was used to estimate the adjusted relative rates (RR), and corresponding 95% confidence interval (CI), of GHPW admissions occurred from the date corresponding to one year after the index visit associated with exposure to recommendations experienced within the first year of follow-up. This implicitly corresponds to adopting an intention-to-treat design, since one-year healthcare exposure was related to the outcomes arisen in the period starting one year after. Adjustments were made for baseline characteristics of cohort members such as gender, age, education years, working condition, family arrangement and comorbidities. Additionally, the so-called Multisource Comorbidity Score (MCS), a new comorbidity index obtained from inpatient diagnostic information and outpatient drug prescriptions, and validated using Italian data [85], was calculated for each cohort member. Patients were categorized as having optimal (MCS=0), good (1-4), intermediate (5-9), poor (10-14) or very poor ($\geq$ 15) comorbidity profile.

Two, we reasoned about two biases that could affect the investigated association, i.e., unmeasured confounding and protopathic bias.

Potential unmeasured confounders (e.g., schizophrenia severity) were taken into account by using a case-only design known as case-crossover [78]. With the latter, we verified whether each patient experiencing the outcome experienced the exposure (i.e., attended at least once the MHS or was covered by ADT for more than 60% of the period, or 80% in a secondary analysis) during the period just before outcome onset (current period) and two delayed reference periods. Therefore, using this approach, the current exposure of each case was contrasted with two previous reference periods within each case patient. A conditional logistic regression model for 1:2 matched data was used to estimate the case-crossover odds ratio (OR), and corresponding 95% CI, for current vs. reference exposure on the risk of admission to GHPW. By comparing cohort members who experienced the outcome with themselves at different time points, the case-crossover design implicitly avoids confounding by subject-specific time-invariant attributes [79].

In addition, we addressed the potential presence of protopathic bias. This occurs when the outcome is associated with an exposure that actually results from early symptoms of the outcome [80]. In our application, increased MHS attendance and ADT persistence before occurrence of emergency admission to GHPW is expected because of symptoms worsening. Hence, a paradoxical positive exposure-outcome association might be observed. For this reason, we used a delayed wash-out time-window between current exposure period and outcome occurrence [81].

The delayed, current and reference time-windows had the same width, which was fixed at 45 days in the main analysis. However, due to arbitrariness in the choice, secondary analyses were also performed by expanding the breadth at 90 days.

A schematic representation of within-person case-crossover design used in this study and widths of delayed, current and reference time-windows used in the main and secondary analyses were reported in **Figure 3.3.1**.

Because the above calculations were separately performed within each considered region, the region-specific estimates were summarized by using a random-effect model. The approach proposed by DerSimonian and Laird was used for estimating such effects [83]. The heterogeneity of estimates between regions was tested by Cochran's Q test and measured with the I^2 statistics (the proportion of between-region variability due to heterogeneity) [84].

The Statistical Analysis System Software (version 9.4; SAS Institute, Cary, NC, USA) was used

to perform the analyses. For all hypotheses tested, two-tailed p-values less than 0.05 or, in an equivalent manner, 95% CI of RR/OR that does not contain the value expected under the null hypothesis, were considered significant.

Results

Patients

The distribution of the exclusion criteria is shown in **Figure 3.3.2**. Among the almost 67 thousands eligible prevalent cases, about 61 thousands were excluded, while 5,770 meet the inclusion criteria and were enrolled into the study cohort. Prevalence and incidence data respectively were 5.0% and 3.1 every 10,000 person-years. Cohort members accumulated 7,569 person-year of follow-up and generated 769 admissions to GHPW (incidence rate: 10.2 every 100 person-years at risk). Their baseline characteristics are shown in **Table 3.3.1**. Mean age was about 44.6 years and 55% of cohort members were men. Most patients had low education (60% had less than 8 years of education) and almost 50% of them were unemployed and lived with the family. Nearly three out of four cohort members (73%) had an optimal or good comorbidity profile. There were not relevant differences among administrative units, if not the higher proportion of missing data in Lazio.

Adherence with recommendations

Cumulative proportion of patients surviving attendance with MHS and ADT in the first year since diagnosis of schizophrenia are shown in **Figure 3.3.3**. The probability of surviving MHS was in average 52%, ranging from 40% in Emilia Romagna to 59% in Lazio. The probability of surviving ADT was in average 51%, ranging from 48% in Emilia Romagna and Palermo to 57 % in Lazio.

Adherence with recommendations and mental health-related admissions

As expected, a likely biased positive exposure-outcome association was observed from the Poisson's regression (**Table 3.3.2**). Conversely, a clear protective effect of adherence with both MHS attendance and ADT coverage, was obtained from the case-crossover approach. There was evidence that both persistence with MHS and ADT coverage had significant main effects being the corresponding admissions to GHPW reductions of 35% (95% CI, 12% to 52%) for patients who regularly attended outpatients services (with respect to those who did not), and of 63% (44% to 76%) and 73% (56% to 84%) respectively for those patients with low and high adherence to ADT (compared to patients who did not used antipsychotic drugs), thus showing a significant trend towards risk reduction as the level of adherence with drug therapy increased.

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project

Still concerning summarized national data, **Figure 3.3.4** reports the trend in case-crossover's ORs according to increasing levels of the combined exposure to MHS regular attendance and ADT persistence. A clear trend towards decreasing outcome risk as the level of combined MHS regular attendance and ADT adherence increase was observed. Compared to patients who did not attend regularly MHS and had no use of antipsychotic drugs, significant GHPW admissions risk reductions were observed for all the other categories of combined exposure to MHS and ADT. With respect to those not persistent to MHS assistance and ADT, patients who regularly attended MHS and were in treatment with ADT had significant risk reductions of 71% (51% to 83%) and 79% (62% to 88%) for low and high drug adherence, respectively. With equal attendance of MHS, or adherence to ADT, patients showed a clear decreasing trend of MHRA risk according to the increasing level of ADT adherence, or MHS attendance, respectively.

Figure 3.3.5 shows that such an evidence did not modify substantially by stratifying analyses neither according to the individual administrative units, nor by modifying criteria for drug coverage and time-windows width definition. As we were not able of obtaining model convergence for Lazio, case-crossover estimates took account only of cohort members from Lombardy, Emilia Romagna and Palermo.

Tables and figures

Table 3.3.1. Baseline characteristics of patients with schizophrenia newly taken in care (incident cases) in three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and in the whole sample. Italy, QUADIM Project, 2015-2016

|	Lombardy (N=1,852)	Emilia-Romagna (N=1,701)	Lazio (N=1,624)	Palermo (N=593)	All regions together (N=5,770)
Gender					
Women	47.8%	44.6%	43.7%	37.4%	44.6%
Men	52.2%	55.4%	56.3%	62.6%	55.4%
Age (years)					
Mean (SD)	47.4 (17.8)	42.6 (12.3)	43.0 (11.9)	45.4 (11.4)	44.6 (13.4)
18-30	21.5%	20.9%	13.4%	18.9%	18.8%
30-39	14.5%	23.3%	15.6%	18.9%	17.9%
40-49	20.7%	25.7%	28.0%	25.1%	24.7%
50-64	43.3%	30.0%	43.0%	37.1%	38.6%
Education years					
0-5	47.2%	10.1%	10.8%	21.9%	23.4%
6-8	22.1%	38.0%	40.9%	72.2%	37.2%
9-13	15.7%	31.0%	30.5%	1.9%	22.9%
≥14	3.4%	7.6%	6.1%	4.0%	5.5%
Missing data	11.7%	13.2%	11.6%	0.0%	10.9%
Job condition					
Employed	46.0%	26.3%	23.7%	15.0%	30.7%
Unemployed	29.5%	45.4%	65.9%	76.2%	49.2%
Invalid	13.9%	7.0%	0.1%	6.4%	7.2%
Missing data	10.6%	21.2%	10.3%	2.4%	12.8%
Family arrangement					
Living with family	72.4%	70.7%	0.0%	32.9%	47.5%
Living in community	4.9%	4.8%	0.0%	7.3%	3.7%
Living alone	14.4%	11.7%	0.0%	6.9%	8.8%
Missing data	8.3%	12.8%	100.0%	53.0%	40.0%
Comorbidities					
0	49.2%	60.3%	70.4%	61.9%	59.8%
1-5	16.0%	17.2%	8.6%	12.3%	13.9%
6-10	29.4%	18.3%	17.2%	21.1%	21.8%
11-15	3.5%	2.6%	2.9%	2.9%	3.0%
≥16	1.9%	1.6%	0.9%	1.9%	1.5%

Table 3.3.2. Association between adherence with recommendations (i.e., regular mental health service attendance and appropriate coverage with antipsychotic agents within the first year since diagnosis of schizophrenia) and outcome (i.e., number of hospital admissions for mental disorders occurred from the second year since diagnosis of schizophrenia). Italy, QUADIM Project, 2015-2016

	# events / Person-months	Relative rate[§]	95% confidence interval[§]
Mental health service attendance[†]			
Discontinuing	164 / 14,836	1.00	Ref.
Regular	190 / 17,456	0.92	0.74 to 1.13
Antipsychotic agents[‡]			
No use	95 / 6,324	1.00	Ref.
Low coverage	185 / 16,455	1.53	1.19 to 1.96
High coverage	74 / 22,160	1.70	1.25 to 2.31

[†]   Attendance was considered regular if the time-span between two consecutive visits was 30 days or shorter, or discontinuing otherwise. User-only approach was used for all patients with at least one mental health outpatient visit

[‡]   Months with antipsychotic agents available allowed to classify patients according whether they did not use drug therapy, or coverage was <60% (low) or ≥ 60% (high). User-only approach was used for all patients with at least one prescription of antipsychotic drugs

[§]   Relative rate (and 95% confidence interval) for the risk of hospital admission for mental disorders, according to the Poisson's model. Estimates are adjusted for covariates listed in Table 3.3.1

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project
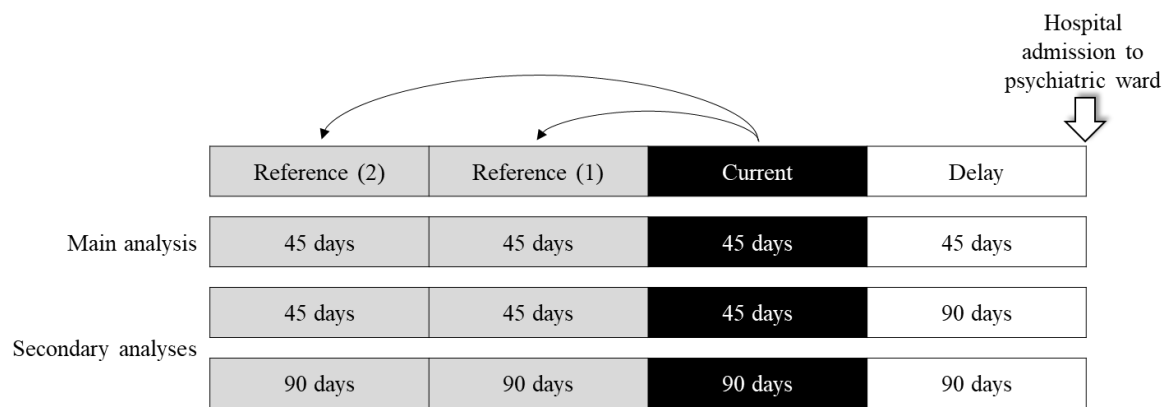
Figure 3.3.1. Schematic representation of within-person case-crossover design used in this study. Different widths of delayed, current and reference time-windows have been considered in the main and secondary analyses.
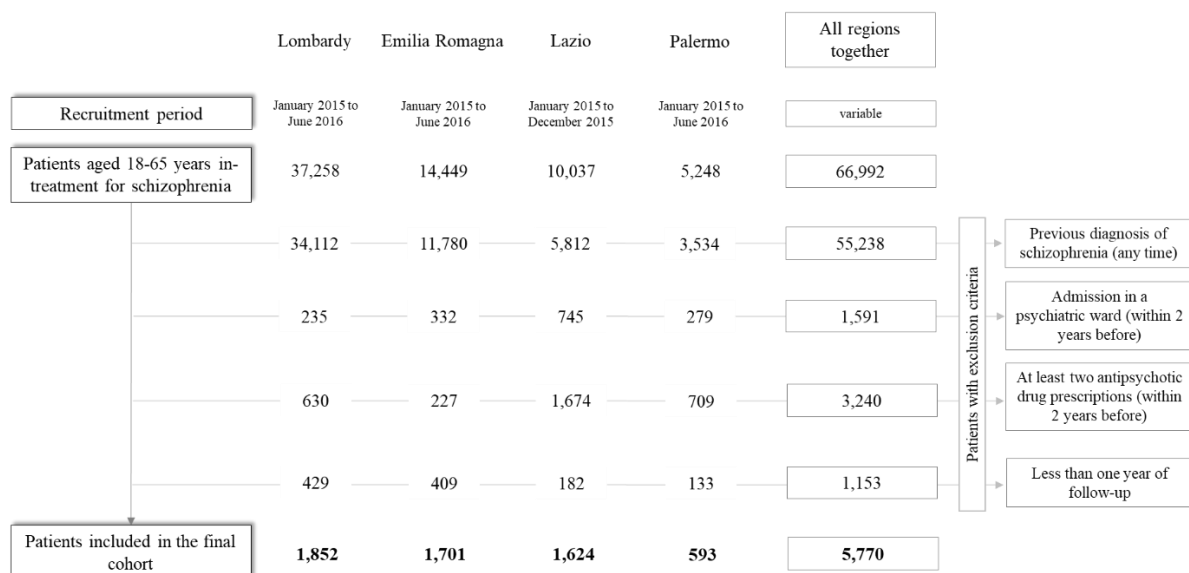
Figure 3.3.2. Flow-chart of inclusion and exclusion criteria in three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and in the whole Italian sample. Italy, QUADIM Project, 2015-2016

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project
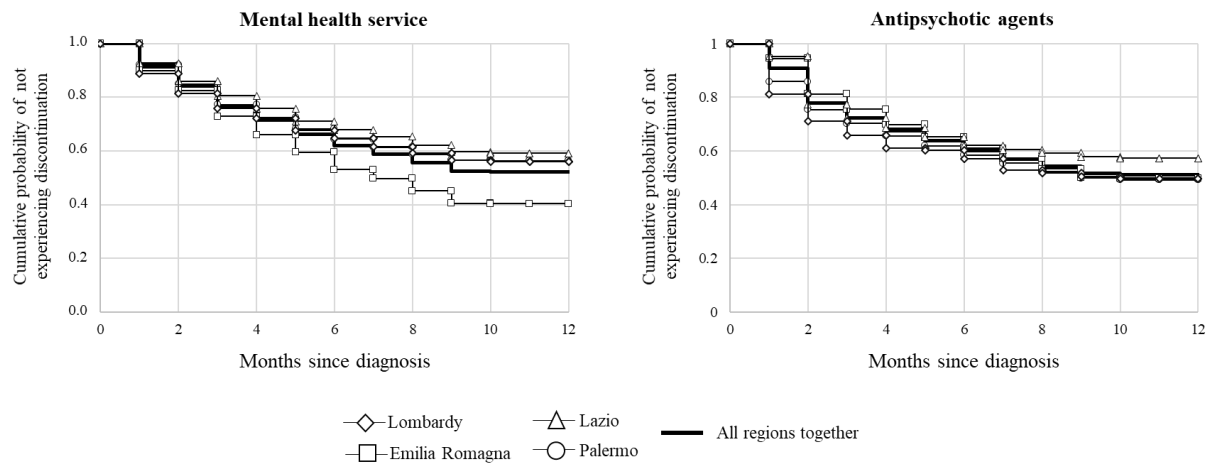
Figure 3.3.3. Cumulative proportion of patients who did not discontinue attendance with mental health services (left box) and therapy with antipsychotic agents in the first year since diagnosis of schizophrenia. Data of three regions (Lombardy, Emilia Romagna and Lazio) and one province (Palermo), and of the whole Italian sample, are pictured. Italy, QUADIM Project, 2015-2016

Footnote. Patients discontinued mental health service attendance whether any visit occurred during a given month (see text). Patients discontinued antipsychotic drug therapy whether there was not coverage during a given month (see text). Cumulative proportions were estimated by means of the life-table method (see text)
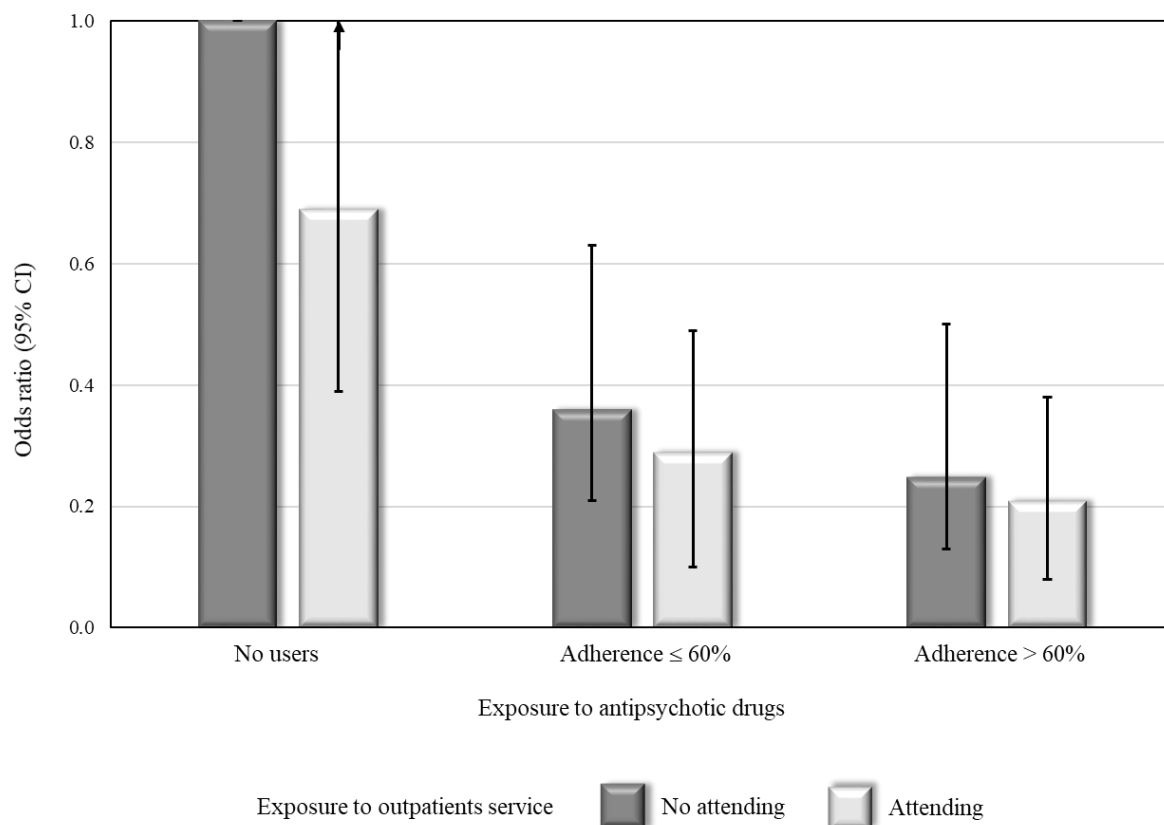
Figure 3.3.4. Summarized case-crossover estimates of the risk reduction of mental health-related hospital admission associated with levels of the combined exposure to (i) mental health services regular attendance and (ii) antipsychotic drug therapy persistence, compared to discontinuing attendance and no use of any antipsychotic drugs. Italy, QUADIM Project, 2015-2016

Footnote. Case-crossover odds ratios, and 95% confidence interval, estimated according to conditional logistic regression contrasting within-patient exposure during current and reference time windows (see Figure 3.3.1). Between-region summarized case-crossover odds ratios (i.e., those obtained by assembling data from Lombardy, Emilia Romagna and Palermo) were estimated by means of a random-effect model, using the DerSimonian and Laird approach
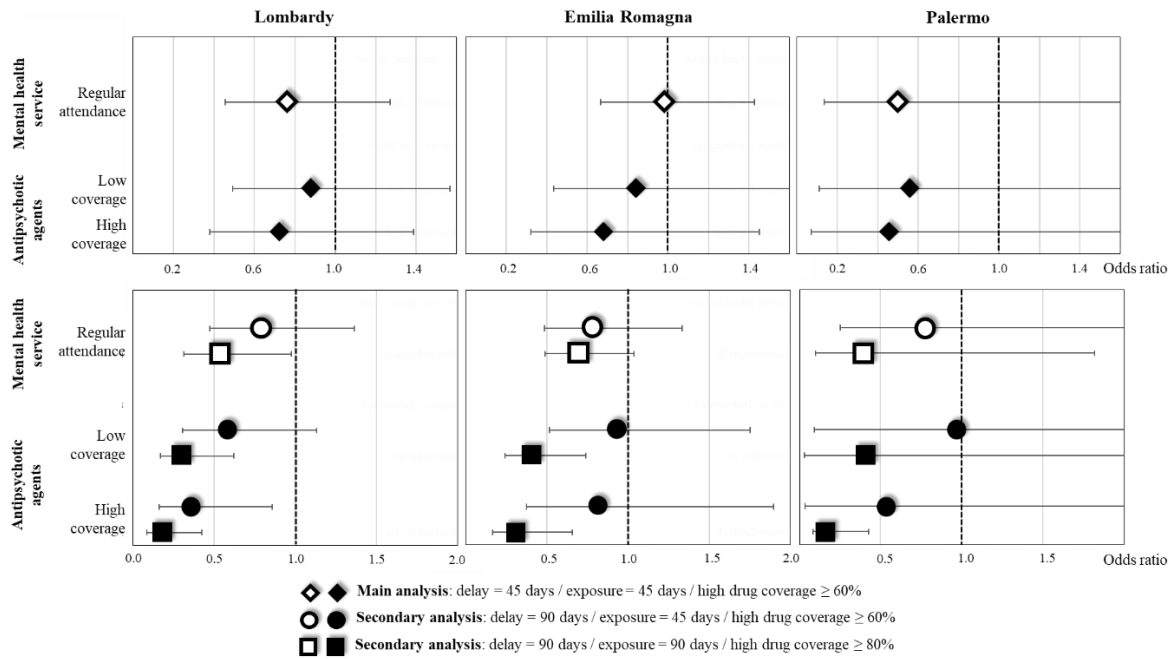
Figure 3.3.X. Case-crossover estimates of the risk reduction of hospital admission for mental disorders associated with adherence to recommendations. The latter were regular attendance of mental health service, compared with discontinuing attendance, and low / high coverage with antipsychotic agents, both compared with no use of antipsychotics. Data of Lombardy, Emilia Romagna and Palermo) are presented. Main and secondary analyses (obtained by varying widths of time-windows and classification criteria for coverage with antipsychotic drugs) are pictured. Italy, QUADIM Project, 2015-2016

Footnote. Case-crossover odds ratios, and 95% confidence interval, estimated according to conditional logistic regression contrasting within-patient exposure during current and reference time windows (see Figure 3.3.1)

Chapter 4

Discussion

The aim of the QUADIM project, and of this thesis was to assess the quality of healthcare pathways provided to patients with SMI (i.e., schizophrenic, depressive, bipolar and personality disorders) assisted by regional DMHs in a real-world setting, using a set of process indicators developed by a panel of experts. For each of the 4 SMI investigated, from the regional HCU databases were identified the cohorts of adult patients affected by this specific mental disorder and taken in care by regional DMHs during the years 2015-2016. The adherence of these patients to the designed process indicators was evaluated during the first 12 months of follow-up, assessing strengths and weaknesses of the 4 regional mental health systems.

One secondary aim of this thesis was the conduction of a validation study for evaluating the association between the most relevant process indicators and measurable clinical outcomes; the underlying idea was to validate some process indicators relating them, as a proxy of the quality of delivered care, with some clinical outcomes, such as admission to hospital psychiatric wards.

Firstly, the cohorts of patients affected by SMI were identified and the prevalence and incidence of each of the 4 SMI investigated were calculated. For each considered SMI, the age-standardized prevalence rates estimated in the 4 regions involved in the QUADIM project were similar to those observed at a national level in the third "Annual Report on Mental Health in Italy, year 2017" [6]. Instead, the estimated age-standardized incidence rates were lower than those reported in the third "Annual Report on Mental Health in Italy, year 2017", since more stringent inclusion/exclusion criteria were adopted in the identification algorithms of the incident cohorts, with the purpose to increase the probability of exclude prevalent cases.

The quality of routine mental healthcare delivered to the identified cohorts was evaluated. For each SMI studied, most patients received an adequate pharmacological treatment although, especially for depressive patients, the proportions of patients discontinuing the pharmacological treatment during the year following the index visit were high.

Many patients resulted well assisted by the territorial MHS, indeed an high proportion of patients were persistent with the attendance with outpatient visits delivered by territorial and day-care facilities of the regional DMHs, Patients with an incident disorder at the onset resulted adequately treated with psychoeducational and psychotherapy sessions, and their families received psychological interventions with a good frequency. Criticisms emerged in the intensity of home visits delivered by the professionals of regional DMHs and, especially for patients affected by personality disorder, in the adherence with the clinical monitoring recommendations for the mood stabilizers drug therapy. Discontinuation of the recommended pharmacological treatment is still an important issue, which needs further attention, especially for patients with an incident disorder, since in the cohorts B and C were observed the highest proportions of patients discontinuing the pharmacological treatment. Furthermore, some indicators showed very heterogeneous results among the different Regions.

As far as the validation study is concerned, this current population-based investigation confirms previous observations that healthcare of schizophrenic patients newly taken in care is frequently abandoned and/or is not adequately followed in the real-life practice [86], even in the Italian setting [28,76]. In addition, evidence of regional variations in the management of schizophrenia within the same country was observed in our investigation. The new important finding, however, is that schizophrenic patients who did not discontinue MHS attendance and the antipsychotic drug therapy had a significant reduction of the GHPW admission risk of 35% and 73%, respectively, a conclusion that expands to a large unselected population the conclusions of recent systematic reviews [87,88]. Moreover, as shown in **Figure 3.3.4**, increased GHPW admission risk reductions were observed with increasing adherence to both MHS and ADT treatment. This finding is very important for reaching a consensus in how to measure and compare the quality of care of schizophrenic patients, to develop process improvements, and to reduce the heterogeneity of clinical practice.

The present validation study, and the QUADIM project as a whole, is unique in several respects. One, the investigation is based on data from a large unselected population, which was made possible since in Italy a cost-free healthcare system involves practically all citizens. Two, our data reflect routine clinical practice and are not affected by selective participation and recall bias. Three, patients were identified from the point of the first visit with the mental health service

in which diagnosis of SMI was made, and the complete sequence of public or accredited healthcare facilities, including mental health care and other services, was known. Finally, a number of sensitivity analyses confirmed the robustness of our findings in the validation study.

Limitations of the study should be taken into account to give the correct interpretation to our results. One, we cannot exclude that some differences in adherence to recommendations between administrative units, might be in part due to heterogeneity in data quality and completeness. However, because healthcare utilization data are needed for reimbursement to public and accredited service providers, incorrect and incomplete reports have legal consequences. Two, bias associated with our inability to account for out-of-pocket clinical evaluations, e.g., psychiatric visits and antipsychotic drugs supplied privately, should be considered [89]. However, as far as the results of the validation study are concerned, the estimates would be unbiased if use of out-of-pocket services similarly affected cohort members regardless whether they experienced or did not experience the outcome (i.e., if no differential misclassification of exposure occurred [90]). Three, adherence with the recommended pharmacological therapy was derived from drug prescriptions, i.e., a widely used method to estimate adherence to treatment in large populations [91], which requires, however, the assumption that the proportion of days covered by a prescription corresponds to the proportion of days of drug use [66].

Finally, as it happens for practically all the studies based on HCU databases, limited amount of available clinical information engenders two further weaknesses [92] in the results of the validation study. First, as patients with frequent controls are expected to have more severe clinical characteristics than those less intensively controlled, because of our impossibility of clinical stratification, we could not directly account for confounders. This seems to be confirmed by our odd finding that the higher was adherence to recommendations during the first year after diagnosis of schizophrenia, the more likely emergency hospital admission was experienced afterwards. Second, as mental healthcare was frequently abandoned, but might be started again in response to worsening symptoms, in the absence of information on symptoms severity, an equal strange positive association between exposure to mental healthcare and outcome onset could be observed due to the so-called protopathic bias [80]. In our application, a case-crossover design [78,79] and a lag-time approach [81] were respectively used to avoid confounding by subject-specific time-invariant attributes and to take into account protopathic bias. These analytical expedients should have provided reliable estimates of the strength of adherence-outcome association.

Conclusions

Improving the quality of care is a leading priority for national health systems, consistent with the aim of improving population health, while maintaining the sustainability of the whole health system [37,93], especially for the mental health system, being composed by a complex network of community mental health teams and a wide range of community-based treatment, rehabilitation, employment and residential care facilities.

Since resident patients of 4 regions from Northern, Central and Southern Italy were considered, the sample recruited is highly representative and the obtained results can be generalized and transferred to the national level. Thus, starting from this multiregional Project, based on several previous italian studies at regional and national level, it will be possible to define quality standards for the health care delivered by the Departments of Mental Health, as well as develop procedures for the design of process indicators and their calculation among the italian Regions.

The availability of a shared software program to implement and calculate the identified process indicators will allow the replication of the analyses not only in the four participating Regions, but in the other Italian Regions that will be interested to the aims of the project. Furthermore, calculation of these indicators will not represent an additional workload in the collection of data for service operators because all the indicators can be calculated from the use of HCU databases.

Further validation studies are needed, in order to validate the association between selected process indicators and measurable clinical outcomes also in patients affected by depressive, bipolar and personality disorders.

This Project, the first in Italy to evaluate the quality of care pathways provided to patients with severe mental disorders on such a large and unselected population, can provide valuable information for service planning policies, starting from the assumption that the information on the quality of care represents a necessary step to reach the improvement of the healthcare quality. Indeed, because benefits for patients and healthcare system are expected from improving adherence with recommendations in patients affected by SMI, as highlighted by the validation study on patients with schizophrenic incident disorder, better awareness about

need for mental healthcare continuity is mandatory. Tight control through active recall must to be considered the cornerstone of national guidance, national audits, and quality improvement incentives politics.

References

1. 2017 National Survey on Drug Use and Health (NSDUH). Available at: https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report.

2. National Institute of Mental Health (NIMH), Health topics. Available at: https://www.nimh.nih.gov/health/statistics/mental-illness.shtml.

3. Slade M, Powell R, Strathdee G. Current approaches to identifying the severely mentally ill. Soc Psychiatry Psychiatr Epidemiol 1997;32:177–84.

4. Substance Abuse and Mental Health Services Administration. Final notice establishing definitions for (1) children with a serious emotional disturbance, and (2) adults with a serious mental illness. Federal Register 1993;58(96):29, 422–429, 425.

5. National Advisory Mental Health Council. Health care reform for Americans with severe mental illness: report of the National Advisory Mental Health Council. American Journal of Psychiatry 1993;150:1447–1465.

6. Italian Ministry of Health. 3rd Italian Annual report on Mental Health, year 2017. Available at: http://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp?lingua=italiano&id=2841.

7. Narrow WE, Regier DA, Norquist G, et al. Mental health services uses by Americans with severe mental illness. Social Psychiatry and Psychiatric Epidemiology 2000;35:147– 155.

8. Ruggeri M, Leese M, Thornicroft G, Bisoffi G, Tansella M. Definition and prevalence of severe and persistent mental illness. Br J Psychiatry 2000;177:149–55.

9. House of Commons Health Select Committee. First Report of the Health Committee: Better Off in the Community? The Care of People who are Seriously Mentally Ill.1994 London: HMSO.

10. Lora A, Bezzi R, Erlicher A. Estimating the prevalence of severe mental illness in mental health services in Lombardy (Italy). Community Ment Health J 2007;43:341–57.

11. Leff J. Care in the Community: Illusion or Reality? 1997 Wiley: London.

12. Thornicroft G, Tansella M. Better Mental Health Care. Cambridge, United Kingdom, 2009 Cambridge University Press.

13. Campbell H, Hotchkiss R, Bradshaw N, Porteous M. Integrated care pathways. BMJ 1998;316:133–7.

14. Riley K. Care pathways. Paving the way. Health Serv J 1998;108:30–1.

15. Vanhaecht K, Panella M, van Zelm R, et al. An overview on the history and concept of care pathways as complex interventions. Int J Care Pathw 2010;14(3):117–23.

16. De Luc K. Developing Care Pathways. 2001 Radcliffe Publishing.

17. Zander K. Integrated Care Pathways: Eleven International Trends. J Integr Care Pathw 2002;6(3):101–7.

18. Hindle D, Yazbeck A-M. Clinical pathways in 17 European Union countries: a purposive survey. Aust Health Rev 2005;29:94–104.

19. Vanhaecht K, Guezo J. SmartGroup on Clinical Pathways. J Integr Care Pathw 9:114–5.

20. Vanhaecht K, De Witte K, Sermeus W. The Care Process Organisation Triangle:A framework to better understand how clinical pathways work. J Integr Care Pathw 2007;11:1–8.

21. Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. Health Technol Assess 2004;8:iii–iv, 1–72.

22. Cunningham S, Logan C, Lockerbie L, et al. Effect of an integrated care pathway on acute asthma/wheeze in children attending hospital: cluster randomized trial. J Pediatr 2008;152:315–20.

23. Rotter T, Kugler J, Koch R, Gothe H, Twork S, van Oostrum JM, et al. A systematic review and meta-analysis of the effects of clinical pathways on length of stay, hospital costs and patient outcomes. BMC Health Serv Res 2008;8:265.

24. Schrijvers G, van Hoorn A, Huiskes N. The care pathway: concepts and theories: an introduction. Int J Integr Care 2012;12.

25. Piano Nazionale di Governo dei Tempi di Attesa - Relazione sullo Stato Sanitario del Paese. Available at: http://www.salute.gov.it/rssp/paginaParagrafoRssp.jsp?sezione=risposte&capitolo=valutazi one&id=2665.

26. Comoretto RI. Assessing healthcare pathways by means administrative data. Phd thesis, 2018 University of Milan-Bicocca.

27. World Health Organization. Everybody's business: strengthening health systems to improve health outcomes: WHO's framework for action. 2007 WHO, Geneva.

28. Lora A. An overview of the mental health system in Italy. Ann Ist Super Sanita 2009;45:5–16.

29. Munk-Jørgensen P. Has deinstitutionalization gone too far? Eur Arch Psychiatry Clin Neurosci 1999;249:136–43.

30. Salize HJ, Schanda H, Dressing H. From the hospital into the community and back again - a trend towards re-institutionalisation in mental health care? Int Rev Psychiatry 2008;20:527–34.

31. Manderscheid RW, Atay JE, Crider RA. Changing trends in state psychiatric hospital use from 2002 to 2005. Psychiatr Serv 2009;60:29–34.

32. Piccinelli M, Politi P, Barale F. Focus on psychiatry in Italy. Br J Psychiatry 2002;181:538–44.

33. The Mental Health System of the Lombardy Region [in Italian]. Milano, Italy, Regione Lombardia, 2009. Available at www.psychiatryonline.it/ital/SSM_LOM BARDIA.pdf.

34. Lora A, Barbato A, Cerati G, Erlicher A, Percudani M. The mental health system in Lombardy, Italy: access to services and patterns of care. Soc Psychiatry Psychiatr Epidemiol 2012;47:447–54.

35. Ministero della Salute. Progetto Obiettivo "Tutela Salute mentale 1998-2000" Available at: http://www.ministerosalute. it/imgs/C_17_pubblicazioni_558_allegato.pdf.

36. Centro Studi e Ricerche in Psichiatria. Una valutazione nazionale dei Centri di Salute Mentale Territoriali Italiani: il Progetto PROG-CSM Fase I - Report al Ministero della Salute (unpublished report). 2008 Torino.

37. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. Health Aff (Millwood) 2008;27:759-69.

38. Thornicroft G, Tansella M. The Mental Health Matrix: a Manual to Improve Services. 1999 University Press: Cambridge.

39. Lora A, Lesage A, Pathare S, Levav I. Information for mental health systems: an instrument for policy-making and system service quality. Epidemiol Psychiatr Sci 2017;26:383–94.

40. World Health Organization. Country Health Information Systems: A Review of the Current Situation and Trends. 2011 WHO: Geneva.

41. World Health Organization. The World Health Report 2001 – Mental Health: New Understanding, New Hope. 2001 WHO: Geneva.

42. Emmerson B, Frost A, Fawcett L, Ballantyne E, Ward W, Catts S. Do clinical pathways really improve clinical performance in mental health settings? Australas Psychiatry 2006;14:395–8.

43. Emmerson B, Fawcett L, Frost A, Lacey M, Todd C, Powell J. A tale of three pathways: the experience of RBWH Mental Health. Australas Psychiatry 2004;12:256–60.

44. Jones A. Implementation of hospital care pathways for patients with schizophrenia. J Nurs Manag 2000;8:215–25.

45. Lock J. How clinical pathways can be useful. An example of a clinical pathway for the treatment of anorexia nervosa in adolescents. Child Adolesc Psychiatr Clin N Am 1999; 4: 331–40.

46. Panella M, Demarchi ML, Carnevale L, et al. The management of schizophrenia through clinical pathways. Value Health 2006; 9: A318.

47. Rayner L. Language, therapeutic relationships and individualized care: addressing these issues in mental health care pathways. J Psychiatr Ment Health Nurs 2005;12:481–7.

48. Wilson A, Tobin M, Ponzio V, et al. Developing a clinical pathway in depression: sharing our experience. Australas Psychiatry 1997; 7: 17–9.

49. Reilly J, Newton R, Dowling R. Implementation of a first presentation psychosis clinical pathway in an area mental health service: the trials of a continuing quality improvement process. Australas Psychiatry 2007;15:14–8.

50. Lora A, Conti V, Leoni O, Rivolta AL. Adequacy of treatment for patients with schizophrenia spectrum disorders and affective disorders in Lombardy, Italy. Psychiatr Serv 2011;62:1079–84.

51. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, et al. The quality of health care delivered to adults in the United States. N Engl J Med 2003;348:2635–45.

52. Institute of Medicine (US) Committee on Crossing the Quality Chasm: Adaptation to Mental Health and Addictive Disorders. Improving the Quality of Health Care for Mental and Substance-Use Conditions: Quality Chasm Series. Washington (DC): National Academies Press (US); 2006.

53. Lora A, Monzani E, Ibrahim B, Soranna D, Corrao G. Routine quality care assessment of schizophrenic disorders using information systems. Int J Qual Health Care 2018;30:157.

54. Regione Lombardia. La qualità della cura nei disturbi mentali gravi. 2013 Milano.

55. Lora A, Cosentino U, Gandini A, et al. Which community care for patients with schizophrenic disorders? Packages of Care provided by Departments of Mental Health in Lombardy (Italy). Epidemiologia e Psichiatria Sociale, 2007;16,4:330-238.

56. Bramesfeld A, Wensing M, Bartels P, Bobzin H, Grenier C, Heugren M, et al. Mandatory national quality improvement systems using indicators: An initial assessment in Europe and Israel. Health Policy 2016;120:1256–69.

57. Saraceno B. Mental health systems research is urgently needed. Int J Ment Health Syst 2007;1:2.

58. Organization for Economic Co-operation and Development. FOCUS ON HEALTH – Making Mental Health Count. 2014 Available at: http://www.oecd. org/els/health-systems/Focus-on-Health-Making-Mental- Health-Count.pdf.

59. Braithwaite J, Hibbert P, Blakely B, Plumb J, Hannaford N, Long JC, et al. Health system frameworks and performance indicators in eight countries: A comparative international analysis. SAGE Open Med 2017;5:2050312116686516.

60. Perry M, Drasković I, van Achterberg T, et al. Development and validation of quality indicators for dementia diagnosis and management in a primary care setting. J Am Geriatr Soc 2010;58(3):557-63.

61. de Beurs E, Warmerdam EH, Oudejans SCC, Spits M, Dingemanse P, de Graaf SDD, et al. Treatment Outcome, Duration, and Costs: A Comparison of Performance Indicators Using Data from Eight Mental Health Care Providers in The Netherlands. Adm Policy Ment Health 2018;45:212–23.

62. Smith M, Butler A, Lesage A, et al. A Comparison of Mental Health Performance Indicators in Canada. International Journal of Population Data Science 2018;3(2):083.

63. Corrao G, Rea F, Di Martino M, Lallo A, Davoli M, DE Palma R, et al. Effectiveness of adherence to recommended clinical examinations of diabetic patients in preventing diabetes-related hospitalizations. Int J Qual Health Care 2018;

64. Conferenza Unificata Stato-Regioni. Definizione dei percorsi di cura da attivare nei Dipartimenti di Salute Mentale per i disturbi schizofrenici, i disturbi dell'umore e i disturbi gravi di personalità. 2014.

65. Ragazzo, C. Regione Lombardia capofila nel File F. Giornale Italiano di Health Technology Assessment 2009;2:119-126.

66. Corrao G, Mancia G. Generating evidence from computerized healthcare utilization databases. Hypertension 2015;65:490–8.

67. Corrao G, Ibrahim B, Nicotra F, Soranna D, Merlino L, Catapano AL, et al. Statins and the risk of diabetes: evidence from a large population-based cohort study. Diabetes Care 2014;37:2225–32.

68. Arfè A, Corrao G. Tutorial: strategies addressing detection bias were reviewed and implemented for investigating the statins-diabetes association. J Clin Epidemiol 2015;68:480–8.

69. Schneeweiss S, Avorn J. A review of uses of health care utilization databases for epidemiologic research on therapeutics. J Clin Epidemiol 2005;58:323–37.

70. Corrao G, Parodi A, Nicotra F, Zambon A, Merlino L, Cesana G, et al. Better compliance to antihypertensive medications reduces cardiovascular risk. J. Hypertens. 2011;29:610–8.

71. Giussani G, Franchi C, Messina P, Nobili A, Beghi E, EPIRES Group. Prevalence and incidence of epilepsy in a well-defined population of Northern Italy. Epilepsia 2014;55:1526–33.

72. Ingrasciotta Y, Giorgianni F, Marcianò I, Bolcato J, Pirolo R, Chinellato A, et al. Comparative Effectiveness of Biosimilar, Reference Product and Other Erythropoiesis-Stimulating Agents (ESAs) Still Covered by Patent in Chronic Kidney Disease and Cancer Patients: An Italian Population-Based Study. PLoS ONE 2016;11:e0155805.

73. Strom BL. Overview of Automated Databases in Pharmacoepidemiology. Textbook of Pharmacoepidemiology 2013;167–71.

74. Rosella LC, Lebenbaum M, Fitzpatrick T, O'Reilly D, Wang J, Booth GL, et al. Impact of diabetes on healthcare costs in a population-based cohort: a cost analysis. Diabet. Med. 2016;33:395–403.

75. Regione Lombardia. Giunta Regionale. Deliberazione n. X/2017 del 01.07.2014. Approvazione del documento Regole per l'accesso ai dati del datawarehouse di Regione Lombardia da parte di enti esterni. Available at: http://normativasan.servizirl.it/port/GetNormativaFile?fileName=4920_ACCESSO%20DA TAWAREHOUSE%20dgr%202017%201.7.2014.pdf.

76. Corrao G, Soranna D, Merlino L, Monzani E, Viganò C, Lora A. Do patterns of mental healthcare predict treatment failure in young people with schizophrenia? Evidence from an Italian population-based cohort study. BMJ Open 2015;5:e007140.

77. Suissa S. Immeasurable time bias in observational studies of drug effects on mortality. Am. J. Epidemiol. 2008;168:329–35.

78. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. Am. J. Epidemiol. 1991;133:144–53.

79. Marshall RJ, Jackson RT. Analysis of case-crossover designs. Stat Med 1993;12:2333–41.

80. Horwitz RI, Feinstein AR. The problem of «protopathic bias» in case-control studies. Am. J. Med. 1980;68:255–8.

81. Arfè A, Corrao G. The lag-time approach improved drug-outcome association estimates in presence of protopathic bias. J Clin Epidemiol 2016;78:101–7.

82. Regione Lombardia. DELIBERAZIONE N° XI / 491 Seduta del 02/08/2018.

83. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.

84. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.

85. Corrao G, Rea F, Di Martino M, De Palma R, Scondotto S, Fusco D, et al. Developing and validating a novel multisource comorbidity score from administrative data: a large population-based cohort study from Italy. BMJ Open 2017;7:e019503.

86. Marder SR. Monitoring treatment and managing adherence in schizophrenia. J Clin Psychiatry 2013;74:e21.

87. Pfammatter M, Junghan UM, Brenner HD. Efficacy of Psychological Therapy in Schizophrenia: Conclusions From Meta-analyses. Schizophr Bull 2006;32:S64–80.

88. Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Salanti G, et al. Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis. Lancet 2012;379:2063–71.

89. Pauly NJ, Talbert JC, Brown J. Low-Cost Generic Program Use by Medicare Beneficiaries: Implications for Medication Exposure Misclassification in Administrative Claims Data. J Manag Care Spec Pharm 2016;22:741–51.

90. Funk MJ, Landi SN. Misclassification in administrative claims data: quantifying the impact on treatment effect estimates. Curr Epidemiol Rep 2014;1:175–85.

91. Halpern MT, Khan ZM, Schmier JK, Burnier M, Caro JJ, Cramer J, et al. Recommendations for evaluating compliance and persistence with hypertension therapy using retrospective data. Hypertension 2006;47:1039–48.

92. Corrao G, Cantarutti A. Building reliable evidence from real-world data: Needs, methods, cautiousness and recommendations. Pulm Pharmacol Ther 2018;53:61–7.

93. Mueser KT, Bond GR, Drake RE, Resnick SG. Models of community care for severe mental illness: a review of research on case management. Schizophr Bull 1998;24:37–74.

94. Pincus HA, Page AEK, Druss B, Appelbaum PS, Gottlieb G, England MJ. Can psychiatry cross the quality chasm? Improving the quality of health care for mental and substance use conditions. Am J Psychiatry 2007;164:712–9.

95. World Health Organization. WHO-AIMS country reports 2015. Available at: http://www.who.int/mental_health/who_aims_country_reports/en/.

96. World Health Organization. Atlas: Mental Health Atlas, 2014. 2015 WHO: Geneva.

97. World Health Organization. Mental Health Systems in Selected Low- and Middle-Income Countries: a Cross National Analysis of 42 Countries using WHO-AIMS Data. 2009 WHO:Geneva.

98. World Health Organization. Mental Health Information Systems. 2005 WHO: Geneva.

99. World Health Organization. Monitoring and Evaluation of Mental Health Policies and Plans. 2007 WHO: Geneva.

100. World Health Organization. Monitoring the Building Blocks of Health Systems: a Handbook of Indicators and Their Measurement Strategies. 2010 WHO: Geneva.

101. Kahneman D. Thinking, Fast and Slow. 2011 Farrar, Straus and Giroux: New York.

102. World Health Organization. Design and Implementation of health Information Systems. 2000 WHO: Geneva.

103. World Health Organization. Organization of Services for Mental Health. 2003 WHO: Geneva.

104. Leginski WA, Croze C, Driggers J, et al. Data Standards for Mental Health Decision Support Systems. A Report of the Task Force to Revise the Data Content and System Guidelines of the Mental Health Statistics Improvement Program. 1989 U.S. Department of Health and Human Services: Washington, DC.

105. Australian Institute of Health and Welfare (AIHW). 2015 Mental Health Available at: http://www.aihw.gov.au/mental-health-data-cubes.

106. Programme for the Integration of Mental Health Data (PRIMHD). 2015 Mental Health Data. Available at: http://www.health.govt.nz/nz-healthstatistics/national-collections-and-surveys/collections/ primhd-mental-health-data.

107. Health and Social Care Information Centre (HSCIS). 2014 Mental Health Bulletin Annual Report from MHMDS Returns 2013–14. Available at: https://www.google.it/search?q=Health+and+Social+Care+Information+Centre+%282014%29.+Mental+Health+Bulletin+Annual+Report+from+MHMDS+Returns+2013+-+14+Mental+Health+Bulletin+Annual+Report+from+MHMDS+Returns+2013-&ie=utf-8&oe=utf-8&gws_rd=cr&ei=xIhtVvXbBoj5UKexoPAK.

108. IHE, Institute of Health Economics. 2007. Mental Health Economic Statistics: In Your Pocket ISBN (print): 978-1- 897443-07-1. Available at: http://www.ihe.ca/publications/mental-healtheconomic-statistics-in-your-pocket.

109. Italian Ministry of Health. 2001 The Italian Mental Health Information System (SISM). Available at: http://www.nsis.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=3012&area=sistemaInformativo&menu=mentale.

110. Italian Ministry of Health. 2001 Functional specifications for the Italian Mental Health Information System (SISM). Available at: http://www.salute.gov.it/imgs/C_17_pagineAree_3014_listaFile_itemName_13_file.pdf.

Appendix I

Mental Health Information Systems

Improving the quality of care is a leading priority for national health systems, consistent with the aim of improving population health, while maintaining the sustainability of the whole health system [37], especially for the mental health system, being composed by a complex network of different types of community mental health teams and a wide range of treatment, rehabilitation, employment and residential care facilities, currently operating in the community. Thus, persuaded that what "gets measured gets done", World Health Organization (WHO) included "monitoring community mental health" through strengthening information systems, as one of the ten recommendations that can make a difference in mental health care [41]. Therefore, reliable and timely health information, being the foundation for effective health services management and public health action [40], is needed in the mental health system by all stakeholders.

Constrained by out-dated tradition and a deficit in training, mental health trails behind the general health system in collecting and analysing standard information [52,94–97].

Mental Health Information Systems (MHIS)

WHO has defined a Mental Health Information System (MHIS) as "a sustainable system for collecting, processing, analysing, disseminating and using information about mental health services and the mental health needs of the population it serves" [98], thus being one of the essential elements for the functioning of an healthcare system, just like financing, governance, human resources and service delivery [40,99,100]. The implementation of an effective MHIS can lead to both more effective governance and service improvement of the health system [101]. Goals, providers, consumers of, and information to be collected by, a MHIS were topic of debate in the last decades.

At the national system level, an MHIS aims to monitor services delivering mental health care and improve their effectiveness and efficacy through better management [102], and the list of stakeholders interested includes not only policy-makers, legislators, planners, managers, but also clinicians, users, patients' families and advocacy non-governmental organisations, that are keen to monitor the quality of care [39].

According to WHO [103], the MHIS should be able to collect information from all formal mental health services (from childhood to elderly), from substance use health services (that often remain separated, and not linkable, for privacy regulations) and from mental health services delivered at the primary care level. Thus, a MHIS collects demographic information and diagnoses of all patients attending mental health services and records all treatments provided to them (outpatient and home visits, day treatment attendance, admissions to general hospital and residential facilities). Furthermore, the MHIS should be also interconnected with the other healthcare utilization (HCU) databases in order to have access to information regarding the whole mental health patients' healthcare consumption.

In a recent review on country health information systems, the WHO indicated which information should be collected to monitor the building blocks of a country's health system [40] and, also considering the question specifically framed by Leginski regarding which information should be collected by a MHIS ("Who receives what services from whom, at what cost and with what effect?" [104]), the minimum information set to be included in database for monitoring mental healthcare includes information:

- At patient level, such as socio-demographic information (e.g., gender, age, marital status, years of education, working condition, family arrangement), history of past contacts with mental health services, ICD-10 diagnoses and physical/psychiatric comorbidities.
- At activity level (e.g., mental health services and treatments provided to mental health patients)
- At outpatient level (i.e., types of interventions delivered and mental health professionals involved)
- At day-care level (e.g., information regarding the sessions of day-care treatments in day-care facilities)
- At inpatient level (i.e., information regarding admissions residential or hospital facilities, such as dates of admission and discharge, voluntary or compulsory status of the recovery, etc.)
- At facility level (i.e., facilities' characteristics such as the personnel, professionals)

Some countries in the last years have incorporated these indications and have established, at a national level, and have established the mandatory collection and communication of a minimum set of

information regarding the services delivered by their own national mental health systems, as was the case in Australia [105], New Zealand [106], UK [107], Canada [108] and Italy [109].

The Italian "Sistema informativo di Salute Mentale" (SISM)

In Italy, the new Healthcare Information System (HIS) represents the reference tool for the quality, efficiency and appropriateness assessment of the National Health Service (NHS), through the availability of information which, for completeness and consistency, supports the Regions and the Ministry of Health (MoH) in the exercise of its functions and, in particular, in its role of guaranteeing the application of the Essential Levels of Assistance by the Regional health services.

The HIS finds its legal basis in the Article 87 of the Law n. 388 of 23rd December 2000 ("Provisions for the preparation of the annual and multi-year financial statements of the State, Financial Law 2001"). Recently the evolution guidelines of the HIS were updated by the Agreement between the State and the italian Regions of July 2016.

The HIS implementation is inserted in a framework aimed at monitoring the balance between cots and quality of the delivered healthcare services. The correct design and development of the HIS required the definition of a common set of information contents in order to allow the interconnection of data of information systems between the regional and national level. Therefore, information regarding the various care areas was identified and the rules for the correct supply of information flows were defined, in order to allow the collection of a homogeneous set of information in the NSIS.

Today, the HIS represents the most important health database at national level, aimed at adequately supporting the Regions and the MoH in planning, coordinating and delivering healthcare services to italian citizens.

The HIS, according to a healthcare pathway logic, has the aim of collecting the information related to the contacts of the single citizen with the different facilities and services of the NHS. Indeed, HIS collects individual data, produced at regional level, related to the provision of healthcare. This set of information also allows the analysis of healthcare pathways provided to patients, the evaluation of the quality of delivered services and the assessment of strengths and weaknesses of the regional health systems [6].

In the HIS' framework, the Italian Mental Health Information System (SISM) was established by a decree of the italian MoH on 15th October 2010, with the aim of collecting information regarding healthcare services and social interventions provided by the NHS to patients affected by mental health diseases and their families. Therefore, data on mental health services in Italy are routinely collected

by this national specific automated system concerning psychiatric care provided by the regional Departments of mental health accredited by the NHS. The SISM is implemented at a region-wide level, i.e., every six months the regional mental health information systems must send to the HIS data on the provided psychiatric care, with a maximum tolerated delay period of sixty days after the end of the survey semester. Any corrections or additions to the transmitted data can be made, but within the month following the sending deadline.

In order to standardize data collection by regional information systems, a document containing the functional specifications was prepared. It contains the characteristics and supply rules for the correct harmonization of the information contents, allowing information to be uniformly encoded by using for each variable the same names, values and formats [109,110].

The SISM gathers information from all Departments of mental health and from private day care and residential facilities and it collects demographic information and the ICD-10, or ICD-9-CM, diagnoses of all patients attending mental health services and records all patients' care episodes in any treatment setting (outpatient and home visits, day treatment attendance, admissions to general hospital and residential facilities). Details of healthcare utilization databases use in the field of mental health research have been reported in more detail elsewhere [76].

Appendix II

DISEASES	ICD-10 codes (for Lombardy Region only)
Schizophrenic spectrum disorder	
Schizophrenia	F20.*
Schizotypal disorder	F21.*
Delusional disorders	F22.*
Brief psychotic disorder	F23.*
Shared psychotic disorder	F24.*
Schizoaffective disorders	F25.*
Other psychotic disorder not due to a substance or known physiological condition	F28.*
Unspecified psychosis not due to a substance or known physiological condition	F29.*
Major depressive disorder	
Depressive episode	F32.*
Recurrent depressive disorder	F33.*
Dysthymia	F34.1
Other persistent mood (affective) disorders	F34.8
Persistent mood (affective) disorder, unspecified	F34.9
Other recurrent mood (affective) disorders	F38.1
Other specified mood (affective) disorders	F38.8
Unspecified mood (affective) disorder	F39
Post-traumatic stress disorder	F43.1
Adjustment disorders	F43.2
Bipolar disorder	
Manic episode	F30.*
Bipolar affective disorder	F31.*
Cyclothymia	F34.0
Other single mood (affective) disorders	F38.0
Personality disorder	
Specific personality disorders	F60.*
Mixed and other personality disorders	F61

DISEASES	ICD-9 CM codes
Schizophrenic spectrum disorder	
Schizophrenic disorders	295.*
Delusional disorders	297.*
Reactive confusion	298.2
Acute paranoid reaction	298.3

Psychogenic paranoid psychosis	298.4
Other and unspecified reactive psychosis	298.8
Unspecified psychosis	298.9
Major depressive disorder	
Major depressive disorder, single episode	296.2
Major depressive disorder, recurrent episode	296.3
Atypical depressive disorder	296.82
Unspecified episodic mood disorder	296.90
Depressive type psychosis	298.0
Dysthymic disorder	300.4
Adjustment disorder with depressed mood	309.0
Prolonged depressive reaction	309.1
Depressive disorder	311.*
Bipolar disorder	
Bipolar I disorder, single manic episode	296.0
Manic disorder, recurrent episode	296.1
Bipolar I disorder, most recent episode (or current) manic	296.4
Bipolar I disorder, most recent episode (or current) depressed	296.5
Bipolar I disorder, most recent episode (or current) mixed	296.6
Bipolar I disorder, most recent episode (or current) unspecified	296.7
Bipolar disorder, unspecified	296.80
Atypical manic disorder	296.81
Other	296.89
Other specified episodic mood disorder	296.99
Excitative type psychosis	298.1
Personality disorder	
Personality disorders	301.*
Dementia	290.x, 294.x, 331.x, 334.x, 335.x
Parkinson's disease	3220.x
Cancer	140.x-208.x
Traumatic injuries	V01-V09
Hyperthyroidism, hyperparathyroidism	242.x, 252.x
Cerebrovascular diseases	430.x – 438.

DRUGS	ATC codes
Antipsychotic agents	N05A (excluded N05AN)
Antidepressant agents	N06A
Mood Stabilizers	N05AN (Lithium) ; N05AH03 , N05AH04 , N05AX12 (other Antipsychotics) ; N03AG01 (Valproate) ; N03AF01 (Carbamazepine) ; N03AX09 (Lamotrigine)
Hypoglycemic drugs	A10
Antihypertensives	C02, C03, C07, C08, C09
Statins	C10AA

Corticosteroids	H02AB
Antineoplastic agents	L01
Anti-thyroid preparations	H03B

OUTPATIENT SERVICES	**Italian Outpatient Codes**
Mental healthcare related outpatient interventions	94.12.1, 94.01.1, 94.08.3, 94.08.4, 94.08.5, 94.08.6, 94.09, 94.19.1, 94.3, 94.42, 94.44

OUTPATIENT VISITS (delivered by territorial and day-care facilities of DMHs)	**Italian Mental Health Information system codes**
Psychiatric visits	01
Clinical psychological interviews	02
Interviews	03
Consultations	04
Medical-legal verification	05
Standardized assessments using tests	06
Individual psychotherapy	07
Couple psychotherapy	08
Family psychotherapy	09
Group psychotherapy	10
Drugs administration	11
Interviews with family members	12
(Individual) informative and psycho-educational interventions aimed at the family	13
(Group) informative and psycho-educational interventions aimed at the family	14
Meetings	15
(Individual) interventions on basic skills	16
(Group) interventions on basic skills	17
(Individual) re-socialization interventions	18
(Group) re-socialization interventions	19
Healthcare facilities stays	20
(Individual) expressive, practical manual and motor interventions	21
(Group) expressive, practical manual and motor interventions	22
Work training	23
Support interventions	24
Interventions for administrative and social problems	25
Network interventions	26

Clinical pathways in patients with severe mental disorders in Italy
The QUADIM project