Relevanz von Behandlungsleitlinien in der Versorgung

Prof. Dr. Peter Falkai
PD Dr. Alkomiet Hasan

LVR Symposium 2015:
Qualität in der Psychiatrie –
Messung, Steuerung, Optimierung
Köln, 29. – 30. Januar 2015

Leitlinien in der klinischen Praxis – Erkennen worauf es ankommt

Kopp B and Rahn KH 2015: Bayer Ärzteblatt; 1-2: 8-12

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Was sind (Behandlungs)Leitlinien?

Leitlinien sind systematisch entwickelte Empfehlungen mit dem Zweck, Ärzte und Patienten bei der Entscheidung über angemessene Maßnahmen der Krankenversorgung (Prävention, Diagnostik, Therapie und Nachsorge) unter spezifischen Umständen zu unterstützen.

Sie geben den Stand des Wissens (Ergebnisse von klinischen Studien und Wissen von Experten) über effektive und angemessene Krankenversorgung zum Zeitpunkt der "Drucklegung" wieder.

Warum brauchen wir Leitlinien?

Ein guter Arzt muss bei jedem Patienten eine **individuelle Entscheidung** unter Berücksichtigung möglichst vieler Faktoren treffen.

Aber, **individuelle Therapieentscheidungen** können mit einer ausreichenden Qualität nur getroffen werden, wenn die EBM Empfehlungen bekannt sind.

Nur so kann eine Abwägung und korrekte Einordnung **des Indiviudalfalls** erfolgen.

Was ist überhaupt Evidenzbasierte Medizin?

Evidence based medicine: what it is and what it isn't

It's about integrating individual clinical expertise and the best external evidence

BMJ VOLUME 312 13 JANUARY 1996

Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS.

"Externe klinische Evidenz führt zur Neubewertung bisher akzeptierter medizinischer Verfahren."

"Ärzte, die Kochbuchmedizin befürchten, werden mit den Advokaten der EBM auf den Barrikaden gehen."

"Die Evolution der EBM wird noch fortschreiten."

http://www.ebm-netzwerk.de/was-ist-ebm/leitartikel-sackett/
BMJ. 1996 Jan 13;312(7023):71-2.

Was ist überhaupt Evidenzbasierte Medizin?

Evidenz (lat. evidentia = Augenscheinlichkeit) bedeutet umgangssprachlich: Augenschein, Offenkundigkeit, völlige Klarheit. „Das ist doch evident" bedeutet somit, dass **etwas nicht weiter hinterfragt werden** muss.

Im Kontext der Evidenzbasierten Medizin hat der Begriff Evidenz eine völlig andere Bedeutung. Hier leitet er sich vom englischen Wort "evidence" (= Aussage, Zeugnis, Beweis, Ergebnis, Unterlage, Beleg) ab und bezieht sich auf die Informationen aus wissenschaftlichen Studien und systematisch zusammengetragenen klinischen Erfahrungen, die einen Sachverhalt erhärten oder widerlegen.

Evidenzbasierte Medizin (EbM = beweisgestützte Medizin) ist demnach der **gewissenhafte, ausdrückliche und vernünftige Gebrauch** der gegenwärtig besten externen, wissenschaftlichen Evidenz für Entscheidungen in der medizinischen Versorgung individueller Patienten.

http://www.ebm-netzwerk.de/was-ist-ebm/grundbegriffe/definitionen/

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Wie bewerte ich überhaupt Evidenz?
Der „Teufel" steckt wie so oft im Detail

WFSBP
Leitlinien
2013/14

Category of Evidence		Description
A		Full Evidence From Controlled Studies is based on: 2 or more double-blind, parallel-group, randomized controlled studies (RCTs) showing superiority to placebo (or in the case of psychotherapy studies, superiority to a "psychological placebo" in a study with adequate blinding) and 1 or more positive RCT showing superiority to or equivalent efficacy compared with established comparator treatment in a three-arm study with placebo control or in a well-powered non-inferiority trial (only required if such a standard treatment exists) In the case of existing negative studies (studies showing non-superiority to placebo or i nferiority to comparator treatment), these must be outweighed by at least 2 more positive studies or a meta-analysis of all available studies showing superiority to placebo and non-inferiority to an established comparator treatment. Studies must fulfil established methodological standards. The decision is based on the primary efficacy measure.
B		Limited Positive Evidence From Controlled Studies is based on: 1 or more RCTs showing superiority to placebo (or in the case of psychotherapy studies, superiority to a"psychological placebo") or a randomized controlled comparison with a standard treatment without placebo control with a sample size sufficient for a non-inferiority trial and no negative studies exist
C		Evidence from Uncontrolled Studies or Case Reports/Expert Opinion
	C1	Uncontrolled Studies. Evidence is based on: 1 or more positive naturalistic open studies (with a minimum of 5 evaluable patients) or a comparison with a reference drug with a sample size insufficient for a non-inferiority trial and no negative controlled studies exist
	C2	Case Reports. Evidence is based on: 1 or more positive case reports and no negative controlled studies exist
	C3	Evidence is based on the opinion of experts in the field or clinical experience
D		Inconsistent Results Positive RCTs are outweighed by an approximately equal number of negative studies
E		Negative Evidence The majority of RCTs studies or exploratory studies shows non-superiority to placebo (or in the case of psychotherapy studies, superiority to a "psychological placebo") or inferiority to comparator treatment
F		Lack of Evidence Adequate studies proving efficacy or non-efficacy are lacking.
Recommendation Grade		Based on
1		Category A evidence and good risk-benefit ratio
2		Category A evidence and moderate risk-benefit ratio
3		Category B evidence
4		Category C evidence
5		Category D evidence

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

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Was gibt es noch für Leitlinien…?

…nur eine kleine Auswahl…

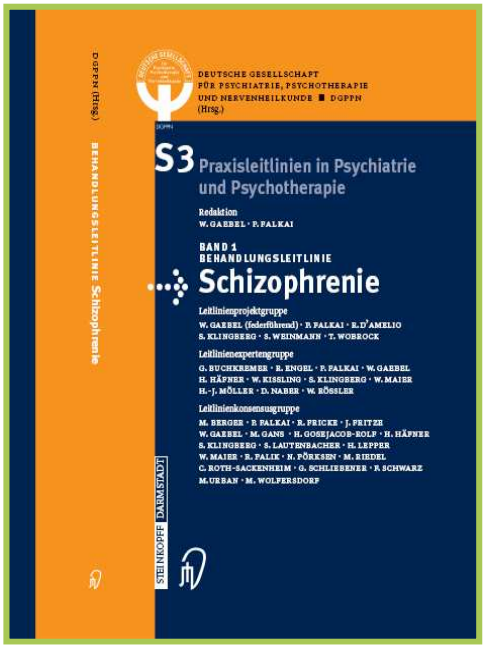
American Psychiatric Association Practice Guidelines

American Psychiatric Association (APA) practice guidelines provide evidence-based recommendations for the assessment and treatment of psychiatric disorders.

APA Steering Committee on Practice Guidelines | Statement of Intent | Copyright, Citation, and Disclaimer | Introduction

Practice Guideline for the Treatment of Patients With Schizophrenia Second Edition

GUIDELINE WATCH (SEPTEMBER 2009): PRACTICE GUIDELINE FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA



The Schizophrenia Patient Outcomes Research Team (PORT): Updated Treatment Recommendations 2009

Julie Kreyenbuhl[1–3], Robert W. Buchanan[4], Faith B. Dickerson[5], and Lisa B. Dixon[2,3]

Schizophrenia Bulletin vol. 36 no. 1 pp. 94–103, 2010
doi:10.1093/schbul/sbp130
Advance Access publication on December 2, 2009

NICE National Institute for Health and Care Excellence

Psychosis and schizophrenia in adults: treatment and management

Issued: February 2014 last modified: March 2014

NICE clinical guideline 178

guidance.nice.org.uk/cg178

Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders

Leitlinien im Vergleich

	DGPPN S3 (2006)	WFSBP (2012/13)	NICE (2009/12)	PORT (2010)	RANZCP (2005)	APA (2004)
Priorisierung der SGA	Ja	Nein	Nein	Nein	Ja	Ja
Phasenspezifische Behandlung	(Ja)	Ja	Ja	(Ja)	(Ja)	Ja
Separate Betrachtung primärer und sekundärer Negativsymptome	Ja	Ja	(Ja)	Nein	Nein	Ja
Behandlungsdauer Ersterkrankung	Mindestens 12 Monate	Mindestens 12 Monate	Nein	Nein	Mindestens 12 Monate	Mindestens 6 Monate
Behandlungsdauer Mehrfacherkrankung	2 bis 5 Jahre, ggf. lebenslang	2 bis 5 Jahre, ggf. lebenslang	Nein	Nein		Langfristige Behandlung
Intermittierende Behandlung	(Ja)	Nein	Nein	Nein	(Ja)	(Ja)
Clozapin-Behandlung bei Behandlungsresistenz	Ja	Ja	Ja	Ja	Ja	Ja
Clozapin >350 ng/ml bei Behandlungsresistenz	Nein	Ja	Ja	Ja	Nein	Nein
Psychosoziale Interventionen	Ja	Nein	Ja	Ja	Ja	Ja
Detaillierte evidenzbasierte Strategien zur Therapie von Nebenwirkungen	Ja	Ja	Nein	Ja	Nein	Ja

Hasan et al. 2013 Nov;84(11):1359-60

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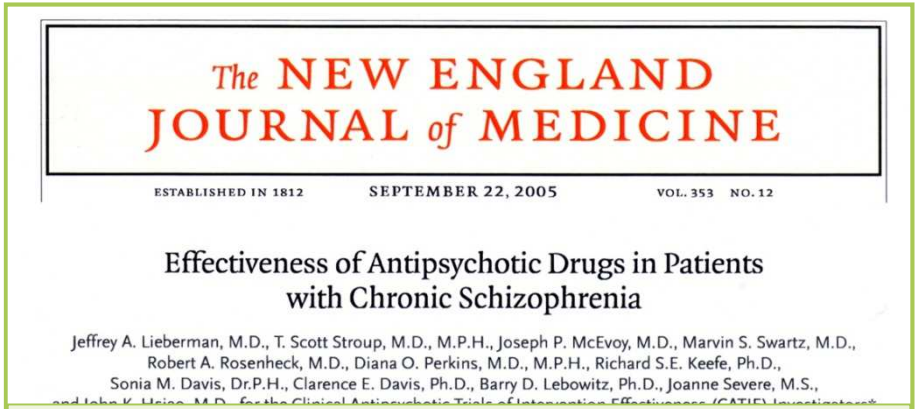
Antipsychotika – typisch oder atypisch?



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 22, 2005 VOL. 353 NO. 12

Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia

Jeffrey A. Lieberman, M.D., T. Scott Stroup, M.D., M.P.H., Joseph P. McEvoy, M.D., Marvin S. Swartz, M.D., Robert A. Rosenheck, M.D., Diana O. Perkins, M.D., M.P.H., Richard S.E. Keefe, Ph.D., Sonia M. Davis, Dr.P.H., Clarence E. Davis, Ph.D., Barry D. Lebowitz, Ph.D., Joanne Severe, M.S.,

Lieberman J et al. 2005: NEJM

Articles

Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial

René S Kahn*, W Wolfgang Fleischhacker*, Han Boter, Michael Davidson, Yvonne Vergouwe, Ireneus P M Keet, Mihai D Gheorghe, Janusz K Rybakowski, Silvana Galderisi, Jan Libiger, Martina Hummer, Sonia Dollfus, Juan J López-Ibor, Luchezar G Hranov, Wolfgang Gaebel, Joseph Peuskens, Nils Lindefors, Anita Riecher-Rössler, Diederick E Grobbee, for the EUFEST study group†

Summary

Background Second-generation antipsychotic drugs were introduced over a decade ago for the treatment of schizophrenia; however, their purported clinical effectiveness compared with first-generation antipsychotic drugs is still debated. We aimed to compare the effectiveness of second-generation antipsychotic drugs with that of a low dose

Lancet 2008; 371: 1085–97
See Comment page 1048
*These authors contributed

Kahn R et al. 2008: The Lancet

Randomized Controlled Trial of the Effect on Quality of Life of Second- vs First-Generation Antipsychotic Drugs in Schizophrenia

Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1)

Peter B. Jones, MD, PhD; Thomas R. E. Barnes, MD, DSc; Linda Davies, MSc; Graham Dunn, PhD; Helen Lloyd, BA; Karen P. Hayhurst, MSc; Robin M. Murray, MD, DSc; Alison Markwick, BA; Shôn W. Lewis, MD

Jones B et al. 2006: Arch Gen Psychiatry

Effectiveness and Cost of Olanzapine and Haloperidol in the Treatment of Schizophrenia

A Randomized Controlled Trial

Rosenheck R et al. 2003: JAMA

Ersterkrankung
Empfehlungen für die antipsychotische Behandlung

Recommendation Table I. Recommendations for the antipsychotic treatment of first-episode schizophrenia patients.

Antipsychotic agent	Category of evidence[a]	Recommendation[b]
Olanzapine	A	1
Quetiapine	A	1
Risperidone	A	1
Clozapine[1]	A	2
Haloperidol	A	2
Amisulpride	B	2
Aripiprazole	B	2
Ziprasidone	B	2
Asenapine[2]	F	–
Iloperidone[2]	F	–
Paliperidone[2]	F	–
Lurasidone[2]	F	–
Sertindole[2]	F	–
Zotepine[2]	F	–

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Mehrfacherkrankung / Relapse

Empfehlungen für die antipsychotische Behandlung

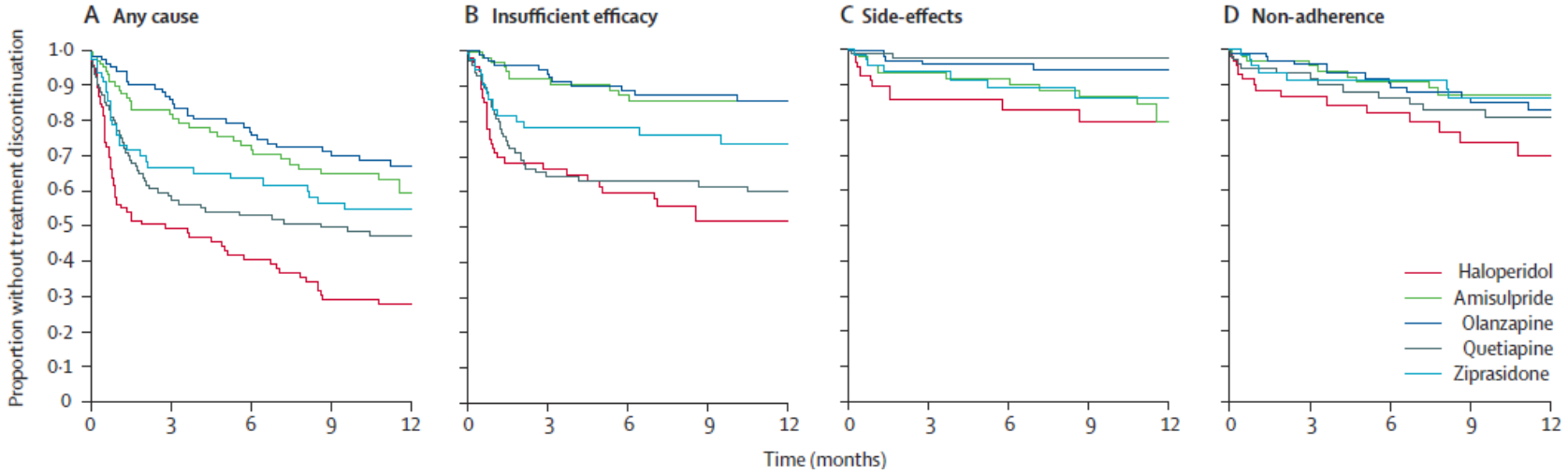
Recommendation Table II. Recommendations for the antipsychotic treatment of multi-episode patients (acute relapse).

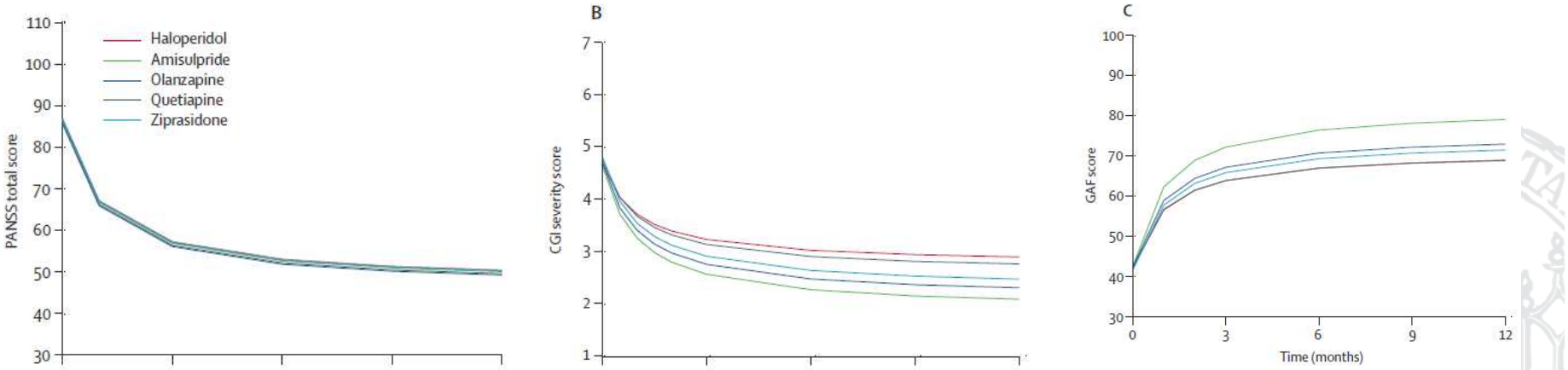
Antipsychotic agent	Category of evidence[a]	Recommendation[b]
Amisulpride	A	1
Asenapine[1]	A	1/2
Aripiprazole	A	1
Clozapine[2]	A	1/2
Haloperidol	A	2
Iloperidone[1]	A	1/2
Olanzapine	A	1
Paliperidone[1]	A	1/2
Quetiapine	A	1
Risperidone	A	1
Sertindole[1,3]	A	1/2
Ziprasidone	A	1
Lurasidone	B	3
Zotepine	B	3

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

EUFEST - Eine der wesentlichen Studien, die eine Änderungen der Empfehlungen bedingt haben





Kahn et al., 2008, Lancet. 29;371(9618):1085-97

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Was bedeutet diese Ergebnisse konkret?

- Die Unterschiede in der Wirksamkeit sind viel kleiner als die Unterschiede in der Verträglichkeit.

- "Taken together, we agree with the investigators [Leucht et al. 2013] that their findings support the idea that each antipsychotic drug needs to be assessed on the basis of its **individual risk-to benefit profile** and that **generalising classifications into first-generation and second-generation antipsychoticss mostly not useful**" (Correl & De Hert, 2013, The Lancet)

- Dieser Gedanke wurde bereits in den 2012 und 2013 publizierten WFSBP Leitlinien für die biologische Behandlung der Schizophrenien konkretisiert.

Augmentation & Behandlungsdauer

Augementationsstrategien
aus den WFSBP Leitlinien 2012 & 2013

Recommendation Table IV. Recommendations for the augmentation of antipsychotic treatment.

Augmentation strategy	Category of evidence[a]	Recommendation[b]	Application for
Carbamazepine add on	E	–	Treatment-resistant schizophrenia
Lamotrigine ad on	D	5	Treatment-resistant schizophrenia
Lamotrigine + Clozapine	B	3	Treatment-resistant schizophrenia
Lithium add on	D/E	–	Treatment-resistant schizophrenia
Lithium add on	B	3	In patients with mood symptoms
Pregabalin add on	C2	4	Treatment-resistant anxiety
Topiramate add on	D	5	Treatment-resistant schizophrenia
Topiramate add on	B	3	Reducing weight gain[1]
Valproate	E	–	Treatment-resistant schizophrenia
Valproate	D	5	Targeting aggression and hostility

[a]Category of evidence: Category of evidence where A = full evidence from controlled studies (see Table I). [b]Safety rating = recommendation grade derived from categories of evidence and additional aspects of safety, tolerability, and interaction potential (see Table I). [1]See part 2 of these guidelines.

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

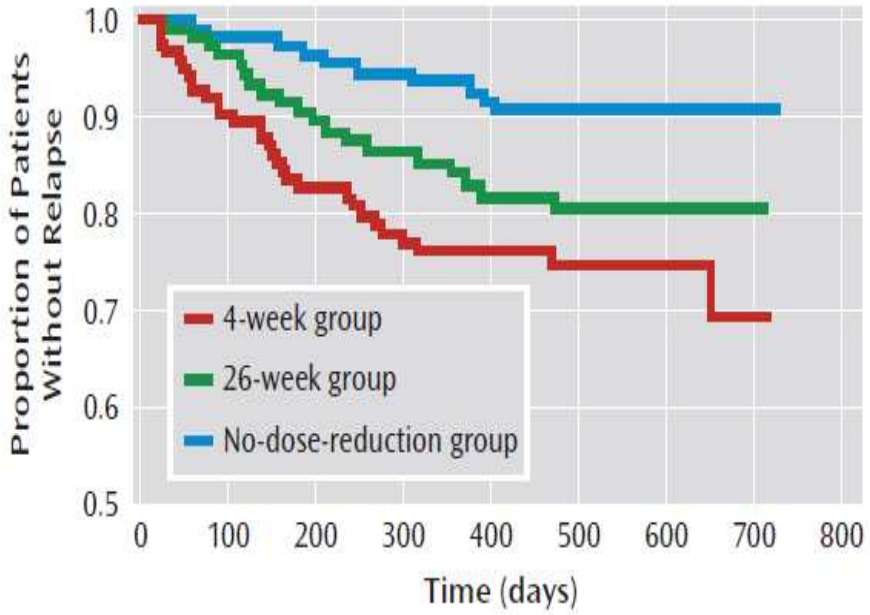
http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

In der Akutbehandlung – ab wann reduzieren?

4-week Group:
Risperidon Dosis wurde nach 4 Wochen halbiert.

26-week Group:
Risperidon Dosis wurde nach 26 Wochen halbiert.

Rispierdon-Dosis vor Reduktion war zwischen 4 und 8 mg/d



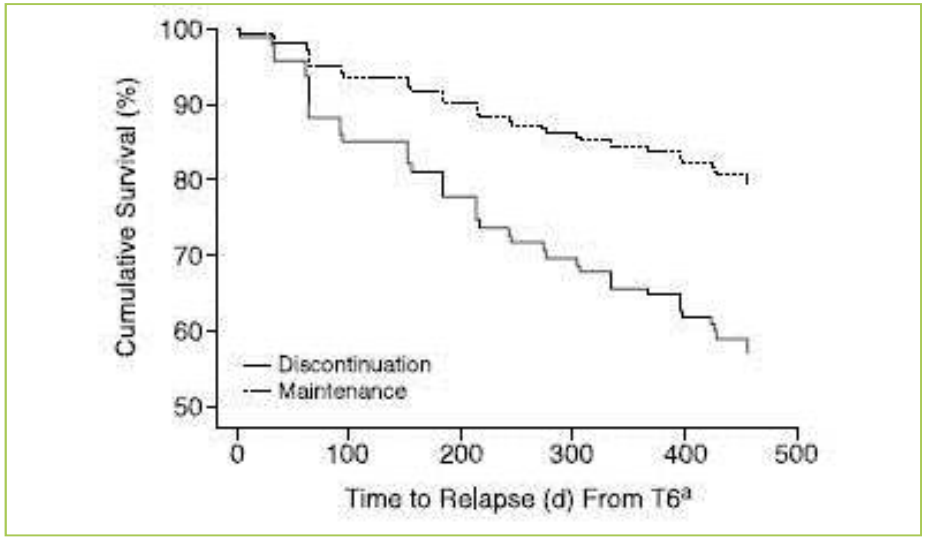
Number at risk								
4-week group	125	111	91	84	68	37	29	5
26-week group	120	104	87	81	65	44	23	3
No-dose-reduction group	129	124	107	99	83	59	30	5
Number with relapse								
4-week group	0	12	21	27	28	29	29	30
26-week group	0	6	12	15	18	19	19	19
No-dose-reduction group	0	2	4	6	9	10	10	10

Wang CY et al. 2010: Am J Psychiatry 167(6):676-85

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

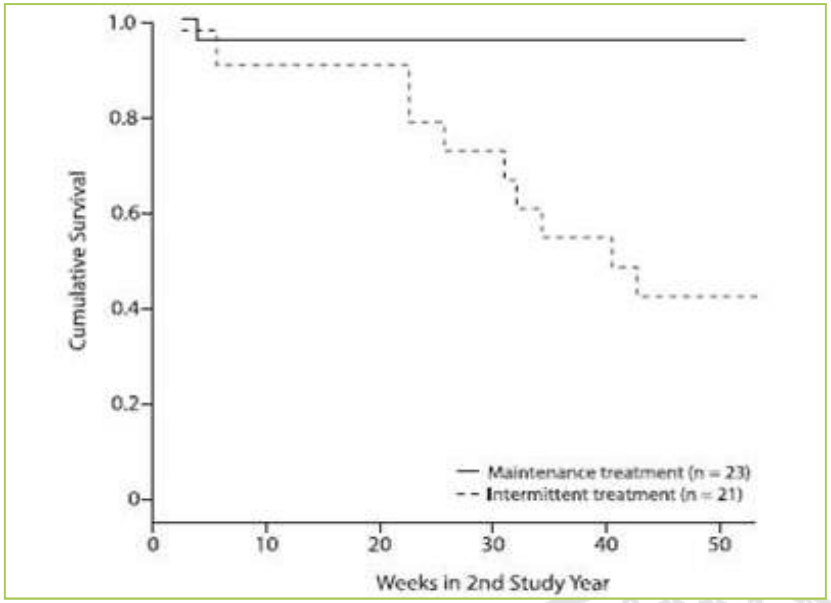
Langzeitbehandlung - Intensität

Relapse rates for discontiuation stategies versus maintenance treatment (survival function)



Wunderink L et al. 2007: J Clin Psychiatry 68(5):654-61

Survival Analysis for clinical deterioration for patients recieving maintenance antipsychotic versus intermittent treatment



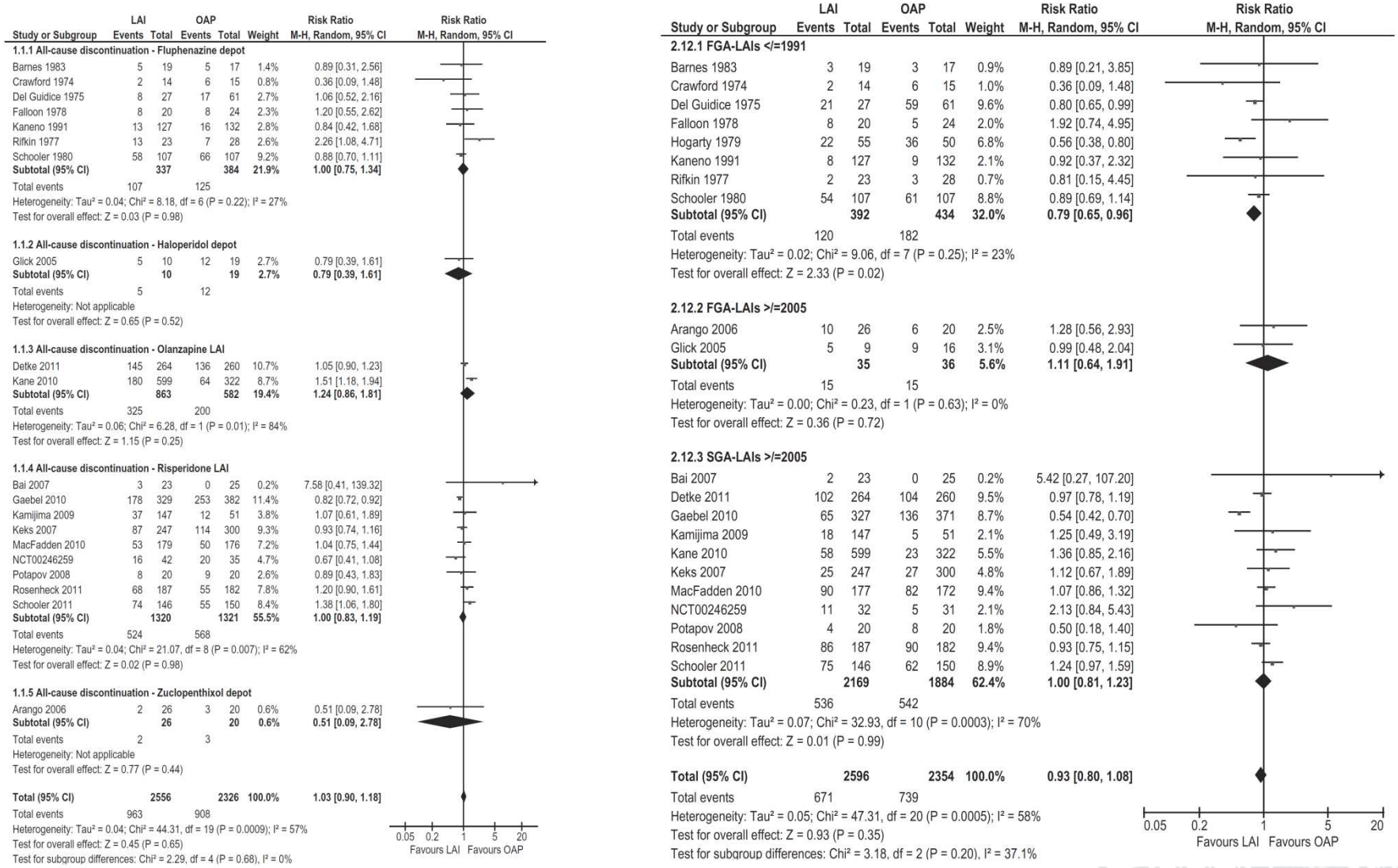
Gaebel W et al. 2010: J Clin Psychiatry 72(2):205-18

- Immer durchgehende Therapie (continuous treatment)!
- Kein intermittent treatment (außer bei Ausnahmen)!

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Depot (long-acting injectables) – neue Mirror-Studien Mataanalyse



All-cause discontinuation (safety/efficacy population).

Kishimoto et al. 2013, Schiz Bulletin 40, 192 – 213

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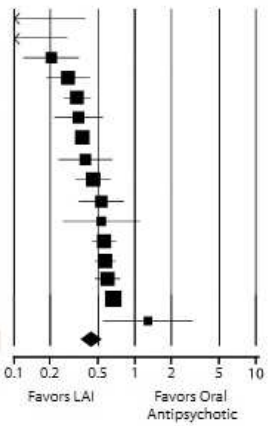
Depot (long-acting injectables) – – neue Mirror-Studien Mataanalyse

Figure 2. Hospitalization Risk

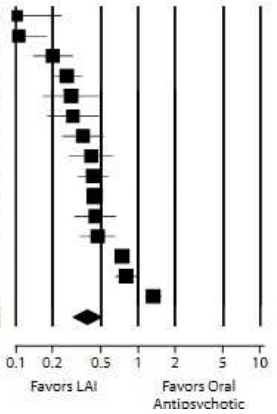
Study	Risk Ratio	Lower Limit	Upper Limit	*Z* Value	*P* Value
Girardi et al, 2010[22]	0.024	0.001	0.397	−2.609	.0091
Beauclair et al, 2005[26]	0.092	0.030	0.282	−4.166	.0000
Arató and Erdős, 1979[32]	0.204	0.119	0.350	−5.761	.0000
Devito et al, 1978[33]	0.281	0.183	0.430	−5.844	.0000
Denham and Adamson, 1971[39]	0.333	0.254	0.438	−7.884	.0000
Morritt, 1974[37]	0.343	0.214	0.550	−4.440	.0000
Lam et al, 2009[24]	0.369	0.327	0.415	−16.569	.0000
Lindholm, 1975[35]	0.391	0.232	0.660	−3.515	.0004
Peng et al, 2011[20]	0.452	0.321	0.636	−4.554	.0000
Gottfries and Green, 1974[36]	0.529	0.341	0.822	−2.831	.0046
Rosa et al, 2012[17]	0.529	0.251	1.116	−1.672	.0944
Chang et al, 2012[16]	0.557	0.437	0.711	−4.697	.0000
Johnson and Freeman, 1972[38]	0.570	0.461	0.704	−5.203	.0000
Crivera et al, 2011[18]	0.597	0.463	0.768	−4.003	.0001
Ren et al, 2011[19]	0.663	0.611	0.720	−9.746	.0000
Svestka et al, 1984[28]	1.286	0.541	3.056	0.569	.5694
	0.430	0.350	0.527	−8.074	.0000



Abbreviation: LAI = long-acting injectable.

Figure 3. Number of Hospitalizations

Study	Rate Ratio	Lower Limit	Upper Limit	*Z* Value	*P* Value
Beauclair et al, 2005[26]	0.103	0.044	0.239	−5.298	.0000
Arató and Erdős, 1979[32]	0.106	0.062	0.182	−8.140	.0000
Waldmann and Neumann, 1984[29]	0.201	0.137	0.296	−8.143	.0000
Denham and Adamson, 1971[39]	0.262	0.192	0.357	−8.437	.0000
Morritt, 1974[37]	0.283	0.165	0.485	−4.590	.0000
Malm, 1971[40]	0.294	0.179	0.484	−4.811	.0000
Devito et al, 1978[33]	0.355	0.239	0.528	−5.113	.0000
Polonowita and James, 1976[34]	0.414	0.269	0.639	−3.990	.0001
Chang et al, 2012[16]	0.430	0.318	0.580	−5.519	.0000
Carswell et al, 2010[21]	0.441	0.381	0.511	−10.983	.0000
Lindholm, 1975[35]	0.447	0.299	0.670	−3.899	.0001
Peng et al, 2011[20]	0.469	0.331	0.666	−4.232	.0000
Ren et al, 2011[19]	0.742	0.682	0.808	−6.898	.0000
Tan et al, 1981[31]	0.800	0.641	0.999	−1.968	.0491
Bourin et al, 1998[27]	1.333	1.125	1.579	3.326	.0009
	0.381	0.283	0.512	−6.397	.0000



Kishimoto et al. 2013, Journal of Clinical Psychiatry 74:10

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Behandlungsresistenz

„Behandlungsresistenz“

Treatment-resistant schizophrenia can be defined as a situation in which a significant improvement of psychopathology and/or other target symptoms has not been demonstrated despite treatment with two different antipsychotics from at least two different chemical classes (at least one should be an atypical antipsychotic) in the previous five years at the recommended antipsychotic dosages for a treatment period of at least 2–8 weeks per drug (Kane et al. 1988a; Lehman et al. 2004; McIlwain et al. 2011; NICE 2002; 2010).

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

„Behandlungsresistenz“

- In cases of treatment-resistant schizophrenia treatment adherence needs to be controlled
- A switch from an initially unsuccessful FGA to another FGA seems to be ineffective (*Category of Evidence A, Recommendation grade 1*) and a switch to an SGA should instead be taken into consideration (*Category of Evidence B, Recommendation grade 3*)
- In individuals with a diagnosed treatment-resistant schizophrenia according to recent definitions, clozapine should be considered as first-line treatment (*Category of Evidence B, Recommendation grade 3*)
- Dependent on the national regulations, patients treated with clozapine should be monitored frequently with regard to haematological side effects/EEG-alterations/cardiac side effects, and a dosage range of 100–900 mg or a blood level of more than 350 ng/ml should be aimed for (*Category of Evidence B/C3, Recommendation grades 3/4*) (Buchanan et al. 2010; Falkai et al. 2005)
- In cases of clozapine intolerance a switch to another SGA, preferentially olanzapine or risperidone, should be performed (*Category of Evidence B, Recommendation grade 3*)
- There are few data to support amisulpride, aripiprazole and quetiapine being effective in monotherapy for the management of treatment-resistant schizophrenia (*Category of Evidence C, Recommendation grade 4*)
- There is no evidence for the efficacy of asenapine, iloperidone, lurasidone and paliperidone in the treatment of these patients (*Category of Evidence F*)
- Dose escalation, unless side effects lead to an earlier drug switching, was previously recommended by an expert consensus statement (Kane et al. 2003), but recent studies do not support this statement (see above)
- Apart from these treatment strategies, special psychotherapeutic (especially cognitive behavioural therapy) and psychosocial interventions to enhance the therapeutic alliance (e.g., adherence therapy, psychoeducation and family interventions) and the usage of long-acting depot antipsychotics should be taken into consideration

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

„Behandlungsresistenz“

- In cases of treatment-resistant schizophrenia treatment adherence needs to be controlled
- A switch from an initially unsuccessful FGA to another FGA seems to be ineffective (*Category of Evidence A, Recommendation grade 1*) and a switch to an SGA should instead be taken into consideration (*Category of Evidence B, Recommendation grade 3*)
- In individuals with a diagnosed treatment-resistant schizophrenia according to recent definitions, clozapine should be considered as first-line treatment (*Category of Evidence B, Recommendation grade 3*)
- Dependent on the national regulations, patients treated with clozapine should be monitored frequently with regard to haematological side effects/EEG-alterations/cardiac side effects, and a dosage range of 100–900 mg or a blood level of more than 350 ng/ml should be aimed for (*Category of Evidence B/C3, Recommendation grades 3/4*) (Buchanan et al. 2010; Falkai et al. 2005)
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Aber in Deutschland, wie in fast ganz Europa wird lieber kombiniert (2, 3, 4 fach Kombinationen), als auf Clozapin umzustellen

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

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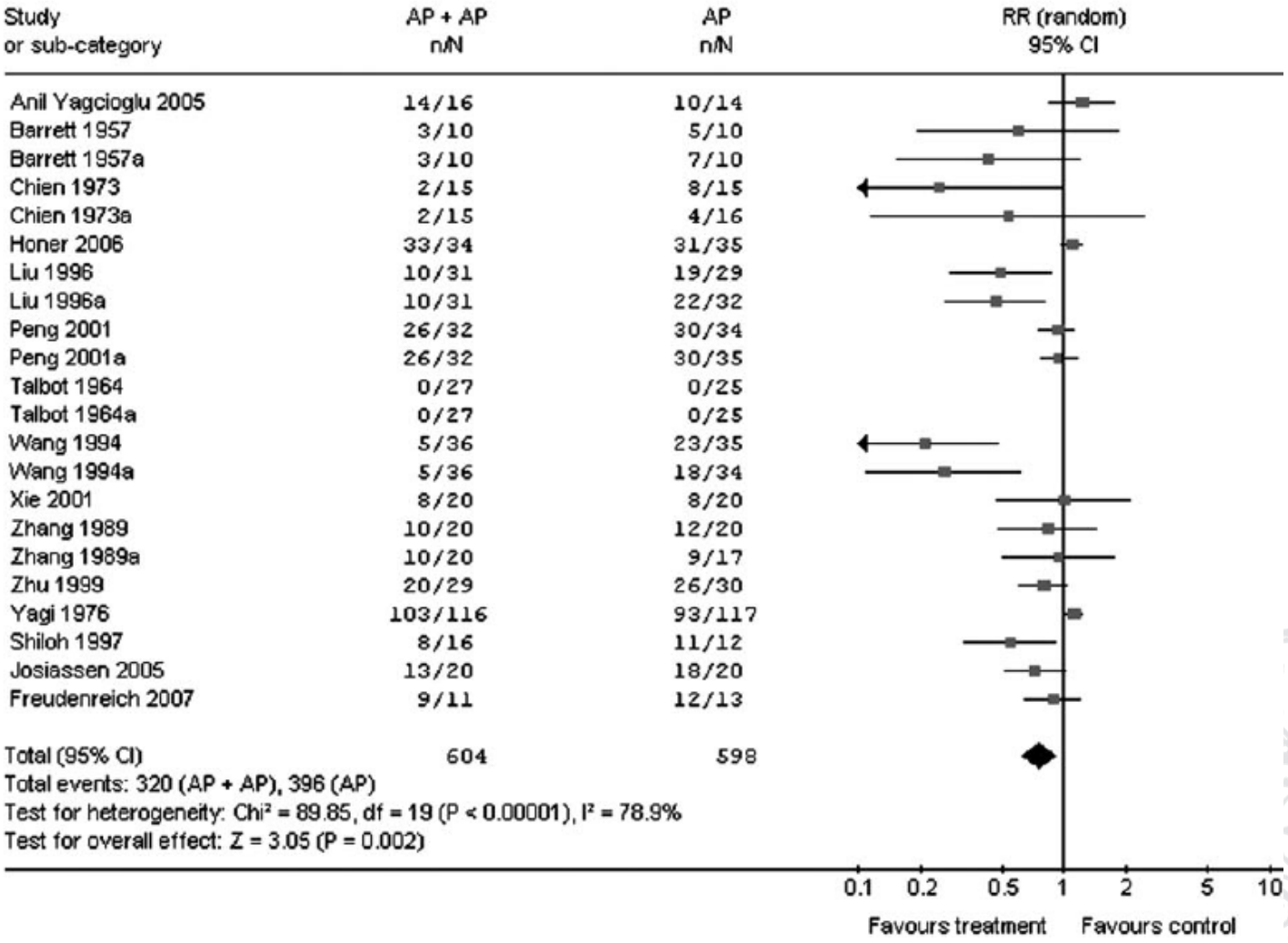
- Apart from these treatment strategies, special psychotherapeutic (especially cognitive behavioural therapy) and psychosocial interventions to enhance the therapeutic alliance (e.g., adherence therapy, psychoeducation and family interventions) and the usage of long-acting depot antipsychotics should be taken into consideration

Spiegelkontrollen: 350 ng/ml

Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Kombinationsbehandlungen



Correll et al. 2008, Schiz Bull

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Kombinationsbehandlungen

There is still only limited evidence for the efficacy of combining different antipsychotics in treatment-resistant schizophrenia. An important question is whether to add one antipsychotic to an ongoing treatment or to lower the dosage of the first antipsychotic agent when combining with another agent.

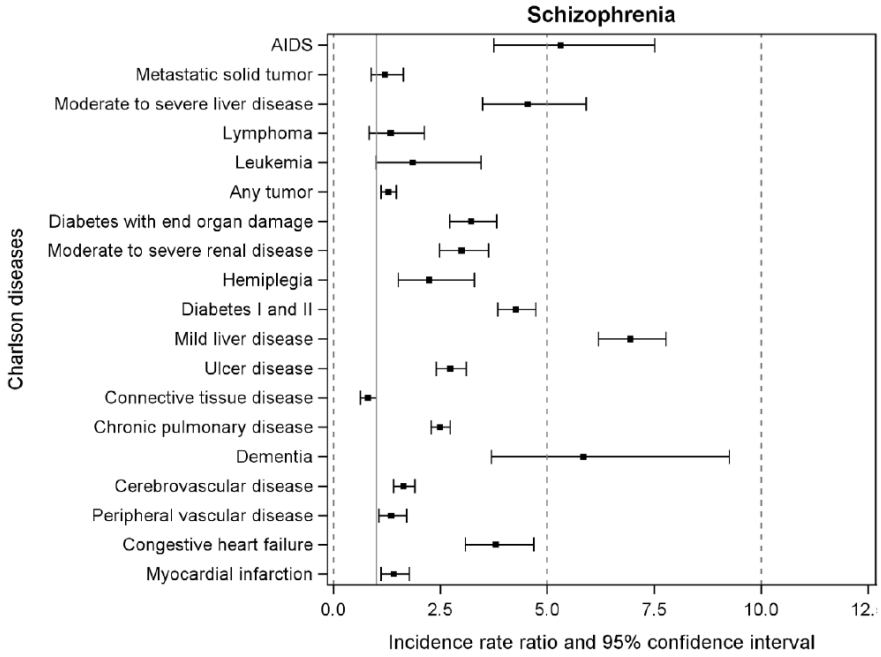
- The combination of clozapine with another SGA (possibly risperidone) might have some advantage compared to monotherapy *(Category of Evidence C, Recommendation grade 4)*
- Antipsychotic monotherapy should be the preferential treatment strategy and, in cases of treatment-resistant schizophrenia, the recommendations set out in our and other guidelines for the management of this disease state should be followed *(Category of Evidence C3, Recommendation grade 4)*
- In certain individual cases an antipsychotic combination therapy might be advisable *(Category of Evidence C3, Recommendation grade 4)* and, in these cases, side effects and clinical responses should be monitored at frequent intervals *(Category of Evidence C3, Recommendation grade 4)*

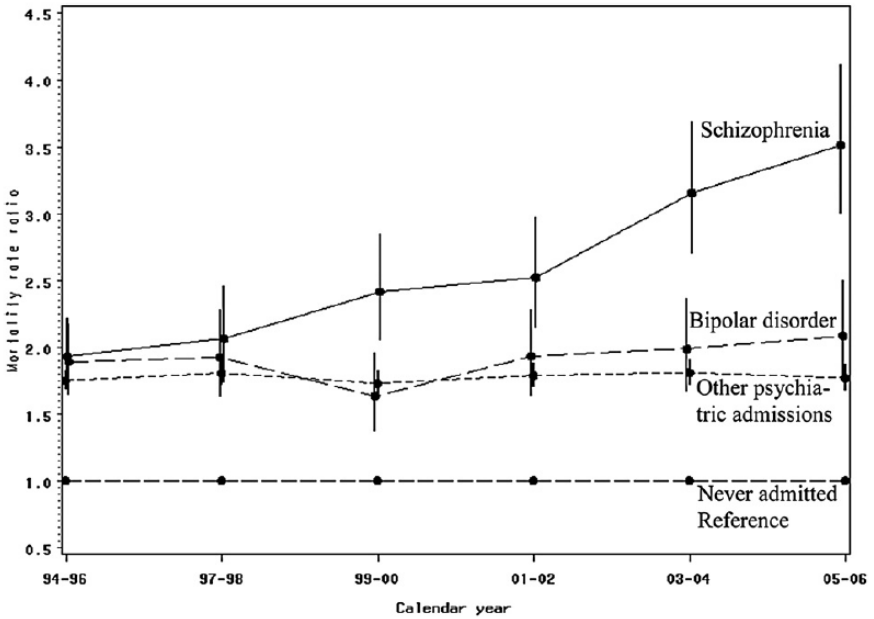
Hasan A et al. 2012: World J Biol Psychiatry; 13: 318-78

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Somatische Komorbidität und Nebenwirkungsmanagment

Somatische Komorbidität





Psychiatrie ist eine moderne medizinische Fachdisziplin und die Beobachtung, dass in vielen Ländern Psychiater „ihre weißen Kittel ausgezogen [...] und vergessen haben, dass Sie Ärzte sind" (47), muss als besorgniserregende Entwicklung gewertet werden. In der Weiterbildung und im klinischen Alltag muss auch den somatischen Befunden Rechnung getragen werden, um in Zukunft die hohe Mortalität dieser schweren Erkrankung zu reduzieren und die Lebensqualität der Betroffenen zu verbessern. Es gibt international

Munk-Larsen et al. 2011 a/b, Hasan et al. 2012
Sartorius et al. 2007

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Was bringen Behandlungsleitlinien für die Versorgungsrealität ?

Effekt von Leitlinien auf Behandlungsqualität – Ergebnisse einer Multicenter-Studie (I)

Eur Arch Psychiatry Clin Neurosci (2010) 260:51–57
DOI 10.1007/s00406-009-0016-2

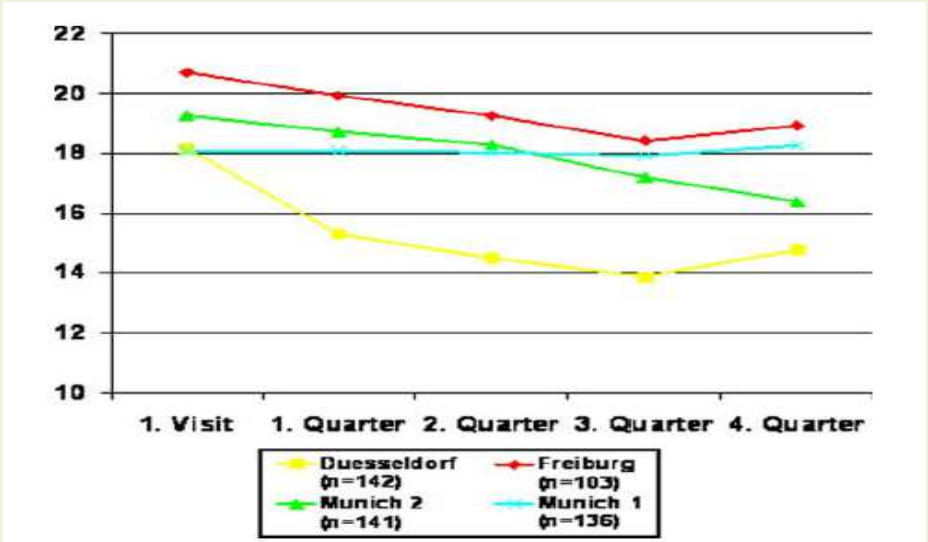
ORIGINAL PAPER

Improving outpatient treatment in schizophrenia: effects of computerized guideline implementation—results of a multicenter-study within the German Research Network on Schizophrenia

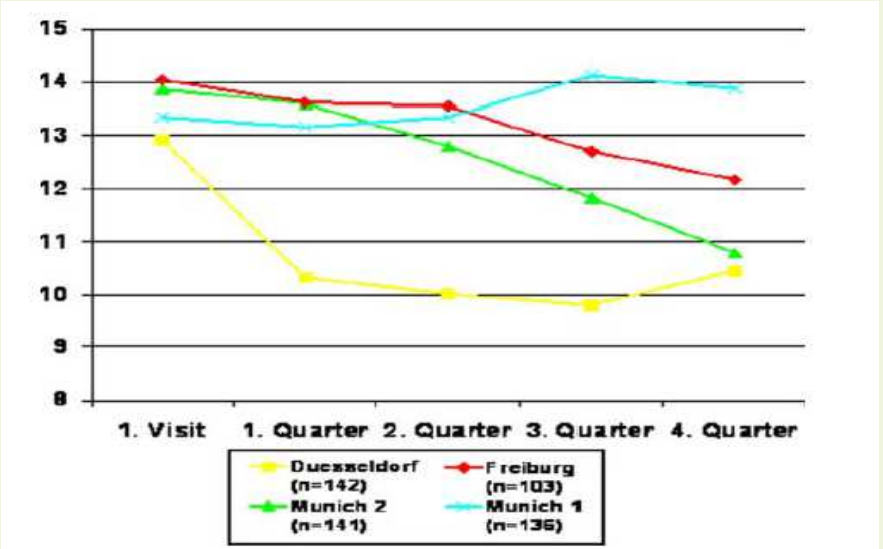
B. Janssen · S. Ludwig · H. Eustermann · R. Menke · M. Haerter · M. Berger · G. Adam · U. Seemann · W. Kissling · W. Gaebel

As a result of the intervention, we observed a strong initial but time-limited improvement with respect to the core aspects of outpatient treatment in schizophrenia in the experimental group

Symptom course in the first treatment year (n=323)
PANSS Negative score



Symptom course in the first treatment year (n=323)
PANSS Positive score



Janssen B et al. 2010: Eur Arch Clin Neurosci; 260: 51-7

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Effekt von Leitlinien auf Behandlungsqualität – Ergebnisse einer Multicenter-Studie (II)

Therapeutic measures prescribed by treating physician at least once in the time between T0 and T4 (in % of patients)

	Psychotherapy	Psychoeducation	Social services	Family Counseling
Duesseldorf	52.5	33.6	1.0	5.4
Freiburg	43.7	10.3	14.9	5.7
Munich 2	6.9	11.5	7.3	3.6
Munich 1	6.9	7.2	11.9	4.1
Chi-square	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P = 0.815$

Good or satisfying medication and appointment adherence at T0 and at T4 (%) rated by treating physician on six-ary compliance scale

	Medication adherence		Appointment adherence	
	1. Quarter	4. Quarter	1. Quarter	4. Quarter
Duesseldorf ($N = 138$)	62.3	68.8	59.3	68.5
Freiburg ($N = 102$)	63.7	71.1	62.1	77.4
Munich 1 ($N = 124$)	87.1	87.6	73.6	76.9
Munich 2 ($N = 136$)	92.6	93.1	83.2	88.3
ANOVA	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P = 0.003$

Janssen B et al. 2010: Eur Arch Clin Neurosci; 260: 51-7

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Implementierung einer Schizophrenie-Leitlinie: klinische Ergebnisse

Implementation of a Schizophrenia Practice Guideline: Clinical Results

Stefan Weinmann, M.D., Dr.P.H.; Susanne Hoerger; Monika Erath; Reinhold Kilian, Dr.P.H.; Wolfgang Gaebel, M.D.; and Thomas Becker, M.D.

After guideline implementation, monotherapy at discharge increased from 39.5% to 67.6% (p = .021) and the incidence of significant neurologic side effects decreased from 26.3% to 7.0% (p = .038)

Guideline adherence by treatment group: Before (pre) and after (post) guideline implementations, N(%)

Guideline Recommendation/Management Principle	Pre (N = 76)	Post (N = 71)	Exp (B)[a]	p Value[b]
Antipsychotic monotherapy in the first week after admission	27 (35.5)	46 (64.8)	0.289	.029
Antipsychotic monotherapy at discharge	30 (39.5)	48 (67.6)	0.266	.021
Atypical antipsychotic monotherapy at discharge	25 (32.9)	39 (54.9)	0.416	.117
Antipsychotic dosage not above recommendation in the first week after admission	57 (75.0)	58 (81.7)	0.780	.718
Antipsychotic dosage not above recommendation at discharge	59 (77.6)	61 (85.9)	0.451	.341
Antipsychotic dosage within recommended range at discharge	46 (60.5)	52 (73.2)	0.591	.357
Adequate therapy of significant depressive symptoms	5 (35.7)[c]	7 (46.7)[d]	0.594	.667
Adequate therapy of significant persistent psychotic symptoms	8 (44.4)[e]	7 (46.7)[f]	0.814	.795
Significant neurological side effects of more than 1 week duration	20 (26.3)	5 (7.0)	0.368	.038
Adequate therapy of significant neurological side effects	11 (55.0)	4 (80.0)	0.547	.313

[a]Exp (B) represents the regression coefficient in the propensity score model equaling the odds ratio of being in the preintervention versus postintervention group.
[b]The p value is given for the propensity score model with baseline total Positive and Negative Syndrome Scale score as covariate.
[c]N = 14 patients with significant depressive symptoms.
[d]N = 15 patients with significant depressive symptoms.
[e]N = 18 patients with significant persistent psychotic symptoms.
[f]N = 15 patients with significant persistent psychotic symptoms.

Weinmann S et al. 2008: J Clin Psychiatry; 69(8): 1299-1306

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Adhärenz zu Leitlinien und Outcome

International Journal for Quality in Health Care 2000; Volume 12, Number 6: pp. 475–482

Performance measurement for schizophrenia: adherence to guidelines for antipsychotic dose

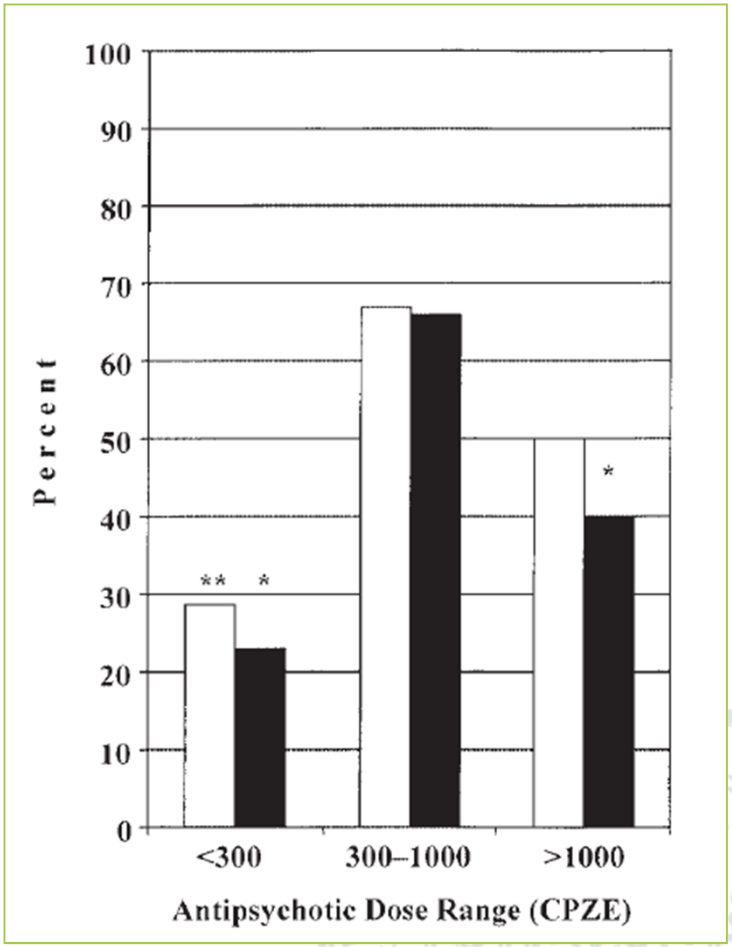
RICHARD R. OWEN[1,2], CAROL R. THRUSH[1,2], JOANN E. KIRCHNER[1,2], ELLEN P. FISCHER[1,2] AND BRENDA M. BOOTH[1,2]

[1]HSR & D Center for Mental Healthcare and Outcomes Research (CeMHOR), Central Arkansas Veterans Healthcare System, and [2]The Centers for Mental Healthcare Research, Department of Psychiatry and Behavioral Sciences, University of Arkansas for Medical Sciences, Little Rock, AR, USA

For the entire sample, linear regression models showed that the performance measure variable was not significantly associated with follow-up symptom severity (BPRS total scores).

Patients prescribed recommended doses had lower adjusted mean BPRS totals than patients prescribed doses either greater than ($P < 0.05$) or less than ($P < 0.05$) recommended

BPRS total score <36 at 6-month follow-up



Entire sample
Oral AP only

Owen PR et al. 2000: Int J Qual Health Care; 12(6): 475-82

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Charakteristika der einbezogenen Studien im Hinblick auf das Verlaufsergebnis

Table 1. Characteristics of included studies addressing process outcomes

Study	Study design	Sample size	Diagnosis	Guideline	Implementation strategy	Process outcome	Positive effect of the implementation strategy as interpreted by the authors
Baandrup *et al.* [7]	Cluster RCT	Pre: 583; Post: 602	Schizophrenia, psychosis	Clinical guidelines with emphasis on reducing/avoiding antipsychotic polypharmacy	Multifaceted educational intervention: educational material, educational outreach visits, reminders, educational meetings	Rates of polypharmacy	No
Baker *et al.* [12]	Before and after study	35	Diagnosis of induded patients is not reported	Clinical practice manual based on the work of the Medical Research Council that established PRN prescribing and administration habits of psychotropic medication, with the aim of improving clinical practice	Educational material, reminder (explicitly agreement of staff to use the manual, which was reiterated by a letter in the manual), quotes from staff and patients, clinical examples, summaries of the previously collected data, a comprehensive bibliography, an outline of the research project	Guideline adherence	No
Chong *et al.* [8]	Before and after study (incl. historical controls)	Pre: 68; Post: 438	First episode psychosis, schizophrenia	Evidence-based treatment algorithm with emphasis on reduction of antipsychotic polypharmacy	Unclear	Rates of polypharmacy	Yes
Mistler *et al.* [9]	Before and after study (incl. historical controls)	Pre: 12; Post: 12	Schizophrenia, psychosis, depression, bipolar disorder	Evidence-based treatment algorithm to optimize single drug regimens and to eliminate redundant medications, based on principles of collaborative care	Unclear	Rate of polypharmacy	Yes
Osborn *et al.* [13]	Cluster RCT	121	Psychosis, schizophrenia, bipolar disorder	Authors refer to the NICE recommendations of routine screening for cardiovascular risk factors for people with severe mental illness	Nurse-led intervention: reminders, educational material, nurse as coordinator	Guideline adherence	Yes
Owen *et al.* [14]	Cluster RCT	349	Schizophrenia	Authors refer to schizophrenia guidelines (not specified)	Practical patient-tailored strategy: educational material, educational meetings, patient interview (adherence barrier assessment and development of patient-tailored strategies to overcome these barriers)	Guideline adherence	No
Sorensen *et al.* [15]	Before and after study	Pre: 104; Post: 96	Schizophrenia, depression	Evidence-based treatment algorithms to standardize pharmacological treatment	Reminders, educational meetings	Guideline adherence	Yes
Weinmann *et al.* [10]	Before and after study	151	Schizophrenia, psychosis	Pharmacological part of the German evidence-based schizophrenia guideline	Educational material, conferences/ courses, audit and feedback, quality circle	Rate of polypharmacy	Yes
Thompson *et al.* [11]	Cluster RCT	Pre: 474; Post: 480	'All diagnosis' (no information available)	Guideline on antipsychotic polypharmacy based on evidence-based sources, induding NICE	Multifaceted intervention: educational material, educational outreach visits, reminders	Rate of polypharmacy	Yes

NICE, National Institute for Clinical Excellence; Post, after guideline implementation; Pre, before guideline implementation; PRN, pro re nata; RCT, randomized controlled trial.

Girlanda F et al. 2013: Curr Op Psychiatry; 28: 369-75

http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/index.html

Charakteristika der einbezogenen Studien im Hinblick auf das Patientenergebnis

Table 2. Characteristics of included studies addressing patient outcomes

Study	Study design	Sample size	Diagnosis	Guideline	Implementation strategy	Patient Outcome	Positive effect of the Implementation strategy as interpreted by the authors
Bauer *et al.* [17]	RCT	330	Bipolar disorder	Evidence-based Veterans Affairs clinical practice guidelines	Collaborative Care Model: educational material, educational meetings, nurse as coordinator, patient education	Number of weeks in any episode	Yes
Bauer *et al.* [18]	RCT	148	Depression, Bipolar disorder	Treatment algorithm to standardize pharmacological treatment	Unclear	Time to remission	Yes
Hudson *et al.* [19]	Cluster RCT	349	Schizophrenia	Authors refer to schizophrenia guidelines (not specified)	Practical patient-tailored strategy: educational material, educational meetings, Patient interview (adherence barrier assessment and development of patient-tailored strategies to overcome these barriers)	Treatment adherence	Yes
Yoshino *et al.* [20]	CCT	240	Depression	Treatment algorithm to standardize pharmacological treatment	Unclear	Remission rates	Yes

CCT, controlled clinical trial; RCT, randomized controlled trial.

Girlanda F et al. 2013: Curr Op Psychiatry; 28: 369-75

Zusammenfassung der Ergebnisse des Vergleichs (1)

Active education + Support for implementation compared with Routine care or Passive dissemination for participants with schizophrenia and related psychosis

Patient or population: participants with schizophrenia and related psychosis
Settings: specialist mental health care
Intervention: Active education + Support for implementation
Comparison: Routine care or Passive dissemination

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Routine care or Passive dissemination	Active education + Support for implementation				
Polypharmacy at follow-up	441 per 1,000	428 per 1,000 (331 to 552)	RR 0.97 (0.75 to 1.25)	310 (two studies)	⊕○○○ very low[1,2]	
Not screened for cardiovascular risk factors	895 per 1,000	635 per 1,000 (429 to 922)	RR 0.71 (0.48 to 1.03)	38 (one study)	⊕○○○ very low[1,3]	
Global state-PANSS total score		Mean global state-PANSS total score-design effect corrected in the intervention groups was **01.30 lower** (10.52 lower to 7.92 higher)		59 (one study)	⊕○○○ very low[4,5]	
Satisfaction with care-ZUF8		Mean satisfaction with care-ZUF8-design effect corrected in the intervention groups was **0.10 higher** (1.96 lower to 2.16 higher)		46 (one study)	⊕○○○ very low[4,5]	

Barbui C et al 2014: Cochrane Database Syst Rev; 1: CD009780

Zusammenfassung der Ergebnisse des Vergleichs (2)

Lack of treatment adherence-design effect corrected	**385 per 1,000**	**346 per 1,000** (169 to 712)	**RR 0.90** (0.44 to 1.85)	52 (one study)	⊕○○○ **very low**[5,6]	
Drug attitude-DAI		Mean drug attitude-DAI-design effect corrected in the intervention groups was **1.40 lower** (3.38 lower to 0.58 higher)		32 (one study)	⊕○○○ **very low**[4,5]	
Quality of life		Mean quality of life-design effect corrected in the intervention groups was **0 higher** (0 to 0 higher)	Not estimable	0 (0)	See comment	No trial reported this outcome

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Risk of bias: rated-'very serious'-Randomisation and allocation poorly described.
[2]Imprecision: rated-'serious'-Only two studies with a pooled treatment estimate ranging from substantial beneficial effect to substantial harmful effect.
[3]Imprecision: rated-'serious'-Only one study with few cases and events.
[4]Risk of bias: rated-'serious'-Groups were not well balanced in terms of length of hospitalisation and psychopathology ratings.
[5]Imprecision: rated-'very serious'-Only one study with few cases.
[6]Risk of bias: rated-'serious'-Groups were not well balanced in terms of ethnic groups and psychopathology ratings.

Barbui C et al 2014: Cochrane Database Syst Rev; 1: CD009780

Domänen der Behandlungsqualität

Strukturen	Prozesse	Ergebnisse
Charakteristika des Arztes/Therapeuten Charakteristika der Einrichtungen/der Gebäude/ der Versorgungsstrukturen Charakteristika der Finanzierung von Leistungen Ausbildungsregelungen Gesetzliche Rahmenbedingungen	Interpersonale Prozesse: •Kommunikationsprozesse und -stile •Entscheidungsfindung •Arten der Zusammenarbeit Behandlungsprozesse: •Prävention •Erkennung von Erkrankungen •Diagnostik •Zugang zu Behandlung •Einzelne Behandlungs-verfahren, Compliance •Koordination •Kontinuität der Behandlung •Sicherheit	Symptome Funktionsniveau Lebensqualität Unerwünschte Wirkungen Zufriedenheit Kosten-Effektivität

Weinmann S et al. 2008: Die Psychiatrie; 5: 266-74

Wie sind die Indikatoren zusammengesetzt und entwickelt?

Ein typischer Indikator setzt sich zusammen aus dem Nenner, d.h. der Zielpopulation, auf die der Indikator angewendet wird, und dem Zähler, d.h. der Anzahl oder dem Anteil der Betroffenen aus der Zielpopulation, die bestimmtes Kriterium erfüllen:

$$\frac{\text{Zahl der Patienten, die im Rahmen eines intensiven Case-Managements betreut werden}}{\text{Zahl der Patienten im Alter von 18-65 Jahren mit einer Schizophrenie und einer komorbiden Suchterkrankung während des Zeitraums eines Jahres}} \times 100 = \ \%$$

Weinmann S et al. 2008: Die Psychiatrie; 5: 266-74

Welchen Kriterien sollten Qualitätsindikatoren genügen?

Kriterien der Validität	Kriterien der Machbarkeit
1. Unterstützung durch ausreichende wissenschaftliche Evidenz oder ausreichenden professionellen Konsens	1. Die notwendigen Informationen sind hochwahrscheinlich in einer typischen Kranken-akte aufzufinden
2. Patienten erfahren erkennbaren gesundheit-lichen Nutzen	2. Schätzungen der Ausprägung eines Qualitätsindikators auf der Basis von Krankenaktendaten sind hochwahrscheinlich reliabel und unverzerrt
3. Großteil der Faktoren stehen unter Kontrolle oder Einfluss der Leistungserbringer	3. Das Fehlen der Dokumentation relevanter Daten zum Qualitäts-indikator ist selbst ein Zeichen für schlechte Qualität

Wobrock T et al. 2010: Die Psychiatrie; 7: 179-89

Zusammenfassung

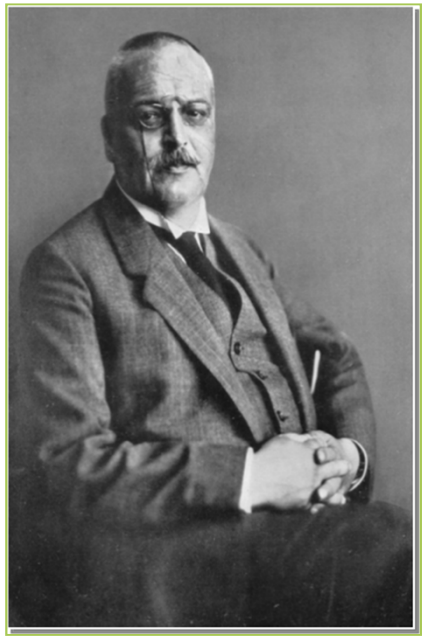
Leitlinien sollen eine Unterstützung darstellen, um mit der Fülle an publizierter Literatur zu neuen Entwicklungen in der Behandlung Schritt zu halten.

Sie sollten eine gute Basis für eine individuelle Therapieentscheidung in der Praxis ermöglichen.

Die Implementierung von Leitlinien in die Behandlungsrealität ist lange Zeit nicht adäquat vorangetrieben worden.

Trotzdem konnten in den letzten Jahren meßbare Fortschritte erzielt werden, die weiter ausgebaut werden müssen und im aktuellen Cochrane Review sehr kritisch bewerten werden.

Die Entwicklung von Qualitätsindikatoren stellen eine gute Möglichkeit dar einen optimalen Behandlungskorridor zu definieren.



Vielen Dank für Ihre Aufmerksamkeit