



Towards a comprehensive routine outcome monitoring program for people with psychotic disorders: The Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS)

Agna A. Bartels-Velthuis^{a,b,1}, Ellen Visser^{a,1}, Johan Arends^c, Gerdina H.M. Pijnenborg^{c,d}, Lex Wunderink^e, Frederike Jörg^{a,e}, Wim Veling^f, Edith J. Liemburg^a, Stynke Castelein^b, Henderikus Knegtering^{a,b}, Richard Bruggeman^{a,g,*}

^a University of Groningen, University Medical Center Groningen, University Center for Psychiatry, Rob Giel Research Center, Hanzeplein 1 (CC72), 9713 GZ Groningen, The Netherlands

^b Lentis Mental Health Institution, Hereweg 80, 9725 AG Groningen, The Netherlands

^c GGZ Drenthe, Mental Health Institution, Dennenweg 9, 9404 LA Assen, The Netherlands

^d University of Groningen, Faculty of Behavioural and Social Sciences, Department of Clinical Psychology & Experimental Psychopathology, Grote Kruisstraat 2/1, 9712 TS Groningen, The Netherlands

^e GGZ Friesland Mental Health Institution, Sixmastraat 2, 8932 PA Leeuwarden, The Netherlands

^f University of Groningen, University Medical Center Groningen, University Center for Psychiatry, Psychosis Department, Hanzeplein 1 (CC60), 9713 GZ Groningen, The Netherlands

^g University of Groningen, University Medical Center Groningen, Department of Pharmacy, Division of Pharmacotherapy and Pharmaceutical Care, A. Deusinglaan 1, 9713 AV Groningen, The Netherlands

ARTICLE INFO

Article history:

Received 10 May 2017

Received in revised form 2 October 2017

Accepted 17 January 2018

Available online 1 February 2018

Keywords:

Severe mental illness

Routine outcome monitoring

Cardiovascular diseases

Metabolic syndrome

Quality of life

ABSTRACT

Background: Patients with psychotic disorders are at risk of developing mental health and social problems, and physical disorders. To monitor and treat these problems when indicated, an annual routine outcome monitoring program, Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS), was developed. This paper presents the background and content of PHAMOUS, implementation of PHAMOUS, characteristics of the patients screened in 2015, and the outcome of patients with three annual screenings between 2011 and 2015.

Methods: PHAMOUS was implemented in four mental health institutions in the Northern Netherlands in 2006. During the PHAMOUS screening, patients are assessed on socio-demographics, psychiatric symptoms, medication, physical parameters, lifestyle, (psycho)social functioning and quality of life, using internationally validated instruments.

Results: In 2015, 1955 patients with psychotic disorders were enrolled in the PHAMOUS screening. The majority (72%) was receiving mental healthcare for ten years or longer. A small group was hospitalized (10%) in the past year. Half of the patients were in symptomatic remission. Less than 10% had a paid job. More than half of the patients fulfilled the criteria for metabolic syndrome (54%). The subsample with three annual screenings from 2011 to 2015 ($N = 1230$) was stable, except the increasing prevalence of high glucose levels and satisfaction with social relationships (Cochran's $Q = 16.33$, $p = .001$ resp. $Q = 14.79$, $p = .001$).

Conclusion: The annual PHAMOUS screening enables to follow the mental, physical and social health problems of patients, which offers a good basis for shared-decision making with regard to updating the annual treatment plan, next to a wealth of data for scientific research.

© 2018 Elsevier B.V. All rights reserved.

1. Introduction

People suffering from severe mental illnesses (SMI) may profit much from a systematic, regular evaluation of their health, as these patients often fail to adequately present their problems, leading to high numbers of unmet needs in mental, physical and psychosocial care (Bellack, 2004; Drake et al., 2000; Patterson and Leeuwenkamp, 2008; Kern et al., 2009). Furthermore, in this population, unhealthy lifestyle factors, such as poor dietary habits, sedentary lifestyle and smoking (de Leon and Diaz, 2005; Vancampfort et al., 2010; De Hert et al., 2009; De Hert

* Corresponding author.

E-mail addresses: a.a.bartels@umcg.nl (A.A. Bartels-Velthuis), e.visser03@umcg.nl (E. Visser), johan.arends@ggzdrenthe.nl (J. Arends), g.h.m.pijnenborg@rug.nl (G.H.M. Pijnenborg), lex.wunderink@ggzfriesland.nl (L. Wunderink), fjorg@umcg.nl (F. Jörg), w.veling@umcg.nl (W. Veling), e.j.liemburg@umcg.nl (E.J. Liemburg), s.castelein@lentis.nl (S. Castelein), h.knegtering@lentis.nl (H. Knegtering), r.bruggeman@umcg.nl (R. Bruggeman).

¹ These authors have made equally significant contributions.

et al., 2011) considerably increase the cardiovascular risk-factors, such as overweight, diabetes, higher cholesterol levels and hypertension (McEvoy et al., 2005; Hasnain et al., 2010; Mitchell et al., 2013), with subsequent cardiovascular problems and high mortality rates (De Hert et al., 2009; De Hert et al., 2011; Vancampfort et al., 2010; Galletly et al., 2012). Also, the frequently reported cannabis use (Peralta and Cuesta, 1992; Hall and Degenhardt, 2000; Richardson, 2010) contributes to the psychotic symptoms (van Os et al., 2009). In addition, people with psychotic disorders, have an increased risk of comorbid mental disorders (e.g. depressive symptoms (Lako et al., 2012a)) and, equally important, the majority of this population has large psychosocial problems.

In the Northern Netherlands, in the early 2000s several pilot studies were conducted on monitoring the physical health of people using anti-psychotics, urged by the emergence of metabolic disturbances due to second generation antipsychotics. For the detection of diabetes, hypertension and metabolic syndrome, regular (at least once a year) measurements of Hb1Ac, blood pressure and waist circumference were introduced.

In order to improve the quality of care for patients with psychotic disorders and other SMI, in 2006, the Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS) was started, implementing a comprehensive ROM-program in four large mental healthcare organizations in the Northern Netherlands. PHAMOUS serves to map the physical, mental and social conditions of these patients, next to the effects of sustained medication intake.

A comprehensive ROM-assessment can be successful in the following domains (Delespaul, 2015): (i) clinical process: continually optimize treatment decisions using repeated assessments; (ii) managerial: to generate management information to optimize strategic choices for the care systems; (iii) accountability: to improve transparency and generate information for external accountability; (iv) science: to provide data to study (course of) mental illness, symptom severity and care needs, and to assess the outcome of real-life implementation of (evidence-based) treatment protocols.

In this paper, we will describe the design (protocol and instruments) and implementation of the actual PHAMOUS screening. Also, the demographic, physical and mental health characteristics of the cohort (2015) will be presented, as well as a three year follow-up of patients with screenings between 2011 and 2015. Next, we will evaluate PHAMOUS in its present form. Finally, future directions, possibilities and challenges will be addressed.

2. Methods

2.1. Implementation of the PHAMOUS screening

All participating organizations in PHAMOUS (Lentis Mental Health Institution, GGZ Friesland Mental Health Institution, GGZ Drenthe Mental Health Institution, and the University Center for Psychiatry of the University Medical Center Groningen) are collaborating in the Rob Giel Research center (RGOc). Since 2010, the RGOc facilitates RoQua (Routine Outcome & Quality Assessment), a safe and reliable software application that can be integrated in electronic patient file systems, allowing to systematically collect clinical data in combination with 'routine outcome' data (for details see van der Krieke et al., 2013).

The aforementioned institutions deliver a broad spectrum of specialized mental healthcare, serving a catchment area of 1.7 million inhabitants in 2015 (Statistics Netherlands). PHAMOUS includes specific questionnaires, interviews, laboratory testing and physical evaluations to assess psychiatric symptomatology, physical and social problems, and quality of life of patients with psychotic disorders. Once a year, the contents of the protocol are updated by a board, consisting of members of all institutions participating in PHAMOUS. A report, composed in RoQua, summarizes the screening results and is, in line with the shared decision making model, discussed with the patient. Subsequently,

patient and clinician formulate a treatment plan for the forthcoming year (see also van der Krieke et al., 2013). The report of the relevant outcomes is sent to the general practitioner (GP), highlighting specific problems and needs (e.g. anomalous outcome on laboratory tests, interviews and questionnaires) and proposing changes in the treatment plan to be performed either by the mental health professionals or the GP. In accordance with the declaration of Helsinki, patients are informed that aggregated and anonymized data may be used for healthcare optimization and scientific research to improve treatment and guidance.

2.2. Study population

All patients fulfilling the DSM-IV criteria for schizophrenia, schizoaffective disorder or other psychotic disorders, aged 18 years and older, are intended to be included in PHAMOUS. No exclusion criteria are used for the PHAMOUS screening.

2.3. Screening and training procedure

Trained research nurses carry out the PHAMOUS screening. Booster sessions are organized regularly to optimize consensus and discuss any problems. In view of turnover of staff and to improve reliability of the measurements, all above-mentioned training procedures are continually, at least yearly, repeated. In each center, a research coordinator is appointed as a contact person assuring the quality, troubleshooting and implementation of PHAMOUS. Duration of the screening per patient, including preparation and administration by the research nurse, is between three and four hours, depending on the condition of the patient.

2.4. Measurements

The yearly PHAMOUS screening consists of measures in the following domains.

Sociodemographic characteristics. Age, gender, living situation, education and daily activities are assessed during the interview with the research nurse.

Psychiatric characteristics. Main diagnosis and comorbidity according to DSM-IV (American Psychiatric Association, 2000), age at onset of first psychotic episode and age at first mental healthcare contact are assessed during the interview. Also, the severity of psychotic symptoms during the past week is assessed with the consensus remission items (Andreasen et al., 2005) of the Positive and Negative Syndrome Scale for Schizophrenia (PANSS; Kay et al., 1987) The mean score of eight items (delusions, conceptual disorganization and hallucinations, blunted affect, social withdrawal and lack of spontaneity, unusual thought content and mannerisms and posturing) was calculated. Symptomatic remission was determined, based on whether patients had a score of three or lower on all eight remission items.

Antipsychotic medication and side effects. The patient brings medication prescriptions at the interview. Types of (antipsychotic) medication (ATC code; Anatomical Therapeutic Chemical classification system, oral or depot, dose, date of starting/stopping) are registered. Haloperidol equivalents of antipsychotic medication were calculated based on the recommendations of Gardner et al. (2010). Present extrapyramidal side effects are assessed by the research nurse by rating presence of akathisia, acute dystonia, tardive dyskinesia, and parkinsonism (scoring options: absent, minor, moderate, severe).

Desired and undesired treatment effects of antipsychotics are evaluated with the brief self-report version of the Subjects' Response to Antipsychotics questionnaire, the SRA-34 (Lako et al., 2013). Mean sum scores of desired effects and of undesired effects were calculated.

Physical characteristics. The following parameters are assessed: the research nurse asks for present somatic diseases (diabetes, cardiovascular diseases, osteoporosis, thyroid abnormalities, hypercholesterolemia and epilepsy); weight and height are measured (to calculate the Body

Mass Index; kg/m²); waist circumference (cm); blood pressure (systolic and diastolic; mm Hg); triglyceride level (mmol/L); glucose level (mmol/L); cholesterol levels (HDL, LDL and total, mmol/L; total cholesterol/HDL ratio). The presence of the metabolic syndrome was determined using the definition of the Adult Treatment Panel III (ATP-III) of the National Cholesterol Education Program (NCEP; Grundy et al., 2005) i.e. three or more of the following criteria: 1) waist circumference ≥88/102 cm (female/male); 2) systolic blood pressure ≥130 or diastolic blood pressure ≥85 mm Hg or receiving antihypertensive drug treatment; 3) HDL-cholesterol <1.30/1.03 mmol (female/male) or receiving lipid-lowering drugs; 4) triglycerides ≥1.7 mmol/L or receiving lipid-lowering drugs; and 5) fasting glucose ≥6.1 mmol/L or receiving anti-diabetic medication(s).

During the interview, eating habits, i.e. number of meals, fruit and vegetables consumption per day/week, and present use of alcohol, nicotine and cannabis are assessed.

(Psycho)social functioning. Inpatient/outpatient status and events in the past year, such as relapse, hospital admissions, suicide attempts or judicial measures, as reported by the patient, are recorded. The patient's case manager completes the Health of the Nation Outcome Scales (HoNOS; Wing et al., 1998), a 12-item questionnaire about problematic behavior and symptoms (scores 0 (no problems)–4 (very severe problems)), covering the past two weeks. Percentage of patients with HoNOS-scores of 3 (moderately severe) and 4 (very severe) were calculated. Four patient groups were distinguished: 1) very severe, ≥2 items with score 3 or 4; 2) moderately severe, one item with score 3 or 4; 3) mild, ≥1 item with score 2; 4) subclinical, each item <2 (Parabiaghi et al., 2005).

The research nurse scores the Global Assessment of Functioning scale (GAF; American Psychiatric Association, 2000) over the past month, in two dimensions (symptom and disability, scores 1–100).

Functional remission over the past six months is assessed on three areas of functioning: daily living and self-care; work, study and house-keeping; and social contacts. These areas are rated by the research nurse on a three-point scale: independent (0), partially independent (1) and dependent (2) functioning (Wiersma et al., 2015).

Quality of life is assessed using the Manchester Short Assessment of Quality of Life (ManSA; Priebe et al., 1999), a 16-item self-report questionnaire, covering several domains of psychosocial functioning in the past week (score 1–7) which is filled in by the patient. Scores 1 and 2, denoting that patients are not satisfied, and scores 6 and 7, denoting that patients are highly satisfied, were counted.

2.5. Statistical analyses

Summary scores of demographic, physical and mental health characteristics of the patients were calculated, using SPSS version 23. Patients with three annual screenings were compared with those who had not using chi-square tests for categorical and t-tests for continuous variables. To test whether distributions differ between the three measurements, non-parametric Cochran's Q tests (for related samples) were performed for dichotomous variables and Friedman tests for continuous variables. p-Values below .01 indicated that results were statistically significant. For statistically significant different distributions post hoc analyses were performed using Wilcoxon signed ranks tests to determine which pairs were different.

3. Results

In 2015, 1955 patients with a psychotic disorder participated. This is 44% of all patients with schizophrenia or another psychotic disorder in the participating institutions. Their sociodemographic and psychiatric characteristics are presented in Table 1 and Table 2 respectively. Anti-psychotic medication and side effects are given in Table 3. Table 4 shows physical and lifestyle characteristics. (Psycho)social functioning is presented in Table 5.

Table 1 Sociodemographic characteristics of patients in PHAMOUS.

| | Total N | Mean/% | SD/N |
|---|---------|--------|------|
| Age, mean (SD) | 1955 | 45.1 | 12.0 |
| Male, % (N) | 1955 | 65.8 | 1286 |
| Living situation | | | |
| Alone | 1900 | 47.8 | 909 |
| With partner/children | | 12.6 | 239 |
| With family/others | | 7.2 | 136 |
| Supported housing | | 15.8 | 300 |
| Long-stay (clinical) | | 12.4 | 235 |
| Other | | 4.3 | 81 |
| Education | | | |
| Lower | 1762 | 24.0 | 422 |
| Middle | | 52.4 | 924 |
| High | | 23.6 | 416 |
| Daily activities: | | | |
| Paid job | 1915 | 9.3 | 179 |
| Supported employment, voluntary work, education | | 36.1 | 691 |
| Household or other | | 54.6 | 1045 |

Table 6 presents the outcome of patients with three annual screenings between 2011 and 2015 (N = 1230). These patients were compared with the other patients of the 2015 cohort (N = 725). The former were older (46 vs 43 years, t(1953) = -6.20, p < .01), had a similar educational level (lower: 23% vs 25%; middle: 53% vs 52%; high: 24% vs 23%, chi-square = 1.13, p = .568) and percentage of males (65% vs 67%, chi-square = 0.49, p = .484). They had a lower age at onset (26 vs 29 years, t(977) = 5.18, p < .001) and a longer illness duration (20 vs 13 years, t(1633) = -12.33, p < .001). Also, more patients lived in supported housing (31% vs 23%, chi-square = 29.50, p < .001) and a higher percentage of patients had schizophrenia (71% vs 46%, chi-square = 191.76, p < .001).

Between 2011 and 2015, the 2015 cohort appeared to improve on psychotic symptoms and quality of life, but the percentage of patients with a metabolic syndrome increased. Except for high glucose level (Cochran's Q = 16.33, p = .001) and high satisfaction with social relationships (Cochran's Q = 14.79, p = .001), these differences were statistically not significant. Post hoc analyses revealed that the percentage of patients with high glucose levels only differed

Table 2 Psychiatric characteristics of patients in PHAMOUS.

| | Total N | Mean/% | SD/N |
|--|---------|--------|------|
| Diagnosis: | | | |
| Schizophrenia, w/wo other disorders | 1955 | 61.8 | 1209 |
| Schizoaffective disorder, w/wo other disorders | | 15.2 | 297 |
| Psychotic disorder, w/wo other disorders | | 23.0 | 449 |
| Axis 1 disorder with personality disorder | | 14.1 | 276 |
| Age at onset first psychotic episode, mean (SD) | 1635 | 26.9 | 9.8 |
| Duration of psychotic symptoms, mean (SD) | | 17.6 | 11.7 |
| <5 years | | 14.4 | 236 |
| 5–10 years | | 14.4 | 236 |
| 10–20 years | | 30.3 | 495 |
| >20 years | | 40.9 | 668 |
| Age at onset first mental health care contact, mean (SD) | 1769 | 27.1 | 10.3 |
| Duration of health care consumption, mean (SD) | | 17.9 | 11.5 |
| <5 years | | 13.4 | 237 |
| 5–10 years | | 14.2 | 251 |
| 10–20 years | | 30.4 | 538 |
| ≥20 years | | 42.0 | 743 |
| Events in the past year, % (N) | | | |
| Relapse psychosis | 1955 | 28.5 | 557 |
| (re)Hospitalized | | 9.9 | 193 |
| Suicide attempt | | 0.9 | 17 |
| Judicial measure (e.g. in custody, compulsory treatment) | 1705 | 12.8 | 219 |
| PANSS (eight remission items) | 1462 | | |
| In remission (<4 on all items), % (N) | | 50.4 | 737 |
| Mean score, mean (SD) | | 1.9 | 0.7 |

Table 3
Antipsychotic medication and side effects of patients in PHAMOUS.

| | Total N | Mean/% | SD/N |
|---|------------|--------|------|
| Antipsychotic medication, % (N) users | 1909 | 94.4 | 1803 |
| Clozapine | 1803 | 34.6 | 624 |
| Olanzapine | | 29.8 | 537 |
| Aripiprazole | | 21.9 | 395 |
| Risperidone | | 19.0 | 342 |
| Quetiapine | | 19.1 | 344 |
| Other | | 25.6 | 462 |
| Haloperidol equivalents, mean (SD) | 1633 | 6.98 | 5 |
| Medication side effects (from minor to severe): | | | |
| Akathisia | 1108 | 13.4 | 148 |
| Acute dystonia | 1100 | 1.7 | 19 |
| Tardive dyskinesia | 1110 | 10.9 | 121 |
| Parkinsonism | 1115 | 18.7 | 209 |
| SRA-34 ^a medication effects | | | |
| Desired effects (mean total out of 10) | 964 | 4.8 | 3.0 |
| Undesired effects (mean total out of 23) | | 8.4 | 5.3 |

^a SRA-34: Subjects' Response to Antipsychotics questionnaire.

significantly between T1 and T2 (Wilcoxon $Z = 2.65$, $p = .008$). Concerning the percentage of patients who were highly satisfied with social relationships, statistically significant differences were found between T1 and T2 (Wilcoxon $Z = 3.86$, $p < .001$), and between T1 and T3 (Wilcoxon $Z = 2.66$, $p = .008$).

4. Discussion

In 2006, the PHAMOUS screening was the first to combine an extensive battery of mental, physical and social parameters into a standard

Table 4
Physical characteristics of patients in PHAMOUS.

| | Total N | Mean/% | SD/N |
|--|------------|--------|------|
| Present somatic diseases, % (N) | | | |
| Diabetes | 1857 | 13.8 | 256 |
| Cardiovascular diseases | 1798 | 12.7 | 228 |
| Osteoporosis | 1763 | 2.0 | 35 |
| Thyroid abnormalities | 1783 | 6.3 | 113 |
| Hypercholesterolemia | 1718 | 22.2 | 382 |
| Epilepsy | 1820 | 3.9 | 71 |
| Metabolic parameters, % (N) | | | |
| BMI ^a (kg/m ²) | | | |
| <18.5 | 1902 | 1.8 | 34 |
| 18.5–25 | | 29.7 | 564 |
| 25–30 | | 35.4 | 674 |
| 30–35 | | 20.7 | 393 |
| >35 | | 12.5 | 237 |
| Waist circumference (women ≥ 88 ; men ≥ 102 cm) | 1842 | 61.2 | 1128 |
| Blood pressure (systolic ≥ 130 or diastolic ≥ 85 mm Hg) or medicated | 1899 | 61.7 | 1171 |
| Triglycerides (≥ 1.7 mmol/L) or medicated | 1389 | 53.6 | 744 |
| HDL-cholesterol (women < 1.3 ; men < 1.03 mmol/L) or medicated | 1387 | 52.9 | 734 |
| Glucose (≥ 6.1 mmol/L) or medicated | 1355 | 37.9 | 514 |
| Metabolic syndrome, % (N) (= at least three of the above) | 1223 | 53.9 | 659 |
| Other blood cholesterol levels, % (N) | | | |
| Total cholesterol ≥ 5 mmol/L | 1314 | 50.8 | 668 |
| LDL-Cholesterol ≥ 3 mmol/L | 1270 | 56.5 | 718 |
| Cholesterol ratio (≥ 5 ; total chol/hdl chol) | 1306 | 31.5 | 411 |
| Lifestyle, % (N) | | | |
| Meals, <3 per day for 4 or more days a week | 1917 | 70.1 | 1344 |
| Fruit, <2 per day | 1637 | 67.9 | 1111 |
| Vegetables, <5 times per week | 1927 | 27.9 | 537 |
| Alcohol user | 1936 | 38.6 | 747 |
| Nicotine user | 1941 | 62.5 | 1214 |
| Cannabis user | 1925 | 13.7 | 264 |

^a Body Mass Index.

Table 5
(Psycho)social functioning of patients in PHAMOUS.

| | Total N | Mean/% | SD/N |
|---|------------|--------|------|
| HoNOS ^a , % (N) (scores from moderately severe to very severe) | | | |
| Overactive, aggressive, disruptive or agitated behaviour | 1609 | 1.9 | 31 |
| Non-accidental self-injury | 1608 | 0.7 | 11 |
| Problem drinking or drug-taking | 1601 | 7.6 | 121 |
| Cognitive problems | 1601 | 6.6 | 105 |
| Physical illness or disability problems | 1606 | 11.8 | 189 |
| Problems associated with hallucinations and delusions | 1602 | 14.1 | 226 |
| Problems with depressed mood | 1598 | 2.6 | 42 |
| Other mental and behavioural problems | 1588 | 18.3 | 290 |
| Problems with relationships | 1603 | 16.1 | 258 |
| Problems with activities of daily living | 1603 | 10.7 | 171 |
| Problems with living conditions | 1598 | 2.0 | 32 |
| Problems with occupation and activities | 1600 | 3.9 | 62 |
| HoNOS, % (N) | | | |
| Subclinical (all scales smaller than score 2) | 1603 | 14.7 | 235 |
| Mild (min of 1 scale with score 2) | | 39.6 | 635 |
| Moderate severe (1 scale with score 3 or 4) | | 21.6 | 347 |
| Very severe (min of 2 scales with score 3 or 4) | | 24.1 | 386 |
| GAF ^b (% (N) with score < 60) | | | |
| Symptoms | 832 | 70.3 | 585 |
| Disabilities | 693 | 68.0 | 471 |
| Functional remission (% (N) independently functioning) | | | |
| Daily living and self-care | 1002 | 37.8 | 379 |
| Work, study and housekeeping | 1005 | 16.5 | 166 |
| Social contacts | 1005 | 47.5 | 477 |
| ManSA ^c - Quality of life, % (N) | | | |
| Very dissatisfied: score 1–2 | | | |
| Life as a whole | 1541 | 7.9 | 121 |
| Living environment | 1543 | 5.5 | 85 |
| Living situation (alone or with others) | 1542 | 6.7 | 103 |
| Daily activities | 1543 | 7.7 | 119 |
| Physical health | 1544 | 11.5 | 177 |
| Psychological health | 1544 | 11.8 | 182 |
| Personal safety | 1536 | 4.8 | 73 |
| Social relationships | 1535 | 9.1 | 139 |
| Family relationships | 1534 | 8.9 | 136 |
| Intimate relationships | 1533 | 11.4 | 175 |
| Sexual life | 1494 | 18.9 | 282 |
| Financial situation | 1538 | 14.6 | 224 |
| Highly satisfied: score 6–7 | | | |
| Life as a whole | 1541 | 38.9 | 599 |
| Living environment | 1543 | 62.6 | 966 |
| Living situation (alone or with others) | 1542 | 52.8 | 814 |
| Daily activities | 1543 | 49.8 | 769 |
| Physical health | 1544 | 37.4 | 577 |
| Psychological health | 1544 | 37.0 | 572 |
| Personal safety | 1536 | 59.5 | 914 |
| Social relationships | 1535 | 38.7 | 594 |
| Family relationships | 1534 | 56.3 | 864 |
| Intimate relationships | 1533 | 42.5 | 651 |
| Sexual life | 1494 | 28.2 | 421 |
| Financial situation | 1538 | 38.8 | 597 |
| ManSA - Quality of life, % (N) | | | |
| Victim of violence | 1540 | 6.0 | 92 |
| Accused of a crime | 1540 | 4.2 | 65 |
| Having a good friend | 1535 | 75.8 | 1164 |
| Spoken with a friend past week | 1534 | 69.5 | 1066 |

^a HoNOS: Health of the Nation Outcome Scales.

^b GAF: Global Assessment of Functioning scale.

^c ManSA: Manchester Short Assessment of Quality of Life.

ROM procedure in the Northern Netherlands. At that time, this procedure could be considered as pioneering work. PHAMOUS is nowadays still focusing on disease management with the aim of optimizing care for a vulnerable patient group and it has a secured ROM position in clinical practice ever since. Implementation was facilitated and supported from start-on by the boards of the participating mental healthcare institutions. The Rob Giel Research center and the RoQua application were pivotal in providing a robust infrastructure, training facilities and a productive research environment. In the most recent year of the study, two thirds of the patients (mean age 45 years) were male, two thirds were

Table 6
Three annual screenings of the 2015-cohort, between 2011 and 2015 (N = 1230, 63% of 1955).

| | T1 ^a | T2 ^b | T3 ^c |
|--|-----------------|-----------------|-----------------|
| Psychotic symptoms | | | |
| PANSS (eight remission items) | | | |
| In remission (<4 on all items), % (N) | 45.8 (445) | 47.3 (469) | 48.0 (454) |
| Mean score, mean (SD) | 2.01 (0.8) | 1.96 (0.7) | 1.96 (0.7) |
| Metabolic syndrome, % (N) (= at least three of the below) | 52.1 (452) | 56.3 (480) | 56.3 (472) |
| Waist circumference (women ≥ 88; men ≥ 102 cm) | 62.8 (728) | 64.1 (750) | 64.4 (752) |
| Blood pressure (systolic ≥ 130 or diastolic ≥ 85 mm Hg) or medicated | 63.6 (762) | 62.8 (756) | 61.7 (742) |
| Triglycerides (≥ 1.7 mmol/L) or medicated | 50.9 (486) | 54.2 (514) | 55.4 (525) |
| HDL-cholesterol (women < 1.3; men < 1.03 mmol/L) or medicated | 49.5 (472) | 53.5 (505) | 54.6 (515) |
| Glucose (≥ 6.1 mmol/L) or medicated [^] | 34.2 (322) | 38.8 (357) | 40.4 (371) |
| Quality of life, ManSA, % (N) | | | |
| Very dissatisfied (score 1–2) | | | |
| Life as a whole | 6.6 (65) | 6.4 (65) | 6.4 (64) |
| Living environment | 5.5 (54) | 3.7 (38) | 4.0 (40) |
| Living situation (alone or with others) | 5.5 (54) | 4.3 (44) | 5.2 (52) |
| Daily activities | 6.5 (64) | 4.2 (43) | 5.9 (59) |
| Physical health | 10.3 (102) | 10.5 (106) | 11.1 (111) |
| Psychological health | 11.5 (114) | 11.5 (116) | 10.6 (106) |
| Personal safety | 3.7 (37) | 4.3 (44) | 4.3 (44) |
| Social relationships | 8.3 (82) | 7.1 (72) | 8.1 (81) |
| Family relationships | 7.0 (69) | 7.0 (69) | 7.2 (71) |
| Intimate relationships | 11.5 (111) | 13.1 (132) | 10.1 (100) |
| Sexual life | 20.0 (189) | 18.9 (184) | 18.0 (174) |
| Financial situation | 13.2 (131) | 13.8 (140) | 12.2 (122) |
| Highly satisfied (score 6–7) | | | |
| Life as a whole | 37.5 (372) | 37.9 (384) | 40.2 (401) |
| Living environment | 59.5 (589) | 60.4 (614) | 65.2 (652) |
| Living situation (alone or with others) | 51.5 (505) | 51.3 (520) | 53.3 (532) |
| Daily activities | 48.4 (480) | 48.9 (497) | 52.3 (522) |
| Physical health | 36.1 (358) | 36.0 (365) | 37.0 (370) |
| Psychological health | 36.1 (358) | 34.8 (353) | 36.2 (362) |
| Personal safety | 56.5 (559) | 56.3 (570) | 59.0 (588) |
| Social relationships | 35.7 (352) | 40.9 (414) | 41.0 (408) |
| Family relationships | 53.6 (529) | 56.7 (574) | 57.0 (565) |
| Intimate relationships | 39.5 (382) | 39.5 (399) | 41.8 (415) |
| Sexual life | 27.1 (256) | 27.1 (264) | 27.9 (270) |
| Financial situation | 38.2 (378) | 38.8 (393) | 40.3 (401) |
| Victim of violence | 4.4 (43) | 5.0 (51) | 4.2 (42) |
| Accused of a crime | 3.1 (31) | 2.4 (24) | 2.9 (29) |
| Having a good friend | 74.0 (730) | 74.3 (753) | 75.3 (748) |
| Spoken with a friend past week | 67.2 (663) | 69.1 (700) | 69.9 (693) |

^a 2011, 2012 or 2013.

^b 2012, 2013 or 2014.

^c 2015.

[^] Significantly different at .01 level.

diagnosed with schizophrenia, nearly half of them lived alone, and only one out of ten had a paid job. Half of them were in symptomatic remission. More than half of the patients fulfilled the criteria of the metabolic syndrome. As measured with the HoNOS, a quarter of the patients were categorized as severe patients. Patients with three annual screenings between 2011 and 2015 (N = 1230) were stable, except for the increasing prevalence of high glucose levels and satisfaction with social relationships.

4.1. Towards a comprehensive ROM-system

Some specific demands are required for any comprehensive ROM-system to function in a productive and sustainable way to improve the provided mental healthcare (Delepaul, 2015).

First, the very first aim of any ROM-system is to improve the clinical process: allowing patients and clinicians to continually optimize treatment decisions using repeated assessments. The report generated by RoQua after the PHAMOUS screening is used in a shared decision-making process to optimize treatment. General practitioners are informed and involved in the treatment as much as possible. The technical and administrative part of the report-generating process is functioning appropriately. However, much work is still to be done in translating the detected problems to treatment indications. Recent studies from

our research group show that a large portion of these problems (e.g. metabolic risks, sexual disturbances and social needs) remained untreated (Tasma et al., 2016; Bruins et al., 2017). To further optimize the process of shared decision-making, computer-assisted programs to empower the patient and the nurse-practitioners have been tested in randomized control trials (van der Krieke et al., 2013) and are now being developed further.

Second, from a managerial perspective, the information provided by PHAMOUS can be aggregated at a higher level, optimizing strategic choices for the healthcare system. For instance, since the metabolic syndrome is highly prevalent in patients using antipsychotics, nurse-practitioners have been instructed to more intensively address these problems, and healthy lifestyle programs have become part of care as usual. Also, based on the reported social needs of chronic patients, guided peer support groups have been developed (Castelein et al., 2008) which are now part of standard care. Also, Individual Placement and Support (IPS) workers are now collaborating within the multidisciplinary team, to improve job prospects (Michon et al., 2014). As for staff education, numerous nurses have been trained to objectively detect extrapyramidal side effects of antipsychotic medication.

Third, a comprehensive ROM-system should improve transparency and (external) accountability. As PHAMOUS aims to include all eligible patients and all instruments are validated questionnaires, data can be

readily used for transparency and external accountability. Since the clinical data on a patient level within PHAMOUS can be combined with care consumption data of the Psychiatric Case Register Northern Netherlands, we are now conducting 'real world' health-economic studies in this population.

Fourth, an important goal of PHAMOUS was to develop a ROM-system that would yield reliable data for research. Initially, the research focus was on metabolic disturbances. For example, Schorr et al. (2009) investigated the prevalence of the metabolic syndrome and showed that the natural course of the metabolic syndrome is dynamic (Schorr et al., 2008). A subsample of patients participated in a genetic study, called PHAMOUS-gene, aiming to detect polymorphisms that may play a role in weight gain in patients using antipsychotics (Vehof et al., 2011b; Vehof et al., 2011a) and to genotype different genes in relation to antipsychotic metabolism and metabolic problems (Risselada et al., 2010; Risselada et al., 2012). Also, the relationship between cannabis use and metabolic parameters in this specific population was studied (Bruins et al., 2016). However, the database provides more unique research opportunities. The course of depressive symptoms and prescribing patterns of antidepressants were examined in a one-year follow-up study (Lako et al., 2012b). Besides, Lako et al. (2013) developed and tested an abbreviated version of the Subjects' Response to Antipsychotics questionnaire (SRA-34; Wolters et al., 2006). They demonstrated that patients using antipsychotic combination therapy were more likely to attribute depressive symptoms to their antipsychotics than patients using antipsychotic monotherapy (Lako et al., 2016). Negative symptoms have also been a central point of interest in our network. The two subdomains of negative symptoms, 'social amotivation' and 'expressive deficits' and their clinical correlates, were now confirmed in a large population with a long illness duration (Stiekema et al., 2016). The current database is available to help researchers and clinicians to identify patients that are eligible for new intervention studies. Thus, Looijmans et al. (2014) used the PHAMOUS framework for a multi-site cluster randomized controlled trial, studying the effects of changing the obesogenic environment of severe mentally ill residential patients.

4.2. New developments and challenges: towards an "iROM"?

As the Dutch mental health system is rapidly changing, the care for SMI patients is no longer the sole terrain of specialized care. Instead, people who have been stable for over six months, with low symptom scores are nowadays referred to primary care (basic-mental healthcare) or to the general practitioners (GPs), who employ mental health nurses to provide low intensity mental healthcare within the GP offices. To serve patients and caregivers in these time-restricted environments, a new abbreviated version of PHAMOUS has been developed. A web-based, or even mobile, 'iROM' version would be feasible, guaranteeing continuity in the ROM-history when patients are referred back and forth between GPs, primary, secondary and tertiary care centers.

Initially, PHAMOUS mainly focused on patients with psychotic disorders using antipsychotic medication. Over time, the scope broadened to patients treated in the same service facilities, most of them diagnosed with other forms of SMI. Therefore, more generic symptom dimension scales need to be developed to assess symptom severity in a more transdiagnostic way. Interestingly, as the early detection program in the Northern Netherlands (On The ROAD) and the first episode psychosis program (PROGR-S; Liemburg et al., 2014) are organized within the same RoQua data structure, trajectory analyses of patients through different stages of SMI are now possible.

In conclusion, over the last decade PHAMOUS has been providing a routine outcome monitor for all patients with a psychotic illness in the large Northern Netherlands region and supports the primary process of decision making. PHAMOUS, combined with mental healthcare consumption databases, also offers pointers to optimize the organization of mental healthcare providing useful information for both healthcare

economics and healthcare planning. Finally, PHAMOUS has built a robust infrastructure for epidemiological and clinical research on interventions and on risk and resilience factors.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Contributors

AABV and EV have designed the study and written the manuscript in close collaboration with HK and RB. All authors contributed to the interpretation of the results and have approved the final manuscript.

Funding/support

The Rob Giel Research center is structurally funded by the following mental health organizations: Lentis, GGZ Friesland, GGZ Drenthe, Mediant, Dimence Groep, and the University Center for Psychiatry of the University Medical Center Groningen.

Acknowledgements

The authors gratefully acknowledge the work of all research nurses, research coordinators and the RoQua team, as well as all efforts of Irene M. Lako PhD, who was involved in the set-up and initial coordination of PHAMOUS.

References

- American Psychiatric Association, 2000. *Diagnostic and Statistical Manual of Mental Disorders, 4th edition*. 4th ed. Author, Washington, DC.
- Andreasen, N.C., Carpenter, W.T., Kane, J.M., Lasser, R.A., Marder, S.R., Weinberger, D.R., 2005. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am. J. Psychiatry* 162 (3), 441–449.
- Bellack, A.S., 2004. Skills training for people with severe mental illness. *Psychiatr. Rehabil. J.* 27 (4), 375–391.
- Bruins, J., Pijnenborg, M.G., Bartels-Velthuis, A.A., Visser, E., van den Heuvel, E.R., Bruggeman, R., Jorg, F., 2016. Cannabis use in people with severe mental illness: the association with physical and mental health—a cohort study. *A Pharmacotherapy Monitoring and Outcome Survey study. J. Psychopharmacol.* 30 (4), 354–362.
- Bruins, J., Pijnenborg, G.H.M., Van den Heuvel, E.R., Visser, E., Corpeleijn, E., Bartels-Velthuis, A.A., Bruggeman, R., Jörg, F., 2017. Persistent low rates of treatment of metabolic risk factors in people with psychotic disorders: a PHAMOUS study. *J. Clin. Psychiatry* <https://doi.org/10.4088/JCP.16m10831>.
- Castelein, S., Bruggeman, R., van Busschbach, J.T., van der Gaag, M., Stant, A.D., Knegtering, H., Wiersma, D., 2008. The effectiveness of peer support groups in psychosis: a randomized controlled trial. *Acta Psychiatr. Scand.* 118 (1), 64–72.
- De Hert, M., Schreurs, V., Vancampfort, D., Van Winkel, R., 2009. Metabolic syndrome in people with schizophrenia: a review. *World Psychiatry.* 8 (1), 15–22.
- De Hert, M., Cohen, D., Bobes, J., Cetkovich-Bakmas, M., Leucht, S., Ndeti, D.M., Newcomer, J.W., Uwakwe, R., Asai, I., Moller, H.J., Gautam, S., Detraux, J., Correll, C.U., 2011. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. *World Psychiatry.* 10 (2), 138–151.
- de Leon, J., Diaz, F.J., 2005. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophr. Res.* 76 (2–3), 135–157.
- Delepaul, P.A., 2015. Routine outcome measurement in the Netherlands - a focus on benchmarking. *Int. Rev. Psychiatr.* 27 (4), 320–328.
- Drake, R., Haley, C., Akhtar, S., Lewis, S., 2000. Causes and consequences of duration of untreated psychosis in schizophrenia. *Br. J. Psychiatry* 177, 511–515.
- Galletly, C.A., Foley, D.L., Waterreus, A., Watts, G.F., Castle, D.J., McGrath, J.J., Mackinnon, A., Morgan, V.A., 2012. Cardiometabolic risk factors in people with psychotic disorders: the second Australian national survey of psychosis. *Aust. N. Z. J. Psychiatry* 46 (8), 753–761.
- Gardner, D.M., Murphy, A.L., O'Donnell, H., Centorrino, F., Baldessarini, R.J., 2010. International consensus study of antipsychotic dosing. *Am. J. Psychiatry* 167 (6), 686–693.
- Grundy, S.M., Cleeman, J.I., Daniels, S.R., Donato, K.A., Eckel, R.H., Franklin, B.A., Gordon, D.J., Krauss, R.M., Savage, P.J., Smith, S.C., Spertus, J.A., Costa, F., 2005. Diagnosis and management of the metabolic syndrome - an American Heart Association/National Heart, Lung, and Blood Institute scientific statement - executive summary. *Circulation* 112 (17), E285–E290.
- Hall, W., Degenhardt, L., 2000. Cannabis use and psychosis: a review of clinical and epidemiological evidence. *Aust. N. Z. J. Psychiatry.* 34 (1), 26–34.
- Hasnain, M., Fredrickson, S.K., Vieweg, W.V.R., Pandurangi, A.K., 2010. Metabolic syndrome associated with schizophrenia and atypical antipsychotics. *Curr. Diab. Rep.* 10 (3), 209–216.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13 (2), 261–276.
- Kern, R.S., Glynn, S.M., Horan, W.P., Marder, S.R., 2009. Psychosocial treatments to promote functional recovery in schizophrenia. *Schizophr. Bull.* 35 (2), 347–361.

- Lako, I.M., Bruggeman, R., Knegtering, H., Wiersma, D., Schoevers, R.A., Slooff, C.J., Taxis, K., 2012a. A systematic review of instruments to measure depressive symptoms in patients with schizophrenia. *J. Affect. Disord.* 140 (1), 38–47.
- Lako, I.M., Taxis, K., Bruggeman, R., Knegtering, H., Burger, H., Wiersma, D., Slooff, C.J., 2012b. The course of depressive symptoms and prescribing patterns of antidepressants in schizophrenia in a one-year follow-up study. *Eur. Psychiatry* 27 (4), 240–244.
- Lako, I.M., Bruggeman, R., Liemburg, E.J., van den Heuvel, E.R., Knegtering, H., Slooff, C.J., Wiersma, D., Taxis, K., 2013. A brief version of the subjects' response to antipsychotics questionnaire to evaluate treatment effects. *Schizophr. Res.* 147 (1), 175–180.
- Lako, I.M., Taxis, K., van den Heuvel, E.R., Leenaars, C.H., Burger, H., Wiersma, D., Slooff, C.J., Knegtering, H., Bruggeman, R., 2016. Altered emotional experiences attributed to antipsychotic medications - a potential link with estimated dopamine D2 receptor occupancy. *Psychiatry Res.* 236, 9–14.
- Liemburg, E.J., Castelein, S., van Es, F., Scholte-Stalenhoef, A.N., van de Willige, G., Smid, H., Visser, E., Knegtering, H., Bruggeman, R., 2014. The psychosis recent onset Groningen survey (PROGR-S): defining dimensions and improving outcomes in early psychosis. *PLoS One* 9 (11), e113521.
- Looijmans, A., Jorg, F., Schoevers, R.A., Bruggeman, R., Stolk, R.P., Corpeleijn, E., 2014. Changing the obesogenic environment of severe mentally ill residential patients: ELIPS, a cluster randomised study design. *BMC Psychiatry* 14 (293).
- McEvoy, J.P., Meyer, J.M., Goff, D.C., Nasrallah, H.A., Davis, S.M., Sullivan, L., Meltzer, H.Y., Hsiao, J., Scott Stroup, T., Lieberman, J.A., 2005. Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the clinical antipsychotic trials of intervention effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. *Schizophr. Res.* 80 (1), 19–32.
- Michon, H., van Busschbach, J.T., Stant, A.D., van Vugt, M.D., van Weeghel, J., Kroon, H., 2014. Effectiveness of individual placement and support for people with severe mental illness in The Netherlands: a 30-month randomized controlled trial. *Psychiatr. Rehabil. J.* 37 (2), 129–136.
- Mitchell, A.J., Vancampfort, D., Sweers, K., van Winkel, R., Yu, W., De Hert, M., 2013. Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—a systematic review and meta-analysis. *Schizophr. Bull.* 39 (2), 306–318.
- Parabiaghi, A., Barbato, A., D'Avanzo, B., Erlicher, A., Lora, A., 2005. Assessing reliable and clinically significant change on health of the nation outcome scales: method for displaying longitudinal data. *Aust. N. Z. J. Psychiatry.* 39 (8), 719–725.
- Patterson, T.L., Leeuwenkamp, O.R., 2008. Adjunctive psychosocial therapies for the treatment of schizophrenia. *Schizophr. Res.* 100 (1–3), 108–119.
- Peralta, V., Cuesta, M.J., 1992. Influence of cannabis abuse on schizophrenic psychopathology. *Acta Psychiatr. Scand.* 85 (2), 127–130.
- Priebe, S., Huxley, P., Knight, S., Evans, S., 1999. Application and results of the Manchester short assessment of quality of life (MANSA). *Int. J. Soc. Psychiatry* 45 (1), 7–12.
- Richardson, T.H., 2010. Cannabis use and mental health: a review of recent epidemiological research. *Int. J. Pharmacol.* 6 (6), 796–807.
- Risselada, A.J., Vehof, J., Bruggeman, R., Wilffert, B., Cohen, D., Al Hadithy, A.F., Arends, J., Mulder, H., 2010. Association between the 1291-C/G polymorphism in the adrenergic alpha-2a receptor and the metabolic syndrome. *J. Clin. Psychopharmacol.* 30 (6), 667–671.
- Risselada, A.J., Vehof, J., Bruggeman, R., Wilffert, B., Cohen, D., Al Hadithy, A.F., Arends, J., Mulder, H., 2012. Association between HTR2C gene polymorphisms and the metabolic syndrome in patients using antipsychotics: A replication study. *The Pharmacogenomics Journal* 12 (62), 62–67.
- Schorr, S.G., Slooff, C.J., Postema, R., Van Oven, W., Schilthuis, M., Bruggeman, R., Taxis, K., 2008. A 12-month follow-up study of treating overweight schizophrenic patients with aripiprazole. *Acta Psychiatr. Scand.* 118 (3), 246–250.
- Schorr, S.G., Slooff, C.J., Bruggeman, R., Taxis, K., 2009. The incidence of metabolic syndrome and its reversal in a cohort of schizophrenic patients followed for one year. *J. Psychiatr. Res.* 43 (13), 1106–1111.
- Statistics Netherlands. .. <http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=03759ned&D1=0-2%2c17&D2=129-132&D3=0-4&D4=25-26&HDR=T&STB=G2%2cG3%2cG1&P=D&VW=T>.
- Stiekema, A.P., Liemburg, E.J., van der Meer, L., Castelein, S., Stewart, R., van Weeghel, J., Aleman, A., Bruggeman, R., 2016. Confirmatory factor analysis and differential relationships of the two subdomains of negative symptoms in chronically ill psychotic patients. *PLoS One* 11 (2), e0149785.
- Tasma, M., Swart, M., Wolters, G., Liemburg, E., Bruggeman, R., Knegtering, H., Castelein, S., 2016. Do routine outcome monitoring results translate to clinical practice? A cross-sectional study in patients with a psychotic disorder. *BMC Psychiatry* 16 (1), 107-016-0817-6.
- van der Krieke, L., Emerencia, A.C., Boonstra, N., Wunderink, L., de Jonge, P., Sytema, S., 2013. A web-based tool to support shared decision making for people with a psychotic disorder: randomized controlled trial and process evaluation. *J. Med. Internet Res.* 15 (10), 205–219.
- van Os, J., Linscott, R.J., Myin-Germeys, I., Delespaul, P., Krabbendam, L., 2009. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychol. Med.* 39 (2), 179–195.
- Vancampfort, D., Knapen, J., Probst, M., van Winkel, R., Deckx, S., Maurissen, K., Peuskens, J., De Hert, M., 2010. Considering a frame of reference for physical activity research related to the cardiometabolic risk profile in schizophrenia. *Psychiatry Res.* 177 (3), 271–279.
- Vehof, J., Al Hadithy, A.F.Y., Burger, H., Snieder, H., Risselada, A.J., Wilffert, B., Cohen, D., Arends, J., Wiersma, D., Mulder, H., Bruggeman, R., 2011a. Association between the ROBO1 gene and body mass index in patients using antipsychotics. *Psychiatr. Genet.* 21 (4), 202–207.
- Vehof, J., Risselada, A.J., Al Hadithy, A.F.Y., Burger, H., Snieder, H., Wilffert, B., Arends, J., Wunderink, L., Knegtering, H., Wiersma, D., Cohen, D., Mulder, H., Bruggeman, R., 2011b. Association of genetic variants of the histamine H1 and muscarinic M3 receptors with BMI and HbA1c values in patients on antipsychotic medication. *Psychopharmacology* 216 (2), 257–265.
- Wiersma, D., Visser, E., Bahler, M., Bruggeman, R., Delespaul, P.A., van der Gaag, M., de Haan, L., Keet, I.P., Nijssen, Y., van Os, J., Pijnenborg, G.H., Slooff, C., Swildens, W., de Vos, A.E., van Weeghel, J., Wunderink, L., Mulder, C.L., 2015. Functional remission of people with serious mental illness (SMI): psychometric properties of a new ROM-instrument. *Tijdschr. Psychiatr.* 57 (6), 395–404.
- Wing, J.K., Beever, A.S., Curtis, R.H., Park, S.B.G., Hadden, S., Burns, A., 1998. Health of the nation outcome scales (HoNOS) - Research and development. *Br. J. Psychiatry* 172, 11–18.
- Wolters, H.A., Knegtering, R., Wiersma, D., van den Bosch, R.J., 2006. Evaluation of the subjects' response to antipsychotics questionnaire. *Int. Clin. Psychopharmacol.* 21 (1), 63–69.