AstraZeneca

| PASS Study Report | |
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# Objective assessment of metabolic monitoring in patients treated with Seroquel® or Seroquel® XL/XR (quetiapine fumarate): use of IMS Disease Analyzer to assess physician behaviour in the UK and Germany

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**Approved by:** Robert Steven Brody — Principal Investigator

12 December 2013 — Date

# PASS INFORMATION

| | |
|---|---|
| **Title** | **Objective assessment of metabolic monitoring in patients treated with Seroquel® or Seroquel® XL/XR (quetiapine fumarate): use of IMS Disease Analyzer to assess physician behaviour in the UK and Germany** |
| **Version identifier of the final study report** | V5.0 |
| **Date of last version of the final study report** | 10 December 2013 |
| **EU PAS register number** | ENCEPP/SDPP/3292 |
| **Active substance** | Quetiapine fumarate<br>Antipsychotic<br>ATC: N05AH04 |
| **Medicinal product** | Seroquel® tablets and<br>Seroquel® extended release tablets (Seroquel® XL/XR) |
| **Product reference** | **Seroquel®:**<br>25 mg: PL 17901/0038<br>100mg: PL 17901/0039<br>150 mg: PL 17901/0041<br>200 mg: PL 17901/0040<br>300 mg: PL 17901/0088<br><br>**Seroquel® XL /XR**<br>50 mg: PL 17901/0249<br>150 mg: PL 17901/0259<br>200 mg: PL 17901/0250<br>300 mg: PL 17901/0251<br>400 mg: PL 17901/0252 |
| **Procedure number** | **NL/H/0156/001-012/PAC**<br>Case number 333147 |
| **Marketing authorisation holder(s)** | **AstraZeneca UK Ltd**<br>600 Capability Green<br>Luton<br>LU1 3LU<br>United Kingdom |
| **Joint PASS** | No |

| | |
|---|---|
| **Research question and objectives** | Educational material was circulated to General Practitioners in the UK and Psychiatrists and Neurologists in Germany on the recommendations included in the SmPCs for metabolic monitoring of patients treated with Seroquel® and Seroquel® XL/XR (quetiapine fumarate).<br>This study's primary objective is to document whether physicians in the UK and Germany perform monitoring of patients treated with quetiapine fumarate (using diagnoses, lab tests, evaluation and measurement and counselling as described below) and to document the frequency range among physicians within the study sample on the following metabolic monitoring parameters:<br>• recording patient weight at treatment initiation,<br>• monitoring of weight of patients receiving on-going treatment,<br>• counselling patients on healthy eating, exercise and healthy lifestyle improvements<br>• monitoring for elevated cholesterol,<br>• monitoring for signs and symptoms of hyperglycaemia,<br>• monitoring of blood glucose in patients with diabetes mellitus, and<br>• monitoring of blood glucose in patients with risk factors for diabetes mellitus for worsening of glycaemic control |
| **Country(-ies) of study** | United Kingdom and Germany |
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# TABLE OF CONTENTS PAGE

# LIST OF TABLES

# LIST OF FIGURES

# 1. ABSTRACT


## Title

Objective assessment of metabolic monitoring in patients treated with Seroquel® or Seroquel XL/XR® (quetiapine fumarate): use of IMS Disease Analyzer to assess physician behaviour in the UK and Germany

Date: 10 December 2013

Main author: Robert S. Brody, AstraZeneca Pharmaceuticals LP

***Keywords***

Quetiapine, metabolic, monitoring, hyperglycaemia, weight, lipids, risk minimisation.

## Rationale and background

Objective assessment of physician conduct of metabolic monitoring of patients treated with quetiapine using electronic medical record (EMR) data.

## Research question and objective

Whether physicians in the UK and Germany monitor patients treated with quetiapine for metabolic risk factors.

## Study design / Setting

EMR data was used in a cross-sectional assessment of activities of UK GPs and German psychiatrists and neurologists regarding patient management following the distribution of metabolic educational materials on quetiapine.

## Subjects and study size, including dropouts

Numbers of practices and eligible patients:

- 93 UK GP practices (887 patients)
- 42 Psychiatry and 145 Neurology practices in Germany (6153 patients)

## Variables and data sources

Outcomes included: weight measurement; cholesterol monitoring; signs and symptoms (s/s) of hyperglycaemia; lifestyle counselling. Key patient variables included: demographics; BMI; prior monitoring activity; antipsychotic and antidepressant prescriptions; prior relevant diagnoses.

## Results

16-67% of UK GP practices and $\leq$ 2% of psychiatry or neurology practices in Germany monitored $\geq$50% of their relevant patients. The highest prevalence of monitoring by UK GPs was for s/s of hyperglycaemia in patients with diabetes (50.6% of eligible patients). The

lowest level of monitoring by UK GPs was assessment of lipids in 27.7% of eligible patients. Other monitoring by UK GPs was performed in 31%-39% of eligible patients. Higher levels of monitoring by GPs were found for each monitoring activity in the 12 months prior to the study period, when monitoring was performed in 45%-81% of eligible patients.

**Conclusions**

Use of the IMS Disease Analyzer database to assess the performance of monitoring by GPs in the UK and specialty physicians in Germany was affected by the completeness of the updates to the database (limiting length of the study period to 7 months in duration) and its application to a comprehensive interdisciplinary (*shared care approach* to) measurement of outcomes. The findings confirm that monitoring of metabolic parameters is being performed to a varying degree by General Practitioners in the UK. Metabolic monitoring was rarely documented among psychiatrists and neurologists in Germany. Following a *shared care approach,* specialists may be interacting with GPs regarding the need for continuing care including metabolic monitoring but this information appears not to be accessible through the EMR.

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Co-Investigator: Soheil Chavoshi, MS, Regional Engagement Lead, Payer & Real World Evidence

Co-Investigator: Dhaval Desai MD, Medical Science Director, Global Clinical Development

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# 2. LIST OF ABBREVIATIONS

| Abbreviation | Full Description |
|---|---|
| ATC | Anatomical Classification system of pharmaceutical products developed and maintained by the European Pharmaceutical Marketing Research Association |
| AZ | AstraZeneca |
| BMI | Body Mass Index |
| CI | Confidence Interval |
| CNS | Central Nervous System |
| CVD | Cardiovascular Disease |
| DA | IMS Disease Analyzer database |
| EMR | Electronic Medical Record |
| ENCePP | European Network of Centres for Pharmacoepidemiology and Pharmacovigilance |
| EphMRA | European Pharmaceutical Market Research Association |
| EU | European Union |
| GP | General Practitioner |
| HDL | High-Density Lipoprotein |
| ICD-10 | International Classification of Diseases - 10 |
| ISEAC | Independent Scientific and Ethical Advisory Committee |
| LDL | Low-Density Lipoprotein |
| LQ | Lower Quartile |
| MDD | Major depressive disorder |
| MEB | Medicines Evaluation Board |
| NICE | National Institute for Health & Clinical Excellence |
| OR | Odds Ratio |
| QOF | The Quality and Outcomes Framework (specific quality measurement in the UK) |
| quetiapine | Inclusive of quetiapine fumarate, Seroquel®, and Seroquel® XL/XR |
| SAP | Statistical Analysis Plan |
| SAS | Statistical Analysis System (Statistical software program) |
| SD | Standard Deviation |
| SmPC | Summary of Product characteristics |
| SOP | Standard Operating Procedures |
| s/s | Signs and Symptoms |
| UK | United Kingdom |
| UQ | Upper Quartile |

# 3. INVESTIGATORS

- Primary Investigator: Robert S Brody, MPH, Director Global Epidemiology, Payer & Real World Evidence[1]

- Co-Investigator: Soheil Chavoshi, MS, Regional Engagement Lead, Payer & Real World Evidence[1]
- Co-Investigator: Dhaval Desai MD, Medical Science Director, Global Clinical Development[1]

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# 4. OTHER RESPONSIBLE PARTIES

IMSWorld Publications Limited (London, United Kingdom) - provided assistance in study preparation, data extraction and aggregation, performed analytics, and assisted with interpretation of the study results.

# 5. MILESTONES

**Table 1 Key study milestones and planned dates of completion**

| Milestone | Planned date | Actual date | Comments |
|---|---|---|---|
| Acceptance of the post approval commitment (Procedure NL/H/0156-/001-012/IB/087) | 03 January 2013 | 03 January 2013 | |
| Registration in the EU PAS register | 31 December 2012 | 31 January 2013 | |
| Finalisation of Statistical Analysis Plan | 03 April 2013 | 05 June 2013 | |
| Start of data collection | 04 April 2013 | 04 April 2013 | Date when data was extracted from the EMR database. |
| End of data collection | 20 June 2013 | 20 June 2013 | Final cleaned dataset prepared for analysis |
| Completion of analyses | 14 June 2013 | 02 July 2013 | |
| ISEAC Approval | 30 July 2013 | 19 September 2013 | This approval was required for analyses conducted using the Disease Analyzer for UK only.<br>Final approval was granted in September 2013 due to additional information requested by the ISEAC review committee. |
| Final report of study results | 31 July 2013 | 10 December 2013 | |

# 6. RATIONALE AND BACKGROUND

AstraZeneca's (AZ's) Seroquel® and Seroquel® XL/XR are indicated for the treatment of schizophrenia, bipolar disorder including manic and depressive episodes, preventing recurrence in maintenance treatment of bipolar disorder as monotherapy or in combination with mood stabilizers. In addition, Seroquel® XL/XR is indicated for prevention of relapse in stable schizophrenic patients who have been maintained on Seroquel® XL/XR; and as add-on treatment for major depressive disorder in patients with a sub-optimal response to antidepressant monotherapy [Seroquel IR composite 2013, Seroquel XR MR composite 2013].

In early 2012, AZ circulated educational materials on the importance of metabolic monitoring of quetiapine fumarate patients to General Practitioners (GPs) in the UK, Psychiatrists and

Neurologists in Germany. These materials were developed in agreement with the Medicines Evaluation Board (MEB), and the relevant local health authorities, to inform practitioners prescribing Seroquel® and Seroquel® XL/XR of labelling revisions recommending monitoring of weight at initiation of treatment and for patients receiving ongoing treatment, monitoring for signs and symptoms of hyperglycaemia, monitoring for hyperlipidaemia, monitoring of blood glucose in patients with diabetes mellitus, and monitoring of blood glucose in patients with risk factors for diabetes mellitus for indicators of worsening glycaemic control. Following EU risk management requirements, AZ needs to assess the effectiveness of these educational materials regarding recommendations for metabolic monitoring included in the Summary of Product characteristics (SmPC) for Seroquel® and Seroquel® XL/XR [SmPC 2013].

This study is one component of an assessment of the effectiveness of risk minimisation activities that included the distribution of educational materials to physicians by AZ. The assessment includes a dual-evidentiary approach (through an objective assessment of outcome indicators for metabolic monitoring determined from electronic medical records (EMR) as proposed in this study, through self-reported physician activities regarding monitoring evaluated in a separate physician survey and through process indicators, i.e., as determined by the receipt of educational materials, through responses to the above mentioned survey). The study was recognized by the MEB as exploratory and was considered a means to arrive at an objective assessment of physician monitoring activity without the subjectivity that might be introduced in a physician survey.

Metabolic abnormalities occur frequently in patients with severe mental illness and affective disorders and the contributions that lifestyle, genetic factors and treatment with antipsychotic drugs play in contributing to increased health risks are of concern. Commonly used pharmacologic treatments for these illnesses may intensify the propensity for development of abnormalities in metabolic parameters [Newcomer 2006]. Guidelines from UK National Institute for Health and Clinical Excellence (NICE) on the management of schizophrenia [NICE 2009] and bipolar disorder [NICE 2006], both of which had been issued several years before the SEROQUEL XR educational materials were distributed, recommend stringent monitoring of metabolic status and cardiovascular risk factors in psychiatric patients receiving antipsychotic drugs. The NICE guidelines recognize the impact of physical co- morbidity in these mental disorders, as well as the scarcity of high-quality research in this field. For patients with a diagnosis of either bipolar disorder or schizophrenia, the guidelines recommend that an annual physical health check is part of the role of primary care.

The majority of GPs in the UK regard themselves as involved in the monitoring and treatment of physical illness and prescribing for mental illness [NICE 2013]. In the UK, NICE provides administrative oversight of the Quality and Outcomes Framework (QOF), which contains groups of indicators, against which general practices score points according to their level of achievement. GPs as members of primary care teams receive an incentive to perform a physical health check and specific assessments for people with a diagnosis of a serious mental illness. As part of the QOF, NICE's role focuses on the clinical and public health domains in the QOF. The following measures are relevant to the practices and patients of UK GPs that were included in the study:

- The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of BMI in the preceding 15 months
- The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of blood pressure in the preceding 15 months
- The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses aged over 40 whose blood cholesterol level has been recorded in the preceding 15 months.
- The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses whose blood glucose level has been recorded in the preceding 15 months

The German guidelines with regard to metabolic monitoring of patients taking antipsychotics were adopted several years before the SEROQUEL XR educational materials were distributed following the recommendations of a consensus conference on Antipsychotic Drugs and Obesity and Diabetes [ADA 2004]. Metabolic investigations for patients treated with antipsychotics include the following assessments at initiation of treatment:

- Body weight (BMI)
- Waist circumference
- Fasting serum glucose
- Fasting blood lipids
- Blood pressure

These assessments are recommended to be repeated during the first four weeks and during the first 3 months of treatment. Weight and waist circumference (as well as blood pressure) are recommended to be measured on an ongoing basis at an interval of 3 months. Fasting serum glucose and blood lipids (a measure of monitoring cholesterol) are recommended to be repeated on an annual basis.

Literature reports from different sources in the US and the EU suggest that there is substantial variation in physician activities involving metabolic monitoring and in most reports a less than optimal proportion of patients are found to have metabolic monitoring ofmodifiable cardiovascular risk factors including lipids and serum glucose parameters [De Hert].

Patients with these severe mental illness have been recognized to exhibit significant metabolic abnormalities at the time of their initial episode of illness and when first being treated [ENCePP 2013]. Given the long-term impact of untreated metabolic risk factors on cardiovascular mortality, especially in populations with a substantially higher risk of death due to cardiovascular disease, the importance of prevention efforts in primary and secondary care to avoid a greater burden on morbidity and mortality in this population is recognised. These observations provide the background and basis for this evaluation to provide an objective assessment of the monitoring activities of physicians who prescribed Seroquel® to patients in two EU countries (representing primary care in the UK and office-based specialist care in Germany) and the impact upon patients.

# 7. RESEARCH QUESTION AND OBJECTIVES

This study supported activities to assess the effectiveness of educational materials in scope of the EU Risk Management Plan and Summary of Product Characteristics (SmPC) for Seroquel® (quetiapine fumarate) tablets and Seroquel® XL/XR extended release tablets with respect to evaluation and monitoring for hyperglycaemia and other metabolic parameters for patients treated with these medications. One component of the assessment proposed in this program involved the evaluation of outcome indicators (evaluation and monitoring of metabolic parameters) by physicians prescribing quetiapine fumarate. This study utilised an Electronic Medical Records (EMR) database as a potential means to assess the monitoring of patients.

The primary objective of this study was to document whether physicians in the UK and Germany performed monitoring of patients treated with Seroquel® or Seroquel® XL/XR or quetiapine fumarate (using lab tests, evaluation and measurement and counselling as described below) by recording the frequency range among physicians within the study sample on the following metabolic monitoring parameters:

- recording patient weight at initiation of treatment,
- monitoring of weight of patients receiving on-going treatment,
- monitoring for elevated cholesterol,
- monitoring for signs and symptoms of hyperglycaemia,
- monitoring of blood glucose in patients with diabetes mellitus,
- monitoring of blood glucose in patients with risk factors for diabetes mellitus for worsening of glycaemic control, and
- counselling patients on healthy eating, exercise and healthy lifestyle improvements.

In order to understand the impact upon patients, the proportion of patients monitored for each of the metabolic parameters listed above was also documented.

# 8. AMENDMENTS AND UPDATES

| Number | Date | Section of study protocol | Amendment or update | Reason |
|---|---|---|---|---|
| 1 | 05 June 2013 | 5.1 | Update to Statistical Analysis Plan (SAP): Modified German specialities to be studied (changed from GPs and psychiatrists to neurologists and psychiatrists in accordance with the speciality groups in Germany who were sent the metabolic educational materials) | Due to confirmation of specialists who were actually sent the educational materials; the confirmation was received after protocol finalisation |
| 2 | 05 June 2013 | 2.1 | Update to SAP: Primary objective was outlined in the protocol around "physicians" and we conducted the analysis at "practice" level | A data limitation within the database used where the level of information available around a patient's medical management was limited to the practice level (and not available for individual physicians) due to privacy regulations in the studied countries |
| 3 | 05 June 2013 | 5.2 | Update to SAP: The date for the qualifying diagnosis was to occur during the 12 months prior to or during the study period. This was extended to include any point in prior history | This change was intended to accommodate physician documentation practice in EMR as only initial diagnoses are recorded and confirmation of active disease is not. |
| 4 | 05 June 2013 | 9.1 | Update to SAP: Multivariate analysis modelling (including additional potential confounders were studied: prior use of antidepressants, history of anxiety or psychosis, diagnosis of metabolic disorder, prior testing of blood glucose, and smoking status) | To evaluate potential confounders and variables that were considered potential explanatory factors, described in the protocol, as possibly influencing the performance of metabolic monitoring |

# 9. RESEARCH METHODS

## 9.1 Study design

This was a cross-sectional assessment of retrospectively collected physician medical management activities related to assessments and performance of metabolic tests recorded in electronic medical record data during encounters with patients in the UK and in Germany following the distribution of metabolic educational materials on Seroquel®. Using the EMR

data, the study informed about period prevalence of recorded monitoring performed by these select physician specialities.

The study design was intended to provide a pragmatic approach to describe the monitoring of patients around the following key metabolic monitoring messages communicated through the distributed educational materials which recommended: monitoring of weight, lipids, metabolic risk concerning signs of hyperglycaemia and changes in glucose for patients with diabetes mellitus or with risk factors for diabetes mellitus. In addition, documentation of the provision of counselling for exercise, nutrition and maintenance of a healthy lifestyle was added as an independent, but related assessment variable.

EMRs are a source of data that include records of evaluation and management activities of physicians in the performance of routine practice including subjective evaluations, objective testing, assessment and planning as part of the general medical care and specialised care provided to patients. There are limitations to evaluation of EMR data, as with any retrospective data not collected for research purposes, such as it cannot confirm undocumented conversations between the patient and practitioner and does not include insight into free text notes, which are shielded for privacy. The assessment of medical monitoring of the patients of interest in a retrospective manner using EMR data however was expected to be more objective than information obtained via surveying physicians about the medical management provided to patients that were undergoing treatment with Seroquel® or Seroquel® XL/XR (quetiapine fumarate), because it used data entered contemporaneously into the records rather than retrospective recall of monitoring behaviour.

The study was conducted in accordance with applicable regulatory requirements, and other applicable guidelines, such as subject privacy requirements and the guiding principles of the Declaration of Helsinki. Consistent with the Declaration's guidelines, the research protocol is publicly available on the ENCePP (European Network of Centres for Pharmacoepidemiology and Pharmacovigilance) website [Office for National Statistics 2011]. A report on study results, including the results of a companion primary research study based upon physician self-reported behaviour regarding metabolic monitoring of patients treated with Seroquel in selected countries in the European Union (EU) will also be made publicly available via the ENCePP website. The Independent Scientific and Ethical Advisory Committee (ISEAC) of the IMS Disease Analyzer Database has reviewed and approved the study concept and design.

## 9.2 Setting

The educational materials were distributed to General Practitioners (GPs) in the UK and to psychiatrists and neurologists in Germany. Therefore, the study evaluated GPs in the UK and office-based psychiatrists and neurologists in Germany. The retrospective observation periods were: from 11 January to 31 July 2012 following the distribution of educational materials to GPs in the UK, and from 13 February to 31 August 2012 following distribution of educational materials to psychiatrists and neurologists in Germany. Patient data was extracted based on the patient eligibility criteria specified in Section 9.3.

## 9.3 Subjects

In order to be considered for the study, patients had to fulfil all of the following inclusion criteria and none of the exclusion criteria.

### 9.3.1 Study inclusion criteria

1. Aged ≥ 18 years as of January 1, 2012. In accordance with privacy policies, the database calculated patient age as of the start of each calendar year.

2. Had active diagnosis, based on ICD-10 diagnosis codes, of one or more of the indications for Seroquel®, Seroquel® XL/XR and quetiapine fumarate: schizophrenia, bipolar disorder or major depressive disorder (MDD), during the observation period (as outlined in Section 9.2, 11 January to 31 July 2012 in the UK and 13 February to 31 August 2012 in Germany) or within the patient's prior history. See Table 2.

**Table 2 ICD-10 diagnosis codes related to inclusion criteria #2's operational definition**

| DISEASE PARAMETER | ICD-10 | DESCRIPTION |
|---|---|---|
| **Schizophrenia** | F20 | Schizophrenia |
| **Bipolar disorder, manic episode** | F30 | Bipolar disorder, manic episode |
| | F31 | Bipolar affective disorder |
| **Major depressive disorder** | F32 | Major depressive disorder, single episode |
| | F33 | Major depressive episode, recurrent |

3. Prescribed Seroquel®, Seroquel® XL/XR or quetiapine fumarate sometime on/after diagnosis of one of the qualifying conditions listed above and during the observation or study period. Prescription of these products was identified by searches for the molecule name 'quetiapine'.

4. Had available history of at least 12 months prior to the observation start date (11 January in UK and 13 February in Germany). For UK patients, date of registration with the practice was used to indicate the beginning of the active patient record. For patients in Germany, a recorded event at least 12 months prior to observation start date met this criterion.

5. Considered an "active" patient within the EMR as of the start and end months of the observation period (i.e., 1 February 2012 and 1 August 2012 in Germany and 1 January 2012 and 1 July 2012 in the UK). Confirmation of active status at the start of observation described above. For UK patients, continued registration with their GP at the close of the observation period (31 July 2012) confirmed active status. In Germany, any observed event on or after 31 August 2012 confirmed active status as of the end of the observation period.

6. Had at least one medical encounter (i.e., office visit, telephone call) during the observation period. This could have included the encounter where Seroquel®, Seroquel® XL/XR or quetiapine fumarate was prescribed.

7. If a German patient, must be under the care of a physician with a speciality of psychiatry or neurology. The UK DA data includes only primary care practices.

### 9.3.2 Study exclusion criteria

1. Patients who were treated only outside of the target timeframe.

2. Patients who were not treated with Seroquel® or Seroquel® XL/XR or quetiapine fumarate inside the target timeframe.

Any physician encounters observed prior to a patient fulfilling all inclusion criteria were excluded from analyses assessing the outcome.

## 9.4 Variables

Data were collected and analysed to assess the seven metabolic monitoring outcomes detailed below.

**Outcome Variables - UK and Germany**

1. Record of patient weight at initiation of quetiapine: Patients considered for evaluation of this endpoint included those new to quetiapine based on having no observed prescriptions for Seroquel®, Seroquel® XL/XR or quetiapine fumarate within the 12-month history period. The proportion of all patients who met study eligibility criteria and were new to quetiapine who had their weight recorded on the same day as they received their first prescription for quetiapine were reported. These patients have also been referred to as newly initiated patients in this report.

2. Monitoring of weight of patients during on-going treatment with quetiapine: All study patients were evaluated for this endpoint. The proportion of study patients who had their weight recorded during the observation period was reported.

3. Monitoring for elevated cholesterol: All study patients were evaluated for this endpoint. Evidence of monitoring included the ordering of lipid panel or component test (i.e., total cholesterol, LDL-cholesterol, HDL-cholesterol, and/or triglycerides) or reviewing/receipt of lipid panel or component test result.

4. Monitoring for signs and symptoms of hyperglycaemia: All study patients were evaluated for this endpoint. Monitoring could include reviewing signs or symptoms for hyperglycaemia (i.e., diagnosis of polyuria, polydipsia, polyphagia, or hyperglycaemia), ordering of blood glucose testing (i.e., blood or urine glucose test, HbA1c testing or diagnosis of elevated blood glucose level), reviewing of blood glucose test results or prescription order for self monitoring blood glucose test strips.

5. Monitoring of blood glucose in patients with diabetes mellitus: This endpoint was assessed only for diabetic patients, derived from diabetes mellitus diagnosis codes

or evidence of anti-diabetic medication use. Monitoring included ordering of blood glucose testing (i.e., blood or urine glucose test or HbA1c testing), reviewing blood glucose test results or prescription order for self monitoring blood glucose test strips.

6. Monitoring of blood glucose in patients with risk factors for diabetes mellitus for worsening of glycaemic control: This endpoint was assessed only for patients with risk factors for diabetes mellitus, not including those with diabetes mellitus. Risk factors for diabetes mellitus were identified in the first encounter during the observation period or during the 12 months of prior history. Monitoring included ordering of blood glucose testing (i.e., blood or urine glucose test or HbA1c testing), reviewing blood glucose test results or prescription order for self monitoring blood glucose strips.

    - Risk factors were defined as: obesity (i.e., recorded or calculated BMI >25[1] or diagnosis of either abnormal weight gain or obesity), pre-diabetes mellitus (i.e., diagnosis of abnormal glucose tolerance test), history of previous cardiovascular disease or diagnosis of metabolic syndrome. As no ICD-10 diagnosis code exists specifically for metabolic syndrome or hyperinsulinemia in Europe, the translation of UK READ code for metabolic syndrome resulted in ICD-10 code E88.9 (metabolic disorders, not otherwise specified), which was utilised knowing that it might include a broader reach than intended.

7. Counselling patients on healthy eating, exercise and healthy lifestyle improvements: All study patients were evaluated for this endpoint. The proportion of patients whose physicians had recorded providing counselling relating to healthy lifestyle factors was reported. Evidence of monitoring included the recording of a diagnosis code indicative of counselling related to lifestyle (e.g., dietary, alcohol, drug, etc.) behaviour.

*[NOTE: Please refer to Tables 1 and 2 in the SAP for comprehensive list of codes]*

Data were collected for all descriptive patient and practice variables listed below:

**Descriptive Practice Variables - Germany**

- Age and gender of physician leader in practice
- Years qualified of physician leader in practice
- Practice speciality (psychiatry or neurology)
- Practice type (single, group)
- Number of physicians in practice
- Practice region
- Number of patients per practice

1 Although BMI >30 is considered the lower limit of the obesity threshold, MEB requested BMI>25 to be included as a risk factor in this study.

**Descriptive Practice Variables - UK**

Physician-level characteristics are not available in Disease Analyzer UK. All physicians in this data are of general practice speciality. The number of patients per practice was reported.

**Descriptive Patient Variables - UK and Germany**

- Age (based on year of birth and increments each first of new year)
- Gender
- Smoking status (current smoker, not currently smoking, unknown)
- Patient's qualifying psychiatric diagnoses (i.e., schizophrenia, bipolar disorder, major depressive disorder; patients may have more than one diagnosis)
- Whether the patient was prescribed other antipsychotic (ATC N05A) medication during the 6 months prior history
- Whether the patient was prescribed other antidepressant (ATC N06A) medication during the 6 months prior history
- Number of visits during the study period
- Whether a lipid panel test was performed during the 12 months prior history
- Whether the patient was identified as having pre-diabetes mellitus, where diagnosis of abnormal glucose tolerance test recorded during the first encounter of the observation period or during the 12 months prior history and the patient was not subsequently categorised as diabetic
- A history of weight recorded during the 12 months prior history
- Most recent BMI. This was categorised as ≤25 or >25 (obese) as well as by <18.5, 18.5-25, >25-30, >30-35 and >35.

**Potential Confounding Variables or Risk Factors for Monitoring of Patients**

The following variables were considered potential confounders or risk factors, either of which could influence the performance of metabolic monitoring of patients. These factors were categorised based on the 12 months prior history, unless otherwise noted. Analysis of confounding and influence of risk factors were performed at the patient level, not at the practice level.

The reported factors were:

- Use of antipsychotics other than Seroquel®, Seroquel® XL/XR or quetiapine fumarate during the 6 months prior history. These were categorised as 0, 1, 2 and 3 or more
- Use of antidepressants during the 6 months prior history. These were categorised as 0, 1, 2 and 3 or more
- Obesity (calculated or recorded as BMI >25)

- Age as of 1 January 2012
- Female gender
- Patient history of anxiety or psychosis based on recorded outpatient diagnosis
- Hospitalisation during the 12 months prior history (UK only; low capture rate within the German data among neurologists and psychiatrics; missing data on hospitalisations were not considered to be reliable indicators of lack of hospitalisations)
- High blood pressure, defined by diagnosis of primary or secondary hypertension or diagnosis of hypertensive heart disease
- Elevated cholesterol, defined by a composite of treatment and diagnosis. Diagnoses included hypercholesterolaemia, hyperglyceridaemia, and hyperlipidaemia. Treatments included statins, lipid regulators combined with other lipid regulators, ion-exchange resins, fibrates and other cholesterol and triglyceride regulators
- Testing for elevated cholesterol, defined by physician's order/review of results from or patient's receipt of total cholesterol, LDL-cholesterol, HDL-cholesterol and/or triglycerides test
- History of diagnosed cardiovascular disease
- History of diabetes mellitus, derived from diabetes mellitus diagnosis or evidence of anti-diabetic medication use
- Testing of blood glucose (blood or urine glucose test or HbA1c testing)
- Metabolic syndrome, where diagnosed. Since a specific ICD-10 diagnosis code for metabolic syndrome or hyperinsulinemia was not found (or used) in DA for EMR from the UK and Germany, the code E88.9 (metabolic disorders, not otherwise specified) was used.
- Smoking status was based on the most recent record during the 12 month history period. The status was categorised as current smoker, not currently smoking or for those without any recording of status, unknown

## 9.5 Data sources and measurement

IMS Disease Analyzer (DA) comprises longitudinal patient-level databases from physician-practice management systems of office-based physicians in France, Germany and the UK. For this study, databases for Germany and the UK were used. The databases include up to 18 years of data drawn from EMRs, offering long-term disease tracking on more than 19 million patients. DA data available by country of interest are summarised in Table 3.

**Table 3 Census population for studied countries and descriptive counts of IMS Disease Analyzer data for the UK and Germany**

| | UK | Germany |
|---|---|---|
| *Census populationestimate for 2012* | 63.2M* | 82M** |
| Patient records | 4.2M | 15.5M |
| Unique physicians | 1,151 | 3,002 |
| Unique practices | 218 | 2,357 |
| Total prescriptions | 206M | 150M |

* Office for National Statistics 2011
** World Bank Population Data 2012

DA encompasses several EMR software partners within each country. IMS secures agreement from physician practices that utilise these software packages to participate in the DA panel. As with any EMR software, there are fixed-format data collection fields as well as free text note fields. Standard practice of what information, how much, and in what format (fixed vs. free text) is collected may vary by physician practice, EMR software used and country. The basis of the data collection within an EMR is encounter-based, indicating that all recorded data revolves around an interaction with the practice, which may include an office visit, referral, telephone call, or laboratory/test results sent to the practice.

In Germany, DA data are collected from participating specialists including psychiatrists and neurologists. More frequently, physician practices in Germany consist of a single practitioner, so EMR encounters are often linkable to a specific physician. UK patients are assigned to a particular GP who coordinates all of the patient's care. Traditionally, UK GP practices are composed of several physicians, making it difficult to link specific EMR encounters to a specific physician within the practice. Therefore, within the UK, physician behaviour may need to be viewed at the practice-level. In both DA data available from the UK and Germany, patients' records of receipt of care from another physician cannot be tracked in the DA data.

Data include basic demographics (gender and age) and medical diagnoses, recorded in ICD-10 (and READ codes in the UK) and linked to physician-written prescriptions and the date of the visit during which the diagnosis was made and/or the prescription was written. Details regarding physician-written prescriptions include the specific medication (only generic name in the UK), form, strength, and the European Pharmaceutical Market Research Association (EphMRA) drug classification ATC code. The total units prescribed and the prescribed units per day (daily dose) may be available. In the UK, the specific quantity of medication supplied is an individual unit count.

The EMR encounter data contain notes on actions taken and the health status recorded during the patient's visit; these notes may be entered by a nurse, physician, or other staff with whom the patient had contact. Notes and entry into fixed fields are based on discussion with the patient as well as the healthcare professional's impressions. Data may include referrals and hospitalisations (although limited); the speciality of the physician to which the patient is referred is also available.

In addition, EMR encounter data may include the patient's height, weight, and smoking status. The German data also include the patient's obesity status and insurance status.

EMR encounter data include:

- ICD-10 diagnosis codes with dates of diagnoses or resolution of condition - to help identify Central Nervous System (CNS) diagnosis as well as risk factors (e.g., high cholesterol, cardiovascular diseases), prior conditions, and relevant family history as well as hyperglycaemia
- Vital and biometric measurements (e.g., blood pressure, weight, height), as recorded per visit
- Lipid panel (includes cholesterol and triglyceride) lab results, as recorded by the practice
- Other lab results, such as blood glucose, as recorded by the practice
- Treatments - prescription orders: date, EphMRA's ATC classification code, dose, form, pack, reason for any switch or stoppage of prior medication; as recorded by the practice
- Notes containing references to diet/exercise counselling or ICD-10 diagnoses/READ codes corresponding to the provision of patient counselling for nutrition, exercise, or maintenance of healthy lifestyle
- Referrals to hospitals or another physician, often noting speciality of "referred to" physician

## 9.6 Bias

The study results must be interpreted within the context of the patient sample studied as outlined in Section 9.3. Selection bias may have accounted for differences in the proportion of patients monitored at the practice level due to the inclusion of prevalent users and patients newly initiated on quetiapine.

There may be underestimation of the frequency of monitoring due to the seven month observation period for the study. This period was defined based upon the constraints imposed by the availability of data from the data source, the IMS Disease Analyzer database at the time of finalisation of the study protocol, contracting for access to the data, and the requirement for evaluation of recorded monitoring of patients in a period closely following distribution of educational material. Since all patients in this study were required to be registered with the physician practice at least 12 months prior to the start of the observation period as well as until the end of the observation period, it was possible to interpret monitoring results performed even if patient/physician encounters were limited to annual physician visits over a 19 month timeframe or based upon other recommended timing and periodicity of monitoring as set forth in national guidelines.

In addition, the selection of a shorter or longer time period following the educational material distribution could provide different results, especially if there were significant changes in local

practice or there were other influences on monitoring frequency contributing to changes in secular trends over time.

The DA databases contain information drawn from panels of clinical practices in the UK and Germany; practices must elect to participate in sharing their EMRs. It is not possible for investigators to identify participating practices to ascertain potential bias attributable to self-selection. Recording of specific variables (*e.g.,* laboratory results, biometric measurements) may vary by physician practice and/or EMR software; therefore, monitoring may be under-represented if monitoring activities were not recorded or were only recorded in the free-text notes fields. EMR data were collected as part of patient care and not specifically for research purposes. Any data entry errors were not detectable and could not be accounted for in the analysis.

The use of specific, IMS and AZ-approved code lists as outlined in Table 2 and in defining the variables in Section 9.3 may be a limitation in comparing study results with other studies using different code lists.

## 9.7 Study size

Given that the study is descriptive in nature and retrospective, all patients meeting the study inclusion criteria were considered for analyses. The primary units of measure were at the practice and patient level. This study reports analyses from 887 patients from 93 GP practices in the UK. In Germany, 1451 patients managed by 42 psychiatry practices and 4702 patients managed by 145 neurology practices were eligible for analyses.

## 9.8 Data transformation

### 9.8.1 Data handling

Data was extracted from the Disease Analyser UK and Germany databases as delimited text files. These were stored and protected from overwriting. All post extraction data processing, creation of analysis datasets, and analyses were conducted with SAS® Version 9.3 (SAS Institute, Cary, NC, USA). Three final analysis datasets were created and locked prior to analysis.

### 9.8.2 Transformations and derived quantities

**Age at any event**

To prevent identification of patients, an anonymized birth date was recorded where the day and month of the date of birth was set to 1 January for every patient in the database.

$$Age\ at\ event\ (years) = \frac{event\ date - anonymised\ birth\ date}{365.25}$$

**Time intervals**

1 month = 30.44 days

1 year = 12 months

1 year = 365 days

**Body mass index (BMI)**

$$BMI\ \left(\frac{kg}{m^2}\right) = \frac{weight(kg)}{(height(m))^2}$$

## 9.9 Statistical methods

### 9.9.1 Main summary measures

Data sets were created for each of the three physician practice groups (UK GPs, German psychiatrists, and German neurologists) and their respective patients. Results were reported separately for each data set.

**Categorisation by percentiles**

Continuous variables requiring categorisation by percentiles were categorised according to the percentile within the analysis data set. Therefore thresholds for quantities categorised in this way may not be consistent between data sets.

**Summary of patient and clinician characteristics**

Summaries of patient characteristics were reported for each analysis data set. Physician characteristics were reported for psychiatrist and neurologist data sets for Germany.

For continuous variables, mean, standard deviation, median, 25$^{th}$ and 75$^{th}$ percentiles, minimum and maximum values and the number of missing values were reported. For categorical variables, the frequency, percentage, and number of missing values were reported. Percentages for categorical variables were based on non-missing values.

**Monitoring of patients**

*Raw proportions*

Analyses of all seven monitoring outcomes follow the same method outlined in this section. The proportion of patients monitored was calculated by:

1. Determining the number of patients eligible to be monitored (denominator)
2. Determining the number of patients monitored (numerator)

The raw counts of denominator (1) and numerator (2) and the proportions of patients monitored (see pre-defined thresholds below) were reported overall for the analysis data set and stratified by the a priori categorisation of practices' patient-volume for the respective patient population (denominator) in the study period.

*Thresholds for monitoring by physician practices*

The categories representing the proportion of patients monitored by each physician practice were: ≥50%, ≥67%, ≥80%, ≥90%, and ≥95%.

*Stratification of practices according to patient-volume*

The categories of practice size were created to present select findings according to the number of patients meeting study eligibility criteria within each practice and included: 0-5, 6-11, 12-34, and 35+ patients.

Practice sizes were categorised using critical values from binomial distributions $B(n, 0.5)$ requiring that $P(X \geq \varphi) \leq 0.025$ where $\frac{\varphi}{n} = p$ and $p$ was a threshold of proportion of patients that were monitored. Requiring the proportions of patients monitored to be greater than 90%, 80%, and 67% resulted in critical values of 6, 12, and 35 patients respectively, and yielding categories of practices as: 35 or more, 12-34, 6-11 patients, and those <6 patients.

*Monitoring in the presence of risk factors*

Odds ratios for the association of explanatory independent variables (including potential confounders and risk factors) with the performance of monitoring were estimated using mixed generalised linear models which included logistic regression models that included a random intercept describing the practice where the patient was managed.

### 9.9.2 Main statistical methods

**Computing environment**

Data was extracted using IMS Disease Analyzer Version 6.3 Build 7 from the December 2012 UK dataset and IMS Disease Analyser Version 6.5 Build 4 from the December 2012 Germany dataset.

Data manipulation and analyses were conducted using SAS 9.3 (SAS Institute, Cary NC). Mixed generalised linear models were fitted in R3.0.1 [Statistical Computing 2013] using the lme4 package [Bates et al 2013].

**Calculation of standard statistics and confidence intervals**

Means, percentiles, maxima, and minima where obtained using PROC MEANS. Frequencies and proportions were calculated using PROC FREQ.

Odds ratios for risk factors were calculated by exponentiation of the coefficient from a fitted mixed logistic regression model. Confidence intervals for odds ratios obtained from mixed logistic regression models were calculated as follows:

$$Lower\ CI\ limit = e^{\beta_i - 1.96 \times \sqrt{\theta_i}}$$

$$Upper\ CI\ limit = e^{\beta_i + 1.96 \times \sqrt{\theta_i}}$$

Where $\beta_i$ is a coefficient from the fitted model and $\sigma_i$ is the diagonal of the variance-covariance from the fitted model.

**Multiple statistical tests**

These analyses employ multiple statistical hypothesis tests with the same samples of patients. No adjustment was made to control the type I error rate.

**Model building: Selection of covariates**

Model building included the following steps:

1. Risk factor selection
2. Backwards selection

Only first order effects were evaluated. Interaction between covariates was not assessed.

*Risk factor selection*

A pool of potential risk factors (Section 9.4) relating to each monitoring activity were provided by AZ based on epidemiological evidence and previous experience in assessment of these issues.

All eligible risk factors were examined using a bivariate cross-tabulation with each monitoring activity. The proportion of patients monitored in each category of the risk factor was reported. Eligible risk factors were those defined as being included for consideration for influencing the monitoring outcome. These eligible risk factors were included in modelling activities provided there was sufficient data and sufficient patients (twenty or more) in each category of the risk factor. Based upon the understanding that recent monitoring of the outcome (i.e., in the past 12 months) may influence the monitoring during the study period, such risk factors were selected to be included *a priori* in the modelling activities regardless of their statistical significance; these and any other risk factors selected *a priori* are described below. Diabetic history was not included in the assessment of the two blood glucose monitoring outcomes as this risk factor was part of the definition of the sub-population being assessed.

*Backwards selection*

A likelihood ratio test was used at each stage of backward selection to determine the significance of a difference between the nested and parent models at the 5% level.

**Reporting results from models**

Risk factors found to be statistically significant at the 5% level in the final model or were *a priori* selected and retained were reported. This includes the numbers of patients in each category of the risk factor, the adjusted odds ratio, and confidence interval.

**Monitoring activities and risk factors**

Monitoring of weight at initiation of quetiapine treatment

Patients identified as newly initiated on quetiapine in the study period were included in these analyses. All risk factors were tabulated. This outcome was not modelled due to the low number of patients weighed on the day of quetiapine initiation.

Monitoring weight during the study period

All patients were included. All risk factors were evaluated, except for obesity which needed to be retained in the model assuming sufficient completeness but regardless of statistical significance.

Monitoring for elevated cholesterol

All patients were included. All risk factors were evaluated, except for previous lipid testing and elevated cholesterol history which needed to be retained in the model assuming sufficient completeness but regardless of statistical significance.

Monitoring for signs and symptoms of hyperglycaemia

All patients were included. All risk factors were evaluated, except for previous testing of blood glucose and history of diabetes which needed to be retained in the model assuming sufficient completeness but regardless of statistical significance.

Monitoring of blood glucose in diabetic patients

Diabetic patients were included. All risk factors were evaluated, except for previous testing of blood glucose which needed to be retained in the model assuming sufficient completeness but regardless of statistical significance.

Monitoring of blood glucose in patients at risk of diabetes

All patients at risk of diabetes were included. Obesity, high blood pressure, a history of cardiovascular disease and previous testing of blood glucose needed to be retained in the model assuming sufficient completeness but regardless of statistical significance.

Monitoring counselling on healthy eating, exercise, and lifestyle improvements during the study period

All patients were included. All risk factors were evaluated, except for hospitalisation in the preceding 12 months which needed to be retained in the model assuming sufficient completeness but regardless of statistical significance.

**Monitoring by practices**

Proportions of patients monitored within each practice

For each practice in an analysis data set, the proportion of eligible patients monitored for each activity was calculated. Eligibility was determined in the same manner described above. Practices have been stratified by the *a priori* selected volumes of eligible patients as described above. Summary statistics were reported to describe the distributions of the proportions across all practices in the stratum. The statistics reported were the median, upper quartile and lower quartile.

All variables were dichotomous unless otherwise noted. See Section 9.4 for definitions of the criteria for categorisation of risk factors and confounders.

### 9.9.3 Missing values

Imputation for missing values was not undertaken for this study. Missing data fields were left incomplete and reported accordingly.

### 9.9.4 Sensitivity analyses

Sensitivity analyses were not conducted on this data.

### 9.9.5 Amendments to the statistical analysis plan (Not applicable)

## 9.10 Quality control

Standard operating procedures (SOPs) were used to guide the conduct of key components of this study. These SOPs include internal quality audits, handling of confidential data, storage and maintenance of archive project documents, quality-control procedures for programming, development of statistical analysis plan, and requirements for review by senior members of the project team.

Analyses datasets and program output were checked for accuracy and integrity according to SOPs. Some of these steps included (but not limited to) checking program logs for errors and warnings, checking output for errors and inconsistencies, and review of all results tables for accuracy.

All key study documents such as the statistical analysis plan and study report were subjected to quality-control review.

# 10. RESULTS

## 10.1 Participants - General Practitioners (United Kingdom)

A total of 98 practices, with 2,646,398 total patients were available from the IMS Disease Analyser (DA) database as of January 2013. Of these, 984 adult (≥18 years) patients were prescribed quetiapine between 11$^{th}$ January and 31$^{st}$ July 2012 and had a prior diagnosed condition (schizophrenia, bipolar disorder, or major depressive disorder) appropriate for the

use of quetiapine. 887 of the patients were registered with the GP practice who had prescribed quetiapine both at least 12 months prior to the start of the study period (indicating they should have patient history of at least 12 months) and as of the end of the study period. As presented in Table 4, application of the inclusion and exclusion criteria reduced the sample by 5 GP practices, leaving a total of 93 GP practices and 887 patients for analysis.

**Table 4 Attrition table of General Physician practices and patients in the UK**

| Step | Description | Patients | Practices |
|---|---|---|---|
| 1 | Entire population of the DA UK as of 1 January 2013 | 2,646,398 | 98 |
| 2 | Prescribed quetiapine during the study period of 11 January and 31 July 2012 *and* had a diagnosis of schizophrenia, bipolar disorder, or major depressive disorder prior to the prescription | 1,037 | 94 |
| 3 | Age ≥18 years on 1 January 2012 | 984 | 94 |
| 4 | Have at least one medical encounter (i.e., office visit, telephone call) during the study period | 984 | 94 |
| 5 | Registered with GP prior to 12 January 2011 (indicating that should have patient history at least 12 months prior to study period[1]) | 916 | 93 |
| 6 | Actively registered with GP as of 31 July 2012[1] | 887 | 93 |

1 UK registration (selection of a particular primary care practice) requires that a person be in residence within a jurisdiction for at least 3 months; therefore, a patient may be treated by a practice with which they are not registered if only temporary resident (<3 months). De-registration involves a patient ending their selection of a primary care practice, presumably done in parallel with registering with another practice. Patients may register, de-register, and then re-register and de-register for a second+ time with the same practice. DA captures the first registration and the most recent de-registration with a practice. Therefore, there is a possibility of missed observations. However, this is considered to represent a small minority of cases, although an exact amount cannot be substantiated.

## 10.2 Descriptive data - General Practitioners (United Kingdom)

There were 887 patients from 93 physician practices that met the eligibility criteria for the study. As indicated in Table 5, the mean (Standard Deviation - SD) was 9.5 (9.2) and the median was 8 patients per practice, with a range of 1 to 56 eligible patients per practice.

**Table 5 Characteristics of UK General Practices in the study**

| **Included in the study** | | | |
|---|---|---|---|
| | *Number of patients* | 887 | |
| | *Number of practices* | 93 | |
| | | | |
| **Number of patients per practice** | | | |
| | *Mean (SD)* | 9.5 | (8.2) |
| | *Median* | 8 | |
| | *[LQ, UQ]* | [4, 12] | |
| | *(min, max)* | (1, 56) | |

Demographic and clinical characteristics of the UK study patients observed by General Practitioners are presented in Table 6. The mean (SD) of all patients included in the study was 50.5 (17.7) years with a median value of 48 years. Approximately two-thirds (65.2%) of the patient population was female. 63.5% of the patients were diagnosed with bipolar disorder, 15.4% with major depressive disorder (MDD) and 9.9% had a diagnosis of schizophrenia. 8.9% of the study population had a combined diagnosis of bipolar disorder and MDD, while 2.1% had a qualifying diagnosis of both bipolar disorder and schizophrenia.

With regard to patients' history of being monitored (in the last 12 months prior to study period), including the presence of important risk factors related to monitoring that were present at the initiation of treatment with quetiapine,

- 39.9% of patients had a lipid panel test performed
- 20% of patients had a history of elevated cholesterol
- 9.6% of patients were classified as having diabetes mellitus and 1% were considered as having pre-diabetes
- among patients without diabetes mellitus, 60% were considered to be at risk for diabetes mellitus on the basis of having one or more risk factors for the disease
- 50.2% of patients had evidence of having their weight measured in the past

Among those patients whose smoking status was known, nearly three quarters (74%) were classified as being current smokers. Most patients had not had any other antipsychotics prescribed in the previous 6 months (90%), with only about 10% of patients having 1 other antipsychotic prescribed during that time. For those who were prescribed other antipsychotics, the 3 most frequent prescriptions were for olanzapine (2.8%), risperidone (2.4%), and aripiprazone (1.4%). Antidepressants were more frequently prescribed in the previous 6 months, with over half of the patients (54%) having 1 prescription, 17% having 2 prescriptions, and 4% having 3 more prescriptions. For those who were prescribed antidepressants, the 3 most frequent prescriptions were for citalopram (15.7%), venlafaxine (14.7%), and mirtazapine (14.2%).

## Table 6 Demographic and clinical characteristics of patients seen in General Practice in the UK

| | | Total number of patients (N=887) | |
|---|---|---|---|
| **Sex n (%)** | | | |
| | *Male* | 309 | (34.8) |
| | *Female* | 578 | (65.2) |
| **Age** | | | |
| | *Mean (SD)* | 50.5 | (17.7) |
| | *Median* | 48 | |
| | *[LQ, UQ]* | [38, 61] | |
| | *(min, max)* | (18, 98) | |
| | | | |
| | *18-24 (<25)* | 42 | (4.7) |
| | *25-39* | 211 | (23.8) |
| | *40-49* | 223 | (25.1) |
| | *50-64* | 229 | (25.8) |
| | *≥65* | 182 | (20.5) |
| **Smoking status n (%)** | | | |
| | *Current smoker* | 365 | (74.0) |
| | *Not currently smoking* | 128 | (26.0) |
| | *Unknown* | 394 | |
| **Qualifying diagnosis n (%)** | | | |
| | *Schizophrenia* | 88 | (9.9) |
| | *Bipolar disorder* | 563 | (63.5) |
| | *Major depressive disorder (MDD)* | 137 | (15.4) |
| | | | |
| | *Bipolar + MDD* | 79 | (8.9) |
| | *Bipolar + Schizophrenia* | 19 | (2.1) |
| | *MDD + Schizophrenia* | 1 | (0.1) |
| | | | |
| | *Schizophrenia + bipolar + MDD* | 0 | (0.0) |
| | | | |
| **Lipid panel testing in prior 12 months n (%)** | | | |
| | *Lipid panel testing in prior 12 months n (%)* | 354 | (39.9) |

## Table 6 Demographic and clinical characteristics of patients seen in General Practice in the UK

| | | **Total number of patients (N=887)** | |
|---|---|---|---|
| **Evidence of diabetes mellitus n (%)** | | | |
| | *Evidence of diabetes mellitus n (%)* | 85 | (9.6) |
| **History of pre-diabetes mellitus excluding diabetic patients n (%)** | | | |
| | *History of pre-diabetes (excluding diabetic patients) n (%)* | 8 | (1.0) |
| **At risk of diabetes mellitus n (%)** | | | |
| | *At risk of diabetes (excluding diabetic patients) n (%)* | 483 | (60.2) |
| **History of elevated cholesterol n (%)** | | | |
| | *History of elevated cholesterol n (%)* | 177 | (20.0) |
| **History of weight monitoring n (%)** | | | |
| | *History of weight measurement in the past 12 months n (%)* | 445 | (50.2) |
| **Prescription of other antipsychotics in prior 6 months n (%)** | | | |
| **Substances** | | | |
| | *aripiprazole* | 12 | (1.4) |
| | *benperidol* | 1 | (0.1) |
| | *chlorpromazine* | 9 | (1.0) |
| | *flupentixol* | 4 | (0.5) |
| | *fluphenazine* | 2 | (0.2) |
| | *levomepromazine* | 2 | (0.2) |
| | *olanzapine* | 25 | (2.8) |
| | *promazine* | 2 | (0.2) |
| | *risperidone* | 21 | (2.4) |
| | *sulpiride* | 3 | (0.3) |
| | *trifluoperazine* | 5 | (0.6) |
| | *zuclopenthixol* | 2 | (0.2) |

## Table 6 Demographic and clinical characteristics of patients seen in General Practice in the UK

| | | Total number of patients (N=887) | |
|---|---|---|---|
| **Number of other antipsychotics prescribed n (%)** | | | |
| | *0* | 802 | (90.4) |
| | *1* | 76 | (8.6) |
| | *2* | 8 | (0.9) |
| | *3* | 1 | (0.1) |
| **Prescription of antidepressants in prior 6 months n (%)** | | | |
| **Substances** | | | |
| | *amitriptyline* | 59 | (6.7) |
| | *citalopram* | 139 | (15.7) |
| | *clomipramine* | 8 | (0.9) |
| | *dosulepin* | 10 | (1.1) |
| | *duloxetine* | 38 | (4.3) |
| | *escitalopram* | 44 | (5.0) |
| | *fluoxetine* | 64 | (7.2) |
| | *fluvoxamine* | 1 | (0.1) |
| | *imipramine* | 2 | (0.2) |
| | *isocarboxazid* | 1 | (0.1) |
| | *lithium* | 72 | (8.1) |
| | *lofepramine* | 12 | (1.4) |
| | *mirtazapine* | 126 | (14.2) |
| | *nortriptyline* | 2 | (0.2) |
| | *paroxetine* | 17 | (1.9) |
| | *phenelzine* | 1 | (0.1) |
| | *reboxetine* | 4 | (0.5) |
| | *sertraline* | 90 | (10.1) |
| | *tranylcypromine* | 1 | (0.1) |
| | *trazodone* | 21 | (2.4) |
| | *trimipramine* | 2 | (0.2) |
| | *tryptophan* | 1 | (0.1) |
| | *valproate_semisodium* | 46 | (5.2) |
| | *venlafaxine* | 130 | (14.7) |

**Table 6 Demographic and clinical characteristics of patients seen in General Practice in the UK**

| | | Total number of patients (N=887) | |
|---|---|---|---|
| **Number of antidepressants prescribed n (%)** | | | |
| | *0* | 223 | (25.1) |
| | *1* | 480 | (54.1) |
| | *2* | 148 | (16.7) |
| | *3* | 29 | (3.3) |
| | *4* | 7 | (0.8) |

Table 7 presents descriptive data on the frequency of visits by patients to their GPs and the status of quetiapine use (as a new user initiating quetiapine or continuing on quetiapine as a prevalent user) at the start of the study period. A mean (SD) number of 14.5 (9.2) visits were made per patient during study period. There were a median of 12 visits per patient during the study period, with the majority of patients (61.7%) having more than 10 visits. One-fifth of all patients analysed (20%) had been initiated on quetiapine during the study, whilst four-fifths (80%) were prevalent users of quetiapine at the start of the study period.

**Table 7 Treatment of patients seen in General Practice in the UK**

| | | Total number of patients (N=887) | |
|---|---|---|---|
| **Number of visits per patient in study period** | | | |
| | *Mean (SD)* | 14.5 | (9.2) |
| | *Median* | 12 | |
| | *[LQ, UQ]* | [8, 18] | |
| | *(min, max)* | (1, 62) | |
| | | | |
| | *1* | 9 | (1.0) |
| | *2* | 16 | (1.8) |
| | *3* | 17 | (1.9) |
| | *4* | 28 | (3.2) |
| | *5* | 26 | (2.9) |
| | *6* | 34 | (3.8) |
| | *7* | 54 | (6.1) |
| | *8* | 50 | (5.6) |
| | *9* | 61 | (6.9) |
| | *10* | 45 | (5.1) |
| | *>10* | 547 | (61.7) |
| | | | |
| **Quetiapine treatment** | | | |
| | *Patients initiated during study n (%)* | 175 | (19.7) |
| | *Prevalent users n (%)* | 712 | (80.3) |

Table 8 presents study findings on risk factors and potential confounding variables believed to potentially have influence in the performance of metabolic monitoring of UK patients in primary care. A total of 60% of patients had a body mass index (BMI) over 25 (i.e., were classed as overweight or obese) with a median BMI of 28 and a BMI range from 12 to 50. Mean (SD) BMI for the study population was 28.9 (7.2).

Using a relative time window of the 12 months prior to the patient's qualification to be in the study, 1.5% had a history including a diagnosis of psychosis or anxiety, 29.8% had been hospitalisation for any reason within the past 12 months, 1% had high blood pressure and 20% had elevated cholesterol. Testing of lipid levels in the prior 12 months were performed for 39.9% of the study population. 3.9% had a history of cardiovascular disease and 9.6% had a history of diabetes. Testing of serum glucose (excluding patients diagnosed with diabetes) in the prior 12 months was performed in 41.5% of patients. None of the patients had a diagnosis of metabolic syndrome.

## Table 8 Risk factors for patients seen in General Practice in the UK

| | | Total number of patients (N=887) | |
|---|---|---|---|
| **Body mass index** | | | |
| | *Unknown* | 62 | |
| | | | |
| | *Mean (SD)* | 28.9 | (7.2) |
| | *Median* | 28 | |
| | *[LQ, UQ]* | [24, 33] | |
| | *(min, max)* | (12, 59) | |
| | | | |
| | *Summary categories n (%)* | | |
| | *Unknown* | 62 | (7.0) |
| | *≤25* | 289 | (32.6) |
| | *>25* | 536 | (60.4) |
| | | | |
| | *Expanded categories n (%)* | | |
| | *Unknown* | 62 | (7.0) |
| | *<18.5* | 22 | (2.5) |
| | *18.5-25.0* | 267 | (30.1) |
| | *>25.0-30.0* | 224 | (25.3) |
| | *>30.0-35.0* | 169 | (19.1) |
| | *>35* | 143 | (16.1) |
| | | | |
| **History with diagnosis of psychosis or anxiety n (%)** | | | |
| | *Yes* | 13 | (1.5) |
| | *No* | 874 | (98.5) |
| | | | |
| **Hospitalisation for any reason in the past 12 months n (%)** | | | |
| | *Yes* | 264 | (29.8) |
| | *No* | 623 | (70.2) |
| | | | |
| **High blood pressure n (%)** | | | |
| | *Yes* | 9 | (1.0) |
| | *No* | 878 | (99.0) |
| | | | |

**Table 8 Risk factors for patients seen in General Practice in the UK**

| | | Total number of patients (N=887) | |
|---|---|---|---|
| **Elevated cholesterol n (%)** | | | |
| | *Yes* | 177 | (20.0) |
| | *No* | 710 | (80.0) |
| | | | |
| **Testing of lipids n (%)** | | | |
| | *Yes* | 354 | (39.9) |
| | *No* | 533 | (60.1) |
| | | | |
| **History of cardiovascular disease n (%)** | | | |
| | *Yes* | 35 | (3.9) |
| | *No* | 852 | (96.1) |
| | | | |
| **History of diabetes mellitus n (%)** | | | |
| | *Yes* | 85 | (9.6) |
| | *No* | 802 | (90.4) |
| | | | |
| **Testing of glucose in the past 12 months (excl. diabetics n=802) n (%)** | | | |
| | *Yes* | 333 | (41.5) |
| | *No* | 469 | (58.5) |
| | | | |
| **Diagnosis of metabolic syndrome** | | | |
| | *No* | 887 | (100) |

## 10.3 Outcome data: summary of outcomes data - General Practitioners (United Kingdom)

Table 9 presents data that summarises monitoring activity performed by primary care practices in the UK between 11 January and 31 July 2012 according to the threshold points relating the proportion of patients in the practices monitored. A total of 72 practices (77% of total practices included in analysis) had patients newly initiated on quetiapine with 3% of these practices monitoring weight for 50% or more of patients who were newly initiated.

All practices included in the analysis (n=93) had patients eligible and had the following results regarding monitoring for at least half (50%) of their patients during the study period: 35% of practices monitored at least half of their patients for weight at least once, 16% of practices monitored at least half of their patients for elevated cholesterol and 23% of practices monitored at least half of their patients for signs and symptoms of hyperglycaemia.

A total of 48 practices (52% of total practices included in analysis) had diabetic patients, with 67% of these practices monitoring 50% or more of their patients for signs and symptoms of hyperglycaemia. A total of 89 practices (96% of total practices included in the analysis) had patients at risk of diabetes, with 30% of these practices monitoring 50% or more of these patients for signs and symptoms of hyperglycaemia. 29% of practices provided counselling on healthy lifestyle at least once in the study period to at least half of their patients.

**Table 9 Summary of monitoring activities performed by GP practices in the UK by proportion of patients monitored**

| | | **Proportion of patients monitored by practice** | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Monitoring activities performed by practices** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of '**A**') | | | | |
| | | | | | | |
| Weight recorded at visit when initial prescription was issued n (%) | *72 (77%)* | 2 (3%) | 1 (1%) | 1 (1%) | 1 (1%) | 1 (1%) |
| | | | | | | |
| Weight recorded at least once in study period n (%) | *93 (100%)* | 33 (35%) | 10 (11%) | 7 (8%) | 5 (5%) | 5 (5%) |
| | | | | | | |
| Monitoring for elevated cholesterol at least once in study period n (%) | *93 (100%)* | 15 (16%) | 5 (5%) | 2 (2%) | 2 (2%) | 2 (2%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia at least once in study period n (%) | *93 (100%)* | 21 (23%) | 4 (4%) | 2 (2%) | 2 (2%) | 2 (2%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *diabetic patients* at least once in study period n (%) | *48 (52%)* | 32 (67%) | 18 (38%) | 18 (38%) | 18 (38%) | 18 (38%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *patients at risk of diabetes* at least once in study period n (%) | *89 (96%)* | 27 (30%) | 7 (8%) | 7 (8%) | 6 (7%) | 6 (7%) |
| | | | | | | |
| Counselling on healthy lifestyle conducted at least once in study period n (%) | *93 (100%)* | 27 (29%) | 11 (12%) | 8 (9%) | 8 (9%) | 7 (8%) |

Table 10 presents the proportion of patients in UK GP practices monitored at least once during the study period of 11 January to 31 July 2012. A total of 175 patients (20% of all patients included for analysis) were newly initiated to quetiapine and, among these patients, only 3.4% had weight recorded at that initial visit.

All patients included in the analysis (n=887) were eligible for the following monitoring outcomes and had the corresponding monitoring results: having weight recorded at any visit (38.7%), having elevated cholesterol monitored at least once in the study period (27.7%) and monitoring for signs and symptoms of hyperglycaemia at least once in the study period (31.9%).

A total of 85 patients (9.5% of the total number of eligible patients) had diabetes with 50.6% of these patients being monitored for signs and symptoms of hyperglycaemia. A total of 483 patients (54% of the total number of eligible patients) were at risk of diabetes with 34.4% of these patients being monitored for signs and symptoms of hyperglycaemia. Only 30.8% of all patients were provided with counselling on healthy lifestyle at least once in the study period.

**Table 10 Summary of monitoring activities performed at least once during the study period by GP practices in the UK**

| Monitoring activity | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|
| | | | |
| Weight recorded at visit when initial prescription was issued | 175 | 6 | (3.4) |
| | | | |
| Weight recorded at least once in study period | 887 | 343 | (38.7) |
| | | | |
| Monitoring for elevated cholesterol at least once in study period | 887 | 246 | (27.7) |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia at least once in study period | 887 | 283 | (31.9) |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *diabetic patients* at least once in study period | 85 | 43 | (50.6) |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *patients at risk of diabetes* at least once in study period | 483 | 166 | (34.4) |
| | | | |
| Counselling on healthy lifestyle conducted at least once in study period | 887 | 273 | (30.8) |

## 10.4 Main results: detailed analyses of outcomes data - General Practitioners (United Kingdom)

Table 11 presents the number of GP practices that monitored the weight of newly initiated quetiapine patients during primary care visits by GP practices (during the study period) according to the number of eligible patients in those practice. Out of a total of 72 practices (77% of total practices included in analysis) that had patients newly initiated on quetiapine, only 2 practices (3%) monitored weight on the date of initial prescription for 50% or more of their patients. Of the practices with 1 to 5 eligible patients, 2 practices (3%) monitored weight for 50% or more of their patients and only 1 practice (1%) monitored weight for 80% or more of their patients. None of the practices with 6 to 11 eligible patients monitored weight for ≥50% of their newly initiated patients on quetiapine. However, this finding was based on a very small number of practices (3 practices).

**Table 11 Monitoring of weight for patients newly initiated on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | **Proportion of patients monitored** | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of '**A**') | | | | |
| | | | | | | |
| **1-5** | *69 (96%)* | 2 (3%) | 1 (1%) | 1 (1%) | 1 (1%) | 1 (1%) |
| | | | | | | |
| **6-11** | *3 (4%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total (% of total studied)** | *72 (77%)* | 2 (3%) | 1 (1%) | 1 (1%) | 1 (1%) | 1 (1%) |

Table 12 presents the proportion of newly initiated quetiapine patients monitored for weight in primary care according to the number of physician visits and risk factors. Among the 175 patients newly initiated on quetiapine, only 6 patients (3.4%) had weight recorded at their initial visit. As the number of patients monitored was very small, a full analysis of monitoring activities according to patient risk factors was not performed. The results for monitoring of patients for each outcome with further breakdown according to the presence/absence of relevant risk factors are presented in Table 12 for completeness; however, caution is advised for those findings based upon small numbers.

**Table 12 Monitoring of weight for patients initiated on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Weight recorded at visit when initial prescription was issued*** | 175 | 6 | (3.4) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 30 | 2 | (6.7) |
| | *No* | 145 | 4 | (2.8) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 106 | 4 | (3.8) |
| | *No* | 69 | 2 | (2.9) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 82 | 3 | (3.7) |
| | *No* | 73 | 3 | (4.1) |
| | *Missing* | 20 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 175 | 6 | (3.4) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 24 | 1 | (4.2) |
| | *No* | 151 | 5 | (3.3) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 43 | 2 | (4.7) |
| | *No* | 132 | 4 | (3.0) |
| | | | | |

**Table 12 Monitoring of weight for patients initiated on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 8 | 0 | (0.0) |
| | *No* | 167 | 6 | (3.6) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 13 | 0 | (0.0) |
| | *No* | 162 | 6 | (3.7) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 64 | 3 | (4.7) |
| | *No* | 111 | 3 | (2.7) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 111 | 5 | (4.5) |
| | *Male* | 64 | 1 | (1.6) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *No* | 172 | 6 | (3.5) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 12 | 0 | (0.0) |
| | *25-39* | 57 | 1 | (1.8) |
| | *40-49* | 40 | 3 | (7.5) |
| | *50-64* | 34 | 1 | (2.9) |
| | *≥65* | 32 | 1 | (3.1) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 175 | 6 | (3.4) |
| | | | | |

**Table 12 Monitoring of weight for patients initiated on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Smoking*** | | | |
| | *Yes* | 68 | 3 | (4.4) |
| | *No* | 20 | 1 | (5.0) |
| | *Missing* | 87 | 2 | (2.3) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 49 | 1 | (2.0) |
| | *No* | 126 | 5 | (4.0) |

Table 13 presents the number of GP practices that monitored weight for patients treated with quetiapine during primary care visits (at any time during the study period) according to the number of eligible patients in those practices. Overall, 33 practices (35% of the total) monitored weight at least once during the study period for ≥50% of their patients and 7 practices (8% of the total) monitored weight for more than 80% of patients. The proportion of practices that monitored 50% or more of their patients' weight during the study period decreased with increasing number of eligible patients in the practice. 49% of practices with 1 to 5 eligible patients monitored 50% or more of their patients' weight, whereas 36% of practices with 6-11 eligible patients and 21% of practices with 12-34 eligible patients monitored 50% or more of their patients' weight during the study period. Since the number of practices with 35 or more eligible patients was less than 5, the impact of small sample size upon the observations for these practices is noted.

**Table 13 Monitoring of weight of patients on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *35 (38%)* | 17 (49%) | 7 (20%) | 6 (17%) | 5 (14%) | 5 (14%) |
| | | | | | | |
| **6-11** | *28 (30%)* | 10 (36%) | 3 (11%) | 1 (4%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *28 (30%)* | 6 (21%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *2 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *93 (100%)* | 33 (35%) | 10 (11%) | 7 (8%) | 5 (5%) | 5 (5%) |

Table 14 presents the proportion of patients monitored for weight during primary care visits at any time during the study period by the number of physician visits and by risk factors. 343 (39%) had weight recorded during visits within the study period. The proportion of patients having monitoring of weight increased with the number of visits to the GP; those patients with the highest quartile of visits (with between 19 and 62 visits) having 49% of patients monitored and those in the lowest quartile of visits (with between 1 and 8 visits) having 25% of patients monitored. The frequency of monitoring of weight at any time during the study period for patients treated with another antipsychotic compared to those not treated with another antipsychotic was observed in 42.4% and 38.3% of patients, respectively. A statistically significant odds ratio (OR) indicating less frequent monitoring of weight for patients prescribed antidepressants with reference to those not prescribed antidepressants was observed at OR= 0.55, with 95% Confidence Interval (CI) of 0.40 - 0.77. The odds ratio indicates more frequent monitoring of weight during the study period for patients with a BMI over 25 with reference to those with a BMI under 25 was observed OR=1.93, with 95% CI (1.42, 2.64). Odds ratios showing an association with an increased chance for monitoring weight were observed for:

- patients with elevated cholesterol with reference to patients without such elevations in cholesterol, OR= 1.71 95% CI (1.21,2.61)
- patients with lipid panel testing performed during the study period in reference to patients without such testing , OR=2.26 95% CI (1.64, 3.12)
- patients with diabetes mellitus in reference to those without such diagnosis, OR=1.81 95% CI (1.07, 3.06)

There were lower odds of monitoring weight among older age groups versus those aged 18 to 39 (the reference group), with patients age 50 to 64 and patients 65 and over with statistically significant lower odds of being monitored compared to the reference group with (OR of 0.61 and 0.48, respectively). The results for those aged 40 to 49 suggest that this group also had lower odds than those aged 18 to 39 (OR=0.80, 95% CI 0.54, 1.19) of having weight monitored, however, these results were not statistically significant.

Factors that were not associated with monitoring of weight during the study period included: prescription with other antipsychotics, history of high blood pressure or cardiovascular disease, prior testing of blood glucose, gender, history of anxiety or psychosis, smoking status, and history of hospitalisation in the past year.

**Table 14 Monitoring of weight of patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Weight recorded at least once in study period n (%)*** | 887 | 343 | (38.7) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-8 visits)* | 234 | 59 | (25.2) |
| | *Q2 (9-12 visits)* | 219 | 80 | (36.5) |
| | *Q3 (13-18 visits)* | 216 | 97 | (44.9) |
| | *Q4 (19-62 visits)* | 218 | 107 | (49.1) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 85 | 36 | (42.4) |
| | *No* | 802 | 307 | (38.3) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 664 | 239 | (36.0) |
| | *No* | 223 | 104 | (46.6) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *0.55* | *(0.40, 0.77)* | |
| | | | | |

**Table 14 Monitoring of weight of patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***BMI >25*** | | | |
| | *Yes* | 536 | 246 | (45.9) |
| | *No* | 289 | 96 | (33.2) |
| | *Missing* | 62 | 1 | (1.6) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.93* | *(1.42, 2.64)* | |
| | | | | |
| | | | | |
| | ***High blood pressure*** | | | |
| | *Yes* | 9 | 3 | (33.3) |
| | *No* | 878 | 340 | (38.7) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 177 | 97 | (54.8) |
| | *No* | 710 | 246 | (34.6) |
| | | | | |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.71* | *(1.12, 2.61)* | |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 354 | 184 | (52.0) |
| | *No* | 533 | 159 | (29.8) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *2.26* | *(1.64, 3.12)* | |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 35 | 14 | (40.0) |
| | *No* | 852 | 329 | (38.6) |
| | | | | |

**Table 14 Monitoring of weight of patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Diabetes*** | | | |
| | *Yes* | 85 | 54 | (63.5) |
| | *No* | 802 | 289 | (36.0) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.81* | *(1.07, 3.06)* | |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 402 | 192 | (47.8) |
| | *No* | 485 | 151 | (31.1) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 578 | 224 | (38.8) |
| | *Male* | 309 | 119 | (38.5) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 13 | 5 | (38.5) |
| | *No* | 874 | 338 | (38.7) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 42 | 13 | (31.0) |
| | *25-39* | 211 | 86 | (40.8) |
| | *40-49* | 223 | 89 | (39.9) |
| | *50-64* | 229 | 90 | (39.3) |
| | *≥65* | 182 | 65 | (35.7) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | ***Adjusted Odds Ratio (95% CI)*** | | | |
| | *Age 18 - 39* | *Reference* | | |
| | *Age 40 - 49* | *0.80* | *(0.54, 1.19)* | |
| | *Age 50 - 64* | *0.61* | *(0.41, 0.93)* | |
| | *Age ≥65* | *0.48* | *(0.30, 0.76)* | |
| | | | | |
| | | | | |

**Table 14 Monitoring of weight of patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *No* | 887 | 343 | (38.7) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 365 | 157 | (43.0) |
| | *No* | 128 | 74 | (57.8) |
| | *Missing* | 394 | 112 | (28.4) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 264 | 104 | (39.4) |
| | *No* | 623 | 239 | (38.4) |

Table 15 presents the number of GP practices that monitored ≥50% or more of their patients for cholesterol levels with lipid panel testing during primary care visits according to the number of eligible patients in those practices. Overall (without regard to number of eligible patients in the practice), 15 practices (16%) performed monitoring of cholesterol with lipid panel testing for 50% or more of their patients and only 2 practices (2%) performed such testing for more than 80% of patients at least once during the study period.

**Table 15 Monitoring of elevated cholesterol for patients on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *35 (38%)* | 6 (17%) | 4 (11%) | 2 (6%) | 2 (6%) | 2 (6%) |
| | | | | | | |
| **6-11** | *28 (30%)* | 5 (18%) | 1 (4%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *28 (30%)* | 4 (14%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *2 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *93 (100%)* | 15 (16%) | 5 (5%) | 2 (2%) | 2 (2%) | 2 (2%) |

Table 16 presents the proportion of patients whose cholesterol was monitored during primary care visits according to the number of physician visits and by risk factors. All patients in the study (n=887) were analysed, and of these patients, 246 (27.7%) had their cholesterol monitored (i.e. lipid levels assessed) at least once during visits within the study period. The proportion of patients having their cholesterol monitored increased with the number of visits to the GP, with those in the highest quartile of visits (with between 19 and 62 visits) having 35.3% of patients monitored and those in the lowest quartile of visits (with between 1 and 8 visits) having 11.1% of patients monitored.

Monitoring of cholesterol was more likely for a range of risk factors associated with cholesterol:

- patients had approximately 1.8 fold increased odds of having their cholesterol monitored if they had a history of elevated cholesterol compared to those who did not OR=1.81 95% CI (1.16, 2.81),
- patients had an approximate 1.8 fold increased odds of having their cholesterol monitored if they had a history of blood lipid testing compared to those who did not OR=1.78 95% CI (1.24, 2.54) and
- an approximate 2.5 fold increased odds of having their cholesterol monitored if they had a diagnosis of diabetes compared to those who were not diagnosed as diabetic OR=2.48 95%CI (1.43, 4.30).

An age-related increase in the frequency of monitoring patients' cholesterol through age 64 was observed. Monitoring had higher odds of occurring among older age groups versus those aged 18 to 39 (the reference group), with those aged 65 and older having approximately twice the odds of being monitored compared to the reference group with an OR=1.96 (95% CI 1.10, 3.50), those aged 50 to 64 having an approximate 4.6 times the odds of being monitored compared to the reference group with an OR=4.55 (95% CI 2.73, 7.58), and those aged 40 to 49 having over 3 times the odds of being monitored compared to the reference group with an OR= 3.19 (95% CI 1.90, 5.33).

Factors that were not associated with monitoring of cholesterol during the study period included: prescription with other antipsychotics or antidepressants, BMI, history of high blood pressure, cardiovascular disease, prior testing of blood glucose, gender, smoking status, and history of hospitalisation in the past year.

**Table 16 Monitoring of elevated cholesterol for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Elevated cholesterol assessed at least once in study period*** | 887 | 246 | (27.7) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-8 visits)* | 234 | 26 | (11.1) |
| | *Q2 (9-12 visits)* | 219 | 68 | (31.1) |
| | *Q3 (13-18 visits)* | 216 | 75 | (34.7) |
| | *Q4 (19-62 visits)* | 218 | 77 | (35.3) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 85 | 26 | (30.6) |
| | *No* | 802 | 220 | (27.4) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 664 | 185 | (27.9) |
| | *No* | 223 | 61 | (27.4) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 536 | 177 | (33.0) |
| | *No* | 289 | 66 | (22.8) |
| | *Missing* | 62 | 3 | (4.8) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *Yes* | 9 | 2 | (22.2) |
| | *No* | 878 | 244 | (27.8) |
| | | | | |

**Table 16 Monitoring of elevated cholesterol for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 177 | 85 | (48.0) |
| | *No* | 710 | 161 | (22.7) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.81* | *(1.16, 2.81)* | |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 354 | 142 | (40.1) |
| | *No* | 533 | 104 | (19.5) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.78* | *(1.24, 2.54)* | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 35 | 8 | (22.9) |
| | *No* | 852 | 238 | (27.9) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 85 | 47 | (55.3) |
| | *No* | 802 | 199 | (24.8) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *2.48* | *(1.43, 4.30)* | |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 402 | 149 | (37.1) |
| | *No* | 485 | 97 | (20.0) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 578 | 152 | (26.3) |
| | *Male* | 309 | 94 | (30.4) |
| | | | | |

**Table 16 Monitoring of elevated cholesterol for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 13 | 8 | (61.5) |
| | *No* | 874 | 238 | (27.2) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 42 | 3 | (7.1) |
| | *25-39* | 211 | 26 | (12.3) |
| | *40-49* | 223 | 69 | (30.9) |
| | *50-64* | 229 | 96 | (41.9) |
| | *≥65* | 182 | 52 | (28.6) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | ***Adjusted Odds Ratio (95% CI)*** | | | |
| | *Age 18 - 39* | *Reference* | | |
| | *Age 40 - 49* | *3.19* | *(1.90, 5.33)* | |
| | *Age 50 - 64* | *4.55* | *(2.73, 7.58)* | |
| | *Age ≥65* | *1.96* | *(1.10, 3.50)* | |
| | | | | |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 887 | 246 | (27.7) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 365 | 108 | (29.6) |
| | *No* | 128 | 48 | (37.5) |
| | *Missing* | 394 | 90 | (22.8) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 264 | 77 | (29.2) |
| | *No* | 623 | 169 | (27.1) |

Table 17 presents the number of GP practices that monitored the majority of their patients for signs and symptoms of hyperglycaemia during primary care visits according to the number of eligible patients in those practices.

Among the practices included in the analysis (n=93), 21 practices (23%) monitored for signs and symptoms of hyperglycaemia for 50% or more of their patients and only 2 practices (2%) monitored hyperglycaemia for more than 80% of patients at least once during the study period. 29% of those practices with smaller numbers of eligible patients (between 1 and 5) monitored 50% or more of their patients, whereas a smaller proportion of practices with higher numbers of eligible patients (for example, 12 to 34 patients) performed monitoring for 50% or more of their patients for hyperglycaemia.

**Table 17 Monitoring for signs and symptoms of hyperglycaemia for patients on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | **Proportion of patients monitored** | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *35 (38%)* | 10 (29%) | 3 (9%) | 2 (6%) | 2 (6%) | 2 (6%) |
| | | | | | | |
| **6-11** | *28 (30%)* | 6 (21%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *28 (30%)* | 5 (18%) | 1 (4%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *2 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *93 (100%)* | 21 (23%) | 4 (4%) | 2 (2%) | 2 (2%) | 2 (2%) |

Table 18 presents the proportion of patients monitored for signs and symptoms of hyperglycaemia during primary care visits by the number of physician visits and by risk factors. Among the patients studied (n=887), 283 (32%) were monitored for signs and symptoms of hyperglycaemia at least once during visits within the study period. The proportion of patients being monitored increased with the number of visits to the GP, with those in the highest quartile of visits (with between 19 and 62 visits) having a frequency of 43.6% patients monitored and those in the lowest quartile of visits (with between 1 and 8 visits) having 14% patients monitored.

Monitoring for signs and symptoms of hyperglycaemia was more likely for a range of risk factors associated with hyperglycaemia: patients had 1.6 times the odds of being monitored if they had a BMI over 25 compared to those who had a BMI less than 25, OR=1.60, 95% CI (1.16, 2.21), over twice the odds if they had a history of elevated cholesterol compared to

those who did not (OR=2.08 (95% CI 1.42, 3.16)), and 1.8 times the odds of being monitored if they had a history of monitoring for hyperglycaemia compared to those who did not OR= 1.76, 95% CI (1.28, 2.41). Monitoring for hyperglycaemia had lower odds of being performed among patients prescribed antidepressants in the prior 6 months OR=0.69 95% CI (0.49, 0.97).

A higher odds of monitoring for hyperglycaemia occurred for patients with a diagnosis of diabetes OR= 1.26 95% CI (0.75, 2.11), although this result was not statistically significant.

An age-related increase in monitoring of patients for signs and symptoms of hyperglycaemia was observed. Factors that were not predictive of the monitoring for signs and symptoms of hyperglycaemia during the study period included: prescription with other antipsychotics or antidepressants, history of high blood pressure or cardiovascular disease, prior testing of blood glucose, gender, smoking status, and history of hospitalisation in the past year.

**Table 18 Monitoring for signs and symptoms of hyperglycaemia for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Monitoring for signs and symptoms of hyperglycaemia at least once in study period*** | 887 | 283 | (31.9) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-8 visits)* | 234 | 32 | (13.7) |
| | *Q2 (9-12 visits)* | 219 | 74 | (33.8) |
| | *Q3 (13-18 visits)* | 216 | 82 | (38.0) |
| | *Q4 (19-62 visits)* | 218 | 95 | (43.6) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 85 | 29 | (34.1) |
| | *No* | 802 | 254 | (31.7) |
| | | | | |

**Table 18 Monitoring for signs and symptoms of hyperglycaemia for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 664 | 202 | (30.4) |
| | *No* | 223 | 81 | (36.3) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *0.69* | *(0.49, 0.97)* | |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 536 | 200 | (37.3) |
| | *No* | 289 | 74 | (25.6) |
| | *Missing* | 62 | 9 | (14.5) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.60* | *(1.16, 2.21)* | |
| | | | | |
| | ***High blood pressure*** | | | |
| | *Yes* | 9 | 2 | (22.2) |
| | *No* | 878 | 281 | (32.0) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 177 | 87 | (49.2) |
| | *No* | 710 | 196 | (27.6) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *2.08* | *(1.42, 3.06)* | |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 354 | 152 | (42.9) |
| | *No* | 533 | 131 | (24.6) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 35 | 10 | (28.6) |
| | *No* | 852 | 273 | (32.0) |
| | | | | |

**Table 18 Monitoring for signs and symptoms of hyperglycaemia for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Diabetes*** | | | |
| | *Yes* | 85 | 43 | (50.6) |
| | *No* | 802 | 240 | (29.9) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.26* | *(0.75, 2.11)* | |
| | | | | |
| | ***Monitoring of hyperglycaemia*** | | | |
| | *Yes* | 402 | 165 | (41.0) |
| | *No* | 485 | 118 | (24.3) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.76* | *(1.28, 2.41)* | |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 578 | 184 | (31.8) |
| | *Male* | 309 | 99 | (32.0) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 13 | 8 | (61.5) |
| | *No* | 874 | 275 | (31.5) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 42 | 7 | (16.7) |
| | *25-39* | 211 | 48 | (22.7) |
| | *40-49* | 223 | 72 | (32.3) |
| | *50-64* | 229 | 87 | (38.0) |
| | *≥65* | 182 | 69 | (37.9) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 887 | 283 | (31.9) |
| | | | | |

**Table 18 Monitoring for signs and symptoms of hyperglycaemia for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Smoking*** | | | |
| | *Yes* | 365 | 113 | (31.0) |
| | *No* | 128 | 55 | (43.0) |
| | *Missing* | 394 | 115 | (29.2) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 264 | 91 | (34.5) |
| | *No* | 623 | 192 | (30.8) |

Table 19 presents the number of GP practices that monitored ≥50% or more of their patients with diabetes mellitus for signs and symptoms of hyperglycaemia during primary care visits (during the study period) according to the number of eligible patients in those practices. A total of 48 practices (52% of all practices included in the study) had patients who were diagnosed as diabetic and therefore eligible for this analysis. Of these practices, 32 (67% of 48 practices) monitored for signs and symptoms of hyperglycaemia for 50% or more of their diabetic patients and only 18 practices (38%) monitored weight for 80% or more of their diabetic patients at least once during the study period. The results were similar for those practices with smaller numbers of eligible patients (between 1 and 5) in that monitoring of 50% or more of patients with diabetes mellitus for hyperglycaemia was performed by 66% of practices and nearly complete ascertainment or greater than 95% of such patients were monitored by 38% of practices.

**Table 19 Monitoring for signs and symptoms of hyperglycaemia for diabetic patients on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *47 (100%)* | 31 (66%) | 18 (38%) | 18 (38%) | 18 (38%) | 18 (38%) |
| | | | | | | |
| **6-11** | *1 (100%)* | 1 (100%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *48 (100%)* | 32 (67%) | 18 (38%) | 18 (38%) | 18 (38%) | 18 (38%) |

Table 20 presents the proportion of patients monitored for signs and symptoms of hyperglycaemia among diabetic patients during primary care visits by the number of physician visits and by risk factors. Among the 85 patients with diabetes mellitus (~10% of all patients included in the study), 43 (50.6%) were monitored for signs and symptoms of hyperglycaemia at least once during visits to GPs within the study period. Those patients with a number of GP visits in the third quartile of frequency (having between 13 and 18 visits) were most likely to monitored (73.1% of all patients).

Having a history of monitoring for hyperglycaemia was an indicator for having nearly a four-fold increase in the odds of being monitored than those who did not have such a history OR=3.90 95% CI (1.14, 13.31).

Factors that were not predictive of the monitoring for signs and symptoms of hyperglycaemia among patients with diabetes mellitus during the study period included: prescription with other antipsychotics or antidepressants, BMI, history of elevated cholesterol, blood lipid testing, cardiovascular disease, prior testing of blood glucose, gender, smoking status, and history of hospitalisation in the past year. Certain factors (i.e., high blood pressure and history of psychosis) were not able to be evaluated because of limitations of sample size in stratification of risk factors.

**Table 20 Monitoring for signs and symptoms of hyperglycaemia for diabetic patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Monitoring for signs and symptoms of hyperglycaemia for diabetic patients at least once in study period*** | 85 | 43 | (50.6) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-8 visits)* | 8 | 0 | (0.0) |
| | *Q2 (9-12 visits)* | 16 | 4 | (25.0) |
| | *Q3 (13-18 visits)* | 26 | 19 | (73.1) |
| | *Q4 (19-62 visits)* | 35 | 20 | (57.1) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 8 | 6 | (75.0) |
| | *No* | 77 | 37 | (48.1) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 66 | 34 | (51.5) |
| | *No* | 19 | 9 | (47.4) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 72 | 38 | (52.8) |
| | *No* | 13 | 5 | (38.5) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *Yes* | 2 | 0 | (0.0) |
| | *No* | 83 | 43 | (51.8) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 59 | 30 | (50.8) |
| | *No* | 26 | 13 | (50.0) |
| | | | | |

**Table 20 Monitoring for signs and symptoms of hyperglycaemia for diabetic patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Blood lipid testing*** | | | |
| | *Yes* | 64 | 32 | (50.0) |
| | *No* | 21 | 11 | (52.4) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 5 | 2 | (40.0) |
| | *No* | 80 | 41 | (51.3) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 85 | 43 | (50.6) |
| | | | | |
| | ***History of monitoring for hyperglycaemia*** | | | |
| | *Yes* | 69 | 39 | (56.5) |
| | *No* | 16 | 4 | (25.0) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *3.90* | *(1.14, 13.31)* | |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 47 | 25 | (53.2) |
| | *Male* | 38 | 18 | (47.4) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 2 | 2 | (100) |
| | *No* | 83 | 41 | (49.4) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 3 | 2 | (66.7) |
| | *25-39* | 11 | 4 | (36.4) |
| | *40-49* | 14 | 10 | (71.4) |
| | *50-64* | 28 | 12 | (42.9) |
| | *≥65* | 29 | 15 | (51.7) |
| | | | | |

**Table 20 Monitoring for signs and symptoms of hyperglycaemia for diabetic patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *No* | 85 | 43 | (50.6) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 32 | 14 | (43.8) |
| | *No* | 22 | 14 | (63.6) |
| | *Missing* | 31 | 15 | (48.4) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 38 | 18 | (47.4) |
| | *No* | 47 | 25 | (53.2) |

Table 21 presents the number of GP practices that monitored the majority of their patients at risk of developing diabetes mellitus for signs and symptoms of hyperglycaemia during primary care visits (during the study period) according to the number of eligible patients in those practices. A total of 89 practices (96% of all practices included in the study) had patients who met the eligibility criteria for having one or more risk factors for diabetes mellitus and were included in the analysis. Of these, 27 practices (30% of 89 practices) monitored for signs and symptoms of hyperglycaemia in patients with diabetes mellitus for 50% or more of their patients and 7 practices (8%) monitored weight for more than 80% of patients at least once during the study period. Practices with smaller numbers of eligible patients tended to monitor more frequently, with 38% of those practices with smaller numbers of eligible patients (between 1 and 5) performing monitoring for signs and symptoms of hyperglycaemia among patients at risk for diabetes in 50% or more of their patients, and a smaller proportion of practices with higher numbers of eligible patients (for example, those with 6-11 patients and 12-34 patients ) monitoring 50% or more of patients for hyperglycaemia in 24% and in 0% of their practices, respectively.

**Table 21 Monitoring for signs and symptoms of hyperglycaemia for patients at risk of diabetes on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *53 (100%)* | 20 (38%) | 6 (11%) | 6 (11%) | 6 (11%) | 6 (11%) |
| | | | | | | |
| **6-11** | *29 (100%)* | 7 (24%) | 1 (3%) | 1 (3%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *7 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *89 (100%)* | 27 (30%) | 7 (8%) | 7 (8%) | 6 (7%) | 6 (7%) |

Table 22 presents the proportion of patients at risk for diabetes monitored for signs and symptoms of hyperglycaemia during primary care visits by the number of physician visits and by risk factors. A total of 483 patients (54% of the total eligible population) were classed as 'at risk' of developing diabetes. Of these patients, 166 (34.4%) were monitored for signs and symptoms of hyperglycaemia at least once during visits within the study period. The proportion of patients being monitored for signs and symptoms of hyperglycaemia was highest (45.8%) for those with the greatest number of visits to the GP, falling into the highest quartile of visits (with between 19 and 62 visits).

A statistically significant lower odds of the performance of monitoring of patients at risk for diabetes for signs and symptoms of hyperglycaemia was observed among patients previously prescribed antidepressants within the past 6 months OR=0.63, 95% CI (0.40, 0.98). Lower odds of monitoring that did not reach statistical significance were associated with BMI >25 (OR=0.84, 95% CI (0.18, 4.04)), and patients with a history of cardiovascular disease (OR=0.60, 95% CI (0.19, 1.88)). Patients at risk of developing diabetes mellitus who also had a history of elevated cholesterol had higher odds of being monitored for signs and symptoms of hyperglycaemia with an OR=1.98 95% CI (1.18, 3.32).

An age-related increase in monitoring of patients at risk for diabetes for signs and symptoms of hyperglycaemia for signs and symptoms of hyperglycaemia was observed through age 64. Monitoring for signs and symptoms for hyperglycaemia had higher odds of occurring among older age groups versus those aged 18 to 39 (the reference group), with those aged 50 to 64 and those aged 40 to 49 years having nearly twice the odds of being monitored compared to the reference group (OR: 1.80 and 95% CIs (1.03, 3.15) for both). The modelling results suggest that those aged 65 years and over also had higher odds of being monitored (OR=1.43, 95% CI (0.75, 2.74)), but this result was not statistically different from the reference group.

Factors that were not associated with monitoring for signs and symptoms of hyperglycaemia among patients with diabetes mellitus during the study period included: prescription with other antipsychotics, history of high blood pressure, blood lipid testing, being diabetic, gender, history of anxiety or psychosis, smoking status, and history of hospitalisation in the past year.

**Table 22 Monitoring for signs and symptoms of hyperglycaemia for patients at risk of diabetes on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | ***Monitoring for signs and symptoms of hyperglycaemia for diabetic patients at least once in study period*** | 483 | 166 | (34.4) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-8 visits)* | 120 | 18 | (15.0) |
| | *Q2 (9-12 visits)* | 125 | 51 | (40.8) |
| | *Q3 (13-18 visits)* | 120 | 43 | (35.8) |
| | *Q4 (19-62 visits)* | 118 | 54 | (45.8) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 51 | 19 | (37.3) |
| | *No* | 432 | 147 | (34.0) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 367 | 118 | (32.2) |
| | *No* | 116 | 48 | (41.4) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *0.63* | *(0.40, 0.98)* | |
| | | | | |

**Table 22 Monitoring for signs and symptoms of hyperglycaemia for patients at risk of diabetes on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***BMI >25*** | | | |
| | *Yes* | 464 | 162 | (34.9) |
| | *No* | 16 | 4 | (25.0) |
| | *Missing* | 3 | 0 | (0.0) |
| | | | | |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *0.84* | *(0.18, 4.04)* | |
| | | | | |
| | ***High blood pressure*** | | | |
| | *Yes* | 7 | 2 | (28.6) |
| | *No* | 476 | 164 | (34.5) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 88 | 44 | (50.0) |
| | *No* | 395 | 122 | (30.9) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.98* | *(1.18, 3.32)* | |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 201 | 85 | (42.3) |
| | *No* | 282 | 81 | (28.7) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 30 | 8 | (26.7) |
| | *No* | 453 | 158 | (34.9) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *0.60* | *(0.19, 1.88)* | |
| | | | | |

**Table 22 Monitoring for signs and symptoms of hyperglycaemia for patients at risk of diabetes on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Diabetes*** | | | |
| | *No* | 483 | 166 | (34.4) |
| | | | | |
| | ***History of monitoring for hyperglycaemia*** | | | |
| | *Yes* | 230 | 91 | (39.6) |
| | *No* | 253 | 75 | (29.6) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.38* | *(0.93, 2.06)* | |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 319 | 108 | (33.9) |
| | *Male* | 164 | 58 | (35.4) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 7 | 4 | (57.1) |
| | *No* | 476 | 162 | (34.0) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 11 | 1 | (9.1) |
| | *25-39* | 120 | 30 | (25.0) |
| | *40-49* | 127 | 48 | (37.8) |
| | *50-64* | 137 | 55 | (40.1) |
| | *≥65* | 88 | 32 | (36.4) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | ***Adjusted Odds Ratio (95% CI)*** | | | |
| | *Age 18 - 39* | *Reference* | | |
| | *Age 40 - 49* | *1.80* | *(1.03, 3.15)* | |
| | *Age 50 - 64* | *1.80* | *(1.03, 3.15)* | |
| | *Age ≥65* | *1.43* | *(0.75, 2.74)* | |
| | | | | |

**Table 22 Monitoring for signs and symptoms of hyperglycaemia for patients at risk of diabetes on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *No* | 483 | 166 | (34.4) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 203 | 70 | (34.5) |
| | *No* | 73 | 27 | (37.0) |
| | *Missing* | 207 | 69 | (33.3) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 141 | 53 | (37.6) |
| | *No* | 342 | 113 | (33.0) |

Table 23 presents the number of GP practices that provided counselling for healthy eating, exercise, or lifestyle practices to majority of their patients during primary care visits (during the study period) according to the number of eligible patients in those practices. Overall, 27 practices (29% of all practices) provided counselling to 50% or more of their patients and 8 practices (9% of total practices) provided counselling to 80% or more of patients at least once during the study period. The proportion of practices providing health/lifestyle counselling to 50% or more of their patients during the study period decreased with increasing number of eligible patients in the practice. 43% of practices with 1 to 5 eligible patients counselled 50% or more of their patients, whereas 25% of practices with 6-11 eligible patients and 18% of practices with 12-34 eligible patients counselled 50% or more of their patients during the study period. Since the number of practices exceeding eligible patients was 2, the impact of small sample size upon the observations for these practices was noted.

**Table 23 Monitoring of healthy eating/ exercise/ lifestyle for patients on quetiapine according to number of eligible patients in practice: by General Practice in the UK**

| | | Proportion of patients counselled | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *35 (100%)* | 15 (43%) | 8 (23%) | 7 (20%) | 7 (20%) | 7 (20%) |
| | | | | | | |
| **6-11** | *28 (100%)* | 7 (25%) | 2 (7%) | 1 (4%) | 1 (4%) | 0 (0%) |
| | | | | | | |
| **12-34** | *28 (100%)* | 5 (18%) | 1 (4%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *2 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *93 (100%)* | 27 (29%) | 11 (12%) | 8 (9%) | 8 (9%) | 7 (8%) |

Table 24 presents the proportion of patients who were provided counselling to promote healthy eating, exercise, or lifestyle practices during primary care visits by the number of physician visits and by risk factors. Overall 273 (30.8%) patients were given counselling to promote healthy eating, exercise, or lifestyle behaviours at least once during visits within the study period. The proportion of patients given counselling increased with the number of visits to the GP, with approximately 40% of patients in the highest quartile of visits (with between 19 and 62 visits) having received counselling, 37% of patients in the third quartile of visits (with between 13 and 18 visits) having received counselling, 29.7% of patients falling into the second quartile (with between 9 and 12 visits) having received counselling, and 17.5% of patients in the lowest quartile (having between 1 and 8 visits) having received counselling.

Patients who had been hospitalised within the past year had increased odds of receiving counselling to promote healthy eating, exercise, or lifestyle behaviours OR= 1.46, 95% CI (1.02, 2.10).

There was no consistent pattern of receiving counselling to promote healthy eating, exercise, or lifestyle behaviours in relation to age of the patient. None of the risk factors studied were found to be associated with the odds of receiving healthy lifestyle counselling.

**Table 24 Monitoring for healthy eating/ exercise/ lifestyle for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Counselling on healthy lifestyle conducted at least once in study period*** | 887 | 273 | (30.8) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-8 visits)* | 234 | 41 | (17.5) |
| | *Q2 (9-12 visits)* | 219 | 65 | (29.7) |
| | *Q3 (13-18 visits)* | 216 | 80 | (37.0) |
| | *Q4 (19-62 visits)* | 218 | 87 | (39.9) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 85 | 27 | (31.8) |
| | *No* | 802 | 246 | (30.7) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 664 | 196 | (29.5) |
| | *No* | 223 | 77 | (34.5) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 536 | 170 | (31.7) |
| | *No* | 289 | 84 | (29.1) |
| | *Missing* | 62 | 19 | (30.6) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *Yes* | 9 | 2 | (22.2) |
| | *No* | 878 | 271 | (30.9) |
| | | | | |

**Table 24 Monitoring for healthy eating/ exercise/ lifestyle for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 177 | 60 | (33.9) |
| | *No* | 710 | 213 | (30.0) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 354 | 118 | (33.3) |
| | *No* | 533 | 155 | (29.1) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 35 | 14 | (40.0) |
| | *No* | 852 | 259 | (30.4) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 85 | 27 | (31.8) |
| | *No* | 802 | 246 | (30.7) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 402 | 129 | (32.1) |
| | *No* | 485 | 144 | (29.7) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 578 | 180 | (31.1) |
| | *Male* | 309 | 93 | (30.1) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 13 | 5 | (38.5) |
| | *No* | 874 | 268 | (30.7) |
| | | | | |

**Table 24 Monitoring for healthy eating/ exercise/ lifestyle for patients on quetiapine, overall, by number of physician visits, and risk factors: patients seen in General Practice in the UK**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Age*** | | | |
| | *<25* | 42 | 12 | (28.6) |
| | *25-39* | 211 | 67 | (31.8) |
| | *40-49* | 223 | 57 | (25.6) |
| | *50-64* | 229 | 77 | (33.6) |
| | *≥65* | 182 | 60 | (33.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 887 | 273 | (30.8) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 365 | 118 | (32.3) |
| | *No* | 128 | 54 | (42.2) |
| | *Missing* | 394 | 101 | (25.6) |
| | | | | |
| | ***Hospitalised in the last year*** | | | |
| | *Yes* | 264 | 90 | (34.1) |
| | *No* | 623 | 183 | (29.4) |
| | | | | |
| | | *Odds ratio* | *(95% CI)* | |
| | *Adjusted Odds Ratio (95% CI)* | *1.46* | *(1.02, 2.10)* | |

Table 25 shows the descriptive statistics including the range, median, values corresponding to the 25$^{th}$ and 75$^{th}$ percentiles for the distribution of proportions of patients who received different metabolic monitoring previously described from GP practices in the primary care setting in the UK. There were 93 GP practices where eligible patients ranged from 1 to 56 in each practice. A median of 40% of patients were monitored for weight at any time during the study period. There were 72 GP practices in the UK with patients initiated on quetiapine ranging from 1 to 11 patients in each practice. Monitoring of weight at the visit in which quetiapine treatment was initiated was not conducted in any of the practices during the study period.

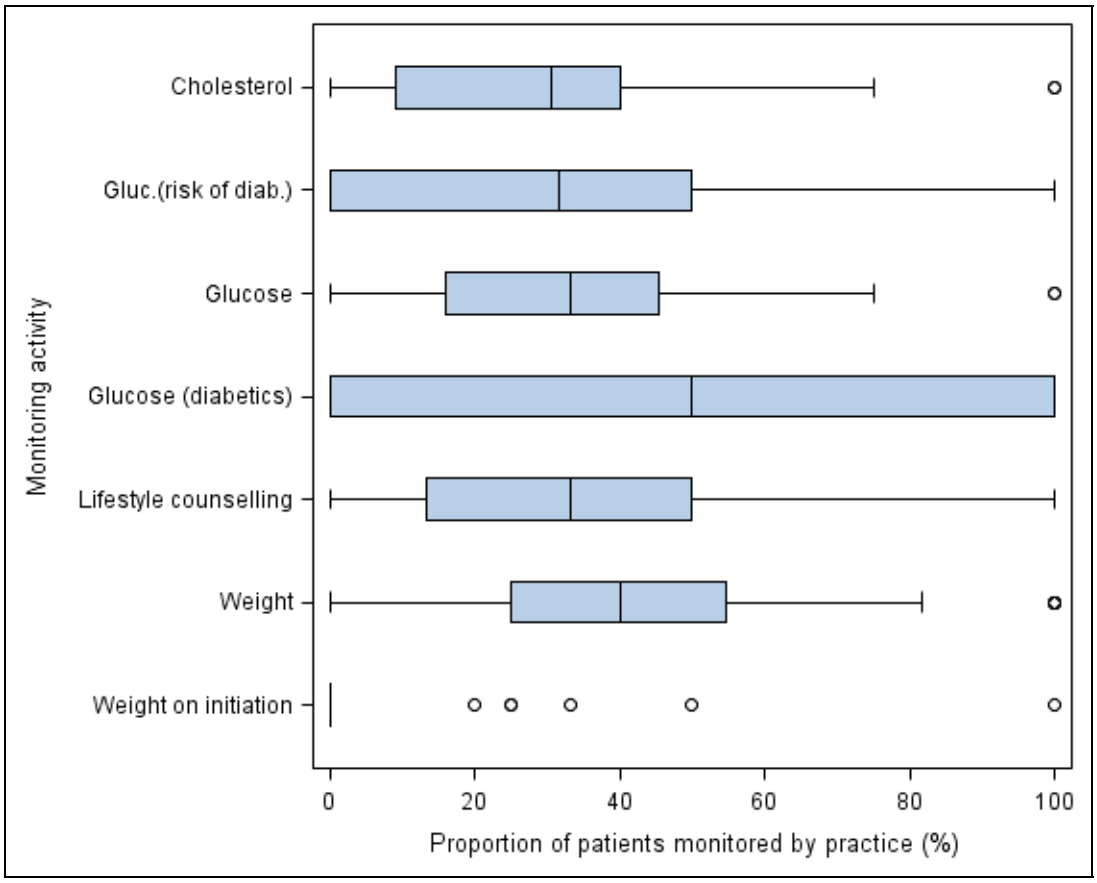
Cholesterol (i.e. lipid level) was monitored for the assessment of hyperlipidaemia with a median of 30% of patients being monitored in UK GP practices. Glucose was monitored for the assessment of hyperglycaemia with a median of 33% of patients being monitored in each

of the UK GP practices. With regard to monitoring related to signs and symptoms of hyperglycaemia, 48 of the GP practices had diabetic patients in the range of 1 and 6 patients; the median proportion of patients monitored for hyperglycaemia was 50% for each practice. There were 89 practices with 1-31 patients with risk factors for developing diabetes mellitus. In this subgroup, the median proportion of patients monitored for hyperglycaemia was 32% for each practice. A median proportion of 33% of patients were provided counselling on adopting healthy lifestyle behaviours. Figure 1 depicts this information in a graphical format.

**Table 25 Monitoring by GP practices in the UK: Distributions of the proportions of patients monitored**

| | | | | **Proportion of patients monitored in the practice** | |
|---|---|---|---|---|---|
| **Monitoring activity** | **Patients** | **Number of practices** | **Range of the number of patients in each practice (min, max)** | **Median** | **[LQ, UQ]** |
| | | | | | |
| **Weight** | *All* | 93 | (1, 56) | 40% | [25%, 55%] |
| | *Initiated on quetiapine* | 72 | (1, 11) | 0% | [0%, 0%] |
| | | | | | |
| **Cholesterol** | *All* | 93 | (1, 56) | 30% | [9%, 40%] |
| | | | | | |
| **Glucose** | *All* | 93 | (1, 56) | 33% | [16%, 45%] |
| | *Diabetics* | 48 | (1, 6) | 50% | [0%, 100%] |
| | *At risk of diabetes* | 89 | (1, 31) | 32% | [0%, 50%] |
| | | | | | |
| **Health counselling** | *All* | 93 | (1, 56) | 33% | [13%, 50%] |

**Figure 1** **Monitoring by practices: Distributions of the proportions of patients monitored by GP practices in the UK (*Descriptive Statistics (Median, [LQ, UQ]) are:* weight on initiation (0%, [0%, 0%]), weight on treatment (40%, [25%, 55%]), lifestyle counselling (33%, [13%, 50%]), glucose monitoring in diabetic patients (50%, [0%, 100%]), glucose monitoring in all patients (33%, [16%, 45%]), glucose monitoring in patients at risk of developing diabetes (32%, [0%, 50%]) and cholesterol monitoring (30%, [9%, 40%]))**




## 10.5 Participants - Psychiatrists (Germany)

Table 26 presents the attrition table of psychiatry practices and patients in Germany. There were 251 office-based psychiatry and neurology practices with data for 1,934,489 patients in the DA by end of January 2013. The inclusion criteria specified in Section 9.3 were applied individually to this patient sample as indicated in the attrition table.

There were 2,294 patients from 56 psychiatry practices aged 18 years and above on 1st January 2012, with one or more of qualifying diagnoses (schizophrenia, bipolar disorder or major depressive disorder) in the medical history, with at least one prescription of quetiapine and with one or more consultations with the psychiatrists between 13 February and 31 August 2012. When the inclusion criteria of active patients within the observational period of 1 February 2012 and 1 August 2012; and availability of 12 months medical history prior to

the observational period were applied, the patient sample sizes reduced to 2,010 and 1,466 respectively. The final criterion in the attrition table was applied to those where the inclusion diagnosis preceded quetiapine prescription which resulted in 1,451 eligible patients in the DA managed by 42 psychiatry practices in Germany for analysis.

**Table 26 Attrition table of psychiatry practices and patients in Germany**

| Step | Description | Patients | Practices |
|---|---|---|---|
| 1 | Adult (≥18 years) patients in DA Germany as of 1 January 2013 (Psychiatry/Neurology) | 1,827,633 | 251 |
| 2 | Prescribed quetiapine between 13 February and 31 August 2012 and at some point in records, have a qualifying diagnosis (schizophrenia, bipolar disorder, or major depressive disorder) | 9,617 | 229 |
| 3 | At least one consultation with psychiatrist between 13 February and 31 August 2012 | 2,294 | 56 |
| 4 | Practices up to reporting standard ensuring that the patient data was reported for the entirety of the study period of 13 February to 31 August 2012 | 2,010 | 46 |
| 5 | Evidence of clinical interaction >12 months before study | 1,466 | 42 |
| 6 | Confirmation that earliest recorded diagnosis preceded quetiapine prescription | 1,451 | 42 |

## 10.6 Descriptive data - Psychiatrists (Germany)

Table 27 provides characteristics of psychiatry practices in which the study patients were observed in Germany that were within the scope of the assessment of EMR data including specialist physicians in Germany. Seventy-nine percent (33 of 42) psychiatry practices were solo practices, while the remaining were group practices. The lead physician within these practices had a mean (SD) age of 52.6 (6.4) years, and the majority (57%) were male. These physicians have been registered for 12.6 years on average and were mostly based in the North Rhine-Westphalia region. There was a median of 25 study patients per practice; eligible patients ranged from 1 to 123 in these psychiatry practices.

## Table 27 Characteristics of psychiatry practices in Germany

| | | Total number of practices (N=42) | |
|---|---|---|---|
| **Total number of doctors (= practices)** | | 42 | |
| **Practice type n (%)** | | | |
| | *Group* | 9 | (21.4) |
| | *Solo* | 33 | (78.6) |
| | | | |
| **Number of doctors in practice n (%)** | | | |
| | *1* | 33 | (78.6) |
| | *2* | 7 | (16.7) |
| | *3* | 1 | (2.4) |
| | *4* | 1 | (2.4) |
| | | | |
| **Doctor age** | | | |
| | *Mean (SD)* | 52.6 | (6.4) |
| | *Median* | 53 | |
| | *[LQ, UQ]* | [47, 56] | |
| | *(min, max)* | (40, 64) | |
| | | | |
| **Speciality n (%)** | | | |
| | *Psychiatry* | 42 | (100) |
| | | | |
| **Sex n (%)** | | | |
| | *Female* | 18 | (42.9) |
| | *Male* | 24 | (57.1) |
| | | | |
| **Years registered** | | | |
| | *Unknown* | 0 | |
| | *Mean (SD)* | 12.6 | (5.7) |
| | *Median* | 13 | |
| | *[LQ, UQ]* | [8, 17] | |
| | *(min, max)* | (2, 27) | |
| | | | |

**Table 27 Characteristics of psychiatry practices in Germany**

| | | Total number of practices (N=42) | |
|---|---|---|---|
| **Practice region n (%)** | | | |
| | *North Rhine-Westphalia* | 9 | (21.4) |
| | *Baden-Wuerttemberg* | 6 | (14.3) |
| | *Bavaria* | 6 | (14.3) |
| | *Schleswig-Holstein, Lower Saxony, Bremen, Hamburg* | 6 | (14.3) |
| | *Thuringia, Saxony* | 6 | (14.3) |
| | *Hessen, Rhineland-Palatinate, Saarland* | 5 | (11.9) |
| | *Berlin* | 2 | (4.8) |
| | *Brandenburg, Mecklenburg-Western Pomerania, Saxony-Anhalt* | 2 | (4.8) |
| | | | |
| **Number of patients per practice included in the study** | | | |
| | *Mean (SD)* | 34.5 | (29.4) |
| | *Median* | 25 | |
| | *[LQ, UQ]* | [16, 43] | |
| | *(min, max)* | (1, 123) | |

Demographic and clinical characteristics of the patients included in the analysis are shown in Table 28. Fifty-eight percent of the patients were female with a median age of 51 years and a mean (SD) age of 51.4 (15.2) years. Over a third (35.6%) of the study population was in the 50 to 64 year age group. Approximately 25% of the study population were in the age band of 40 to 49 years.

Most patients (44% and 46% respectively) were either Members or Retirees in terms of their insurance status. Patients on private medical insurance were low at 4%, and dependents only represented 6% of the sample. Smoking status of patients was not available for 99% of the patient population.

46.2% of the patients were diagnosed with bipolar disorder, 18.5% had a diagnosis of schizophrenia and 9.6% with major depressive disorder (MDD). 11.6% of the study population had a combined diagnosis of bipolar disorder and MDD, while 9.9% had a qualifying diagnosis of both bipolar disorder and schizophrenia. 2.2% of patients had MDD and schizophrenia, and 1.9% of patients had a diagnosis of all three conditions.

Few patient electronic records exhibited recorded diagnoses or biometric measures that identified risk factors for development of diabetes mellitus (58 patients or 4%) while less than 1% (n=9 patients) had evidence of being diagnosed or treated for diabetes mellitus. Only 30 patients (2%) had evidence of lipid panel testing in the 12 months prior to the study period while prior monitoring of elevated cholesterol and weight were lower than 1%.

The majority (67%) of the study population were not prescribed any other antipsychotic medications in the 6 months prior to the observation period. Among those prescribed other antipsychotics, 24% of the patients were prescribed one and approximately 9% were prescribed two or more antipsychotics, respectively. Risperidone, promethazine, and aripiprazole were the most frequently prescribed antipsychotic medications.

The majority (~60%) of patients were prescribed at least one antidepressant during the 6 months prior to the observation period, with 39% of patients being prescribed only one, 15.8% prescribed two, and 4.8% prescribed 3 or more antidepressants. Citalopram, venlafaxine, and mirtazapine were the most frequently prescribed antidepressants received by approximately 15.1%, 14.7%, and 8.1% of patients, respectively.

**Table 28 Demographic and clinical characteristics of patients seen in psychiatry practices in Germany**

| | | **Number of patients (N=1451)** | |
|---|---|---|---|
| **Sex n (%)** | | | |
| | *Male* | 606 | (41.8) |
| | *Female* | 845 | (58.2) |
| | | | |
| **Age** | | | |
| | *Mean (SD)* | 51.4 | (15.2) |
| | *Median* | 51 | |
| | *[LQ, UQ]* | [41, 60] | |
| | *(min, max)* | (19, 94) | |
| | | | |
| | *18-24 (<25)* | 44 | (3.0) |
| | *25-39* | 268 | (18.5) |
| | *40-49* | 357 | (24.6) |
| | *50-64* | 516 | (35.6) |
| | *≥65* | 266 | (18.3) |
| | | | |
| **Insurance status n (%)** | | | |
| | *Dependant* | 82 | (5.7) |
| | *Member* | 637 | (43.9) |
| | *Privately insured* | 64 | (4.4) |
| | *Retiree* | 668 | (46.0) |

## Table 28 Demographic and clinical characteristics of patients seen in psychiatry practices in Germany

| | | Number of patients (N=1451) | |
|---|---|---|---|
| **Smoking status n (%)** | | | |
| | *Current smoker* | 15 | (88.2) |
| | *Not currently smoking* | 2 | (11.8) |
| | *Unknown* | 1434 | |
| | | | |
| **Qualifying diagnosis n (%)** | | | |
| | *Schizophrenia* | 269 | (18.5) |
| | *Bipolar disorder* | 671 | (46.2) |
| | *Major depressive disorder (MDD)* | 139 | (9.6) |
| | | | |
| | *Bipolar + MDD* | 168 | (11.6) |
| | *Bipolar + Schizophrenia* | 144 | (9.9) |
| | *MDD + Schizophrenia* | 32 | (2.2) |
| | | | |
| | *Schizophrenia + bipolar + MDD* | 28 | (1.9) |
| | | | |
| | | | |
| **Lipid panel testing in prior 12 months n (%)** | | | |
| | *Lipid panel testing in prior 12 months n (%)* | 30 | (2.1) |
| | | | |
| **Evidence of diabetes mellitus n (%)** | | | |
| | *Evidence of diabetes mellitus n (%)* | 9 | (0.6) |
| | | | |
| **History of pre-diabetes mellitus excluding diabetic patients n (%)** | | | |
| | *History of pre-diabetes (excluding diabetic patients) n (%)* | 0 | (0.0) |
| | | | |
| **At risk of diabetes mellitus n (%)** | | | |
| | *At risk of diabetes (excluding diabetic patients) n (%)* | 58 | (4.0) |
| | | | |
| **History of elevated cholesterol n (%)** | | | |
| | *History of elevated cholesterol n (%)* | 7 | (0.5) |

## Table 28 Demographic and clinical characteristics of patients seen in psychiatry practices in Germany

| | | Number of patients (N=1451) | |
|---|---|---|---|
| **History of weight monitoring n (%)** | | | |
| | *History of weight monitoring n (%)* | 8 | (0.6) |
| | | | |
| **Prescription of other antipsychotics in prior 6 months** | | | |
| **Substances n (%)** | | | |
| | *AMISULPRIDE* | 30 | (2.1) |
| | *ARIPIPRAZOLE* | 58 | (4.0) |
| | *ASENAPINE* | 2 | (0.1) |
| | *BENPERIDOL* | 7 | (0.5) |
| | *BROMPERIDOL* | 1 | (0.1) |
| | *CHLORPROTHIXENE* | 29 | (2.0) |
| | *CLOZAPINE* | 11 | (0.8) |
| | *FLUPENTIXOL* | 25 | (1.7) |
| | *FLUPHENAZINE* | 7 | (0.5) |
| | *FLUSPIRILENE* | 2 | (0.1) |
| | *HALOPERIDOL* | 37 | (2.5) |
| | *LEVOMEPROMAZINE* | 29 | (2.0) |
| | *MELPERONE* | 38 | (2.6) |
| | *OLANZAPINE* | 29 | (2.0) |
| | *PALIPERIDONE PALMITATE* | 11 | (0.8) |
| | *PERAZINE* | 31 | (2.1) |
| | *PERPHENAZINE* | 6 | (0.4) |
| | *PIMOZIDE* | 1 | (0.1) |
| | *PIPAMPERONE* | 51 | (3.5) |
| | *PROMETHAZINE* | 74 | (5.1) |
| | *PROTHIPENDYL* | 35 | (2.4) |
| | *RISPERIDONE* | 90 | (6.2) |
| | *SERTINDOLE* | 1 | (0.1) |
| | *SULPIRIDE* | 13 | (0.9) |
| **Substances n (%)** | *THIORIDAZINE* | 1 | (0.1) |
| | *TIAPRIDE* | 11 | (0.8) |
| | *ZIPRASIDONE* | 8 | (0.6) |
| | *ZUCLOPENTHIXOL* | 4 | (0.3) |

## Table 28 Demographic and clinical characteristics of patients seen in psychiatry practices in Germany

| | | Number of patients (N=1451) | |
|---|---|---|---|
| **Number of other antipsychotics prescribed n (%)** | | | |
| | *0* | 971 | (66.9) |
| | *1* | 352 | (24.3) |
| | *2* | 104 | (7.2) |
| | *3 or more* | 24 | (1.7) |
| | | | |
| **Prescription of antidepressants in prior 6 months** | | | |
| **Substances n (%)** | | | |
| | *AGOMELATINE* | 61 | (4.2) |
| | *AMITRIPTYLINE* | 45 | (3.1) |
| | *BUPROPION* | 50 | (3.4) |
| | *CITALOPRAM* | 219 | (15.1) |
| | *CLOMIPRAMINE* | 18 | (1.2) |
| | *DOXEPIN* | 41 | (2.8) |
| | *DULOXETINE* | 80 | (5.5) |
| | *ESCITALOPRAM* | 22 | (1.5) |
| | *FLUOXETINE* | 50 | (3.4) |
| | *FLUVOXAMINE* | 1 | (0.1) |
| | *HYPERICUM PERFORATUM* | 2 | (0.1) |
| | *IMIPRAMINE* | 52 | (3.6) |
| | *LITHIUM* | 103 | (7.1) |
| | *MAPROTILINE* | 6 | (0.4) |
| | *MIANSERIN* | 1 | (0.1) |
| | *MIRTAZAPINE* | 117 | (8.1) |
| | *MOCLOBEMIDE* | 6 | (0.4) |
| | *NORTRIPTYLINE* | 19 | (1.3) |
| | *OPIPRAMOL* | 31 | (2.1) |
| **Substances n (%)** | *PAROXETINE* | 25 | (1.7) |
| | *REBOXETINE* | 7 | (0.5) |
| | *SERTRALINE* | 70 | (4.8) |
| | *TRANYLCYPROMINE* | 3 | (0.2) |
| | *TRAZODONE* | 10 | (0.7) |
| | *VENLAFAXINE* | 214 | (14.7) |

**Table 28 Demographic and clinical characteristics of patients seen in psychiatry practices in Germany**

| | | Number of patients (N=1451) | |
|---|---|---|---|
| **Number of antidepressants prescribed n (%)** | | | |
| | *0* | 586 | (40.4) |
| | *1* | 566 | (39.0) |
| | *2* | 229 | (15.8) |
| | *3 or more* | 70 | (4.8) |

Table 29 presents descriptive data on the number of physician visits and quetiapine prescription status (as new users initiating quetiapine or as prevalent users, continuing on quetiapine treatment) for patients who were managed by psychiatrists in Germany. Patients had a mean (SD) of 4.7 (3.3) visits and a median of 4 visits to their psychiatrist during the observational period. There were only 17.8% of patients newly initiated on quetiapine versus 82.2% ongoing users of the medication at the start of the study period.

**Table 29 Treatment of patients seen in psychiatry practices in Germany**

| | | Total number of patients (N=1451) | |
|---|---|---|---|
| **Number of visits per patient in study period** | | | |
| | *Mean (SD)* | 4.7 | (3.3) |
| | *Median* | 4 | |
| | *[LQ, UQ]* | [2, 6] | |
| | *(min, max)* | (1, 41) | |
| | | | |
| | *1* | 103 | (7.1) |
| | *2* | 273 | (18.8) |
| | *3* | 242 | (16.7) |
| | *4* | 242 | (16.7) |
| | *5* | 171 | (11.8) |
| | *6* | 136 | (9.4) |
| | *7* | 85 | (5.9) |
| | *8* | 59 | (4.1) |
| | *9* | 39 | (2.7) |
| | *10* | 28 | (1.9) |
| | *>10* | 73 | (5.0) |
| | | | |
| **Quetiapine treatment** | | | |
| | *Patients initiated during study n (%)* | 259 | (17.8) |
| | *Prevalent users n (%)* | 1192 | (82.2) |

Table 30 presents study findings on risk factors and potential confounding variables believed to potentially have influence in the performance of metabolic monitoring for the study population managed by psychiatrists in Germany. Body mass index (BMI) was recorded in the medical notes for 51 of 1451 patients or approximately 4% of the study population. The mean (SD) BMI was 27.6 (6.3) indicating these patients were, on average, overweight. 182 patients (12.5%) had a prior diagnosis of psychosis or anxiety. None of the patients had a recorded history of high blood pressure and very few patients (<1%) had elevated cholesterol recorded in their medical history. Evidence of lipid testing was available for only 2.1% of patients. There was 1% or less of patients with a recorded history of cardiovascular disease or diabetes mellitus. Glucose testing among the 1,442 non-diabetic patients was recorded for only 1.7% of patients. There were no patients with a recorded diagnosis of metabolic syndrome.

## Table 30 Risk factors for patients seen in psychiatry practices in the Germany

| | | Total number of patients (N=1451) | |
|---|---|---|---|
| **Body mass index** | | | |
| | *Unknown* | 1400 | |
| | | | |
| | *Mean (SD)[n=51]* | 27.6 | (6.3) |
| | *Median* | 27 | |
| | *[LQ, UQ]* | [25, 31] | |
| | *(min, max)* | (17, 49) | |
| | | | |
| | *Summary categories n (%)* | | |
| | *Unknown* | 1400 | (96.5) |
| | *≤25* | 16 | (1.1) |
| | *>25* | 35 | (2.4) |
| | | | |
| | *Expanded categories n (%)* | | |
| | *Unknown* | 1400 | (96.5) |
| | *<18.5* | 4 | (0.3) |
| | *18.5-25.0* | 12 | (0.8) |
| | *>25.0-30.0* | 21 | (1.4) |
| | *>30.0-35.0* | 9 | (0.6) |
| | *>35* | 5 | (0.3) |
| | | | |
| **History with diagnosis of psychosis or anxiety n (%)** | | | |
| | *Yes* | 182 | (12.5) |
| | *No* | 1269 | (87.5) |
| | | | |
| **High blood pressure n (%)** | | | |
| | *No* | 1451 | (100) |
| | | | |
| **Elevated cholesterol n (%)** | | | |
| | *Yes* | 7 | (0.5) |
| | *No* | 1444 | (99.5) |
| | | | |

**Table 30 Risk factors for patients seen in psychiatry practices in the Germany**

| | | Total number of patients (N=1451) | |
|---|---|---|---|
| **Testing of lipids n (%)** | | | |
| | *Yes* | 30 | (2.1) |
| | *No* | 1421 | (97.9) |
| | | | |
| **History of cardiovascular disease n (%)** | | | |
| | *Yes* | 19 | (1.3) |
| | *No* | 1432 | (98.7) |
| | | | |
| **History of diabetes mellitus n (%)** | | | |
| | *Yes* | 9 | (0.6) |
| | *No* | 1442 | (99.4) |
| | | | |
| **Testing of glucose in the past 12 months (excl. diabetics n=1442) n (%)** | | | |
| | *Yes* | 25 | (1.7) |
| | *No* | 1417 | (98.3) |
| | | | |
| **Diagnosis of metabolic syndrome** | | | |
| | *No* | 1451 | (100) |

## 10.7 Outcome data: summary of outcomes data - Psychiatrists (Germany)

Table 31 provides a summary of German psychiatry practices' metabolic monitoring activities. A total of 38 practices had newly initiated patients on quetiapine during the study period. None of these practices monitored patients' weight when quetiapine was initially prescribed. There was only one practice which indicated monitoring of 50% or more of their patients for weight during ongoing visits and where lipids were assessed for elevated cholesterol. None of the 42 practices monitored 50% or more of their patients in the assessment for signs and symptoms of hyperglycaemia during the study period. There were 6 practices (14% of total practices) with diabetic patients on quetiapine, and none of them monitored 50% or more of their patients for signs and symptoms of hyperglycaemia during the study period. Of the 19 practices (45% of total practices) with patients at risk of developing diabetes who were also prescribed quetiapine, none of them monitored 50% or more of their patients for signs and symptoms of hyperglycaemia during the study period either. None of the practices recorded providing lifestyle counselling for 50% or more of their quetiapine patients.

**Table 31 Summary of monitoring activities performed by psychiatric practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Monitoring activities performed by practices** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| Weight recorded at visit when initial prescription was issued n (%) | *38 (90%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Weight recorded at least once in study period n (%) | *42 (100%)* | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) |
| | | | | | | |
| Monitoring for elevated cholesterol at least once in study period n (%) | *42 (100%)* | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia at least once in study period n (%) | *42 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *diabetic patients* at least once in study period n (%) | *6 (14%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *patients at risk of diabetes* at least once in study period n (%) | *19 (45%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Counselling on healthy lifestyle conducted at least once in study period n (%) | *42 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 32 provides a summary of the patients who were monitored by psychiatry practices in Germany for the main outcomes of this study. Only 2 (0.8%) patients were monitored out of 259 patients initiated on quetiapine for weight at the visit associated with initial prescription. Similarly, less than 1% of patients had their weight monitored at any time during the study period. There was 1% (n=14) of patients whose cholesterol was monitored and 1% (n=10) of

patients monitored for signs and symptoms of hyperglycaemia at least once during the study period. None of the 9 diabetic patients in this study population were monitored for signs and symptoms of hyperglycaemia, while only 7% (n=4) of patients who were considered to be at risk of developing diabetes had a record of being monitored. None of the patients had a recording of being provided with counselling on adopting healthy lifestyle behaviours (*e.g.* advice on healthy eating, importance of exercise, and positive changes to lifestyle).

**Table 32 Summary of monitoring activities performed for patients treated with quetiapine by psychiatrists in Germany**

| Monitoring activities performed on patients | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|
| | | | |
| Weight recorded at visit when initial prescription was issued | 259 | 2 | 0.8% |
| | | | |
| Weight recorded at least once in study period | 1451 | 6 | 0.4% |
| | | | |
| Monitoring for elevated cholesterol at least once in study period | 1451 | 14 | 1.0% |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia at least once in study period | 1451 | 10 | 0.7% |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *diabetic patients* at least once in study period | 9 | 0 | 0% |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *patients at risk of diabetes* at least once in study period | 58 | 4 | 6.9% |
| | | | |
| Counselling on healthy lifestyle conducted at least once in study period | 1451 | 0 | 0% |

## 10.8 Main results: detailed analyses of outcomes data - Psychiatrists (Germany)

Table 33 presents the number of psychiatry practices in Germany that monitored the majority of patients newly initiated on quetiapine for weight according to the number of eligible patients in those practices. It can be observed that none of the practices in the respective stratification of number of eligible patients in practice monitored 50% or more of their patients for weight upon initiation of quetiapine.

**Table 33 Monitoring of weight for patients initiated on quetiapine: by psychiatry practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *24 (57%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *7 (18%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *6 (16%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *1 (3%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total practices with newly initiated patients** | *38 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 34 presents the proportion of newly initiated quetiapine patients whose weight was monitored by psychiatry practices in Germany according to the number of physician visits and by risk factors. As the number of patients monitored for weight at the time of initiation of quetiapine treatment was very small, a complete analysis of weight monitoring activity according to patient risk factors is not presented in detail. Of the 259 patients who were newly initiated on quetiapine during the study period, only 2 patients (1%) had a record of weight measurement at the time of that initial prescription. One of these patients was prescribed other antipsychotic medications during the prior 6 months. The two patients who had their weight monitored were also previously prescribed antidepressants and had a BMI>25. These two patients did not have high blood pressure, elevated cholesterol, blood lipid testing, cardiovascular disease (CVD), diabetes, history of blood glucose testing, a history of anxiety/psychosis, or metabolic syndrome.

## Table 34 Monitoring of weight for patients initiated on quetiapine: patients seen in psychiatry practices in Germany

| | | Total number of patients | Total number of patients monitored | % patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Weight recorded at visit when initial quetiapine prescription was issued*** | 259 | 2 | (0.8) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 68 | 1 | (1.5) |
| | *No* | 191 | 1 | (0.5) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 146 | 2 | (1.4) |
| | *No* | 113 | 0 | (0.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 6 | 2 | (33.3) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 251 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 259 | 2 | (0.8) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 258 | 2 | (0.8) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *No* | 256 | 2 | (0.8) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *No* | 256 | 2 | (0.8) |
| | | | | |

**Table 34 Monitoring of weight for patients initiated on quetiapine: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % patients monitored |
|---|---|---|---|---|
| | ***Diabetes*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 258 | 2 | (0.8) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *No* | 256 | 2 | (0.8) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 152 | 1 | (0.7) |
| | *Male* | 107 | 1 | (0.9) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 33 | 0 | (0.0) |
| | *No* | 226 | 2 | (0.9) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 7 | 0 | (0.0) |
| | *25-39* | 51 | 0 | (0.0) |
| | *40-49* | 61 | 0 | (0.0) |
| | *50-64* | 88 | 1 | (1.1) |
| | *≥65* | 52 | 1 | (1.9) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 259 | 2 | (0.8) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *Missing* | 256 | 2 | (0.8) |

Table 35 presents the number of psychiatry practices in Germany that monitored the majority of their patients prescribed quetiapine (both new and established users of the medication) for weight according to the number of eligible patients in their practice. It can be observed that most of the practices in their respective stratification groups did not meet the minimum reporting threshold of monitoring 50% or more of their quetiapine patients for weight during

ongoing visits. There was one practice that monitored weight for 95% or more of their patients on quetiapine.

**Table 35 Monitoring of weight of patients on quetiapine: by psychiatry practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *5 (12%)* | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) |
| | | | | | | |
| **6-11** | *1 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *22 (52%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *14 (33%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *42 (100%)* | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) |

Table 36 describes the weight monitoring of patients prescribed quetiapine managed by office based psychiatry practices in Germany according to the number of physician visits and risk factors. As the number of patients monitored for weight was very small, a complete analysis of this monitoring activity according to patient risk factors is not presented in detail. Of the 1,451 patients, less than 1% (n=6) had evidence of weight measurement during the study period. Only one of these patients was prescribed an antipsychotic other than quetiapine and 4 patients were prescribed antidepressants. All of the monitored patients had a BMI exceeding 25. These 6 patients did not have high blood pressure, elevated cholesterol, CVD, diabetes, history of anxiety/psychosis, or metabolic syndrome.

## Table 36 Monitoring of weight of patients on quetiapine: patients seen in psychiatry practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Weight recorded in study period*** | 1451 | 6 | (0.4) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 376 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 484 | 3 | (0.6) |
| | *Q3 (5-6 visits)* | 307 | 0 | (0.0) |
| | *Q4 (7-41 visits)* | 284 | 3 | (1.1) |
| | | | | |
| **Risk factors : Total n (% monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 480 | 1 | (0.2) |
| | *No* | 971 | 5 | (0.5) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 865 | 4 | (0.5) |
| | *No* | 586 | 2 | (0.3) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 35 | 6 | (17.1) |
| | *No* | 16 | 0 | (0.0) |
| | *Missing* | 1400 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 1451 | 6 | (0.4) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 7 | 0 | (0.0) |
| | *No* | 1444 | 6 | (0.4) |
| | | | | |

## Table 36 Monitoring of weight of patients on quetiapine: patients seen in psychiatry practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Blood lipid testing*** | | | |
| | *Yes* | 30 | 1 | (3.3) |
| | *No* | 1421 | 5 | (0.4) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 19 | 0 | (0.0) |
| | *No* | 1432 | 6 | (0.4) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 9 | 0 | (0.0) |
| | *No* | 1442 | 6 | (0.4) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 25 | 1 | (4.0) |
| | *No* | 1426 | 5 | (0.4) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 845 | 3 | (0.4) |
| | *Male* | 606 | 3 | (0.5) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 182 | 0 | (0.0) |
| | *No* | 1269 | 6 | (0.5) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 44 | 1 | (2.3) |
| | *25-39* | 268 | 0 | (0.0) |
| | *40-49* | 357 | 0 | (0.0) |
| | *50-64* | 516 | 3 | (0.6) |
| | *≥65* | 266 | 2 | (0.8) |
| | | | | |

**Table 36 Monitoring of weight of patients on quetiapine: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *No* | 1451 | 6 | (0.4) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 15 | 1 | (6.7) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 1434 | 5 | (0.3) |

Table 37 presents the number of psychiatry practices in Germany that monitored cholesterol levels of the majority of their patients treated with quetiapine according to the number of eligible patients in those practices. It can be observed that most of the practices in their respective stratification groups did not meet the minimum reporting threshold of lipids panel monitoring for 50% or more of their quetiapine patients. There was one practice that monitored 95% or more of their patients on quetiapine.

**Table 37 Monitoring of elevated cholesterol for patients on quetiapine: by psychiatry practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *5 (12%)* | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) |
| | | | | | | |
| **6-11** | *1 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *22 (52%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *14 (33%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *42 (100%)* | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) |

Table 38 presents an analysis of monitoring cholesterol of patients prescribed quetiapine by office-based psychiatry practices in Germany according to the number of physician visits and risk factors. As the number of patients with lipid levels monitored was very small, a complete analysis of this monitoring activity according to patient risk factors was not performed. Of the 1,451 study patients, there was evidence of cholesterol monitoring for only 14 patients (1%).

Only four of these patients were prescribed other antipsychotics in the prior 6 months, although half the monitored patients were previously prescribed antidepressants. None of the monitored patients had high blood pressure and interestingly, none had elevated cholesterol recorded in their medical history. None of the monitored patients had recorded diabetes, CVD, or metabolic syndrome.

**Table 38 Monitoring of elevated cholesterol for patients on quetiapine: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Elevated cholesterol assessed at least once in study period*** | 1451 | 14 | (1.0) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 376 | 2 | (0.5) |
| | *Q2 (3-4 visits)* | 484 | 6 | (1.2) |
| | *Q3 (5-6 visits)* | 307 | 3 | (1.0) |
| | *Q4 (7-41 visits)* | 284 | 3 | (1.1) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 480 | 4 | (0.8) |
| | *No* | 971 | 10 | (1.0) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 865 | 7 | (0.8) |
| | *No* | 586 | 7 | (1.2) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 35 | 4 | (11.4) |
| | *No* | 16 | 1 | (6.3) |
| | *Missing* | 1400 | 9 | (0.6) |
| | | | | |

**Table 38 Monitoring of elevated cholesterol for patients on quetiapine: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***High blood pressure*** | | | |
| | *No* | 1451 | 14 | (1.0) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 7 | 0 | (0.0) |
| | *No* | 1444 | 14 | (1.0) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 30 | 2 | (6.7) |
| | *No* | 1421 | 12 | (0.8) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 19 | 0 | (0.0) |
| | *No* | 1432 | 14 | (1.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 9 | 0 | (0.0) |
| | *No* | 1442 | 14 | (1.0) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 25 | 4 | (16.0) |
| | *No* | 1426 | 10 | (0.7) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 845 | 9 | (1.1) |
| | *Male* | 606 | 5 | (0.8) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 182 | 1 | (0.5) |
| | *No* | 1269 | 13 | (1.0) |
| | | | | |

**Table 38 Monitoring of elevated cholesterol for patients on quetiapine: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Age*** | | | |
| | *<25* | 44 | 1 | (2.3) |
| | *25-39* | 268 | 1 | (0.4) |
| | *40-49* | 357 | 6 | (1.7) |
| | *50-64* | 516 | 5 | (1.0) |
| | *≥65* | 266 | 1 | (0.4) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 1451 | 14 | (1.0) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 15 | 1 | (6.7) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 1434 | 13 | (0.9) |

Table 39 presents the number of psychiatry practices in Germany that have monitored patients treated with quetiapine for signs and symptoms of hyperglycaemia according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold for monitoring at least 50% of their quetiapine patients for signs and symptoms of hyperglycaemia.

**Table 39 Monitoring of signs and symptoms of hyperglycaemia in patients on quetiapine: by psychiatry practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *5 (12%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *1 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *22 (52%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *14 (33%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *42 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 40 provides analysis of hyperglycaemia monitoring for patients prescribed quetiapine managed by psychiatry practices in Germany by the number of physician visits and risk factors. As the number of patients monitored for hyperglycaemia was very small, a complete analysis of this monitoring activity according to patient risk factors was not performed. Of the 1,451 patients, there was evidence of blood glucose assessment for 10 patients (1%). Half of these patients were not previously prescribed other antipsychotics, while the remaining half was prescribed other antipsychotics in the 6 months prior to the observation period. None of the monitored patients had high blood pressure, elevated cholesterol, CVD, diabetes, or metabolic syndrome. 6.7% of patients monitored were tested for lipids previously and 8% of patients monitored were also tested for blood glucose prior to the study period.

## Table 40 Monitoring of hyperglycaemia in patients on quetiapine: patients seen in psychiatry practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Blood glucose assessed at least once in study period*** | 1451 | 10 | (0.7) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 376 | 1 | (0.3) |
| | *Q2 (3-4 visits)* | 484 | 3 | (0.6) |
| | *Q3 (5-6 visits)* | 307 | 3 | (1.0) |
| | *Q4 (7-41 visits)* | 284 | 3 | (1.1) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 480 | 5 | (1.0) |
| | *No* | 971 | 5 | (0.5) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 865 | 4 | (0.5) |
| | *No* | 586 | 6 | (1.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 35 | 4 | (11.4) |
| | *No* | 16 | 0 | (0.0) |
| | *Missing* | 1400 | 6 | (0.4) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 1451 | 10 | (0.7) |
| | | | | |

## Table 40 Monitoring of hyperglycaemia in patients on quetiapine: patients seen in psychiatry practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 7 | 0 | (0.0) |
| | *No* | 1444 | 10 | (0.7) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 30 | 2 | (6.7) |
| | *No* | 1421 | 8 | (0.6) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 19 | 0 | (0.0) |
| | *No* | 1432 | 10 | (0.7) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 9 | 0 | (0.0) |
| | *No* | 1442 | 10 | (0.7) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 25 | 2 | (8.0) |
| | *No* | 1426 | 8 | (0.6) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 845 | 7 | (0.8) |
| | *Male* | 606 | 3 | (0.5) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 182 | 1 | (0.5) |
| | *No* | 1269 | 9 | (0.7) |
| | | | | |

**Table 40 Monitoring of hyperglycaemia in patients on quetiapine: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Age*** | | | |
| | *<25* | 44 | 1 | (2.3) |
| | *25-39* | 268 | 1 | (0.4) |
| | *40-49* | 357 | 6 | (1.7) |
| | *50-64* | 516 | 2 | (0.4) |
| | *≥65* | 266 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 1451 | 10 | (0.7) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 15 | 1 | (6.7) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 1434 | 9 | (0.6) |

Table 41 presents the number of psychiatry practices in Germany that monitored patients with diabetes treated with quetiapine for signs and symptoms of hyperglycaemia according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold for monitoring at least 50% of their patients with diabetes mellitus in their practices for signs and symptoms of hyperglycaemia.

**Table 41 Monitoring of signs and symptoms of hyperglycaemia for diabetic patients on quetiapine: by psychiatry practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *6 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total practices with diabetic patients** | *6 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 42 presents analyses data for monitoring of signs and symptoms of hyperglycaemia among diabetic patients who were prescribed quetiapine by psychiatry practices in Germany by the number of physician visits and risk factors. As the number of patients with diabetes

mellitus monitored for signs and symptoms of hyperglycaemia was very small, a complete analysis of this monitoring activity according to patient risk factors is not presented in detail. There were only 9 diabetic patients in the study population. As can be observed from Table 42, there was no recorded evidence of glucose assessment for any of these patients in this sub-group by German psychiatrists.

**Table 42 Monitoring of hyperglycaemia for diabetic patients on quetiapine: patients seen in Psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Glucose assessed at least once in study period*** | 9 | 0 | (0.0) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 3 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 2 | 0 | (0.0) |
| | *Q3 (5-6 visits)* | 0 | 0 | (0.0) |
| | *Q4 (7-41 visits)* | 4 | 0 | (0.0) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 5 | 0 | (0.0) |
| | *No* | 4 | 0 | (0.0) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 4 | 0 | (0.0) |
| | *No* | 5 | 0 | (0.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Missing* | 9 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 9 | 0 | (0.0) |
| | | | | |

**Table 42 Monitoring of hyperglycaemia for diabetic patients on quetiapine: patients seen in Psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 5 | 0 | (0.0) |
| | *No* | 4 | 0 | (0.0) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 8 | 0 | (0.0) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 8 | 0 | (0.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 9 | 0 | (0.0) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *No* | 9 | 0 | (0.0) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 5 | 0 | (0.0) |
| | *Male* | 4 | 0 | (0.0) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *No* | 9 | 0 | (0.0) |
| | | | | |
| | ***Age*** | | | |
| | *25-39* | 1 | 0 | (0.0) |
| | *50-64* | 5 | 0 | (0.0) |
| | *≥65* | 3 | 0 | (0.0) |
| | | | | |

**Table 42 Monitoring of hyperglycaemia for diabetic patients on quetiapine: patients seen in Psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *No* | 9 | 0 | (0.0) |
| | | | | |
| | ***Smoking*** | | | |
| | *Missing* | 9 | 0 | (0.0) |

Table 43 presents the number of psychiatry practices in Germany that have monitored the majority of their patients who were at risk of developing diabetes and treated with quetiapine for signs and symptoms of hyperglycaemia according to numbers of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold for monitoring 50% or more of their quetiapine patients at risk for developing diabetes for signs and symptoms of hyperglycaemia.

**Table 43 Monitoring of signs and symptoms of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: by psychiatry practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *17 (89%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *1 (5%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *1 (5%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total practices with patients at risk for diabetes** | *19 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 44 provides analysis of monitoring for signs and symptoms of hyperglycaemia among patients at risk of developing diabetes who have been prescribed quetiapine according to the number of German psychiatrist visits and risk factors. This was based on recordings of blood glucose assessment amongst the 58 patients who were considered to be at risk of developing diabetes. As the number of patients monitored was very small, a complete analysis of this monitoring activity according to patient risk factors is not presented in detail. Seven percent (n=4) of patients had evidence of monitoring for signs and symptoms of hyperglycaemia

during the observation period. Three of these patients were also previously prescribed other antipsychotics, while two were previously prescribed antidepressants. All 4 monitored patients had a BMI>25. These monitored patients did not have high blood pressure, elevated cholesterol, or CVD. Only one out of the 4 patients had a history of blood glucose testing.

**Table 44 Monitoring of signs and symptoms of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Glucose assessed at least once in study period*** | 58 | 4 | (6.9) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 7 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 22 | 1 | (4.5) |
| | *Q3 (5-6 visits)* | 12 | 2 | (16.7) |
| | *Q4 (7-41 visits)* | 17 | 1 | (5.9) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 20 | 3 | (15.0) |
| | *No* | 38 | 1 | (2.6) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 42 | 2 | (4.8) |
| | *No* | 16 | 2 | (12.5) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 35 | 4 | (11.4) |
| | *Missing* | 23 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 58 | 4 | (6.9) |
| | | | | |

**Table 44 Monitoring of signs and symptoms of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 57 | 4 | (7.0) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 5 | 1 | (20.0) |
| | *No* | 53 | 3 | (5.7) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 18 | 0 | (0.0) |
| | *No* | 40 | 4 | (10.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *No* | 58 | 4 | (6.9) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 4 | 1 | (25.0) |
| | *No* | 54 | 3 | (5.6) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 31 | 3 | (9.7) |
| | *Male* | 27 | 1 | (3.7) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 6 | 1 | (16.7) |
| | *No* | 52 | 3 | (5.8) |
| | | | | |

**Table 44 Monitoring of signs and symptoms of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Age*** | | | |
| | *<25* | 3 | 0 | (0.0) |
| | *25-39* | 7 | 1 | (14.3) |
| | *40-49* | 12 | 2 | (16.7) |
| | *50-64* | 22 | 1 | (4.5) |
| | *≥65* | 14 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 58 | 4 | (6.9) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 8 | 1 | (12.5) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 48 | 3 | (6.3) |

Table 45 presents the number of psychiatry practices in Germany that have provided counselling on the importance of healthy eating, exercise, and lifestyle for patients to the majority of their patients prescribed quetiapine according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups recorded providing lifestyle counselling for 50% or more of the study patients.

**Table 45 Monitoring of healthy eating/exercise/lifestyle counselling of patients: by psychiatry practices in Germany**

| | | Proportion of patients counselled | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *5 (12%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *1 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *22 (52%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *14 (33%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *42 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 46 presents findings regarding the provision of counselling to promote healthy lifestyle behaviours to patients who were prescribed quetiapine by psychiatry practices in Germany according to the number of physician visits and risk factors. There was no recorded evidence of the provision of such counselling to patients during the observation period. As can be observed, there was no evidence of this monitoring even one time for the study patients during the observation period.

**Table 46 Monitoring of healthy eating/exercise/lifestyle counselling: patients seen in psychiatry practices in Germany**

| | | **Total number of patients** | **Total number of patients monitored** | **% Patients monitored** |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Counselling on healthy lifestyle conducted at least once in study period*** | 1451 | 0 | (0.0) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 376 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 484 | 0 | (0.0) |
| | *Q3 (5-6 visits)* | 307 | 0 | (0.0) |
| | *Q4 (7-41 visits)* | 284 | 0 | (0.0) |
| | | | | |

## Table 46 Monitoring of healthy eating/exercise/lifestyle counselling: patients seen in psychiatry practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 480 | 0 | (0.0) |
| | *No* | 971 | 0 | (0.0) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 865 | 0 | (0.0) |
| | *No* | 586 | 0 | (0.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 35 | 0 | (0.0) |
| | *No* | 16 | 0 | (0.0) |
| | *Missing* | 1400 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 1451 | 0 | (0.0) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 7 | 0 | (0.0) |
| | *No* | 1444 | 0 | (0.0) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 30 | 0 | (0.0) |
| | *No* | 1421 | 0 | (0.0) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 19 | 0 | (0.0) |
| | *No* | 1432 | 0 | (0.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 9 | 0 | (0.0) |
| | *No* | 1442 | 0 | (0.0) |
| | | | | |

**Table 46 Monitoring of healthy eating/exercise/lifestyle counselling: patients seen in psychiatry practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 25 | 0 | (0.0) |
| | *No* | 1426 | 0 | (0.0) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 845 | 0 | (0.0) |
| | *Male* | 606 | 0 | (0.0) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 182 | 0 | (0.0) |
| | *No* | 1269 | 0 | (0.0) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 44 | 0 | (0.0) |
| | *25-39* | 268 | 0 | (0.0) |
| | *40-49* | 357 | 0 | (0.0) |
| | *50-64* | 516 | 0 | (0.0) |
| | *≥65* | 266 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 1451 | 0 | (0.0) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 15 | 0 | (0.0) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 1434 | 0 | (0.0) |

Table 47 presents descriptive statistics including the range, median and values corresponding to the 25$^{th}$ and 75$^{th}$ percentiles for the proportions of patients who received different metabolic monitoring previously described from German psychiatry practices. There were 42 psychiatry practices with eligible patients. Ninety percent (n=38) of these practices had patients initiated on quetiapine during the study period and the monitoring of weight was either poorly recorded or not performed. Fourteen percent (n=6) of practices had diabetic patients and 45% (n=19) of the practices had patients who were at risk of developing diabetes. Monitoring for signs and symptoms of hyperglycaemia was not in evidence or sparsely conducted among both subset

populations. Overall, the level of monitoring presented in the table reveals that the performance and recording of metabolic monitoring among patients treated with quetiapine in psychiatry practices in Germany was extremely low.

**Table 47 Monitoring by psychiatry practices in the Germany: Distributions of the proportions of patients monitored**

| | | | | Proportion of patients monitored in the practice | |
|---|---|---|---|---|---|
| **Monitoring activity** | **Patients** | **Number of practices** | **Range of the number of patients in each practice (min, max)** | **Median** | **[LQ, UQ]** |
| | | | | | |
| **Weight** | *All* | 42 | (1, 123) | 0% | [0%, 0%] |
| | *Initiated on quetiapine* | 38 | (1, 90) | 0% | [0%, 0%] |
| | | | | | |
| **Cholesterol** | *All* | 42 | (1, 123) | 0% | [0%, 0%] |
| | | | | | |
| **Glucose** | *All* | 42 | (1, 123) | 0% | [0%, 0%] |
| | *Diabetics* | 6 | (1, 3) | 0% | [0%, 0%] |
| | *At risk of diabetes* | 19 | (1, 14) | 0% | [0%, 0%] |
| | | | | | |
| **Health counselling** | *All* | 42 | (1, 123) | 0% | [0%, 0%] |

## 10.9 Participants - Neurologists (Germany)

Table 48 presents the attrition table of neurology practices and patients in Germany that were within the scope of the assessment of EMR data including specialist physicians in Germany. There were 251 office-based psychiatry and neurology practices with data for 1,934,489 patients in the DA by end of January 2013. The inclusion criteria specified in Section 9.3 were applied individually to this patient sample as indicated in the attrition table.

There were 7,323 patients from 173 office-based neurology practices aged 18 years and above on 1st January 2012, with one or more of qualifying diagnoses (schizophrenia, bipolar disorder or major depressive disorder) in the medical history, with at least one prescription of quetiapine and with one or more consultations with the Neurologists between 13 February and 31 August 2012. When the inclusion criteria of active patients within the observational period of 1 February 2012 and 1 August 2012; and availability of 12 months medical history prior to the observational period were applied, the patient sample sizes reduced to 5,934 and 4,750 respectively. The final criterion in the attrition table was applied to those where the inclusion diagnosis preceded quetiapine prescription which resulted in 4,702 eligible patients in the DA managed by 145 neurology practices in Germany for analysis.

**Table 48 Attrition table of neurology practices and patients in Germany**

| Step | Description | Patients | Practices |
|---|---|---|---|
| 1 | Patients in psychiatry or neurology practices within the German DA as of 1 January 2013 that were aged 18 years or older in 2012 | 1,827,633 | 251 |
| 2 | Prescribed quetiapine during the study period of 13 February and 31 August 2012 and had a qualifying diagnosis of schizophrenia, bipolar disorder, or major depressive disorder at some point in the EMR | 9,617 | 229 |
| 3 | At least one consultation with a neurologist during the study period | 7,323 | 173 |
| 4 | Practices up to reporting standard ensuring that the patient data was reported for the entirety of the study period | 5,934 | 146 |
| 5 | Evidence of clinical interaction >12 months before study (indicating that should have patient history at least 12 months prior to study period) | 4,750 | 145 |
| 6 | Initial qualifying diagnosis mentioned in step 2 confirmed as preceding quetiapine prescription | 4,702 | 145 |

## 10.10 Descriptive data - Neurologists (Germany)

Table 49 provides characteristics of neurology practices in Germany in which the study patients were observed. Among the 145 practices with study patients, 80% (n=117) were solo practices, while the remaining were group practices. The lead physicians within these practices had a mean (SD) age of 55.3 (6.3) years, and three-quarters of them were male (74%). These physicians have been registered for 16.2 years on average and the just more than one-quarter (28%) were based in the Hessen -- Rhineland-Palatinate -- Saarland region. Practices had a mean (SD) of 32 (27.4) patients and a median of 27 patients. Eligible patients ranged from 1 to 207 in hese neurology practices.

**Table 49 Characteristics of neurology practices in Germany**

| | | **Total number of practices (N=145)** | |
|---|---|---|---|
| **Total number of practices** | | 145 | |
| | | | |
| **Practice type n (%)** | | | |
| | *Group* | 28 | (19.3) |
| | *Solo* | 117 | (80.7) |
| | | | |
| **Number of doctors in practice n (%)** | | | |
| | *1* | 117 | (80.7) |
| | *2* | 20 | (13.8) |
| | *3* | 6 | (4.1) |
| | *4* | 2 | (1.4) |
| | | | |

## Table 49 Characteristics of neurology practices in Germany

| | | Total number of practices (N=145) | |
|---|---|---|---|
| **Doctor age** | | | |
| | *Mean (SD)* | 55.3 | (6.3) |
| | *Median* | 55 | |
| | *[LQ, UQ]* | [50, 60] | |
| | *(min, max)* | (41, 73) | |
| | | | |
| **Speciality n (%)** | | | |
| | *Neurology* | 145 | (100) |
| | | | |
| **Sex n (%)** | | | |
| | *Female* | 38 | (26.2) |
| | *Male* | 107 | (73.8) |
| | | | |
| **Years registered** | | | |
| | *Unknown* | 1 | |
| | *Mean (SD)* | 16.2 | (7.1) |
| | *Median* | 16 | |
| | *[LQ, UQ]* | [10, 22] | |
| | *(min, max)* | (3, 32) | |
| | | | |
| **Practice region n (%)** | | | |
| | *Hessen, Rhineland-Palatinate, Saarland* | 41 | (28.3) |
| | *North Rhine-Westphalia* | 22 | (15.2) |
| | *Bavaria* | 17 | (11.7) |
| | *Brandenburg, Mecklenburg-Western Pomerania, Saxony-Anhalt* | 17 | (11.7) |
| | *Schleswig-Holstein, Lower Saxony, Bremen, Hamburg* | 15 | (10.3) |
| | *Baden-Wuerttemberg* | 14 | (9.7) |
| | *Berlin* | 11 | (7.6) |
| | *Thuringia, Saxony* | 8 | (5.5) |
| | | | |

**Table 49 Characteristics of neurology practices in Germany**

| | | Total number of practices (N=145) | |
|---|---|---|---|
| **Number of patients per practice included in the study** | | | |
| | *Mean (SD)* | 32.4 | (27.4) |
| | *Median* | 27 | |
| | *[LQ, UQ]* | [14, 46] | |
| | *(min, max)* | (1, 207) | |

Demographic and clinical characteristics of the study patients managed by German neurologists are presented in Table 50. More than half of patients (62%) were female and had a median age of 55 years and a mean (SD) age of 57 (17.2) years. Nearly 33% of the study population were aged 65 years and over, closely followed by 31% of the study population who were 50-64 years of age. Only 2% of patients were aged between 18 and 25 years.

Thirty-five percent of patients were Members of the public insurance and approximately 56% were Retirees. Only 5% of patients had private medical insurance. Smoking status was only available for 3 patients from the total study population of 4,702.

44.8% of the patients were diagnosed with bipolar disorder, 20.4% had a diagnosis of schizophrenia and 7.4% with major depressive disorder (MDD). 9.9% of the study population had a combined diagnosis of bipolar disorder and MDD, while 13.2% had a qualifying diagnosis of both bipolar disorder and schizophrenia. 1.8% of patients had MDD and schizophrenia, and 2.6% of patients had a diagnosis of all three conditions.

Few patient electronic records included recorded diagnoses or biometric measures that identified risk factors for development of diabetes mellitus (only 6% of patients (n=282) and only 1% (n=52) had evidence of being diagnosed or treated for diabetes mellitus. Evidence of lipid panel testing and elevated cholesterol in the 12 months prior to the observational period occurred in only 1% of the study patients while prior monitoring of weight occurred for less than 1% of patients.

The majority of patients (65%) were not prescribed any other antipsychotic medication in the 6 months prior to the observation period. Among those that were previously prescribed antipsychotics, 25% were prescribed only one and 10% prescribed two or more antipsychotics. A variety of antipsychotic medications were prescribed; risperidone, promethazine, and pipamperone were the most frequently prescribed at 6%, 5% and 4%, respectively.

Over half of the study patients (56%) were prescribed antidepressants during the 6 months prior to the observation period. Among these patients, 38% were prescribed only one antidepressant, while 15% were prescribed two and 3% of patients were prescribed 3 or more antidepressants. A wide variety of antidepressant medications were prescribed to this study

population; citalopram, venlafaxine, and mirtazapine were prescribed at the highest frequency for approximately 15%, 12% and 10% of patients, respectively.

**Table 50 Demographic and clinical characteristics of patients seen in neurology practices in Germany**

| | | **Total number of patients (N=4702)** | |
|---|---|---|---|
| **Sex n (%)** | | | |
| | *Male* | 1780 | (37.9) |
| | *Female* | 2922 | (62.1) |
| | | | |
| **Age** | | | |
| | *Mean (SD)* | 57.0 | (17.2) |
| | *Median* | 55 | |
| | *[LQ, UQ]* | [45, 71] | |
| | *(min, max)* | (19, 99) | |
| | | | |
| | *18-24 (<25)* | 86 | (1.8) |
| | *25-39* | 671 | (14.3) |
| | *40-49* | 946 | (20.1) |
| | *50-64* | 1458 | (31.0) |
| | *≥65* | 1541 | (32.8) |
| | | | |
| **Insurance status n (%)** | | | |
| | *Dependant* | 209 | (4.4) |
| | *Member* | 1630 | (34.7) |
| | *Privately insured* | 253 | (5.4) |
| | *Retiree* | 2610 | (55.5) |
| | | | |
| **Smoking status n (%)** | | | |
| | *Current smoker* | 1 | (33.3) |
| | *Not currently smoking* | 2 | (66.7) |
| | *Unknown* | 4699 | |
| | | | |

## Table 50 Demographic and clinical characteristics of patients seen in neurology practices in Germany

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **Qualifying diagnosis n (%)** | | | |
| | *Schizophrenia* | 941 | (20.4) |
| | *Bipolar disorder* | 2101 | (44.8) |
| | *Major depressive disorder (MDD)* | 366 | (7.4) |
| | | | |
| | *Bipolar + MDD* | 453 | (9.9) |
| | *Bipolar + Schizophrenia* | 640 | (13.2) |
| | *MDD + Schizophrenia* | 84 | (1.8) |
| | | | |
| | *Schizophrenia + bipolar + MDD* | 117 | (2.6) |
| | | | |
| **Lipid panel testing in prior 12 months n (%)** | | | |
| | *Lipid panel testing in prior 12 months n (%)* | 33 | (0.7) |
| | | | |
| **Evidence of diabetes mellitus n (%)** | | | |
| | *Evidence of diabetes mellitus n (%)* | 52 | (1.1) |
| | | | |
| **History of pre-diabetes mellitus excluding diabetic patients n (%)** | | | |
| | *History of pre-diabetes (excluding diabetic patients) n (%)* | 0 | (0.0) |
| | | | |
| **At risk of diabetes mellitus n (%)** | | | |
| | *At risk of diabetes (excluding diabetic patients) n (%)* | 282 | (6.1) |
| | | | |
| **History of elevated cholesterol n (%)** | | | |
| | *History of elevated cholesterol n (%)* | 26 | (0.6) |
| | | | |

## Table 50 Demographic and clinical characteristics of patients seen in neurology practices in Germany

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **History of weight monitoring n (%)** | | | |
| | *History of weight monitoring n (%)* | 21 | (0.4) |
| | | | |
| **Prescription of other antipsychotics in prior 6 months** | | | |
| **Substances n (%)** | | | |
| | *AMISULPRIDE* | 95 | (2.0) |
| | *ARIPIPRAZOLE* | 139 | (3.0) |
| | *ASENAPINE* | 9 | (0.2) |
| | *BENPERIDOL* | 11 | (0.2) |
| | *BROMPERIDOL* | 4 | (0.1) |
| | *CHLORPROTHIXENE* | 113 | (2.4) |
| | *CLOZAPINE* | 60 | (1.3) |
| | *FLUPENTIXOL* | 104 | (2.2) |
| | *FLUPHENAZINE* | 32 | (0.7) |
| | *FLUSPIRILENE* | 29 | (0.6) |
| | *HALOPERIDOL* | 125 | (2.7) |
| | *LEVOMEPROMAZINE* | 74 | (1.6) |
| | *MELPERONE* | 227 | (4.8) |
| | *OLANZAPINE* | 118 | (2.5) |
| | *PALIPERIDONE PALMITATE* | 24 | (0.5) |
| | *PERAZINE* | 65 | (1.4) |
| | *PERPHENAZINE* | 6 | (0.1) |
| | *PIMOZIDE* | 3 | (0.1) |
| | *PIPAMPERONE* | 206 | (4.4) |
| | *PROMETHAZINE* | 252 | (5.4) |
| | *PROTHIPENDYL* | 91 | (1.9) |
| | *RISPERIDONE* | 300 | (6.4) |
| | *SERTINDOLE* | 2 | (0.0) |
| | *SULPIRIDE* | 20 | (0.4) |
| | *THIORIDAZINE* | 8 | (0.2) |
| | *TIAPRIDE* | 50 | (1.1) |
| | *ZIPRASIDONE* | 49 | (1.0) |
| | *ZUCLOPENTHIXOL* | 45 | (1.0) |

## Table 50 Demographic and clinical characteristics of patients seen in neurology practices in Germany

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **Number of other antipsychotics prescribed n (%)** | | | |
| | *0* | 3048 | (64.8) |
| | *1* | 1191 | (25.3) |
| | *2* | 348 | (7.4) |
| | *3 or more* | 115 | (2.4) |
| | | | |
| **Prescription of antidepressants in prior 6 months** | | | |
| **Substances n (%)** | | | |
| | *AGOMELATINE* | 93 | (2.0) |
| | *AMIPTYPTYLINE* | 155 | (3.3) |
| | *BUPROPION* | 91 | (1.9) |
| | *CITALOPRAM* | 708 | (15.1) |
| | *CLOMIPRAMINE* | 51 | (1.1) |
| | *DOXEPIN* | 146 | (3.1) |
| | *DULOXETINE* | 194 | (4.1) |
| | *ESCITALOPRAM* | 42 | (0.9) |
| | *FLUOXETINE* | 117 | (2.5) |
| | *FLUVOXAMINE* | 8 | (0.2) |
| | *HYPERICUM PERFORATUM* | 7 | (0.1) |
| | *IMIPRAMINE* | 185 | (3.9) |
| | *LITHIUM* | 305 | (6.5) |
| | *MAPROTILINE* | 12 | (0.3) |
| | *MIANSERIN* | 3 | (0.1) |
| | *MIRTAZAPINE* | 478 | (10.2) |
| | *MOCLOBEMIDE* | 10 | (0.2) |
| | *NORTRIPTYLINE* | 23 | (0.5) |
| | *OPIPRAMOL* | 108 | (2.3) |
| | *PAROXETINE* | 107 | (2.3) |
| | *REBOXETINE* | 8 | (0.2) |
| | *SERTRALINE* | 158 | (3.4) |
| | *TRANYLCYPROMINE* | 15 | (0.3) |
| | *TRAZODONE* | 27 | (0.6) |
| | *VENLAFAXINE* | 575 | (12.2) |

**Table 50 Demographic and clinical characteristics of patients seen in neurology practices in Germany**

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **Number of antidepressants prescribed n (%)** | | | |
| | *0* | 2088 | (44.4) |
| | *1* | 1776 | (37.8) |
| | *2* | 693 | (14.7) |
| | *3 or more* | 145 | (3.1) |

Table 51 presents descriptive data on the number of physician visits and quetiapine prescription status (as new users initiating quetiapine or as prevalent users, continuing on quetiapine) for patients who were managed by neurologists in Germany. Patients had a mean (SD) of 5.0 (3.5) visits and a median of 4 visits to their neurologist within the study period. Most patients had 2 to 5 visits to their neurologist, while 10% of patients visited their specialist 10 times or more. There were 16% of patients newly initiated on quetiapine during the study period of 13 February through 31 August 2012, while the 84% of patients were continuing on quetiapine treatment at the start of the study period.

**Table 51 Treatment of patients seen in neurology practices in Germany**

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **Number of visits per patient in study period** | | | |
| | *Mean (SD)* | 5.0 | (3.5) |
| | *Median* | 4 | |
| | *[LQ, UQ]* | [2, 7] | |
| | *(min, max)* | (1, 27) | |
| | | | |
| | *1* | 406 | (8.6) |
| | *2* | 805 | (17.1) |
| | *3* | 733 | (15.6) |
| | *4* | 673 | (14.3) |
| | *5* | 496 | (10.5) |
| | *6* | 390 | (8.3) |
| | *7* | 294 | (6.3) |
| | *8* | 242 | (5.1) |
| | *9* | 171 | (3.6) |
| | *10* | 104 | (2.2) |
| | *>10* | 388 | (8.3) |
| | | | |
| **Quetiapine treatment** | | | |
| | *Patients initiated during study n (%)* | 749 | (15.9) |
| | *Prevalent users n (%)* | 3953 | (84.1) |

Table 52 presents study findings on the risk factors and potential confounding variables believed to potentially have influence in the performance of metabolic monitoring for the study population managed by German neurologists. Body mass index (BMI) or the component parts (weight and height) were recorded in the patient EMRs for 2% of the study population who were patients of neurologists. Among these patients, the mean (SD) BMI was 29.5 (7.4) indicating these patients were on average overweight and bordering on being obese. Of the study population, 632 patients (13%) had a diagnosis of psychosis or anxiety. None of the 4,702 study patients had a history of high blood pressure and only 1% had elevated cholesterol recorded in their medical history. Evidence of lipid testing was available for 33 (1%) patients. Fewer than 5% of patients had a confirmed history of cardiovascular disease or diabetes mellitus. Less than 1% of the non-diabetic patients had a record of previous glucose testing. There was only one patient with a recorded diagnosis of metabolic syndrome.

## Table 52 Risk factors for patients seen in neurology practices in Germany

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **Body mass index** | | | |
| | *Unknown* | 4620 | |
| | | | |
| | *Mean (SD)[n=82]* | 29.5 | (7.4) |
| | *Median* | 28 | |
| | *[LQ, UQ]* | [25, 34] | |
| | *(min, max)* | (16, 54) | |
| | | | |
| | *Summary categories n (%)* | | |
| | *Unknown* | 4620 | (98.3) |
| | *≤25* | 24 | (0.5) |
| | *>25* | 58 | (1.2) |
| | | | |
| | *Expanded categories n (%)* | | |
| | *Unknown* | 4620 | (98.3) |
| | *<18.5* | 2 | (0.0) |
| | *18.5-25.0* | 22 | (0.5) |
| | *>25.0-30.0* | 26 | (0.6) |
| | *>30.0-35.0* | 17 | (0.4) |
| | *>35* | 15 | (0.3) |
| | | | |
| **History with diagnosis of psychosis or anxiety n (%)** | | | |
| | *Yes* | 632 | (13.4) |
| | *No* | 4070 | (86.6) |
| | | | |
| **High blood pressure n (%)** | | | |
| | *No* | 4702 | (100) |
| | | | |
| **Elevated cholesterol n (%)** | | | |
| | *Yes* | 26 | (0.6) |
| | *No* | 4676 | (99.4) |
| | | | |

**Table 52 Risk factors for patients seen in neurology practices in Germany**

| | | Total number of patients (N=4702) | |
|---|---|---|---|
| **Testing of lipids n (%)** | | | |
| | *Yes* | 33 | (0.7) |
| | *No* | 4669 | (99.3) |
| | | | |
| **History of cardiovascular disease n (%)** | | | |
| | *Yes* | 209 | (4.4) |
| | *No* | 4493 | (95.6) |
| | | | |
| **History of diabetes mellitus n (%)** | | | |
| | *Yes* | 52 | (1.1) |
| | *No* | 4650 | (98.9) |
| | | | |
| **Testing of glucose in the past 12 months (excl. diabetics n=4650) n (%)** | | | |
| | *Yes* | 16 | (0.3) |
| | *No* | 4634 | (99.7) |
| | | | |
| **Diagnosis of metabolic syndrome** | | | |
| | *Yes* | 1 | (0.0) |
| | *No* | 4701 | (100) |

## 10.11 Outcome data: summary of outcomes data - Neurologists (Germany)

Table 53 provides a summary of the German neurology practices' metabolic monitoring activities. A total of 128 practices had newly initiated patients on quetiapine during the study period; none of these practices recorded weight for 50% or more of their newly initiated quetiapine patients. None of the 145 practices reached the reporting threshold of monitoring for signs and symptoms of hyperglycaemia or hyperlipidaemia during the study period for at least 50% of their patients. Among the 85 practices with patients at risk of developing diabetes, only one achieved monitoring for at least 50% of their patients during the study period. None of the neurology practices recorded providing counselling on adopting lifestyle behaviours for at least 50% of their quetiapine patients.

**Table 53 Summary of monitoring activities performed by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| Weight recorded at visit when initial prescription was issued | *128 (88%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Weight recorded at least once in study period | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Monitoring for elevated cholesterol at least once in study period | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia at least once in study period | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *diabetic patients* at least once in study period | *37 (26%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *patients at risk of diabetes* at least once in study period | *85 (59%)* | 1 (1%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| Counselling on healthy lifestyle conducted at least once in study period | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 54 provides a summary of the patients who were monitored by office-based neurology practices in Germany for the main outcomes of this study. Only 1 (<1%) patient was monitored out of 749 patients initiated on quetiapine for weight at the visit associated with the initial prescription. Similarly, <1% of the study patients had their weight monitored at any time during the study period. Very few patients (<1%) had cholesterol (i.e. lipid levels)

assessed or were monitored for signs and symptoms of hyperglycaemia. None of the 52 diabetic patients in this study population were monitored for signs and symptoms of hyperglycaemia, while only 1% of the patients considered at risk for developing diabetes were monitored. None of the patients had any recording of being provided with counselling on adopting healthy lifestyles (e.g. advice on healthy eating, importance of exercise, and positive changes to lifestyle).

**Table 54 Summary of monitoring activities performed for patients treated with quetiapine by neurologists in Germany**

| Monitoring activities performed on patients | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|
| | | | |
| Weight recorded at visit when initial prescription was issued | 749 | 1 | 0.1% |
| | | | |
| Weight recorded at least once in study period | 4702 | 15 | 0.3% |
| | | | |
| Monitoring for elevated cholesterol at least once in study period | 4702 | 16 | 0.3% |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia at least once in study period | 4702 | 7 | 0.1% |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *diabetic patients* at least once in study period | 52 | 0 | 0% |
| | | | |
| Monitoring for signs and symptoms of hyperglycaemia for *patients at risk of diabetes* at least once in study | 282 | 2 | 0.7% |
| | | | |
| Counselling on healthy lifestyle conducted at least once in study period | 4702 | 0 | 0% |

## 10.12 Main results: detailed analyses of outcomes data - Neurologists (Germany)

Table 55 presents the number of neurology practices in Germany that monitored the majority of patients newly initiated on quetiapine for weight according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold for weight monitoring for at least 50% of their newly initiated patients.

**Table 55 Monitoring of weight for patients initiated on quetiapine: by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *75 (59%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *35 (27%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *17 (13%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *1 (1%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total practices with newly initiated patients** | *128 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 56 presents the proportion of newly initiated quetiapine patients whose weight was monitored by neurology practices in Germany according to the number of physician visits and risk factors. As the number of patients monitored for weight at the time of initiation of quetiapine treatment was very small, a complete analysis of weight monitoring activity according to patient risk factors is not presented in detail. Of the 749 patients (16% of total study population) who were newly initiated on quetiapine during the study period, only one patient (<1%) had a record of weight measurement at the time of initial prescription. This patient was not prescribed other antipsychotics or other antidepressants in the 6 months prior to the observation period. This patient was female, within the age range of 40 to 49 years, was not obese (BMI ≤25), did not have high blood pressure, elevated cholesterol, blood lipid testing, cardiovascular disease (CVD), diabetes, history of blood glucose testing, history of anxiety/psychosis, or metabolic syndrome.

## Table 56 Monitoring of weight for patients initiated on quetiapine: patients seen in neurology practices in Germany

| | | Total number of patients | Number of patients monitored | % Monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Weight recorded at visit when initial prescription was issued*** | 749 | 1 | (0.1) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 211 | 0 | (0.0) |
| | *No* | 538 | 1 | (0.2) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 399 | 0 | (0.0) |
| | *No* | 350 | 1 | (0.3) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 11 | 0 | (0.0) |
| | *No* | 6 | 1 | (16.7) |
| | *Missing* | 732 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 749 | 1 | (0.1) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *No* | 746 | 1 | (0.1) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 3 | 0 | (0.0) |
| | *No* | 746 | 1 | (0.1) |
| | | | | |

**Table 56 Monitoring of weight for patients initiated on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Number of patients monitored | % Monitored |
|---|---|---|---|---|
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 32 | 0 | (0.0) |
| | *No* | 717 | 1 | (0.1) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 7 | 0 | (0.0) |
| | *No* | 742 | 1 | (0.1) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 2 | 0 | (0.0) |
| | *No* | 747 | 1 | (0.1) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 500 | 1 | (0.2) |
| | *Male* | 249 | 0 | (0.0) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 108 | 0 | (0.0) |
| | *No* | 641 | 1 | (0.2) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 15 | 0 | (0.0) |
| | *25-39* | 89 | 0 | (0.0) |
| | *40-49* | 138 | 1 | (0.7) |
| | *50-64* | 242 | 0 | (0.0) |
| | *≥65* | 265 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 749 | 1 | (0.1) |
| | | | | |
| | ***Smoking*** | | | |
| | *No* | 1 | 0 | (0.0) |
| | *Missing* | 748 | 1 | (0.1) |

Table 57 presents the number of neurology practices in Germany that monitored weight for patients prescribed quetiapine (both new and established users of the medication) according to the number of eligible patients in their practice. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold of monitoring weight for at least 50% of their patients prescribed quetiapine.

**Table 57 Monitoring of weight of patients on quetiapine: by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *16 (11%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *15 (10%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *59 (41%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *55 (38%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 58 describes the weight monitoring of patients prescribed quetiapine managed by neurology practices in Germany according to the number of physician visits and risk factors. As the number of patients monitored for weight was very small, a complete analysis of this monitoring activity according to patient risk factors is not presented in detail. Of the 4,702 patients studied, less than 1% (n=15) had evidence of weight measurement during the study period. Three of these patients were previously prescribed other antipsychotics and 8 were previously prescribed antidepressants. Nineteen percent of the patients with BMI>25 were monitored for weight, whereas only 12% of the patients with BMI≤25 had their weight monitored. None of the monitored patients had high blood pressure, CVD, diabetes, history of blood glucose testing, or metabolic syndrome.

## Table 58 Monitoring of weight of patients on quetiapine: patients seen in neurology practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Weight recorded in study period*** | 4702 | 15 | (0.3) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2)* | 1211 | 2 | (0.2) |
| | *Q2 (3-4)* | 1406 | 7 | (0.5) |
| | *Q3 (5-7)* | 1180 | 5 | (0.4) |
| | *Q4 (8-27)* | 905 | 1 | (0.1) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 1654 | 3 | (0.2) |
| | *No* | 3048 | 12 | (0.4) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 2614 | 8 | (0.3) |
| | *No* | 2088 | 7 | (0.3) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 58 | 11 | (19.0) |
| | *No* | 24 | 3 | (12.5) |
| | *Missing* | 4620 | 1 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 4702 | 15 | (0.3) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 26 | 1 | (3.8) |
| | *No* | 4676 | 14 | (0.3) |
| | | | | |

**Table 58 Monitoring of weight of patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Blood lipid testing*** | | | |
| | *Yes* | 33 | 1 | (3.0) |
| | *No* | 4669 | 14 | (0.3) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 209 | 0 | (0.0) |
| | *No* | 4493 | 15 | (0.3) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 52 | 0 | (0.0) |
| | *No* | 4650 | 15 | (0.3) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 18 | 0 | (0.0) |
| | *No* | 4684 | 15 | (0.3) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 2922 | 10 | (0.3) |
| | *Male* | 1780 | 5 | (0.3) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 632 | 1 | (0.2) |
| | *No* | 4070 | 14 | (0.3) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 86 | 0 | (0.0) |
| | *25-39* | 671 | 3 | (0.4) |
| | *40-49* | 946 | 3 | (0.3) |
| | *50-64* | 1458 | 4 | (0.3) |
| | *≥65* | 1541 | 5 | (0.3) |
| | | | | |

**Table 58 Monitoring of weight of patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 4701 | 15 | (0.3) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 4699 | 15 | (0.3) |

Table 59 presents the number of neurology practices in Germany that have monitored cholesterol by assessing lipid levels of the majority of patients treated with quetiapine according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold for monitoring cholesterol levels for hyperlipidaemia for at least 50% of their patients prescribed quetiapine.

**Table 59 Monitoring of elevated cholesterol for patients on quetiapine: by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *16 (11%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *15 (10%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *59 (41%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *55 (38%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 60 presents an analysis of cholesterol monitoring among patients prescribed quetiapine and managed by office-based neurology practices in Germany according to the number of physician visits and risk factors. As the number of patients with cholesterol levels monitored was very small, a complete analysis of this monitoring activity according to patient risk

factors was not performed. Of the 4,702 patients studied, there was evidence of cholesterol monitoring for less than 1% (n=16). Six patients monitored were prescribed other antipsychotics and 9 prescribed antidepressants during the 6 months prior to the observation period. None of the monitored patients had either high blood pressure or elevated cholesterol in their medical histories. Additionally, none of the monitored patients had diabetes, history of anxiety/psychosis, or metabolic syndrome, and only 2 of the monitored patients had a history of cardiovascular disease. Twelve percent (4 out of 33 patients) that had prior cholesterol testing were monitored for elevated cholesterol during the study period, whereas almost none of the patients with no prior cholesterol testing were monitored.

**Table 60 Monitoring of elevated cholesterol for patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Elevated cholesterol assessed at least once in study period*** | 4702 | 16 | (0.3) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 1211 | 5 | (0.4) |
| | *Q2 (3-4 visits)* | 1406 | 3 | (0.2) |
| | *Q3 (5-7 visits)* | 1180 | 4 | (0.3) |
| | *Q4 (8-27 visits)* | 905 | 4 | (0.4) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 1654 | 6 | (0.4) |
| | *No* | 3048 | 10 | (0.3) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 2614 | 9 | (0.3) |
| | *No* | 2088 | 7 | (0.3) |
| | | | | |

**Table 60 Monitoring of elevated cholesterol for patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***BMI >25*** | | | |
| | *Yes* | 58 | 0 | (0.0) |
| | *No* | 24 | 0 | (0.0) |
| | *Missing* | 4620 | 16 | (0.3) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 4702 | 16 | (0.3) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 26 | 0 | (0.0) |
| | *No* | 4676 | 16 | (0.3) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 33 | 4 | (12.1) |
| | *No* | 4669 | 12 | (0.3) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 209 | 2 | (1.0) |
| | *No* | 4493 | 14 | (0.3) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 52 | 0 | (0.0) |
| | *No* | 4650 | 16 | (0.3) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 18 | 1 | (5.6) |
| | *No* | 4684 | 15 | (0.3) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 2922 | 11 | (0.4) |
| | *Male* | 1780 | 5 | (0.3) |
| | | | | |

**Table 60 Monitoring of elevated cholesterol for patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 632 | 0 | (0.0) |
| | *No* | 4070 | 16 | (0.4) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 86 | 0 | (0.0) |
| | *25-39* | 671 | 5 | (0.7) |
| | *40-49* | 946 | 3 | (0.3) |
| | *50-64* | 1458 | 8 | (0.5) |
| | *≥65* | 1541 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 4701 | 16 | (0.3) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 4699 | 16 | (0.3) |

Table 61 presents the number of neurology practices in Germany that have monitored patients treated with quetiapine for signs and symptoms of hyperglycaemia according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold of monitoring 50% or more of their patients for signs and symptoms of hyperglycaemia.

**Table 61 Monitoring of signs and symptoms of hyperglycaemia in patients on quetiapine: by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *16 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *15 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *59 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *55 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 62 provides analysis of monitoring for signs and symptoms of hyperglycaemia among patients prescribed quetiapine and managed by office-based neurology practices in Germany by the number of physician visits and risk factors. As the number of patients monitored for signs and symptoms of hyperglycaemia was very small, a complete analysis of this monitoring activity according to patient risk factors was not performed. Of the 4,702 patients studied, there was evidence of blood glucose assessment for only 7 patients (<1%). Among the patients with blood glucose testing in the prior 12 months, 11% (2 out of 18 patients) were monitored for signs and symptoms of hyperglycaemia during the study period as compared to less than 1% of patients without prior blood glucose testing. Less than 1% of patients monitored had other risk factors, including being previously prescribed other antipsychotics or antidepressants, previous monitoring of high blood pressure, elevated cholesterol, diabetes, or metabolic syndrome.

## Table 62 Monitoring of hyperglycaemia in patients on quetiapine: patients seen in neurology practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Blood glucose assessed at least once in study period*** | 4702 | 7 | (0.1) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 1211 | 2 | (0.2) |
| | *Q2 (3-4 visits)* | 1406 | 2 | (0.1) |
| | *Q3 (5-7 visits)* | 1180 | 1 | (0.1) |
| | *Q4 (8-27 visits)* | 905 | 2 | (0.2) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 1654 | 2 | (0.1) |
| | *No* | 3048 | 5 | (0.2) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 2614 | 4 | (0.2) |
| | *No* | 2088 | 3 | (0.1) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 58 | 0 | (0.0) |
| | *No* | 24 | 0 | (0.0) |
| | *Missing* | 4620 | 7 | (0.2) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 4702 | 7 | (0.1) |
| | | | | |

## Table 62 Monitoring of hyperglycaemia in patients on quetiapine: patients seen in neurology practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 26 | 0 | (0.0) |
| | *No* | 4676 | 7 | (0.1) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 33 | 0 | (0.0) |
| | *No* | 4669 | 7 | (0.1) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 209 | 2 | (1.0) |
| | *No* | 4493 | 5 | (0.1) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 52 | 0 | (0.0) |
| | *No* | 4650 | 7 | (0.2) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 18 | 2 | (11.1) |
| | *No* | 4684 | 5 | (0.1) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 2922 | 5 | (0.2) |
| | *Male* | 1780 | 2 | (0.1) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 632 | 1 | (0.2) |
| | *No* | 4070 | 6 | (0.1) |
| | | | | |

**Table 62 Monitoring of hyperglycaemia in patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Age*** | | | |
| | *<25* | 86 | 0 | (0.0) |
| | *25-39* | 671 | 2 | (0.3) |
| | *40-49* | 946 | 0 | (0.0) |
| | *50-64* | 1458 | 3 | (0.2) |
| | *≥65* | 1541 | 2 | (0.1) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 4701 | 7 | (0.1) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 4699 | 7 | (0.1) |

Table 63 presents the number of neurology practices in Germany that monitored patients with diabetes mellitus treated with quetiapine for signs and symptoms of hyperglycaemia according to the number of eligible patients in those practices. It can be observed that none of the practices in their respective stratification groups met the minimum reporting threshold of monitoring at least 50% of patients with diabetes mellitus in their practices for signs and symptoms of hyperglycaemia.

**Table 63 Monitoring of signs and symptoms of hyperglycaemia for diabetic patients on quetiapine: by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *37 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total practices with diabetic patients** | *37 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 64 presents analyses of monitoring for signs and symptoms of hyperglycaemia among diabetic patients who were prescribed quetiapine by office-based neurology practices in

Germany according to the number of physician visits and risk factors. There were 52 diabetic patients in the study population, and none of these patients had recorded evidence of monitoring.

**Table 64 Monitoring of signs and symptoms of hyperglycaemia for diabetic patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Glucose assessed at least once in study period*** | 52 | 0 | (0.0) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 8 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 13 | 0 | (0.0) |
| | *Q3 (5-7 visits)* | 20 | 0 | (0.0) |
| | *Q4 (8-27 visits)* | 11 | 0 | (0.0) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 17 | 0 | (0.0) |
| | *No* | 35 | 0 | (0.0) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 29 | 0 | (0.0) |
| | *No* | 23 | 0 | (0.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Missing* | 52 | 0 | (0.0) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 52 | 0 | (0.0) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 12 | 0 | (0.0) |
| | *No* | 40 | 0 | (0.0) |

**Table 64 Monitoring of signs and symptoms of hyperglycaemia for diabetic patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 2 | 0 | (0.0) |
| | *No* | 50 | 0 | (0.0) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 14 | 0 | (0.0) |
| | *No* | 38 | 0 | (0.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 52 | 0 | (0.0) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 2 | 0 | (0.0) |
| | *No* | 50 | 0 | (0.0) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 30 | 0 | (0.0) |
| | *Male* | 22 | 0 | (0.0) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 8 | 0 | (0.0) |
| | *No* | 44 | 0 | (0.0) |
| | | | | |
| | ***Age*** | | | |
| | *25-39* | 1 | 0 | (0.0) |
| | *40-49* | 8 | 0 | (0.0) |
| | *50-64* | 16 | 0 | (0.0) |
| | *≥65* | 27 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *No* | 52 | 0 | (0.0) |
| | | | | |

**Table 64 Monitoring of signs and symptoms of hyperglycaemia for diabetic patients on quetiapine: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Smoking*** | | | |
| | *Missing* | 52 | 0 | (0.0) |

Table 65 presents the number of German neurology practices that have monitored the majority of their patients who were at risk of developing diabetes and treated with quetiapine for signs and symptoms of hyperglycaemia according to the number of eligible patients in those practices. It can be observed that only one practice with between 1 and 5 eligible patients monitored ≥50% of its patients who were at risk of developing diabetes for signs and symptoms of hyperglycaemia.

**Table 65 Monitoring of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: by neurology practices in Germany**

| | | Proportion of patients monitored | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *69 (81%)* | 1 (1%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *14 (16%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *2 (2%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total practices with patients at risk of diabetes** | *85 (100%)* | 1 (1%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 66 presents analysis of monitoring for signs and symptoms of hyperglycaemia among patients at risk of developing diabetes who have been prescribed quetiapine according to the number of visits to German neurologists and risk factors. As the number of patients monitored was very small, a complete analysis of this monitoring activity according to patient risk factors is not presented in detail. Among the 282 study patients at risk for developing diabetes, 2 patients had evidence of monitoring. One of these patients was prescribed other antipsychotics and both were prescribed antidepressants in the prior 6 months before the observation period. Neither of these patients had high blood pressure, elevated cholesterol, CVD, or anxiety/psychosis. Although these patients were at risk of developing diabetes, there was no evidence of blood lipid testing or blood glucose testing in the prior 12 months.

## Table 66 Monitoring of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: patients seen in neurology practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Glucose assessed at least once in study period*** | 282 | 2 | (0.7) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 58 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 80 | 1 | (1.3) |
| | *Q3 (5-7 visits)* | 78 | 0 | (0.0) |
| | *Q4 (8-27 visits)* | 66 | 1 | (1.5) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 112 | 1 | (0.9) |
| | *No* | 170 | 1 | (0.6) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 174 | 2 | (1.1) |
| | *No* | 108 | 0 | (0.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 58 | 0 | (0.0) |
| | *Missing* | 224 | 2 | (0.9) |
| | | | | |
| | ***High blood pressure*** | | | |
| | *No* | 282 | 2 | (0.7) |
| | | | | |

**Table 66 Monitoring of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 6 | 0 | (0.0) |
| | *No* | 276 | 2 | (0.7) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 7 | 0 | (0.0) |
| | *No* | 275 | 2 | (0.7) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 195 | 2 | (1.0) |
| | *No* | 87 | 0 | (0.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *No* | 282 | 2 | (0.7) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 2 | 0 | (0.0) |
| | *No* | 280 | 2 | (0.7) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 163 | 1 | (0.6) |
| | *Male* | 119 | 1 | (0.8) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 36 | 0 | (0.0) |
| | *No* | 246 | 2 | (0.8) |
| | | | | |
| | ***Age*** | | | |
| | *<25* | 1 | 0 | (0.0) |
| | *25-39* | 26 | 0 | (0.0) |
| | *40-49* | 38 | 0 | (0.0) |
| | *50-64* | 79 | 2 | (2.5) |
| | *≥65* | 138 | 0 | (0.0) |
| | | | | |

**Table 66 Monitoring of hyperglycaemia in quetiapine prescribed patients at risk of developing diabetes: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Metabolic syndrome*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 281 | 2 | (0.7) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 279 | 2 | (0.7) |

Table 67 presents the number of German neurology practices' that have provided counselling on the importance of healthy eating, exercise, and lifestyle to the majority of their patients prescribed quetiapine according to the number of eligible patients in those practice. It was observed that none of the practices in their respective stratification groups met the minimum reporting threshold of providing lifestyle counselling to at least 50% of their quetiapine patients.

**Table 67 Monitoring of healthy eating/exercise/lifestyle counselling of patients: by neurology practices in Germany**

| | | Proportion of patients counselled | | | | |
|---|---|---|---|---|---|---|
| | | **≥50%** | **≥67%** | **≥80%** | **≥90%** | **≥95%** |
| **Eligible patients in practice** | **Number of practices - 'A' (% of total in study)** | Number of practices (% of **'A'**) | | | | |
| | | | | | | |
| **1-5** | *16 (11%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **6-11** | *15 (10%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **12-34** | *59 (41%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **35+** | *55 (38%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | | | | | | |
| **Total** | *145 (100%)* | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table 68 presents data on the provision of counselling to promote healthy lifestyle behaviours to patients who were prescribed quetiapine by German neurology practices according to the number of physician visits and risk factors. There was no recorded evidence of the provision of such counselling to patients during the observation period.

**Table 68 Monitoring of healthy eating/exercise/lifestyle counselling: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| **Monitoring** | | | | |
| | ***Counselling on healthy lifestyle conducted at least once in study period*** | 4702 | 0 | (0.0) |
| | | | | |
| | *Monitoring by number of visits by patients to the doctor* | | | |
| | | | | |
| | *Q1 (1-2 visits)* | 1211 | 0 | (0.0) |
| | *Q2 (3-4 visits)* | 1406 | 0 | (0.0) |
| | *Q3 (5-7 visits)* | 1180 | 0 | (0.0) |
| | *Q4 (8-27 visits)* | 905 | 0 | (0.0) |
| | | | | |
| **Risk factors : Total n (%monitored)** | | | | |
| | ***Prescribed other antipsychotics*** | | | |
| | *Yes* | 1654 | 0 | (0.0) |
| | *No* | 3048 | 0 | (0.0) |
| | | | | |
| | ***Prescribed antidepressants*** | | | |
| | *Yes* | 2614 | 0 | (0.0) |
| | *No* | 2088 | 0 | (0.0) |
| | | | | |
| | ***BMI >25*** | | | |
| | *Yes* | 58 | 0 | (0.0) |
| | *No* | 24 | 0 | (0.0) |
| | *Missing* | 4620 | 0 | (0.0) |
| | | | | |

## Table 68 Monitoring of healthy eating/exercise/lifestyle counselling: patients seen in neurology practices in Germany

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***High blood pressure*** | | | |
| | *No* | 4702 | 0 | (0.0) |
| | | | | |
| | ***Elevated cholesterol*** | | | |
| | *Yes* | 26 | 0 | (0.0) |
| | *No* | 4676 | 0 | (0.0) |
| | | | | |
| | ***Blood lipid testing*** | | | |
| | *Yes* | 33 | 0 | (0.0) |
| | *No* | 4669 | 0 | (0.0) |
| | | | | |
| | ***Cardiovascular disease*** | | | |
| | *Yes* | 209 | 0 | (0.0) |
| | *No* | 4493 | 0 | (0.0) |
| | | | | |
| | ***Diabetes*** | | | |
| | *Yes* | 52 | 0 | (0.0) |
| | *No* | 4650 | 0 | (0.0) |
| | | | | |
| | ***History of blood glucose testing*** | | | |
| | *Yes* | 18 | 0 | (0.0) |
| | *No* | 4684 | 0 | (0.0) |
| | | | | |
| | ***Sex*** | | | |
| | *Female* | 2922 | 0 | (0.0) |
| | *Male* | 1780 | 0 | (0.0) |
| | | | | |
| | ***History of anxiety or psychosis*** | | | |
| | *Yes* | 632 | 0 | (0.0) |
| | *No* | 4070 | 0 | (0.0) |
| | | | | |

**Table 68 Monitoring of healthy eating/exercise/lifestyle counselling: patients seen in neurology practices in Germany**

| | | Total number of patients | Total number of patients monitored | % Patients monitored |
|---|---|---|---|---|
| | ***Age*** | | | |
| | *<25* | 86 | 0 | (0.0) |
| | *25-39* | 671 | 0 | (0.0) |
| | *40-49* | 946 | 0 | (0.0) |
| | *50-64* | 1458 | 0 | (0.0) |
| | *≥65* | 1541 | 0 | (0.0) |
| | | | | |
| | ***Metabolic syndrome*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 4701 | 0 | (0.0) |
| | | | | |
| | ***Smoking*** | | | |
| | *Yes* | 1 | 0 | (0.0) |
| | *No* | 2 | 0 | (0.0) |
| | *Missing* | 4699 | 0 | (0.0) |

Table 69 presents descriptive statistics including the range, median and values corresponding to the 25$^{th}$ and 75$^{th}$ percentiles for the proportions of patients who received different metabolic monitoring previously described from German neurology practices. Among the 145 neurology practices included in the study, 88% (n=128) had patients that were initiated on quetiapine, 26% had confirmed diabetic patients, and 59% had patients identified as at risk for developing diabetes. However, the proportion of patients receiving metabolic monitoring among these subset populations was very low. Overall, the level of monitoring presented in the table reveals that the performance and recording of metabolic monitoring among patients treated with quetiapine in neurology practices in Germany was very low.

**Table 69 Monitoring by neurology practices in the Germany: Distributions of the proportions of patients monitored**

| | | | | Proportion of patients monitored in the practice | |
|---|---|---|---|---|---|
| **Monitoring activity** | **Patients** | **Number of practices** | **Range of the number of patients in each practice (min, max)** | **Median** | **[LQ, UQ]** |
| | | | | | |
| **Weight** | *All* | 145 | (1, 207) | 0% | [0%, 0%] |
| | *Initiated on quetiapine* | 128 | (1, 166) | 0% | [0%, 0%] |
| | | | | | |
| **Cholesterol** | *All* | 145 | (1, 207) | 0% | [0%, 0%] |
| | | | | | |
| **Glucose** | *All* | 145 | (1, 207) | 0% | [0%, 0%] |
| | *Diabetics* | 37 | (1, 3) | 0% | [0%, 0%] |
| | *At risk of diabetes* | 85 | (1, 16) | 0% | [0%, 0%] |
| | | | | | |
| **Health counselling** | *All* | 145 | (1, 207) | 0% | [0%, 0%] |

## 10.13 Other analyses

No other analyses were conducted.

## 10.14 Adverse events/adverse reactions

The objectives of the study did not include analyzing adverse events or adverse reactions.

# 11. DISCUSSION

## 11.1 Key results - General Practitioners (UK)

Among the Disease Analyzer (DA) data from UK GPs, 887 adult patients managed by 93 practices met all the inclusion and exclusion criteria for the evaluation of metabolic monitoring in this study. There was an average (SD) of 9.5 patients (8.2) and a median of 8 patients per practice. Patients had a median of 12 visits during the observation period of 11 January to 31 July 2012. The study patients' median age was 48 years (mean (SD) = 50.5 (17.7) years), and 65% of the patients were female. The most common diagnosis for inclusion in the study was bipolar disorder (64% of patients), followed by major depressive disorder (15%) and then schizophrenia (11%); with at least 11% of patients having 2 or more of these conditions.

Of the 887 patients, 551 (62%) experienced at least one of the studied metabolic monitoring activities during the observation period. A summary of monitoring activity rates and

frequency performed on patients prescribed quetiapine during the observation period by UK GPs are presented below.

**Monitoring of weight for patients newly initiated on quetiapine**

Among the 72 GP practices with patients newly initiated on quetiapine (representing 77% of total GP practices included in analysis), only 2 practices (3%) monitored weight during the consultation when quetiapine was initially prescribed for 50% or more of their patients.

A total of 175 patients (20% of all patients included in the analysis) were newly initiated on quetiapine, and among these, only 6 patients (3%) had weight recorded at the visit on the date of initiation of quetiapine treatment. Given the low sample size of patients being monitored, modelling on the risk factors associated with this outcome was not conducted. However, prior weight monitoring may play an influential role; 445 patients (50% of the total patient population) had their weight monitored during the 12 months prior to the study period.

**Monitoring of weight for patients receiving treatment with quetiapine**

A total of 33 GP practices (35% of the total) monitored weight at any visit during the study period for 50% or more of their patients and only 7 practices (8%) monitored 80% or more of their patients.

A total of 343 patients (39%) had their weight monitored during visits within the study period, with an increased proportion having weight recorded with an increasing number of visits to the GP. Factors associated with reduced odds of monitoring of weight during ongoing treatment included having been prescribed antidepressants in the prior 12 months (OR=0.55) and being aged either 50-64 or >64 years as compared to the youngest age group (18-39) (OR=0.48 and OR=0.61, respectively). Factors associated with higher odds of having weight monitored during at least one visit during the observation period included having BMI >25 (OR=1.93), having either elevated cholesterol (OR=1.71) or prior lipid testing (OR=2.26) during the 12 months prior to the study period, or having a diagnosis of diabetes mellitus (OR=1.81). Having a prior recording of weight (in general, not specific to the result indicating obesity or non-obesity) was not a tested model covariate; however, 50% of all patients had been monitored for weight in the 12 months prior to the study period.

**Monitoring for elevated cholesterol for patients receiving treatment with quetiapine**

A total of 15 GP practices (16% of total) monitored for elevated cholesterol for 50% or more of their patients and only 2% monitored 80% or more of their patients.

40% of patients had lipid panel testing and 20% were recorded as having elevated cholesterol during the 12 months prior to the study period. A total of 246 patients (28%) had their lipid panels assessed at least once during the study period. The proportion of patients having their lipids tested increased with the number of visits to the GP, with those having 8 or fewer visits only representing 11% of patients monitored.

Factors associated with higher odds of being monitored for elevated cholesterol included having during the prior 12 months either elevated cholesterol (OR=1.81) or prior lipid testing

(OR=1.78), having diabetes mellitus (OR=2.48), and being within the age ranges of 40-49 or 50-64 years compared to patients in the age range of 18-39 years (ORs=3.19 and OR=4.55, respectively).

**Monitoring for signs and symptoms of hyperglycaemia for patients receiving treatment with quetiapine**

21 (23% of total) GP practices monitored 50% or more of their patients for signs and symptoms of hyperglycaemia and 2 practices (2%) monitored 80% or more of their patients.

42% of the patients (including patients with diabetes mellitus and patients without diabetes mellitus in aggregate) had received glucose testing in the prior 12 months. A total of 32% of patients were monitored for hyperglycaemia at least once during the observation period, with an increasing proportion of patients having their blood glucose assessed with increasing number of visits to the GP.

The risk factor associated with reduced odds of a patient being monitored for signs and symptoms of hyperglycaemia was receipt of a prescription for antidepressants in the prior 6 months (OR=0.69). Factors associated with increased odds of being monitored for signs and symptoms of hyperglycaemia included having BMI>25; OR=1.60, having elevated cholesterol in the prior 12 months (OR=2.08), having diabetes (OR=1.26) and having testing of glucose in the prior 12 months (OR=1.76).

**Monitoring for signs and symptoms of hyperglycaemia among patients with diabetes mellitus receiving treatment with quetiapine**

A total of 48 GP practices (52% of total practices) had patients with diabetes mellitus. Overall, 32 of these practices (67%) monitored 50% or more of their patients with diabetes mellitus for signs and symptoms of hyperglycaemia and 18 practices (38%) monitored 80% of more of their patients.

Of the 85 patients with diabetes mellitus (10% of all study patients), 51% were monitored for hyperglycaemia during the study period. Patients had nearly 4 times the odds of being monitored for hyperglycaemia if they had a history of blood glucose testing in comparison to those who did not have a recording of such a test (OR= 3.90). No other demographic or risk factors were found to be significantly associated with having monitoring for signs and symptoms of hyperglycaemia performed.

**Monitoring for signs and symptoms of hyperglycaemia among those at risk of diabetes**

A total of 89 GP practices (96% of total practices included in analysis) had patients at risk of developing diabetes mellitus. Overall, 30% of practices monitored 50% or more of their patients at risk for diabetes for signs and symptoms of hyperglycaemia and 8% of practices monitored 80% or more of their patients at risk for diabetes.

A total of 483 non-diabetic patients (60%) were at risk for diabetes mellitus. Of these patients, 166 (34%) had plasma glucose testing performed. The proportion of patients monitored increased for patients having 9 or more visits during the observation period; 89% of the

patients at risk for diabetes mellitus who were monitored for signs and symptoms of hyperglycaemia were categorised within the top three categories according to number of physician visits ranging from 9-62 visits to the physician during the study period.

Prescriptions of antidepressants during the 6 months prior to the beginning of the study period reduced the odds of having a glucose monitoring during the study period (OR=0.63). Patients possessing other risk factors including having BMI>25 and a history of cardiovascular disease demonstrated reduced odds of monitoring but these results did not reach statistical significance.

Factors associated with increased odds for patients at risk of diabetes being monitored for signs and symptoms of hyperglycaemia included having elevated cholesterol in the prior 12 months (OR=1.98) or being within the age ranges of 40-49 and 50-64 years compared to age range of 18-39 years (both OR=1.80). Similarly, higher odds of monitoring with glucose testing in the prior 12 months and patients of older age (≥65 years) as compared to the youngest age group (18-39 years) were not statistically significant.

**Monitoring for healthy lifestyle counselling**

Of the 93 GP practices, 29% (n=27) counselled 50% or more of their patients to promote adoption of healthy lifestyle behaviours and 9% (n=8) monitored 80% or more of their patients. Proportionally, patients whose number of physician visits fell within the lowest quartile (1-8 visits) were monitored less often than those in the top 3 quartiles.

A total of 273 patients (31%) were provided healthy eating/exercise/lifestyle counselling at least once during the observation period. The odds of counselling was 1.5 fold higher among patients hospitalised in the year prior to the observation period (OR=1.46). All other demographic and tested risk factors were not found to be associated with the performance of counselling at a significant level.

In summary, the performance of metabolic monitoring by GP practices in the UK was subject to variation with the highest levels of monitoring being performed for signs and symptoms of hyperglycaemia among patients with diabetes mellitus, for which 67% of GP practices monitored 50% or more of their patients and 38% of practices monitored 80% or more of patients. The monitoring for hyperglycaemia among those at risk for diabetes mellitus was lower with 30% of practices monitoring 50% or more of their patients.

Monitoring of weight for 50% or more of patients was performed by 35% of GP practices. Counselling promoting adoption of healthy lifestyle behaviours was documented for 50% or more of patients in 29% of GP practices.

The proportions of patients monitored by GPs followed the trend in the performance by practices with the highest levels of monitoring observed for hyperglycaemia among patients with diabetes at 51%, serum glucose monitoring for 42% overall and 34% of those patients at risk for developing diabetes mellitus; monitoring of weight for 39% patients ongoing quetiapine treatment, counselling to promote healthy behaviours for 31% and monitoring of cholesterol for 28% of patients seen in GP practices.

## 11.2 Key results - Psychiatrists (Germany)

Among the 42 psychiatry practices in Germany identified in the DA (representing 1,451 adult quetiapine patients), 79% were solo practices. There were slightly more male practitioners (57%) and overall, the psychiatrists had a median age of 53 years and a median of 13 years of registration. There were a median of 25 patients per practice. Each patient had a median of 4 visits each during the observation period.

The patients seen in German psychiatry practices, just over half (58%) were female, with a median age of 51 years and a mean (SD) age of 51.4 (15.2) years. Approximately 36% of the study population were 50-64 years of age. The majority (90%) of patients were either members of public insurance or were retirees, with nearly an equal split (44% and 46%, respectively). The most common diagnosis for inclusion in the study was bipolar disorder (46% of patients), followed by schizophrenia (19%) and then major depressive disorder (~10%); with ~26% of patients having 2 or more of these conditions. In the 6 months prior to the study period, 33% of patients had at least one prescription for another antipsychotic although 60% of patients had at least one prescription for an antidepressant.

Only 1.5% of the 1451 study patients experienced at least one of the metabolic monitoring activities during the study period. Weight and elevated cholesterol were the only activities for which 50% or more of German psychiatry practice patients were monitored during the observation period for the study. This level of monitoring was performed at only one psychiatry practice for each activity and it was not possible to determine whether this was the same practice or two different psychiatry practices. Additional details on metabolic monitoring performed on patients prescribed quetiapine during the observation period by German psychiatry practices are presented below. Due to the low number of patients monitored, modelling of factors predictive of monitoring exercises were not conducted for the patients seen in psychiatry practices in Germany.

### Monitoring of weight for patients newly initiated on quetiapine

Among the 42 psychiatry practices, 90% had at least one patient newly initiated on quetiapine during the study period. Newly initiated patients represented 18% (n=259) of the study sample; of these patients, 3% had their weight monitored in the prior 12 months and 1% had their weight monitored at the visit where quetiapine was initiated.

### Monitoring of weight for patients receiving treatment with quetiapine

One psychiatry practice (2% of the 42 analysed) monitored weight during at least one visit in the study period for more than 95% of its patients; however, this was a practice having between 1 and 5 eligible patients. Less than 1% of patients (n=6) had their weight monitored during visits within the study period.

### Monitoring for elevated cholesterol among patients receiving treatment with quetiapine

One psychiatry practice (2% of the 42 analysed) monitored for elevated cholesterol during at least one visit in the study period for more than 95% of its patients; however, this was a

practice having between 1 and 5 eligible patients. 1% of patients (n=14) had their cholesterol assessed at least once during the study period.

**Monitoring for signs and symptoms of hyperglycaemia for patients receiving treatment with quetiapine**

None of the psychiatry practices met the minimum reporting threshold for monitoring at least 50% of their patients. Only 10 patients (1%) were monitored for signs and symptoms of hyperglycaemia.

**Monitoring for signs and symptoms of hyperglycaemia among patients with diabetes mellitus receiving treatment with quetiapine**

There were 9 patients (1%) across 6 psychiatry practices (14%). None of these diabetic patients were monitored for signs and symptoms of hyperglycaemia.

**Monitoring for hyperglycaemia among those at risk of developing Diabetes**

There were 19 (45%) psychiatry practices representing 58 (4%) patients identified as being at risk for developing diabetes; none of these practices met the minimum reporting threshold for monitoring at least 50% of their patients. Across all 19 practices, only 7% (n=4) of the at-risk patients were monitored for signs and symptoms of hyperglycaemia.

**Monitoring for healthy lifestyle counselling**

Across the 42 psychiatry practices, there was no evidence of patients being counselled to promote adoption of healthy lifestyle behaviours.

In summary, the performance and/or recording of metabolic monitoring among patients treated with quetiapine in psychiatry practices in Germany was very low.

## 11.3 Key results - Neurologists (Germany)

Among the analysed 145 office-based neurology practices in Germany representing 4,702 adult quetiapine patients, 81% were solo practices. Approximately 74% of the physicians were male and across all physicians, the median age was 55 years and they had a median of 16 years registration. There was a median of 27 patients per practice. Each patient had a median of 4 visits during the study period.

62% of the patients were female, and overall, they had a median age of 55 years and a mean (SD) age of 57 (17.2) years. Approximately one-third of patients fell into each of the older age groups, 50-64 years and ≥65 years (31% and 33% respectively). 35% of patients were members of public insurance and over half (56%) were retirees. 45% of the patients were diagnosed with bipolar disorder, 20% had a diagnosis of schizophrenia and 7% with major depressive disorder (MDD). Approximately 25% of the study population had a combined diagnosis of two conditions and ~3% of patients had a diagnosis of all three conditions of schizophrenia, bipolar disorder and MDD. Thirteen percent (n=632) of patients had a history of psychosis or anxiety based on diagnosis. In the 6 months prior to the study period, ~35% of

patients were given one or more prescriptions for another antipsychotic and ~56% of patients were prescribed at least one antidepressant.

Less than 1% of the 4,072 study patients experienced at least one of the monitoring activities during the study period. Across the monitoring activities, only one practice performed monitoring for at least 50% of its patients; this was monitoring for signs and symptoms of hyperglycaemia among patients at risk for developing diabetes. More detail on monitoring activities performed on patients prescribed quetiapine during the study period by neurology practices in Germany are presented below. Due to the low number of patients monitored, modelling exercises were not conducted.

**Monitoring of weight for patients newly initiated on quetiapine**

Among the 145 neurology practices, 88% (n=128) had at least one patient newly initiated on quetiapine during the observation period. Newly initiated patients represented 16% (n=749) of the study sample. Only 1 patient (<1%) had their weight monitored at the quetiapine-initiating visit.

**Monitoring of weight for patients receiving treatment with quetiapine**

None of the neurology practices met the minimum reporting threshold for monitoring weight across any visit for at least 50% of their patients. 15 (0.3%) patients had their weight monitored during at least one visit within the study period.

**Monitoring for elevated cholesterol among patients receiving treatment with quetiapine**

None of the neurology practices met the minimum reporting threshold for monitoring elevated cholesterol for at least 50% of their patients. 16 (0.3%) patients had their cholesterol assessed during the study period.

**Monitoring for signs and symptoms of hyperglycaemia for patients receiving treatment with quetiapine**

None of the neurology practices met the minimum reporting threshold for monitoring for signs and symptoms of hyperglycaemia for at least 50% of their patients. Only 7 (0.1%) patients had their glucose assessed for signs and symptoms of hyperglycaemia during the study period.

**Monitoring for signs and symptoms of hyperglycaemia among patients with diabetes mellitus receiving treatment with quetiapine**

52 patients (1%) across 37 neurology practices (26%) had diabetes and none of them were monitored for signs and symptoms of hyperglycaemia.

**Monitoring for signs and symptoms of hyperglycaemia among those at risk of developing Diabetes**

There were 85 (59%) neurology practices representing 282 (1%) patients identified as being at risk for developing diabetes; one practice monitored at least 50% of its patients for signs and symptoms of hyperglycaemia. Across the 282 at-risk patients, only 2 (0.7%) were monitored for signs and symptoms of hyperglycaemia.

**Monitoring for healthy lifestyle counselling**

Across the 145 neurology practices, there was no evidence of patients being counselled regarding promotion of healthy lifestyle behaviours.

In summary, the performance and/or recording of metabolic monitoring among patients treated with quetiapine in neurology practices in Germany was very low.

## 11.4 Limitations

The LifeLink™ EMR-EU databases such as DA have limitations consistent with other EMR databases:

- Results should be viewed in context with the study period, clinical definitions used, specialities and countries studied, and geographical and physician representation within the database.
- Patients and physicians included in the database are a reflection of the respective populations, but results may not be generalisable to all patients and all practices in each country, as data is collected only from physicians who have agreed to participate in the EMR panel.
- Patients that visit multiple physician practices within a country's DA panel will be assigned different identification numbers (one for each physician practice) and therefore will appear as two distinct patients within DA.
- Patient data for care sought outside the DA practices is not observed. However, this study's primary objective was to evaluate monitoring activity referenced in educational materials distributed to the physician specialities studied. *Shared care* arrangements between primary care physicians and specialists involved with provision of secondary care may be in place within local communities in the two countries evaluated in this study, however the tracking of patients across practice settings for different physician specialities (GP vs psychiatry or neurology) was not possible using the DA database.
- The EMR contains information about prescriptions written and does not confirm if medications were dispensed or consumed.
- Some data about a patient may be under-represented (e.g., counselling) due to recording made in physician notes only, which were not fully accessible in the DA database due to privacy regulations. Depending on each practice's medical record keeping practices, tests or actions may be performed but not necessarily recorded. This includes the recording of notifications or results of services performed outside of the practice. For purposes of this study, only recorded information in the EMR and actions or physicians' plans was considered.
- In the DA, test results would only be captured if they were entered in the appropriate categories and not if these were in the physician notes or any 'free-text' sections.

- The observation windows of the study were limited to seven months and were specific to following the distribution of educational materials. The completeness of the DA database for historical periods beyond those defined was not possible at the time of protocol finalisation and therefore this is recognised as a limitation.
- Country-specific incentives such as the Quality and Outcomes Framework (QOF) in the UK may have impacted a physician's decision to perform monitoring or to record metabolic monitoring of a specific type. The evaluation of the incentives received by practices participating in the DA is not possible and is outside the scope of this evaluation. However it is possible to conjecture about the decision process of the physician although it cannot be definitively assessed in a DA database study.
- Data from retrospective database studies can demonstrate associations between factors and outcome measures (such as the performance of metabolic monitoring) but such findings generally cannot be used to demonstrate a causal link on the basis of a quasi-experimental study design based upon a cross-sectional assessment of period prevalence of metabolic monitoring activity.

## 11.5 Interpretation - General Practitioners (UK)

The study represented a novel attempt to use electronic health data recorded in the IMS Disease Analyzer (DA) database as a means of objectively defining outcome measures for the evaluation of General Practitioner's metabolic monitoring activity over a seven month period. During the study period between 16-67% of General Practitioner practices analyzed performed monitoring activity for ≥50% of their relevant patients. The highest prevalence of monitoring activity (as measured by impact upon patients) involved the evaluation of signs and symptoms of hyperglycemia in patients with diabetes, which was performed for 50.6% of eligible patients. The lowest level of monitoring was for elevated cholesterol through assessment of lipid levels for 27.7% of eligible patients. All other monitoring activities were performed for 31% to 39% of eligible patients.

Results for GPs in the UK showed that the proportion of practices monitoring weight for 50% or more of patients initiated on quetiapine was very low (3%). The following are offered as possible explanations for the low prevalence of monitoring of weight for patients treated with quetiapine:

- Patients included in the DA EMR may have been initiated on treatment by psychiatrists or other speciality physicians and this data was not part of the IMS DA record. In the analysis performed the characterization of patients having been initiated on treatment, included in the EMR, might not reflect the patient's actual course of treatment due to this deficit. In addition, in this study the monitoring of weight at initiation was required to have an entry on the same day as initiation of quetiapine. Results may indicate that in real world practice, the physician applies more discretion to monitoring of weight early in the course of treatment based on the physician-patient relationship and prior interactions. Therefore, the prevalence of monitoring of weight at initiation of quetiapine may have been underestimated.

In addition, GPs may not have considered the need for monitoring of weight when the care of the patient was transferred from a specialist to the GP.

- There was a high prevalence of weight measurement in the 12 months prior to the study period. This may have impacted the prevalence of weight measurement during the study period.
- GPs may not have considered monitoring of weight on the basis of UK QOF guidelines, which recommend monitoring weight every 15 months (NHS, 2013).
- Physicians always have discretion to manage their patients as they deem appropriate. In doing so, they may consider guidelines and product labelling. This may have influenced the measurement of weight during office visits during the study period.

The modelling of factors associated with each monitoring activity performed by GPs in the UK provides additional insight into influences on the GP's decision to perform monitoring. These are worthy of consideration in placing these data into context and attempting to understand enabling factors and barriers to preventative health monitoring in the primary care setting. In addition, these observations should be considered when these findings are compared to the experience of similar health initiatives in other populations. As previously described, there may be other incentives involved in influencing the performance of monitoring by GPs in the UK that cannot be taken into account alongside the clinical factors that were evaluated in this study. The modelling results indicated that the following factors were associated with higher odds of patients being monitored for weight at any time during ongoing treatment with quetiapine: BMI ≥25, history of diabetes, and prior testing of lipids for elevated cholesterol.

Patients aged between 40-49 and 50-64 years had a 3 to 4.5 fold increase in the odds of having their weight monitored than patients in the age range of 18-39 years. Patients aged ≥65 years did not have statistically significant elevated odds for being monitored compared to those aged 18-39 years.

Modelling of factors influencing the monitoring for signs and symptoms of hyperglycaemia results varied according to patient subpopulation. Among all patients, factors indicating higher odds of monitoring for signs and symptoms of hyperglycaemia were obesity, having prior elevated cholesterol, and having prior lipid testing. Among patients with diabetes mellitus, the only factor associated with monitoring was having prior lipid testing performed. Among patients with risk factors for developing diabetes patients, factors indicating higher odds of monitoring were: prior elevated cholesterol and age range of 40-64 years (with reference to patient's age: 18-39 years).

Just over one-quarter of practices recorded counselling ≥50% of their patients on adopting lifestyles. This activity may have been under-reported in the DA EMR as some physicians may consider this as part of a standard plan to promote adoption of a healthy lifestyle among patients and may not document the discussion.

Additionally, with each monitoring outcome, it was observed that patients falling into the lowest quartile of number of visits to the GP (1-8 visits) were monitored less frequently than

patients in the three other categories referencing a higher number of visits to GPs during the study period. Potential explanations for higher monitoring rates among patients with more frequent visits to their GP includes: increased number of visits provided a greater opportunity for being monitored, the increase may be a reflection of the severity of the patients' underlying illness, or may represent patients having a greater risk for development of conditions that the metabolic monitoring activities were intended to uncover.

It is worth noting that higher levels of monitoring were found for each monitoring activity in the 12 months prior to the study period and the levels of monitoring were found to have been performed for 45% to 81% of eligible patients. This finding suggests that awareness on the part of General Practitioners in the UK can be considered to equate to a process indicator if one considers physician awareness as an important component of risk minimisation activity.

## 11.6 Interpretation - Psychiatrists and Neurologists (Germany)

Monitoring outcomes were low amongst both psychiatry and neurology practices in Germany. Metabolic monitoring including monitoring of weight, performance of lipid testing for elevated cholesterol, and monitoring of plasma glucose were not documented among specialist physicians. German guidelines suggest that these metabolic parameters be measured at the initiation of an antipsychotic medication. In Germany, specialist physicians are not likely to perform holistic physical health assessment of patients. The guidelines for metabolic monitoring in Germany relate a schedule of assessment that is not documented in the IMS EMR data describing evaluation and measurement performed on patients. Factors drawn from healthcare delivery and the scope of specialty practice influencing the performance of monitoring were unable to be evaluated.

We expected higher levels of monitoring activity from specialist physicians to be documented in their Electronic Health Records in the DA database. This could be postulated on the presumption that specialists are most frequently the initiators of antipsychotic treatments, have greater familiarity with treatment using quetiapine and other atypical antipsychotics, have greater awareness of guidelines in these disorders, have unique access to medical speciality journals and access medical information in a distinct manner independent of the educational materials distributed by AstraZeneca. As a result this would be expected to foster a greater awareness of the recommendations regarding metabolic monitoring by specialists and a lower awareness of monitoring by general practice physicians unless received in communications from a specialist physician. Following the initiation of treatment with quetiapine by a specialist, the need for continuing treatment and monitoring, is transferred to the GP. The expectation regarding the performance, recording and sharing of metabolic monitoring results between physicians and recorded by specialist physicians in the electronic health records may not be accessible through the DA EMR (for example -extracted from correspondence and entered into the DA EMR data record). Data entered into text fields was not available due to restrictions imposed by privacy regulations, and EMR are not generally shared across sites, so that the specialist physician would not be entering data into the same record as the primary care physician.

Beyond DA's limitations around assessing patients under *shared care* arrangements, the study objectives were to assess metabolic monitoring rates among German neurologists and psychiatrists. (*Shared care* arrangements comprise a team approach to care, with both primary and secondary care practitioners contributing to elements of a patient's overall care package, communicating effectively and working together to make the patient's care as seamless as possible.)

The finding that only 1.5% of study patients experienced at least one of the monitoring activities during the study period suggests that these German specialists do not monitor or at least do not document such activity. It may very well be that although psychiatrists and neurologists prescribe quetiapine, they are not involved with management of certain aspects of patients' physical health involving metabolic monitoring.

## 11.7 Generalisability

The goal of this study was to objectively assess the activities of physicians and the impact upon patients with respect to the recommendations for metabolic monitoring presented in labelling of Seroquel® and Seroquel® XL/XR. The study included patients treated with quetiapine for approved indications. The database, as described previously, is representative of the physician specialities analysed within their respective countries, but all results may not be generalisable to all patients diagnosed with schizophrenia, bipolar disorder, or MDD that are treated with quetiapine or to all GPs in the UK or neurologists or psychiatrists within Germany treating such patients. Additionally, these results do not reflect the behaviour of physician specialists with patients of a similar composition to those reported in this study.

Physician practices self-select into the DA EMR panels. However, to arrive at a sample that is representative of the country's physicians, IMS follows a sampling frame that extends invitations to physician practices to join the panel based on their profile. Invitations are extended in a manner to be consistent with data based on available information from country specific medical associations [Becher et al 2009]. The recruitment is limited to practices using EMR software platforms with which IMS has partnerships.

The validity of the database is supported by external peer-reviewed publications that assessed the validity and generalisability of the DA database [Statistical Computing 2013]. Note that the analyses in this latter referenced work did not specifically focus on this particular population, but provided an assessment of healthcare benchmarks against other available data sources.

# 12. OTHER INFORMATION (NOT APPLICABLE)

# 13. CONCLUSION

This study represented a novel attempt to utilise electronic health data recorded in the IMS Disease Analyzer (DA) database as objective outcome measures for the evaluation of physician metabolic monitoring activity over a seven month period, which followed the distribution of metabolic educational materials that targeted general practitioners and speciality physicians in the EU. During this study period between 16-67% of General Practitioner practices in the UK and $\leq$ 2% of psychiatry or neurology practices in Germany monitored ≥50% of their relevant patients. ).

The observation that monitoring or at least recording of such is rarely documented in the DA Electronic Medical Record database by German neurologists and psychiatrists runs counter to the expectation that specialist physicians should be more likely than general practitioners/primary care physicians to be aware of the recommendations for monitoring of these patients. This could be postulated on the presumption that specialists are most frequently the initiators of antipsychotic treatments, have greater familiarity with treatment using quetiapine and other atypical antipsychotics, have greater awareness of guidelines, have unique access to medical speciality journals and access medical information in a distinct manner independent of the educational materials distributed by AstraZeneca. This expected greater awareness of the recommendations regarding metabolic monitoring is not reflected through analysis of their activities in the DA Electronic Medical Record.

The outcomes for GPs in the UK found that the highest prevalence of monitoring activity (as measured by impact upon patients) involved the evaluation of signs and symptoms of hyperglycaemia in patients with diabetes, which was performed for 50.6% of eligible patients. The lowest level of monitoring by GPs in the UK was the assessment of lipid levels for 27.7% of eligible patients. The performance of all other monitoring activities by GPs in the UK was performed for 31% to 39% of eligible patients.

The completeness of updates to the IMS DA database prevented data collection over a longer time interval. This limitation may have had a more significant impact on the prevalence estimates of monitoring performed by GPs in the UK.

It is worth noting that higher levels of monitoring by GPs were found for each monitoring activity in the 12 months prior to the study period. During this period monitoring was performed for between 45% to 81% of eligible patients. This finding suggests awareness of recommendations for monitoring by a significant proportion of General Practitioners in the UK. This can be considered to equate to a process indicator if one considers that such physician awareness requires a prerequisite knowledge to influence behaviour and therefore can be considered important contributing factors in defining process measures for risk minimisation.

The results from this analysis are not able to be merged with data on whether these specific practices or the physicians completing the EMRs actually received the educational materials distributed by AstraZeneca, whether the materials were read, or whether other interventions or guidelines were influential in the physician's actions upon receiving the educational materials.

One of the lessons learned from this study includes the recognition that in a database analysis, physician judgements and rationale for metabolic monitoring action or inaction are difficult to quantify; they can only be discerned from prevalent evaluation and measurement activities that relate to coded procedures, laboratory tests, and diagnostic information that is captured. It is very likely that the recording of a patient's signs and symptoms as part of subjective and objective assessments performed by physicians may not be recorded completely in defined fields in an Electronic Medical Record such as DA. In addition, correspondence between specialist and generalist regarding metabolic monitoring were not available for evaluation in this study. The ability to define the presence of such information via text mining was not within the scope of this evaluation.

On the basis of data available in the IMS DA Electronic Medical Record database, this study provides a limited objective assessment of physician activity and the impact upon patients regarding the performance of metabolic monitoring during a 7-month window following the distribution of metabolic educational materials.

This study identified limits to the use of electronic health records for assessing metabolic monitoring. Despite these limitations, the study did demonstrate associations between the presence of recorded risk factors and the performance of metabolic monitoring for GPs in the UK. In order to more fully appreciate the effectiveness of risk minimisation activities associated with the distribution of educational materials to physicians, it is important to consider the results of this study with the physician survey (Assessment of physician behaviour regarding metabolic monitoring of patients treated with SEROQUEL® (quetiapine fumarate) Tablets and SEROQUEL® (quetiapine fumarate) Extended Release Tablets in selected countries in the European Union (EU) (Study D1443C00127)) which will further inform on these topics.

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