

Effects of an electronic reminder system on guideline concordant treatment of psychotic disorders: results from a pilot feasibility trial

Irina Franke, MD,¹ Sarah Thier, MSc,² Anita Riecher-Rössler, MD PhD^{3*}

¹ Department of Forensic Psychiatry, University of Basel Psychiatric Clinics, Basel, Switzerland

² Department of Child and Adolescent Psychiatry, University of Basel Psychiatric Clinics, Basel, Switzerland

³ Center for Gender Research and Early Detection, University of Basel Psychiatric Clinics, Basel, Switzerland

*Corresponding author

Prof. Dr. med. Anita Riecher-Rössler
Center for Gender Research and Early Detection
University of Basel Psychiatric Clinics
Kornhausgasse 7
CH-4051 Basel, Switzerland
E-mail: anita.riecher@upkbs.ch
Phone: +41 61 325 81 61
Fax: +41 61 325 81 60

Conflicts of Interest

Sarah Thier worked for more&g as a scientific co-worker, which developed the program

M.E.M.O.R.E.S. She confirms having worked independently.

Anita Riecher-Rössler and Irina Franke declare no conflicts of interest.

Abstract

Background: Adherence to evidence-based guidelines is essential for the treatment outcome of psychotic disorders. Previous studies showed that IT-supported pathways are able to increase guideline adherence in psychiatric care. This paper describes a pilot study on the development of an electronic recall-reminder-system (RRS) for supporting guideline-adherent treatment in outpatient care of patients with chronic psychotic disorders and analyses its feasibility.

Methods: Guidelines were integrated in the RRS software M.E.M.O.R.E.S. Software training for the staff was provided. We compared the number of conducted vs. guideline-recommended interventions 6 months before and after implementation. Subsequently both the caregivers' and the patients' satisfaction with the RRS was evaluated.

Results: Guideline adherence in general was low and the RRS was barely used. After its implementation a significant increase was observed in chemogram-check-ups and diagnostics regarding cardiovascular risks (esp. ECG). Both patients and professionals described problems with integrating the RRS in their daily routine and questioned the usefulness of the guidelines for chronically ill, although they basically approved its importance and usefulness.

Conclusions: Participants appreciated the idea of supporting guideline adherence with an IT-system, but there seemed to be major obstacles to implementation: caregivers appear to be concerned of being exposed or questioned, technical difficulties might lead to avoidance, and there seems to be a lack of knowledge and awareness about the health risks for individuals with psychotic disorders. Possibly guidelines adapted for the chronically ill would find more acceptance. Technical simplifications and better information should be considered prior to further attempts to implement IT-supported guidelines in order to increase acceptance.

Keywords: clinical guidelines, guideline adherence, psychotic disorders, treatment, IT-pathway-systems, acceptance

Zusammenfassung

Hintergrund: Die Einhaltung evidenzbasierter Behandlungsleitlinien ist wesentlich für das Behandlungsergebnis bei psychotischen Erkrankungen. Studien haben gezeigt, dass IT-unterstützte Behandlungspfade die Leitlinienadhärenz in der psychiatrischen Versorgung erhöhen können. Diese Arbeit beschreibt eine Pilotstudie über die Entwicklung eines elektronischen Erinnerungssystems (recall-reminder-system, RRS) zur Unterstützung leitlinienbasierter Therapie in der ambulanten Behandlung von psychotischen Erkrankungen und untersucht die Machbarkeit.

Methoden: Die Behandlungsleitlinien wurden in die RRS-Software M.E.M.O.R.E.S integriert. Die Fachpersonen erhielten Schulungen für den Gebrauch der Software. Es wurde die Zahl der durchgeführten Interventionen 6 Monate vor und nach der Implementierung des RRS verglichen. In der Folge wurde ausserdem die Zufriedenheit von Patienten und Fachpersonen mit dem System evaluiert.

Ergebnisse: Die Leitlinienadhärenz war allgemein niedrig und das RRS wurde kaum verwendet. Nach der Implementierung war ein signifikanter Anstieg bei der Durchführung von Blutuntersuchungen und der Kontrolle kardiovaskulärer Risiken (insbesondere EKG-Untersuchungen) zu verzeichnen. Sowohl Patienten wie auch Fachpersonen beschrieben Schwierigkeiten, das RRS in die tägliche Routine zu integrieren, obwohl sie der Wichtigkeit und Nützlichkeit des Systems grundsätzlich zugestimmt haben.

Fazit: Die Unterstützung leitlinienorientierter Behandlung mit einem IT-System wurde von den Teilnehmenden positiv bewertet, es schienen allerdings grosse Hürden bei der praktischen Umsetzung zu bestehen: Fachpersonen befürchten möglicherweise, hinterfragt oder blossgestellt zu werden, technische Schwierigkeiten reduzieren die Akzeptanz für die Anwendung des Systems und es scheinen Informationsdefizite und fehlende Achtsamkeit bezüglich der Gesundheitsrisiken von Personen mit psychotischen Erkrankungen zu bestehen. Technische Vereinfachungen und bessere Wissensvermittlung vor dem Einsatz

leitlinienbasierter Behandlungsprogramme sollten in Erwägung gezogen werden, um die Akzeptanz zu erhöhen.

Keywords: Behandlungsleitlinien, Leitlinieneinhaltung, psychotische Erkrankungen, Behandlung, IT-Behandlungspfad, Akzeptanz

Background

Several national expert panels have published evidence-based guidelines for the treatment of mental disorders including schizophrenia [1-3]. Guideline-concordant treatment leads to a better outcome for schizophrenic patients regarding psychopathology, hospitalization rates and mortality [4-6]. Recent data from the RAISE study also showed that comprehensive treatment for first episode psychosis can be implemented and improves functional and clinical outcomes [7]. Individuals with severe mental illness, including schizophrenia, have a mortality risk 1.5–2.5 times higher than the general population [8-10]. As antipsychotic medication seems to contribute to this risk [11-15], important aspects of treatment quality in schizophrenia include diagnostic procedures (e.g. MRI, EEG) and regular controls of medication side effects to lessen the risk for somatic comorbidities. Patients suffering from schizophrenic disorders exhibit an increased mortality rate due to cardiovascular conditions and are often incapable of dealing with the risk factors appropriately [16, 17]. Various studies claim that the management of cardiovascular risks in patients with severe mental illness needs to be improved [18-22].

Factors contributing to a generally low guideline adherence in medical care are: technical factors (e.g. hardware, software, usability, integration and interface), organisation-related factors (e.g. finances, management, training, feedback), logistic factors (e.g. system design, work flow, compatibility), behavioural factors (user satisfaction, settings, expectations and interdisciplinary collaboration) and professional/informational factors (e.g. clinical experience, clinical relevance of the topic, communication processes), and also different patient-related obstacles (e.g. opposing cultures, educational, cognitive and attitude differences, no adherence to recommendations) [23, 24].

IT-supported systems can improve guideline-concordant treatment. The popularity of such applications is increasing [25, 26]. Using guideline-based electronic treatment algorithms

leads to increased guideline adherence, resulting in a rise of conducted laboratory examinations and drug screenings. Furthermore, more adequate doses of neuroleptics were prescribed and a reduction in the length of inpatient stay was found [5, 27, 28]. Nevertheless, other recommended interventions such as psychoeducation programmes, cognitive trainings, assessment of global level of functioning or of positive and negative symptoms had been conducted only moderately, if not poorly [27, 29].

This paper presents the results of a pilot prospective intervention study investigating whether guideline adherence in outpatient treatment of schizophrenia could be increased by implementing an electronic recall reminder system (RRS) that informs mental health professionals about upcoming guideline-recommended interventions and patients about upcoming appointments. Furthermore, we analysed the acceptance of the system.

Methods

Development of the RRS

The most widely used and accepted guidelines for psychotic disorders in the German speaking countries were screened. Then the S3-practice guidelines by the German association of psychiatry, psychotherapy and neurology (DGPPN) [1] were combined with current pharmacological treatment guidelines [30], as the DGPPN guideline did not give exact recommendations regarding monitoring of medication. Further interventions included psychosocial interventions (e.g. psychoeducation) and structured clinical assessments (psychopathology, side effects). Altogether there were 48 guidelines. Most of them were medication guidelines and referred to monitoring side effects such as weight gain, glucose levels or dyslipidemia. The physical examinations included blood tests and diagnostic procedures (ECG, EEG, weight, waist size). Furthermore, the guidelines included specific therapeutic interventions, such as psychoeducation, assessment of medication adherence (therapeutic drug monitoring) or information about side effects and contraception. This

information was supplied to the electronic RRS software “M.E.M.O.R.E.S” (Medical Monitoring and Recalling System) [31]. It was implemented at the workplace of each professional. All users received special training, and a written user guide was deposited at each study site.

Diagnoses were confirmed according to DSM-IV and the Basel Screening Instrument for Psychosis [32]. The appointment adherence was assessed by the German translation of the Service Engagement Scale (SES) [33]. It was completed by the caregivers at the time of the RRS-implementation (t_i) and at the end of the study (t_e). The medication adherence was assessed by the Medication Adherence Rating Scale (MARS) [34].

Implementation of the Study

Between November 2011 and May 2012 patients were recruited at 3 psychiatric outpatient departments of the University of Basel Psychiatric Clinics (UPK) and at 3 private psychiatric practices (former patients of the mentioned outpatient departments). As resident psychiatrists did not conduct all physical examinations themselves, 4 general practitioners took part as well. Mental health care professionals included psychiatrists and psychiatric nurses. The compliance with appointments was the primary outcome measure of the study. Guideline adherence and user satisfaction were the secondary outcome parameters. Patients received CHF 10 (\approx 11 \$) for participation.

After having registered the patient in the RRS, the professional had to choose the way of communication (text message, e-mail, or letter) and the applicable guidelines. The program then displayed the date and content of recommended interventions. According to this, the patient automatically received a message and was asked to arrange an appointment. The therapist had the option to consult the RRS about the recommendation, but was obliged to decide individually which interventions were realized. Afterwards the therapist confirmed the

examination as completed or noted why it was not done. Any unconfirmed intervention was displayed as missed.

After recruitment of patients the performed interventions were measured for 6 months without applying the reminder function of the RRS (“pre-phase”) by evaluating the electronic records. In the subsequent 6 months the procedure was repeated with the active RRS (“post-phase”). Changes in guideline adherence were measured by comparing the number of interventions during pre- and post-phase.

The satisfaction with the RRS was assessed with semi-structured questionnaires. Professionals were asked for satisfaction with software, customer support by the provider and with the study itself. Patients were asked for their satisfaction with the messages and the study, and whether it led to an increased frequency of examinations or higher treatment costs.

Data were assessed using the Statistical Package for the Social Sciences (SPSS) 20. To analyse the differences between pre- and post-phase, the Wilcoxon test was used for non-parametric and the T-test for parametric variables (level of significance $p=0.05$).

The study was approved by the local Ethical Committee.

Inclusion/exclusion criteria

Patients had to be between 14 and 65 years of age and diagnosed with schizophrenia. Exclusion criteria were harmful substance use or addiction (excluding cannabis), organic brain syndromes, insufficient language skills, severe negative symptoms and acute psychotic episodes.

Statistical Analysis

A power calculation estimated a required sample size of 43 patients to reach a power of 90% ($\alpha=0.05$). We assumed a drop-out rate of 20%. Therefore, 54 patients would have had to be

recruited, in order to show an improvement in appointment adherence by 10% due to the application of the RRS.

The statistical analysis was done with the Statistical Package of the Social Sciences 20 (SPSS 20). Besides the descriptive analyses of sociodemographic and clinical data, we analyzed differences in the means of the frequencies of diagnostic and therapeutic interventions in pre- and post-phase. The differences of the means were assessed by using parametric or non-parametric tests depending on the distribution of the data, to find out whether there were differences in pre- and post-phases regarding the number and duration of hospitalizations, guideline adherence and kept appointments.

Additionally, to determine whether the included, excluded and refusing patients differed with respect to age and gender, the ANOVA-test for interval-scaled data (age) and the χ^2 -test for nominal-scaled data were performed.

Results

Participants

After having identified 200 patients, a majority of them had to be excluded or refused participation. Finally only 20 patients could be included. The main reason for exclusion was poor language skills (29,4%), the main reasons for refusing participation were perceived additional strain due to study participation (16.4%), refusal of using electronic devices (11.9%), satisfaction with actual treatment (11.9%) and unwillingness to take part in studies in general (9.7%) or because of previous study participation (6.7%). Included, excluded and refusing individuals did not differ regarding age and gender. The participating 13 health care professionals comprised 6 psychiatric nurses, 3 specialists of psychotherapy and psychiatry and 4 general practitioners.

Dropout rate

At the end of the post-phase complete data of only 18 patients were available for further analyses: one included patient did not have an appointment arranged during the whole study period, the other patient's practitioner fell sick. For evaluating patients' satisfaction with text messages data of 17 participants were available as 3 patients did not receive text messages (only the professional did). For further analyses of user satisfaction, data of all 20 participants were available.

Guideline adherence

Laboratory and other diagnostic measures

Table 1 shows the proportion of performed vs. recommended examinations.

Insert Table 1 about here

The results show that guideline concordant monitoring of drug therapy is done in less than 50% of the cases in the pre-phase and increases to over 90% in the post-phase. During the post-phase, a significant increase could be observed regarding chemogram-analyses and a tendency to more haematogram-analyses. Also the controls of blood pressure and ECG increased significantly.

Clinical assessment and psychosocial interventions

Recommendations included assessment of side effects, changes of psychopathology and psychoeducation. We found that side effects, compliance and use of illegal substances were assessed quite regularly. Psychoeducation was performed either irregular or not at all. A written treatment plan was not available. We found no significant differences between pre- and post-phases (see Table 2).

Insert Table 2 about here

Reasons for not complying with guidelines

Health care professionals:

- Professional competence:

Appointments were often held by psychiatric nurses who thought that assessing the patient's physical state and psychopathology is a task obliged to the physician. Psychiatrists did not see the patients at each consultation. They assessed psychopathology and physical state only when major changes were observed.

- Physical focus:

Current treatment focussed on the patients' mental stability and enabling them to manage daily routine; aspects of physical health were not considered to be part of the treatment. Psychiatrists in private practice generally did not perform physical examinations and delegated this to general practitioners.

- Long-term treatment:

Some of the recommendations were considered as unimportant for long-term patients; regular assessment of psychopathology was considered as unnecessary when there were no obvious changes; psychoeducation was not supposed to be a treatment focus for chronically ill people. It was also stated that some examinations had taken place before the study period.

- Organisational obstacles:

Some of the procedures do require a registration process (ECG). Additionally, not all instruments were available at all treatment locations.

- Irregular application:

Pulse rate and blood pressure were only measured "when needed"; body weight only if there were signs of weight gain.

- Assumed relevance:

Additional measurement of waist size wasn't done, when weight was controlled. Some examinations (ECG, EEG or blood glucose) were considered necessary only in case of previously suspicious findings.

- No written documentation:

Written treatment plans including regular assessments and check-ups did not exist or were not updated regularly.

RRS user acceptance (professionals)

The users stated the following reasons for not using the RRS service:

- Lack of integration of the RRS in hospital and medical software systems.
- Inflexibility: the system should have been more adaptable to individual treatment intervals and demands.
- Difficulties in handling: confusing and non-intuitive system.
- Questionable viability of guidelines: the physical focus of the guidelines was considered as discouraging; furthermore, own standards of care already existed.
- Study related obstacles: no detailed information on the scope of the study.
- Top-down support: no instructions on implementing the system by the direct superior; undefined responsibility.
- Patients "requiring" guideline-concordant treatment could not be reached.
- Low acceptance by patients: use of mobile phone was refused, the telephone turned off, change of phone number or no credit; text messages were considered more invasive than e.g. e-mails.

The following positive aspects of the RRS were mentioned:

- Appreciation of the basic idea of the system (overview of existing guidelines, recommendations).
- Lower risk of forgetting examinations.

- Support in daily work, increased integration of treatment standards in routine care.

RRS user acceptance (patients)

The results are displayed in Table 3. The results show that many patients had difficulties in understanding the content and purpose of the study. At the end of the study still a majority of the patients was convinced they should be reminded on arranged appointments via text messages, although they showed up to their appointments regularly anyway. The impression of several patients that their treatment did not change during the course of the study or through the RRS might indicate that they did not perceive additional strain. Only 10% of the participants stated that their treatment costs increased due to study-related examinations.

Insert Table 3 about here

Discussion

We found relatively poor guideline concordance both in the pre-phase as in the post-phase. The RRS only led to a moderate increase in laboratory controls (chemogram and haematogram analyses) and diagnostic examinations (ECG, EEG, weight, blood pressure). This result is supported by other studies [5, 27]. Other interventions like assessment of side effects and compliance were performed quite regularly with and without the RRS. Therapeutic interventions (e.g. psychoeducation) were not performed more often after the implementation of the RRS, which is in accordance to other study results as well [27, 29]. It is remarkable that psychoeducation was not considered to be necessary in chronically ill individuals. Reasons for that decision were not given. Some recommendations, as for example a written documentation of a treatment plan, were not realized at all.

A further result of our pilot study was that the RRS, designed as a supporting tool for clinicians, was only partly applied. The finding that most of the professionals basically approved the idea of guideline implementation indicates that there is general awareness for its

potential usefulness. On the other hand, there seem to be major opposing factors. The users' statements on their satisfaction with the RRS included aspects which have already been described as obstacles for a successful guideline implementation in literature: technical, organisational and professional factors [23, 24]. These obstacles might be eliminated by better institutional support from top down or by improving technical skills and support. Another important reason for the low acceptance was the limited readiness of patients and professionals to take part in a study.

Health care professionals criticized, that some guidelines were not applicable for every stage of psychosis and gave that as a reason why they did not follow some recommendations. For example the question occurred how often psychoeducational interventions should be performed with chronically ill individuals. So some recommendations might need to be adapted to increase acceptance. On the other hand controlling cardiovascular risk under antipsychotic medication is important for individuals with first episode as well as chronic psychoses. Acceptance of comprehensive treatment might increase when guidelines become more flexible and more focussed on shared decision making.

A distinct separation of "physical" and "mental" health care of individuals with severe mental illness should be avoided as it can cause under-supply. Therefore it seems necessary to raise awareness towards aspects of physical health among professionals involved in the care of chronically mentally ill persons. In our study some patients expressed they had expected an improvement of their physical treatment by participating in the study.

The main limiting factor of this study is its low number of patients included and the diversity of included professionals. Furthermore, the selected study sites may have contributed to a selection of chronically ill people and therefore the sample is not representative for schizophrenia patients. Since the RRS was not applied as supposed, the significant results may be explained due to other factors as well. Another limitation might be the short duration of the study; probably there would have been a higher acceptance if the users would have had

more time to get used to the RRS. All results may also have been influenced by the study sample of professionals which included almost 50% psychiatric nurses (the most common form of institutionalised outpatient care in Switzerland).

Despite the evident problems in the present study, the feasibility of IT-supported treatment pathways should be further addressed, as they might be able to improve the quality of mental health care.

Ethical Standards Statement

All procedures followed were in accordance with the ethical standards of the local ethics committee (EKNZ, formerly EKBB) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of Informed Consent

Informed consent was obtained from all patients for being included in the study.

Tables

Table 1 Guideline adherence, documented examinations

	Pre-phase	Post-phase	P
Intervention	(n=17)	(n=18)	
	% (SD)	% (SD)	
Follow-up documentation	90.64 (14.18)	90.11 (15.78)	1.0
Therapeutic drug monitoring	30.96 (27.05)	91.68 (16.65)	.122
Laboratory check-ups (haemogram)	24.91 (36.78)	45.86 (43.27)	.067
Laboratory check-ups (chemogram)	22.64 (33.83)	44.91 (44.93)	.050
Diagnostics (ECG, EEG, blood pressure, weight)	12.26 (29.19)	28.78 (34.31)	.011

SD = Standard Deviation

Table 2 Clinical assessments and psychosocial interventions

Intervention	Number of patients receiving interventions	Number of patients where interventions were recommended	Total number of interventions recommended	Number of patients receiving interventions	Number of patients where interventions were recommended	Total number of interventions recommended
	Pre-phase (n=17)	Pre-Phase	Pre-phase	Post-phase (n=18)	Post-Phase	Post-phase
Assessment of side effects ¹	16	17	35	17	18	34
Assessment of compliance ¹	12	13	17	14	6	6
Substance use ¹	9	16	44	11	18	45
Pregnancy test (4 female patients) ¹	0	4	8	0	4	7
Psychoeducation ²	individually	3	6	individually	0	0
Treatment plan ³	0	10	10	0	3	3

¹ Recommended twice in the first month of treatment, then quarterly

² Recommended twice in the first month of treatment, then individually

³ Recommended annually

Table 3 Patient satisfaction (n=17 for reminders, n=20 for whole course)

Item	Yes % (n)	No % (n)	Don't Know % (n)
Were you informed sufficiently about the aims of the reminding messages?	88.2 (15)	11.8 (2)	0
Were you content with the reminders?	94.1 (16)	5.9 (1)	0
Was the effort caused by the reminders bearable?	94.1 (16)	5.9 (1)	0
Did the reminders cause you to show up on treatment appointments more regularly?	11.8 (2)	82.4 (14)	5.8 (1)
Did the reminders improve your treatment quality?	29.4 (5)	70.6 (12)	0
Would you like to continue the reminder function after the study is finished?	47.1 (8)	52.9 (9)	0
Did you receive more examinations during the course of the study than before?	20.0 (4)	80.0 (16)	0
If yes, were the additional examinations bearable?	100 (4)	0	
Did your treatment costs increase during your participation in the study?	10.0 (2)	90.0 (16)	0
What did you like about the study?	<ul style="list-style-type: none"> • The patient is responsible for arranging an appointment or not • Appointment reminding function was convenient • The study involved little effort • The regular treatment was not interrupted • Interest in the patient's perspective • Reminders support in terms of structuring the day and one's motivation • The study's duration of one year contributed to the study being taken seriously • The study supports research and help to other mentally ill persons • It was unclear why it was necessary to participate in the study, as I showed up to appointments regularly anyway • If an appointment had been missed, it was stressful to arrange a new one • Being asked to arrange an appointment by the reminder was tenacious • A larger effect concerning physical check-ups (e.g. weight and discussing physical changes) was expected 		
What did you dislike about the study?	<ul style="list-style-type: none"> • There were no prompts sent in advance to arranged appointments • The long talk at the beginning of the study was stressful • The study reminds of the own disorder • Text messages were annoying, as appointments had already been arranged • Text messages were received at inconvenient times • If certain examinations would have been performed more often, they would have had to be paid by the patients • The study caused higher costs 		

References

1. *Deutsche Gesellschaft für Psychiatrie und Psychotherapie (ed.). Behandlungsleitlinie Schizophrenie. S3 Praxisleitlinien in Psychiatrie und Psychotherapie 2006, Darmstadt: Steinkopff.*
2. *Practice guideline for the treatment of patients with schizophrenia. American Psychiatric Association. The American journal of psychiatry, 1997. 154(4 Suppl): p. 1-63.*
3. Health, N.C.C.f.M., *Psychosis and Schizophrenia in Adults: Treatment and Management.* 2014, Royal College of Psychiatrists: London.
4. Miller, A., et al., *The Texas Medication Algorithm Project antipsychotic algorithm for schizophrenia: 2003 update.* J Clin Psychiatry, 2004. **65**(4): p. 500-8.
5. Janssen, B., et al., *[Guideline conformity and outcome of inpatient treatment for schizophrenia. A clinical comparison].* Nervenarzt, 2005. **76**(3): p. 315-26.
6. Cullen, B.A., et al., *Guideline-concordant antipsychotic use and mortality in schizophrenia.* Schizophr Bull, 2013. **39**(5): p. 1159-68.
7. Kane, J.M., et al., *Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program.* American Journal of Psychiatry, 2015. **173**(4): p. 362-372.
8. Harris, E.C. and B. Barraclough, *Excess mortality of mental disorder.* The British Journal of Psychiatry, 1998. **173**(1): p. 11-53.
9. Chang, C.-K., et al., *All-cause mortality among people with serious mental illness (SMI), substance use disorders, and depressive disorders in southeast London: a cohort study.* BMC psychiatry, 2010. **10**(1): p. 1.
10. Hoang, U., R. Stewart, and M.J. Goldacre, *Mortality after hospital discharge for people with schizophrenia or bipolar disorder: retrospective study of linked English hospital episode statistics, 1999-2006.* BMJ, 2011. **343**: p. d5422.
11. Roden, D.M., *Drug-induced prolongation of the QT interval.* New England Journal of Medicine, 2004. **350**(10): p. 1013-1022.
12. Ray, W.A., et al., *Atypical antipsychotic drugs and the risk of sudden cardiac death.* New England Journal of Medicine, 2009. **360**(3): p. 225-235.
13. Stahl, S., L. Mignon, and J. Meyer, *Which comes first: atypical antipsychotic treatment or cardiometabolic risk?* Acta Psychiatrica Scandinavica, 2009. **119**(3): p. 171-179.
14. Crump, C., et al., *Comorbidities and mortality in persons with schizophrenia: a Swedish national cohort study.* American Journal of Psychiatry, 2013. **170**(3): p. 324-333.
15. Kiviniemi, M., et al., *Antipsychotics and mortality in first-onset schizophrenia: prospective Finnish register study with 5-year follow-up.* Schizophrenia research, 2013. **150**(1): p. 274-280.
16. Hennekens, C.H., et al., *Schizophrenia and increased risks of cardiovascular disease.* American heart journal, 2005. **150**(6): p. 1115-21.
17. Kilbourne, A.M., et al., *Cardiovascular disease and metabolic risk factors in male patients with schizophrenia, schizoaffective disorder, and bipolar disorder.* Psychosomatics, 2007. **48**(5): p. 412-7.
18. Arbus, C., et al., *Health management of older persons with chronically medicated psychotic disorders: the results of a survey in France.* International psychogeriatrics / IPA, 2012. **24**(3): p. 496-502.

19. De Hert, M., et al., *Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC)*. *Eur Psychiatry*, 2009. **24**(6): p. 412-24.
20. De Hert, M., J. Peuskens, and R. van Winkel, *Mortality in patients with schizophrenia*. *Lancet*, 2009. **374**(9701): p. 1591; author reply 1592-3.
21. Correll, C.U., et al., *Cardiometabolic risk in patients with first-episode schizophrenia spectrum disorders: baseline results from the RAISE-ETP study*. *JAMA psychiatry*, 2014. **71**(12): p. 1350-1363.
22. Vancampfort, D., et al., *Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis*. *World Psychiatry*, 2015. **14**(3): p. 339-347.
23. Cochrane, L.J., et al., *Gaps between knowing and doing: understanding and assessing the barriers to optimal health care*. *J Contin Educ Health Prof*, 2007. **27**(2): p. 94-102.
24. Shcherbatykh, I., et al., *Methodologic issues in health informatics trials: the complexities of complex interventions*. *J Am Med Inform Assoc*, 2008. **15**(5): p. 575-80.
25. Kilbourne, A.M., *E-health and the transformation of mental health care*. *Psychiatr Serv*, 2012. **63**(11): p. 1059.
26. Hilty, D.M., et al., *The effectiveness of telemental health: a 2013 review*. *Telemed J E Health*, 2013. **19**(6): p. 444-54.
27. Godemann, F., et al., *[Guideline compliance in the treatment of schizophrenic patients. Introduction of a computer-assisted treatment pathway]*. *Nervenarzt*, 2010. **81**(5): p. 584-93.
28. van Dijk, M.K., et al., *The effectiveness of adhering to clinical-practice guidelines for anxiety disorders in secondary mental health care: the results of a cohort study in the Netherlands*. *J Eval Clin Pract*, 2012.
29. Markkula, N., R. Alvarado, and A. Minoletti, *Adherence to guidelines and treatment compliance in the Chilean national program for first-episode schizophrenia*. *Psychiatr Serv*, 2011. **62**(12): p. 1463-9.
30. Benkert, O., Hippus, H, (eds.), *Kompendium der Psychiatrischen Pharmakotherapie*. 2011, Heidelberg: Springer Medizin Verlag.
31. GmbH, m.g.e.-H.; Available from: <http://moreandg.com/index.php/memores>
32. Riecher-Rossler, A., et al., *[The Basel Screening Instrument for Psychosis (BSIP): development, structure, reliability and validity]*. *Fortschr Neurol Psychiatr*, 2008. **76**(4): p. 207-16.
33. Tait, L., M. Birchwood, and P. Trower, *A new scale (SES) to measure engagement with community mental health services*. *Journal of Mental Health*, 2002. **11**(2): p. 191-198.
34. Thompson, K., J. Kulkarni, and A. Sergejew, *Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses*. *Schizophrenia research*, 2000. **42**(3): p. 241-247.