Update Depression (2018-2020)

Dr. med. Christian Imboden

Update-Veranstaltung BBgD
12. November 2020

PRIVATKLINIK WYSS
SEIT 1845

Changes in the global burden of depression from 1990 to 2017: Findings from the Global Burden of Disease study

Qingqing Liu[a,b,1], Hairong He[a,1], Jin Yang[a,b], Xiaojie Feng[a,b], Fanfan Zhao[a,b], Jun Lyu[a,b,*]

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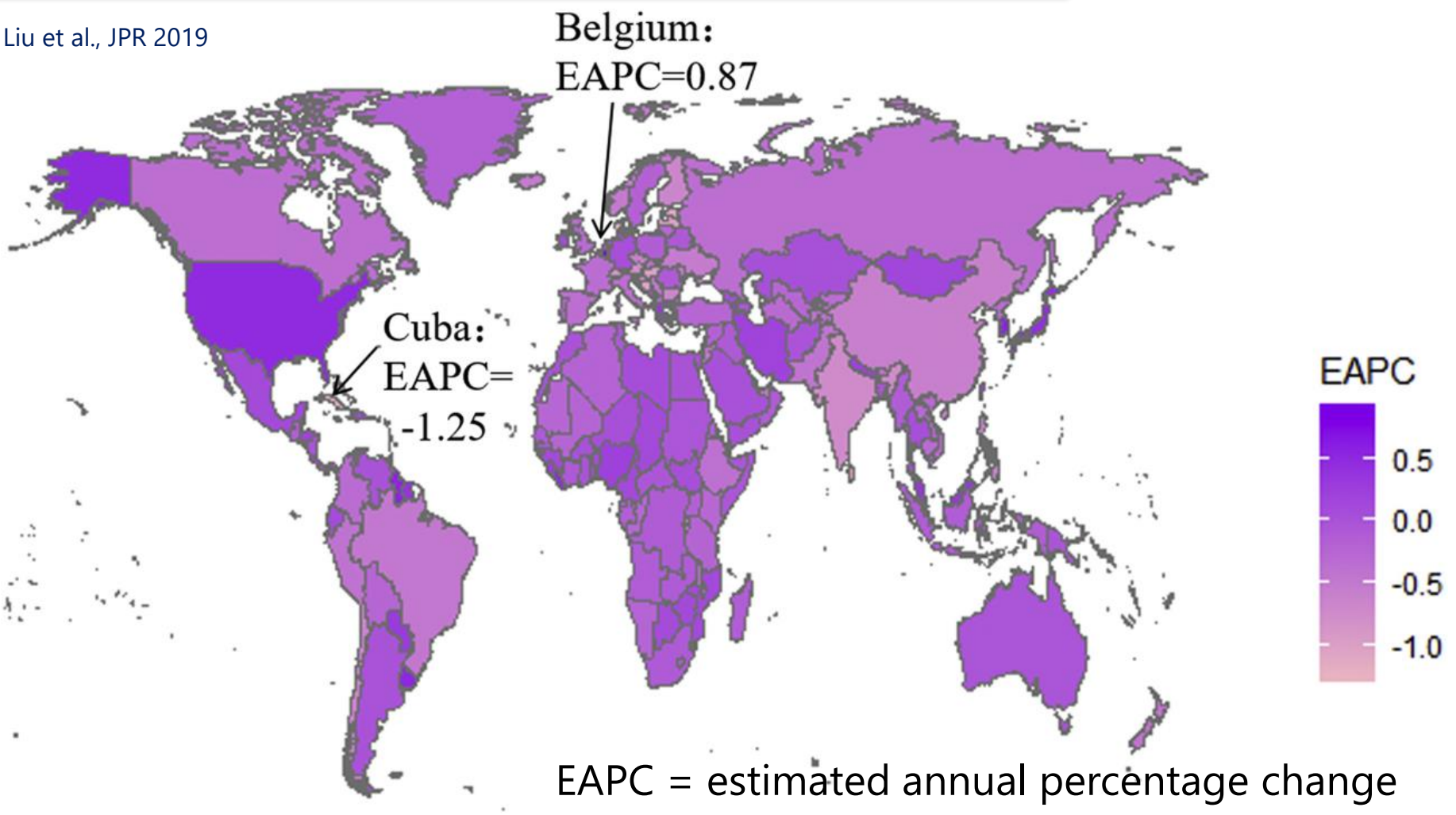
[b] School of Public Health, Xi'an Jiaotong University Health Science Center, Xi'an, Shaanxi, China

Liu et al., JPR 2019



EAPC = estimated annual percentage change

Liu et al., JPR 2019

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Wichtigste Studien 2018 - 2020

1. Pharmakologische Therapien
2. Nicht-pharmakologische Therapien
3. Sport & Depression
4. Depression und Demenz

Antidepressiva

Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis

Andrea Cipriani, Toshi A Furukawa, Georgia Salanti*, Anna Chaimani, Lauren Z Atkinson, Yusuke Ogawa, Stefan Leucht, Henricus G Ruhe, Erick H Turner, Julian P T Higgins, Matthias Egger, Nozomi Takeshima, Yu Hayasaka, Hissei Imai, Kiyomi Shinohara, Aran Tajika, John P A Ioannidis, John R Geddes*

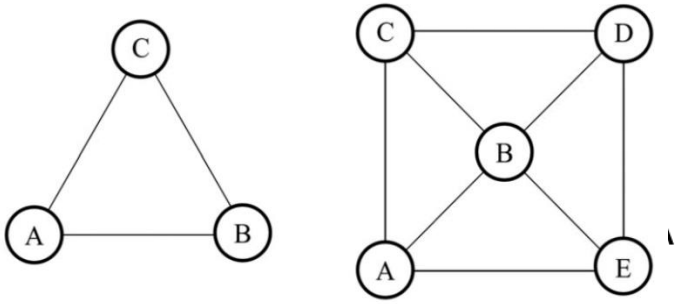
Lancet 2018

BMJ Open 2019

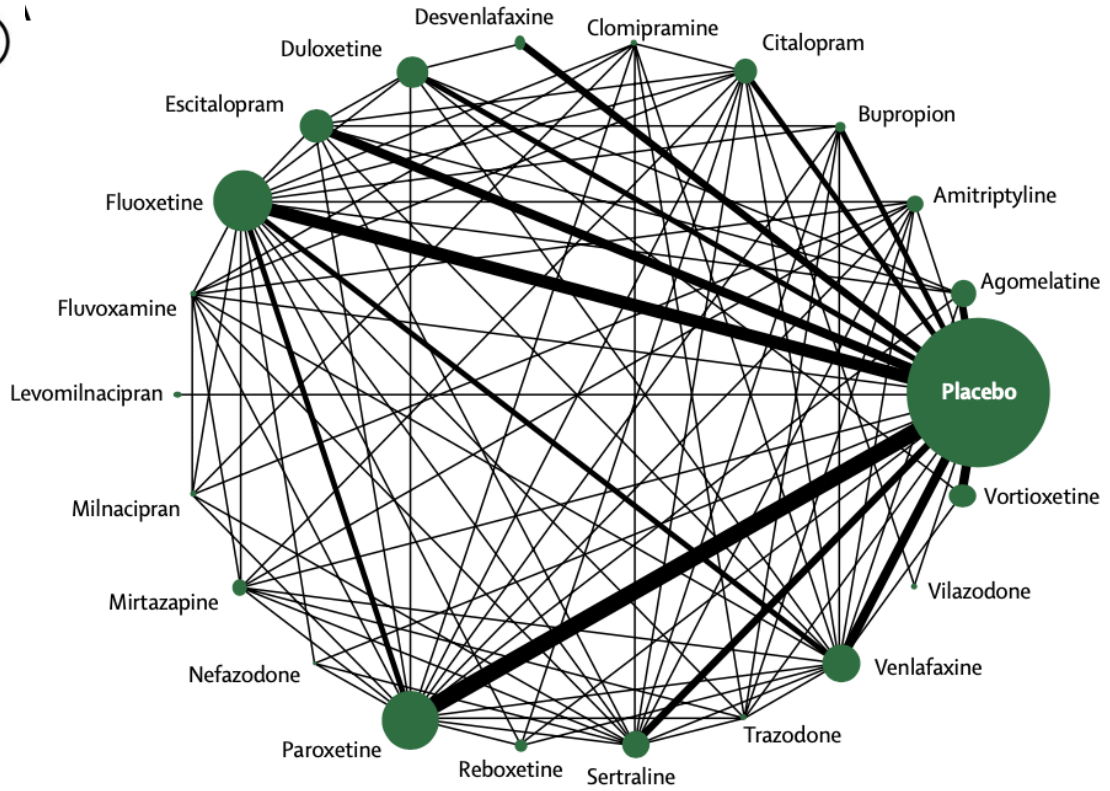
Considering the methodological limitations in the evidence base of antidepressants for depression: a reanalysis of a network meta-analysis

Klaus Munkholm, Asger Sand Paludan-Müller, Kim Boesen

Cipriani-Studie 2018 – Netzwerk-Metaanalyse



Efthimiou et al. 2016



Cipriani et al., Lancet 2018

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Cipriani-Studie 2018 – Netzwerk-Metaanalyse

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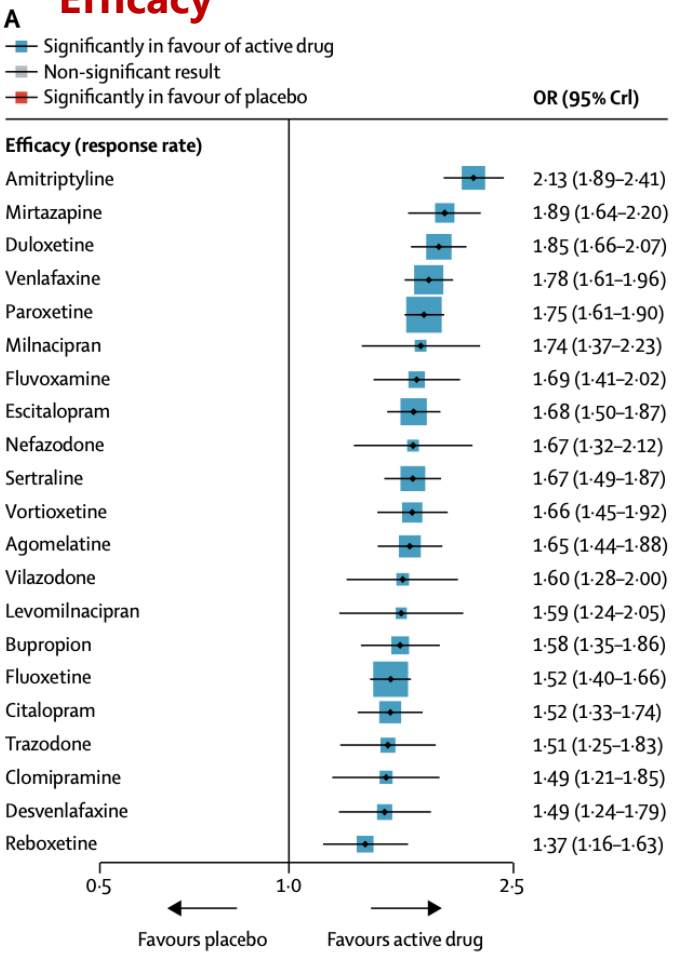
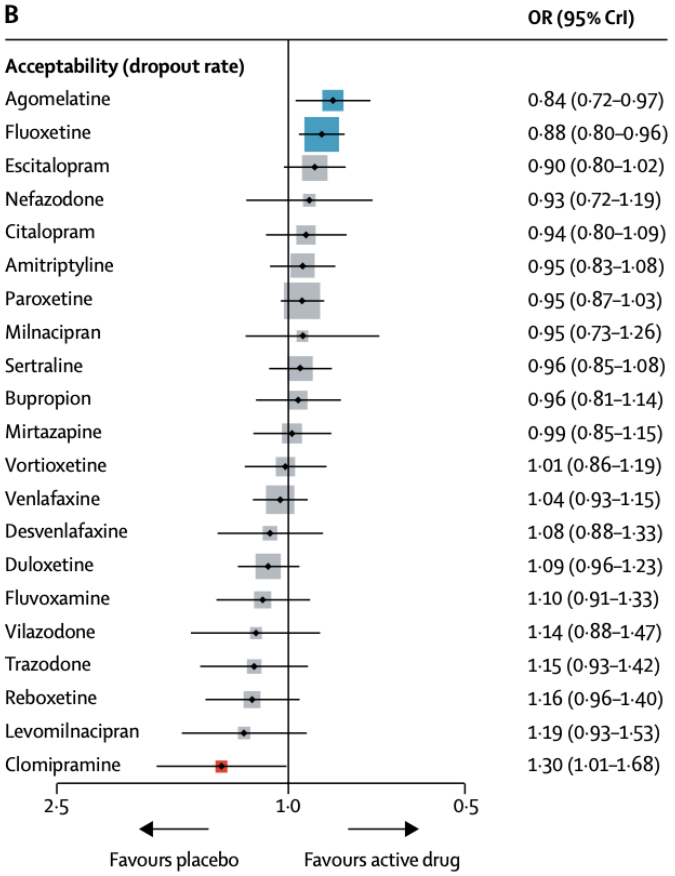
Efficacy



Acceptability (Discontinuation)



«The random-effects summary SMD for all antidepressants was 0.30 (95% CI 0.26–0.34; p<0·0001»

Cipriani et al., Lancet 2018

Munkholm et al: Reanalyse Cipriani-Daten

Cochrane Handbook's risk of bias tool and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) → Risk of bias

- **«Placebo-run-in»** von 1 Woche → höhere Efektstärke (P=0.05):
  - Pat. In Placebo-Gruppe mit initialer Verbesserung (PLC-responders) werden ausgeschlossen
  - Absetzphänomen↑ bei Umstellung AD → PLC → Dropouts ↑
  - Pat. Die früher (ohne UAW) ein AD hatten und in Studie auch AD haben bessere Wahrscheinlichkeit, dieses zu tolerieren.
- **Effektstärke in publizierten Studien höher** als in unpublizierten ($p<0.0001$)

- → Deutlich konservativere Beurteilung der Evidenzstärke
- → **Tiefere Effektivität von AD vs. PLC: Durchschnittlich 1.97 Punkte (Hamilton)**

Munkholm et al., BMJ Open 2019

Munkholm et al: Klinische Relevanz Cipriani-Daten

- Minimal clinically relevant difference (MCID) vs. Signifikanz
- Vorgeschlagen seien 7 Punkte im Hamilton → SMD von ≥0.875
  - Leucht et al. (2013): Kliniker können Unterschiede von ≤ 3 Punkten auf dem Hamilton nicht wahrnehmen
  - **Cipriani: SMD 0.3 für AD**

"The evidence does not support definitive conclusions regarding the benefits of antidepressants for depression in adults. ***It is unclear whether antidepressants are more efficacious than placebo****."*

Schlussfolgerungen:
- Daten von Cipriani et al. (2018) müssen kritisch gesehen werden
- Wirksamkeit von AD sei nicht klar (benefits and harms) → Führe dazu, dass andere Wirksame Therapien zu wenig angewendet würden.
- *Anforderungen an Studien über Wirksamkeit von AD:* Industrieunabhänig, in grossen Populationen ohne AD-Erfahrung, über längere Zeit, Mit Patienten-relevanten Endpunkten (keine Skalen)

Munkholm et al., BMJ Open 2019

Kritik an Munkholm et al. (2019)

- Hauptziel von Cipriani et al. (2018) war nicht Wirksamkeit von AD generell, sondern Vergleich verschiedener AD → Andere Methodik gewählt

- Frage ob AD generell Wirksam sind sollte eher auf der Ebene der einzelnen Wirkstoffe beurteilt werden → weniger Heterogeneität

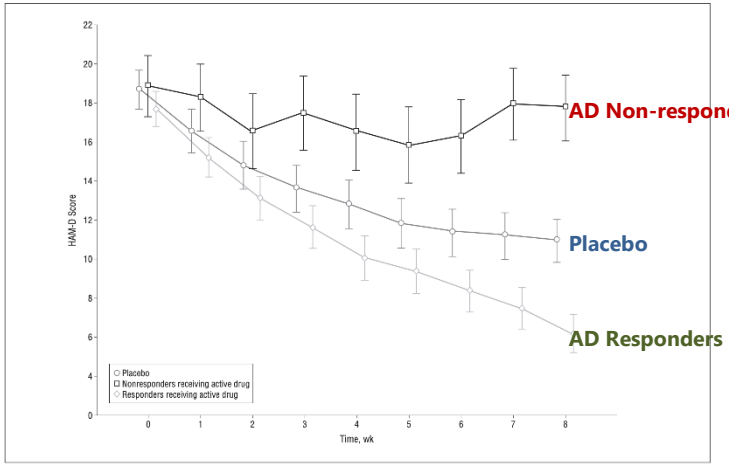
- Bei den 1.97 Punkten Verbesserung im Hamilton sind alle Patienten abgebildet, auch diejenigen, die nicht auf ein AD angesprochen haben → Verzerrung zu Ungunsten der Wirkung bei Patienten die ansprechen
  - Responders vs. Non-responders
  - Ansprechen auf erste Behandlung bei knapp 40% (Warden et al., STAR*D 2007)

- Ausgewählte Studienpopulation (Vorschlag Munkholm: AD-naive patienten) versus „Real-life evidence“ beispielsweise aus der STAR*D Studie.

Individual Differences in Response to Antidepressants
A Meta-analysis of Placebo-Controlled Randomized Clinical Trials

Marta M. Maslej, PhD; Toshiaki A. Furukawa, MD, PhD; Andrea Cipriani, MD, PhD; Paul W. Andrews, PhD, JD; Benoit H. Mulsant, MD, MS, FRCPC

- Varianz → bei heterogener Antwort auf eine Medikation höher
- **Grössere (systematische) interindividuelle Unterschiede → Höhere Varianz**
  - Ein Teil der Probanden spricht gut an, ein Teil wenig bis gar nicht
  - Heterogenität der behandelten Erkrankung



Guerguieva et al., Arch Gen Psychiatry 2011

Maslej et al., JAMA Psych 2020

Individual Differences in Response to Antidepressants
A Meta-analysis of Placebo-Controlled Randomized Clinical Trials

Marta M. Maslej, PhD; Toshiaki A. Furukawa, MD, PhD; Andrea Cipriani, MD, PhD; Paul W. Andrews, PhD, JD; Benoit H. Mulsant, MD, MS, FRCPC

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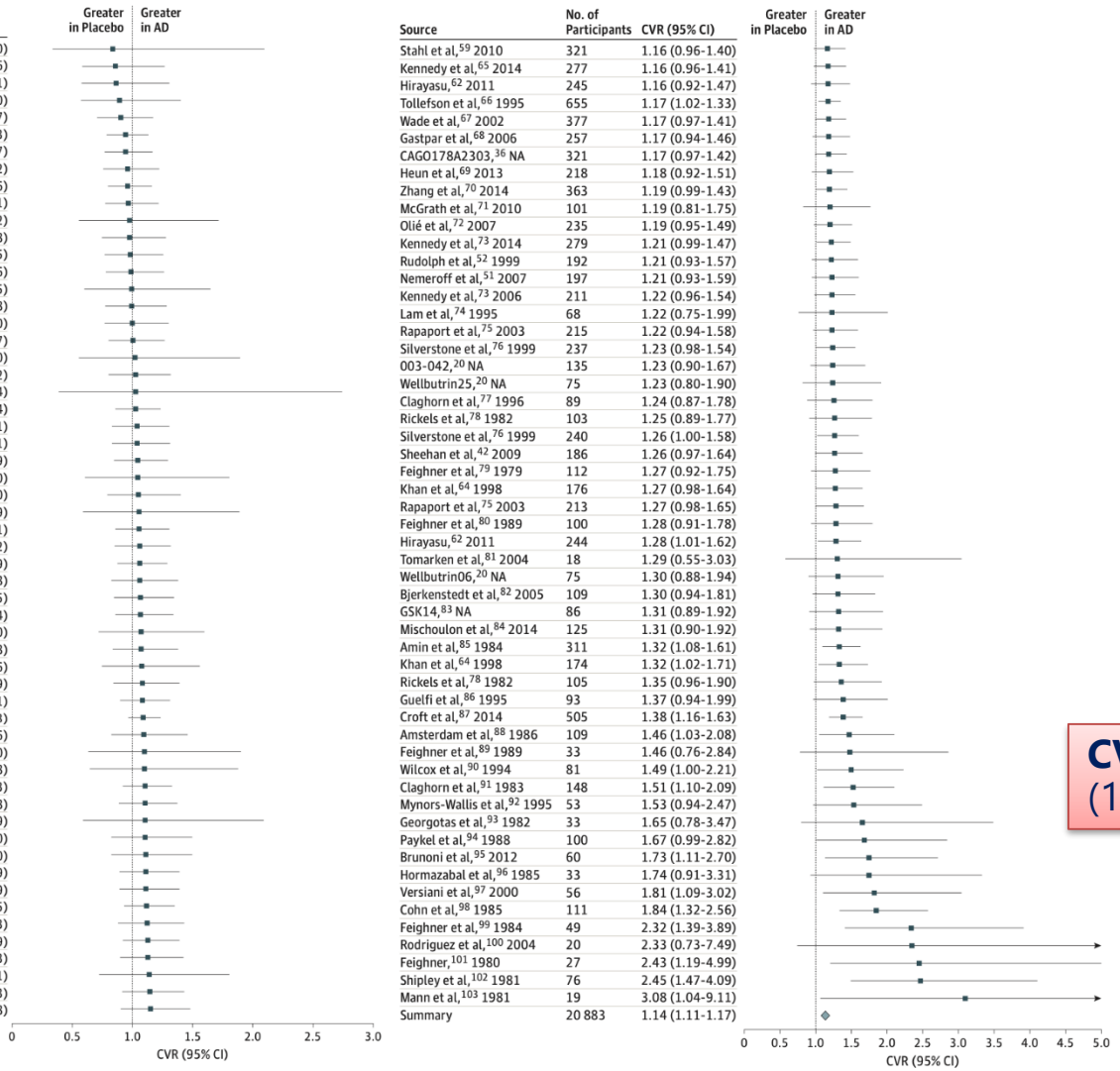
CVR = Coefficient of variation ratios → Höhere Varianz in AD → grössere Unterschiede zwischen Probanden die profitieren und solchen, die nicht profitieren als bei PLC-Antwort

Source	No. of Participants	CVR (95% CI)
MIR84064,[20] NA	30	0.84 (0.33-2.10)
Barber et al,[33] 2011	105	0.86 (0.58-1.26)
Wellbutrin 25,[20] NA	73	0.87 (0.58-1.31)
Study 032a,[34] NA	47	0.90 (0.57-1.40)
Schatzberg et al,[35] 2006	195	0.91 (0.70-1.17)
CAGO178A2303,[36] NA	320	0.94 (0.78-1.13)
CL3-20098-024,[37] NA	304	0.94 (0.77-1.17)
PZ/111,[38] NA	213	0.96 (0.76-1.22)
Zajecka et al,[39] 2010	323	0.96 (0.80-1.16)
FDA248,[40] NA	260	0.97 (0.77-1.21)
WELL029,[20] NA	39	0.98 (0.56-1.72)
003-048,[20] NA	238	0.98 (0.75-1.28)
Sheehan et al,[42] 2009	194	0.98 (0.77-1.25)
PZ/111,[38] NA	211	0.99 (0.78-1.26)
Norton et al,[43] 1984	58	1.00 (0.60-1.65)
PZ/109,[38] NA	207	1.00 (0.78-1.28)
Schatzberg et al,[35] 2006	189	1.00 (0.77-1.30)
FDA246,[40] NA	248	1.01 (0.80-1.27)
Moreno et al,[44] 2005	46	1.03 (0.55-1.90)
Roffman et al,[45] 1982	188	1.03 (0.80-1.32)
MIR84062,[20] NA	30	1.03 (0.39-2.74)
CL3-20098-024,[37] NA	453	1.03 (0.86-1.24)
FDA246,[40] NA	249	1.04 (0.83-1.31)
FDA248,[40] NA	261	1.04 (0.83-1.31)
CL3-20098-022,[37] NA	276	1.05 (0.85-1.29)
Fava et al,[46] 1998	73	1.05 (0.61-1.80)
Hirayasu,[47] 2011	196	1.05 (0.79-1.40)
Study 25,[48] NA	38	1.06 (0.59-1.89)
CL3-20098-022,[37] NA	280	1.06 (0.86-1.31)
CL3-20098-023,[49] NA	278	1.06 (0.85-1.32)
AK1102365,[50] NA	315	1.06 (0.87-1.29)
Nemeroff et al,[51] 2007	201	1.06 (0.82-1.38)
FDA246,[40] NA	243	1.07 (0.84-1.35)
FDA247,[40] NA	217	1.07 (0.86-1.34)
845,[20] NA	82	1.07 (0.72-1.60)
Rudolph et al,[52] 1999	200	1.07 (0.84-1.38)
Fava et al,[53] 2005	90	1.08 (0.75-1.56)
Study015,[34] NA	221	1.08 (0.84-1.39)
Zajecka et al,[39] 2010	328	1.08 (0.90-1.31)
Schneider et al,[54] 2003	728	1.09 (0.97-1.23)
Hirayasu,[47] 2011	201	1.10 (0.82-1.46)
Fava et al,[46] 1998	74	1.10 (0.64-1.90)
Studie009,[34] NA	47	1.10 (0.64-1.88)
Sheehan et al,[55] 2009	406	1.10 (0.92-1.33)
Loo et al,[56] 2002	280	1.11 (0.89-1.38)
PAR279MDUK,[57] NA	29	1.11 (0.59-2.09)
003-042,[20] NA	135	1.11 (0.82-1.50)
003-042,[20] NA	135	1.11 (0.82-1.50)
Rickels et al,[58] 1985	245	1.11 (0.89-1.39)
Loo et al,[56] 2002	271	1.11 (0.89-1.39)
Stahl et al,[59] 2010	324	1.12 (0.93-1.35)
Lineberry et al,[60] 1990	216	1.12 (0.88-1.43)
Iwata et al,[61] 2013	467	1.13 (0.92-1.39)
Hirayasu,[62] 2011	243	1.13 (0.90-1.43)
Roth et al,[63] 1990	56	1.14 (0.72-1.81)
CL3-20098-023,[49] NA	274	1.15 (0.92-1.43)
Khan et al,[64] 1998	182	1.15 (0.90-1.48)
Stahl et al,[59] 2010	321	1.16 (0.96-1.40)
Kennedy et al,[65] 2014	277	1.16 (0.96-1.41)
Hirayasu,[62] 2011	245	1.16 (0.92-1.47)
Tollefson et al,[66] 1995	655	1.17 (1.02-1.33)
Wade et al,[67] 2002	377	1.17 (0.97-1.41)
Gastpar et al,[68] 2006	257	1.17 (0.94-1.46)
CAGO178A2303,[36] NA	321	1.17 (0.97-1.42)
Heun et al,[69] 2013	218	1.18 (0.92-1.51)
Zhang et al,[70] 2014	363	1.19 (0.99-1.43)
McGrath et al,[71] 2010	101	1.19 (0.81-1.75)
Olié et al,[72] 2007	235	1.19 (0.95-1.49)
Kennedy et al,[73] 2014	279	1.21 (0.99-1.47)
Rudolph et al,[52] 1999	192	1.21 (0.93-1.57)
Nemeroff et al,[51] 2007	197	1.21 (0.93-1.59)
Kennedy et al,[73] 2006	211	1.22 (0.96-1.54)
Lam et al,[74] 1995	68	1.22 (0.75-1.99)
Rapaport et al,[75] 2003	215	1.22 (0.94-1.58)
Silverstone et al,[76] 1999	237	1.23 (0.98-1.54)
003-042,[20] NA	135	1.23 (0.90-1.67)
Wellbutrin25,[20] NA	75	1.23 (0.80-1.90)
Claghorn et al,[77] 1996	89	1.24 (0.87-1.78)
Rickels et al,[78] 1982	103	1.25 (0.89-1.77)
Silverstone et al,[76] 1999	240	1.26 (1.00-1.58)
Sheehan et al,[42] 2009	186	1.26 (0.97-1.64)
Feighner et al,[79] 1979	112	1.27 (0.92-1.75)
Khan et al,[64] 1998	176	1.27 (0.98-1.64)
Rapaport et al,[75] 2003	213	1.27 (0.98-1.65)
Feighner et al,[80] 1989	100	1.28 (0.91-1.78)
Hirayasu,[62] 2011	244	1.28 (1.01-1.62)
Tomarken et al,[81] 2004	18	1.29 (0.55-3.03)
Wellbutrin06,[20] NA	75	1.30 (0.88-1.94)
Bjerkenstedt et al,[82] 2005	109	1.30 (0.94-1.81)
GSK14,[83] NA	86	1.31 (0.89-1.92)
Mischoulon et al,[84] 2014	125	1.31 (0.90-1.92)
Amin et al,[85] 1984	311	1.32 (1.08-1.61)
Khan et al,[64] 1998	174	1.32 (1.02-1.71)
Rickels et al,[78] 1982	105	1.35 (0.96-1.90)
Guelfi et al,[86] 1995	93	1.37 (0.94-1.99)
Croft et al,[87] 2014	505	1.38 (1.16-1.63)
Amsterdam et al,[88] 1986	109	1.46 (1.03-2.08)
Feighner et al,[89] 1989	33	1.46 (0.76-2.84)
Wilcox et al,[90] 1994	81	1.49 (1.00-2.21)
Claghorn et al,[91] 1983	148	1.51 (1.10-2.09)
Mynors-Wallis et al,[92] 1995	53	1.53 (0.94-2.47)
Georgotas et al,[93] 1982	33	1.65 (0.78-3.47)
Paykel et al,[94] 1988	100	1.67 (0.99-2.82)
Brunoni et al,[95] 2012	60	1.73 (1.11-2.70)
Hormazabal et al,[96] 1985	33	1.74 (0.91-3.31)
Versiani et al,[97] 2000	56	1.81 (1.09-3.02)
Cohn et al,[98] 1985	111	1.84 (1.32-2.56)
Feighner et al,[99] 1984	49	2.32 (1.39-3.89)
Rodriguez et al,[100] 2004	20	2.33 (0.73-7.49)
Feighner,[101] 1980	27	2.43 (1.19-4.99)
Shipley et al,[102] 1981	76	2.45 (1.47-4.09)
Mann et al,[103] 1981	19	3.08 (1.04-9.11)
Summary	20 883	1.14 (1.11-1.17)

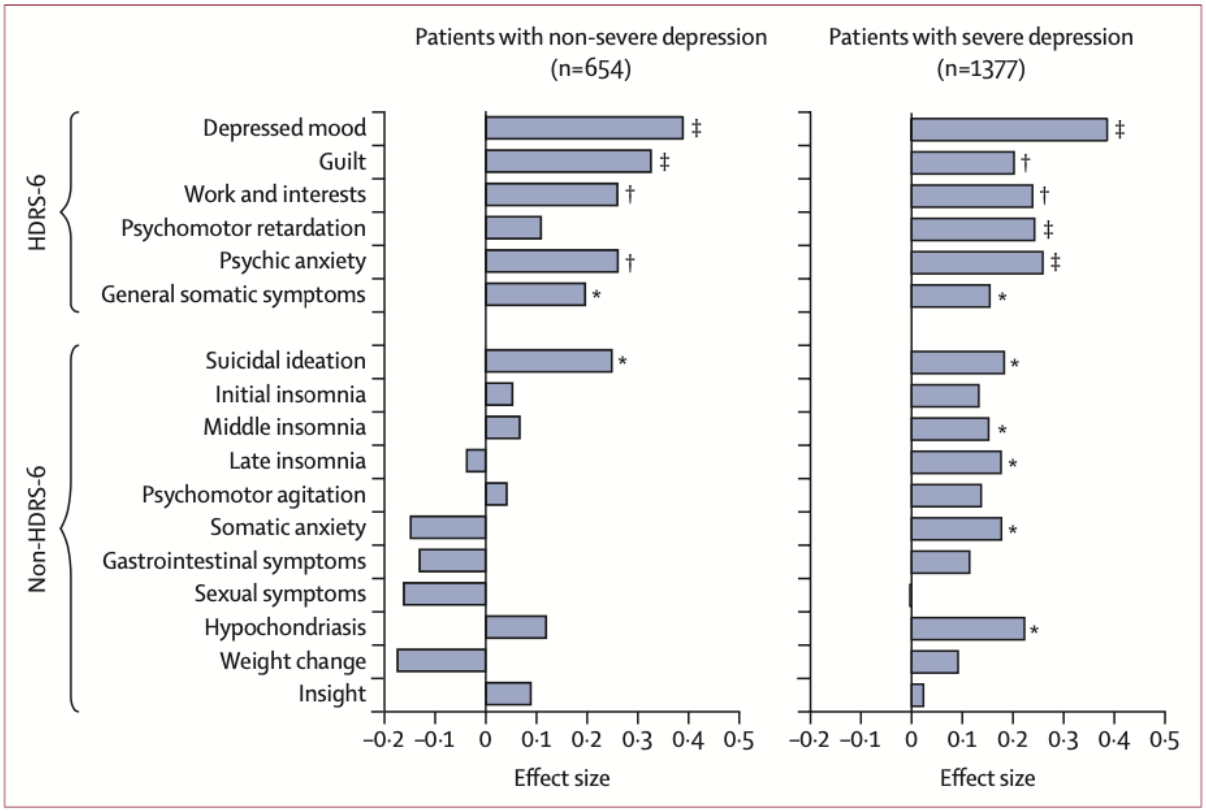


CVR = 1.14
(1.11 – 1.17)

Maslej et al., JAMA Psych 2020

Influence of baseline severity on the effects of SSRIs in depression: an item-based, patient-level post-hoc analysis

Fredrik Hieronymus, Alexander Lisinski, Staffan Nilsson, Elias Eriksson



Post-hoc Analyse:
28 Placebo-kontrollierte SSRI-Studien

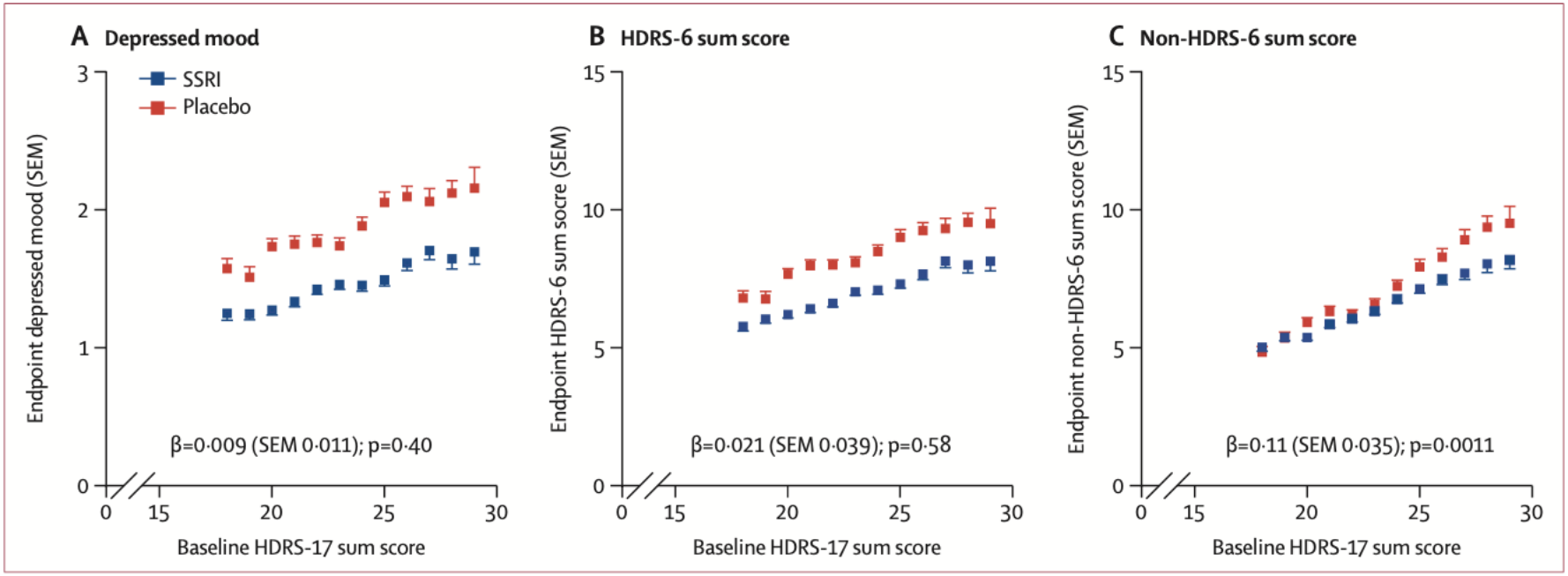
N=8'262 Patienten

Citalopram
Paroxetin
Sertralin

Fluoxetin (als aktive Kontrollgrupe)

Hieronymus et al., Lancet Psych 2019

Depressive Kernsymptomatik vs. gesamte HDRS



Hieronymus et al., Lancet Psych 2019

Impact of pharmacogenomics on clinical outcomes in major depressive disorder in the GUIDED trial: A large, patient- and rater-blinded, randomized, controlled study

John F. Greden[a,*], Sagar V. Parikh[a], Anthony J. Rothschild[b], Michael E. Thase[c], Boadie W. Dunlop[d], Charles DeBattista[e], Charles R. Conway[f], Brent P. Forester[g], Francis M. Mondimore[h], Richard C. Shelton[i], Matthew Macaluso[j], James Li[k], Krystal Brown[l], Alexa Gilbert[k], Lindsey Burns[k], Michael R. Jablonski[k], Bryan Dechairo[k,l]

- **G**enomics **U**sed to **I**mprove **DE**pression **D**ecisions (GUIDED)
- GeneSight® Psychotropic test (Assurex Health Inc.)

- **Outpatients (N = 1167) diagnosed with MDD and with a patient- or clinician-reported inadequate response to at least one antidepressant**

GeneSight®:
Genotyp über 59 Allele und Varianten über 8 Gene

(CYP1A2, CYP2C9, CYP2C19, CYP3A4, CYP2B6, CYP2D6, HTR2A, SLC6A4)

Greden et al., JPR 2019

GeneSight® Psychotropic
COMBINATORIAL PHARMACOGENOMIC TEST

genesight

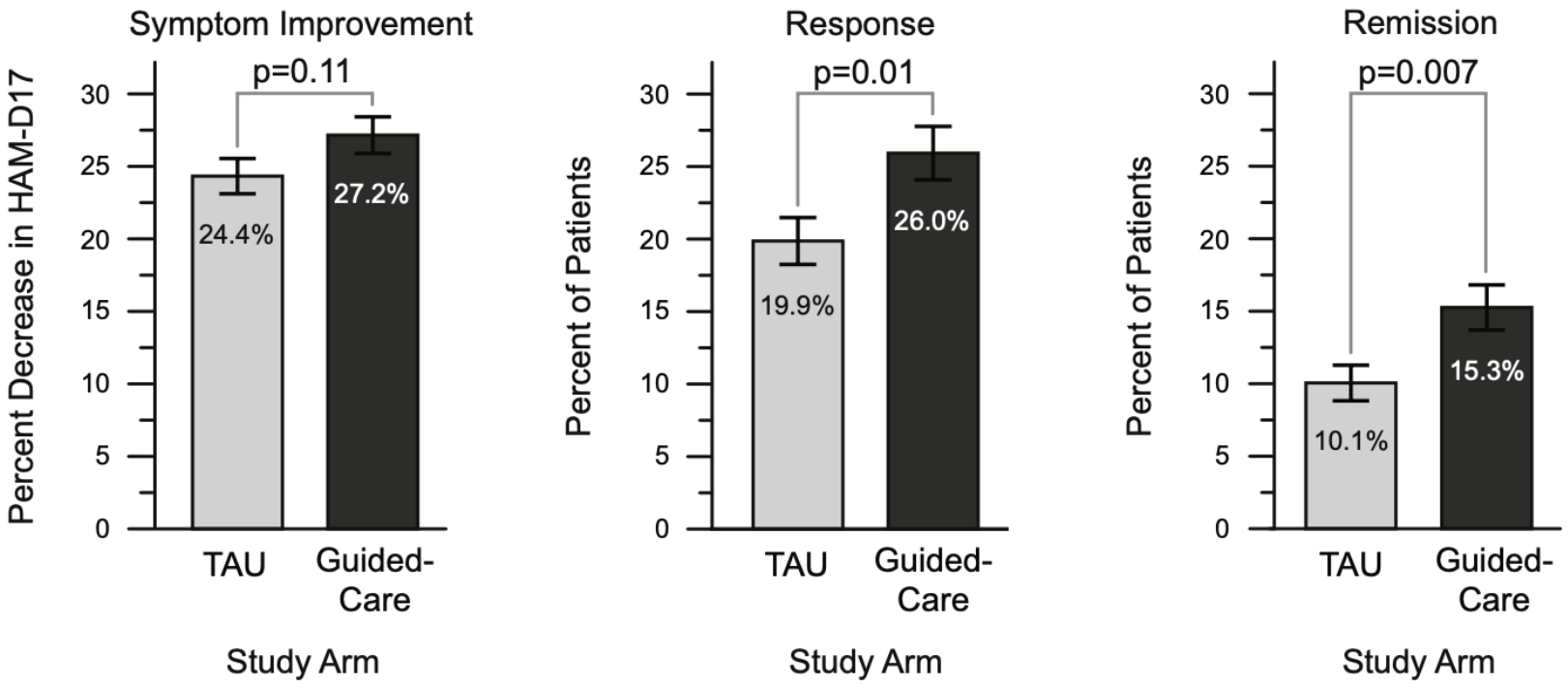
Patient, Sample
DOB: 7/22/1984
Order Number: 9904
Report Date: 6/22/2016
Clinician: Sample Clinician
Reference: 1456CIP

Questions? Call 855.891.9415 or email medinfo@assurexhealth.com

ANTIDEPRESSANTS

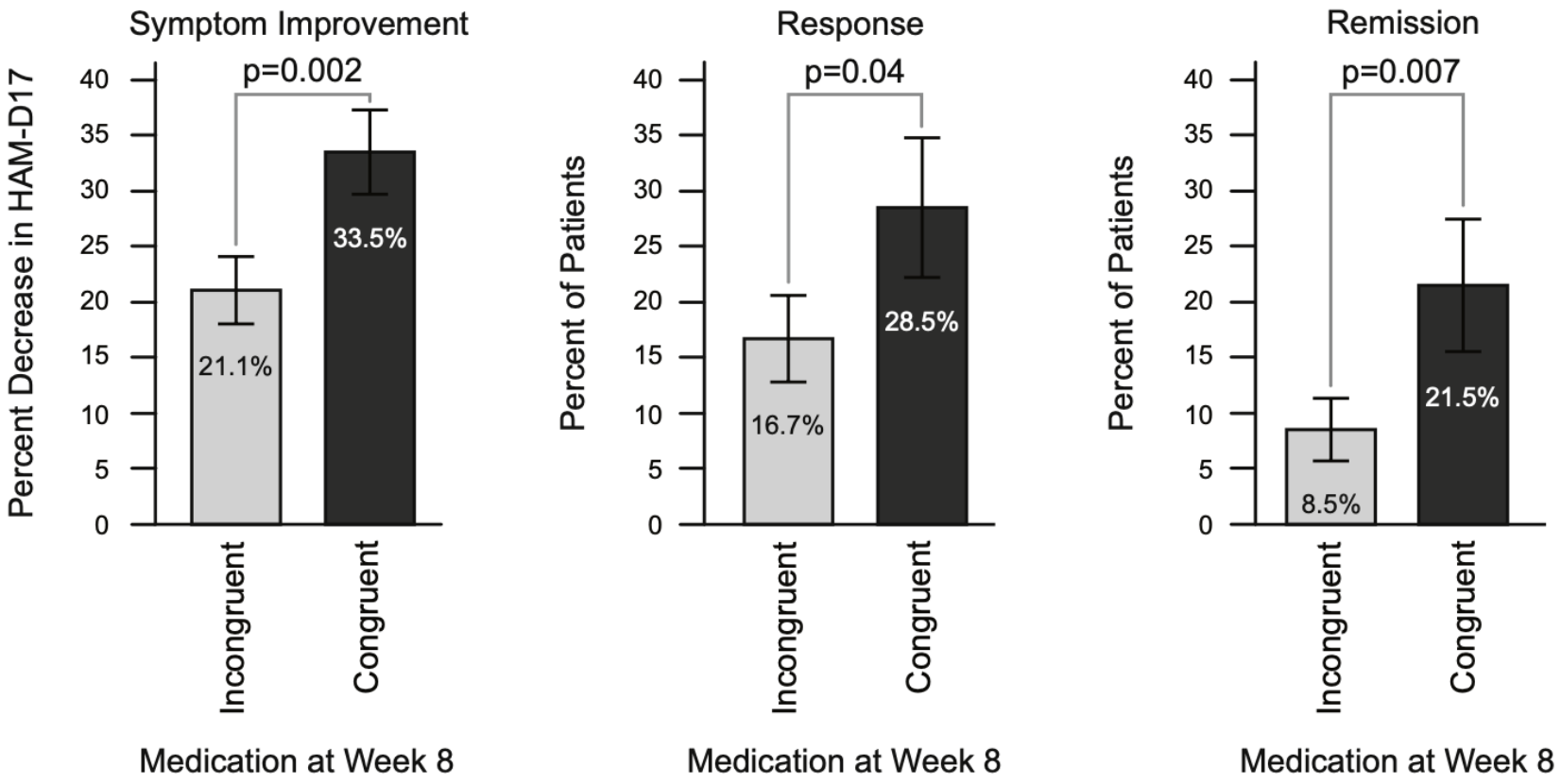
USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION		SIGNIFICANT GENE-DRUG INTERACTION	
desvenlafaxine (Pristiq®)	**trazodone** (Desyrel®)	1	**bupropion** (Wellbutrin®)	1,6
levomilnacipran (Fetzima®)	**venlafaxine** (Effexor®)	1	**mirtazapine** (Remeron®)	1,6
vilazodone (Viibryd®)	**selegiline** (Emsam®)	2	**amitriptyline** (Elavil®)	3,8
	fluoxetine (Prozac®)	1,4	**clomipramine** (Anafranil®)	1,6,8
	citalopram (Celexa®)	3,4	**desipramine** (Norpramin®)	1,6,8
	escitalopram (Lexapro®)	3,4	**doxepin** (Sinequan®)	1,6,8
	sertraline (Zoloft®)	3,4	**duloxetine** (Cymbalta®)	1,6,8
			imipramine (Tofranil®)	1,6,8
			nortriptyline (Pamelor®)	1,6,8
			vortioxetine (Trintellix®)	1,6,8
			fluvoxamine (Luvox®)	1,4,6,8
			paroxetine (Paxil®)	1,4,6,8

GUIDED-Care versus TAU



Greden et al., JPR 2019

Reanalyse alle Patienten



Greden et al., JPR 2019

Adjunctive antidepressants in bipolar depression: A cohort study of six- and twelve-months rehospitalization rates

Yahav Shvartzman[a], Amir Krivoy[a,b,c], Avi Valevski[a,b], Shay Gur[a,b], Abraham Weizman[a,b,c], Eldar Hochman[a,b,c,*]

[a]*Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel*
[b]*Geha Mental Health Center, Petach-Tikva, Israel*
[c]*Laboratory of Biological Psychiatry, Felsenstein Medical Research Center, Petach-Tikva, Israel*

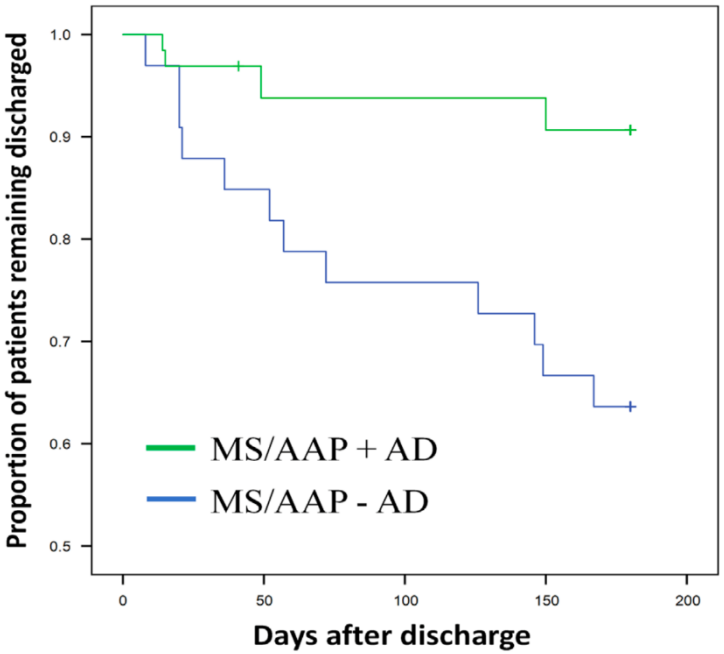
- Vergleich der Rehosp.-Rate von Pat. Mit Bipolar I Störung, Behandlung mit Mood Stabilizer (MSs) und/oder Atypikum (AAPs)
  - Mit AD
  - Ohne AD

- Endpunkte: Rehospitalisationsrate (6 Mte / 1 Jahr)

- N = 98, Hospitalisation mit depressiver Episode bei BP I

Shvartzman et al., Europ Neuropsychopharm 2018

Fig. 1 Time to rehospitalization due to any type of mood episode within six months following discharge according to the treatment at discharge (Kaplan-Meier survival analysis).



AAP, atypical antipsychotic; AD, antidepressant; MS, mood stabilizer.

Table 3 Adjusted hazard ratios for rehospitalization by adjunctive AD treatment at discharge from index depressive hospitalization (cox regression survival analysis).

	β	χ2	Adjusted Hazards ratio[a]	P value	95% CI
Six months following discharge					
Due to any type of mood episode	-2.517	9.160	0.081	0.002	0.016-0.412
Due to manic episode	-1.951	2.982	0.142	0.84	0.016-1.301
Due to depressive episode	-2.499	8.261	0.082	0.004	0.015-0.452
One year following discharge					
Due to any type of mood episode	-1.906	8.483	0.149	0.004	0.041-0.536
Due to manic episode	-2.1	2.146	0.122	0.143	0.007-2.033
Due to depressive episode	-2.21	8.379	0.110	0.004	0.025-0.490

AD, antidepressant.
[a]Adjusted for: age at first hospitalization, length of index hospitalization, number of pervious hospitalizations and presence of psychotic features at index hospitalization.

Shvartzman et al., Europ Neuropsychopharm 2018

Effect of Continuing Olanzapine vs Placebo on Relapse Among Patients With Psychotic Depression in Remission
The STOP-PD II Randomized Clinical Trial

Alastair J. Flint, MB; Barnett S. Meyers, MD; Anthony J. Rothschild, MD; Ellen M. Whyte, MD; George S. Alexopoulos, MD; Matthew V. Rudorfer, MD; Patricia Marino, PhD; Samprit Banerjee, PhD; Cristina D. Pollari, MPH; Yiyuan Wu, MS; Aristotle N. Voineskos, MD, PhD; Benoit H. Mulsant, MD; for the STOP-PD II Study Group

- N = 126 Pat. mit psychotischer Depression unter SERT & OLAN
  - Remission psychotische Sy
  - Remission oder Fast-Remission depressive Sy

Figure 2. Probability of Not Experiencing a Relapse

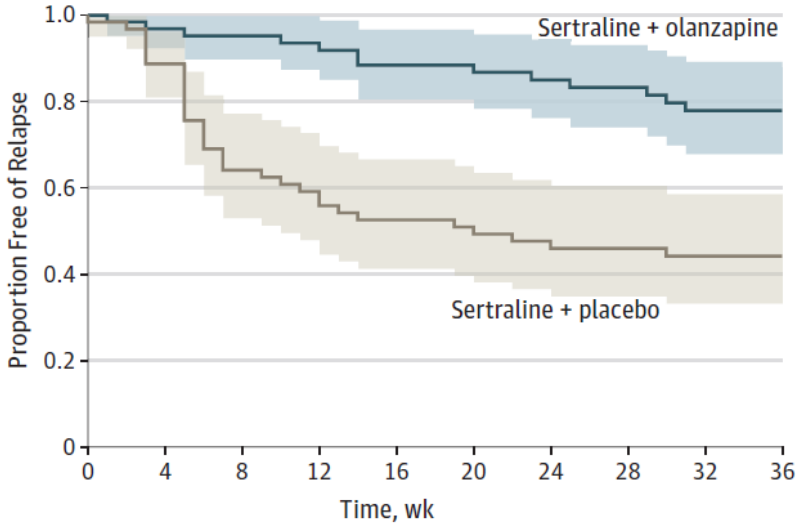


Table 3. Number of Relapse Events[a]

	Sertraline + Olanzapine	Sertraline + Placebo
Depression, no psychosis	5	18
Psychosis, no depression	0	1
Depression and psychosis	4	11
Suicide plan or attempt	0	3
Mania or hypomania	0	0
Psychiatric hospitalization[b]	6	11

Flint et al., JAMA 2019

JAMA Psychiatry | Original Investigation

Efficacy of Esketamine Nasal Spray Plus Oral Antidepressant Treatment for Relapse Prevention in Patients With Treatment-Resistant Depression

A Randomized Clinical Trial

Ella J. Daly, MD; Madhukar H. Trivedi, MD; Adam Janik, MD; Honglan Li, MD, PhD; Yun Zhang, PhD; Xiang Li, PhD; Rosanne Lane, MAS; Pilar Lim, PhD; Anna R. Duca, BSN; David Hough, MD; Michael E. Thase, MD; John Zajecka, MD; Andrew Winokur, MD, PhD; Ilona Divacka, MBA, MD; Andrea Fagiolini, MD; Wiesław J. Cubała, MD, PhD; István Bitter, MD, PhD; Pierre Blier, MD, PhD; Richard C. Shelton, MD; Patricio Molero, MD, PhD; Husseini Manji, MD; Wayne C. Drevets, MD; Jaskaran B. Singh, MD

- Phase III Studie

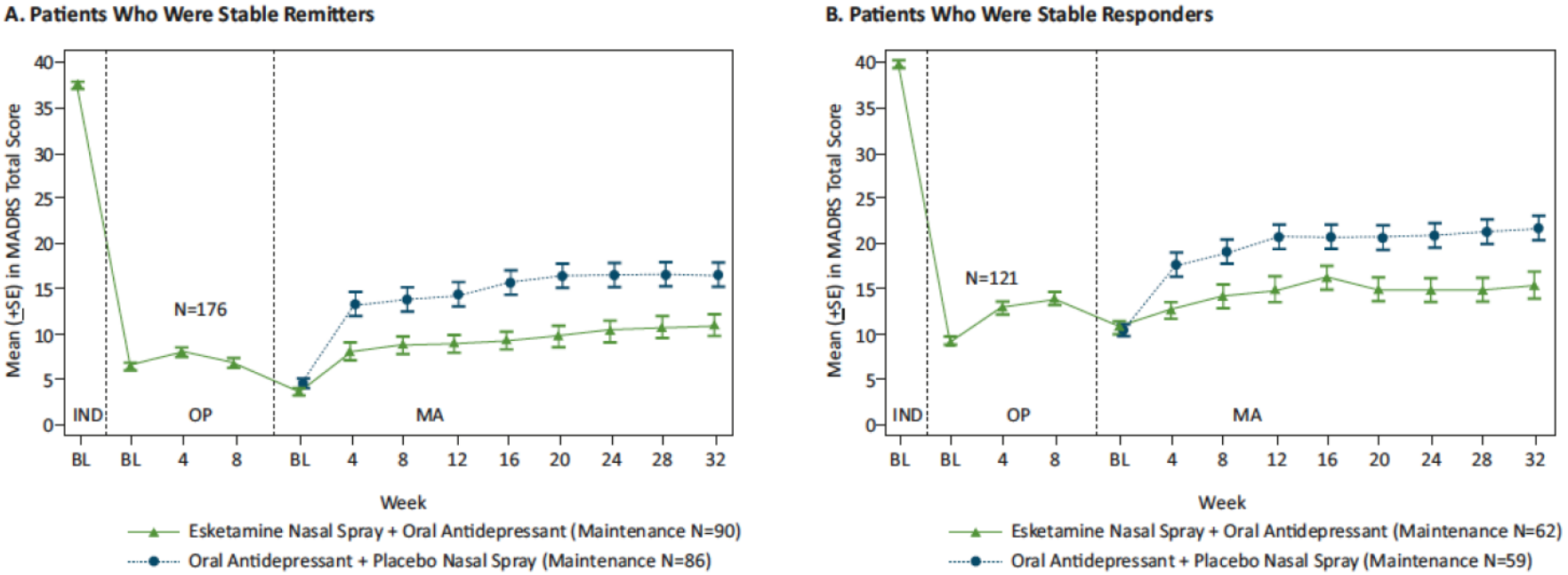
- N = 455 Pat. mit TRD → **Optimization phase:**
  - 16 Wochen Esketamin + AD

Response or Remission?

- N = 297 Pat. (Response/Remission) → **Withdrawal phase:**
  - Esketamin oder PLC (+AD)
  - Wöchentlich bis 2-wöchentlich (gem. Algorithmus)

Daly et al., JAMA Psych 2019

MADRS-Scores über die gesamte Studie



Abbreviations: IND=Induction, OP=Optimization, MA=Maintenance

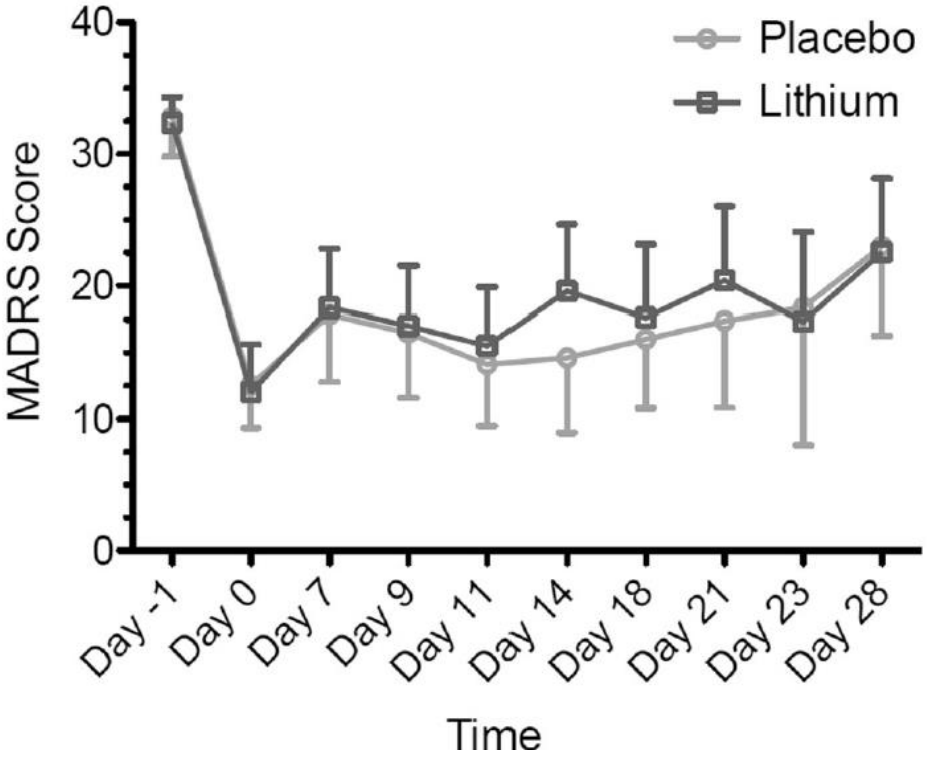
Daly et al., JAMA Psych 2019

Lithium continuation therapy following ketamine in patients with treatment resistant unipolar depression: a randomized controlled trial

Sara Costi[1], Laili Soleimani[1], Andrew Glasgow[2], Jess Brallier[2], John Spivack[3], Jaclyn Schwartz[4], Cara F. Levitch[5], Samantha Richards[1], Megan Hoch[1], Elizabeth Wade[6], Alison Welch[1], Katherine A. Collins[1], Adriana Feder[1], Dan V. Iosifescu[7,8], Dennis S. Charney[9,10] and James W. Murrough[1,9,10]

N = 34 Pat. mit TRD und **Response nach einmaliger Ketamin-Infusion** (0.5mg/kg)

- Randomisierung Li oder PLC
- Weitere drei Infusionen Ketamin und Aufdosierung Li oder PLC
- Endpunkt MADRS Tag 28 (14 Tage nach letzter Ketamin-Infusion)



Costi et al., Neuropsychopharm 2019

Nicht-Pharmakologische Therapien

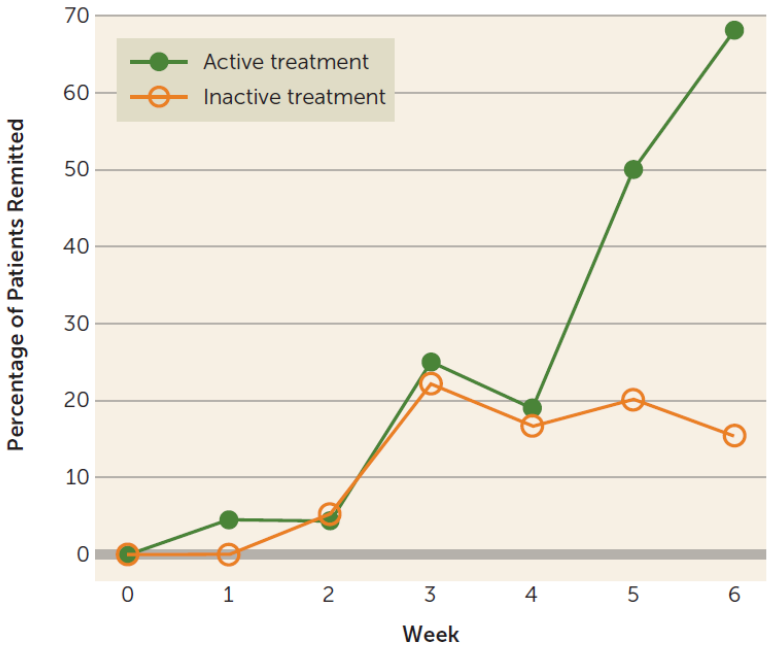
Adjunctive Bright Light Therapy for Bipolar Depression: A Randomized Double-Blind Placebo-Controlled Trial

Dorothy K. Sit, M.D., James McGowan, B.A., Christopher Wiltrout, B.S., Rasim Somer Diler, M.D., John (Jesse) Dills, M.L.S., James Luther, M.A., Amy Yang, M.S., Jody D. Ciolino, Ph.D., Howard Seltman, M.D., Ph.D., Stephen R. Wisniewski, Ph.D., Michael Terman, Ph.D., Katherine L. Wisner, M.D., M.S.

N = 46 depressive Pat. mit Bipolar I oder II Störung

- Stabile stimmungsstabilisierende Medikation
- **Lichttherapie (Mittags):**
  - 7'000 Lux weisses Licht
  - 50 Lux rotes Licht (PLC)
  - *Auftitrierung auf max. 60min/d (je nach Klinik). Beginn mit 15'*

FIGURE 1. Remission Rates Across Study Weeks for Patients With Bipolar Depression Treated with Active (Bright White Light) or Inactive (Dim Red Light) Light Therapy[a]



[a] Significant difference in remission rates between the active treatment group (68.2%) and the inactive treatment group (22.2%) (odds ratio=7.50, 95% CI=1.80, 31.28, p=0.003; adjusted odds ratio=12.64, 95% CI=2.16, 74.08, p=0.004).

Sit et al., Am J Psychiatry 2018

Effectiveness of preventive cognitive therapy while tapering antidepressants versus maintenance antidepressant treatment versus their combination in prevention of depressive relapse or recurrence (DRD study): a three-group, multicentre, randomised controlled trial

Claudi L H Bockting, Nicola S Klein, Hermien J Elgersma, Gerard D van Rijsbergen, Christien Slofstra, Johan Ormel, Erik Buskens, Jack Dekker, Peter J de Jong, Willem A Nolen, Aart H Schene, Steven D Hollon, Huibert Burger

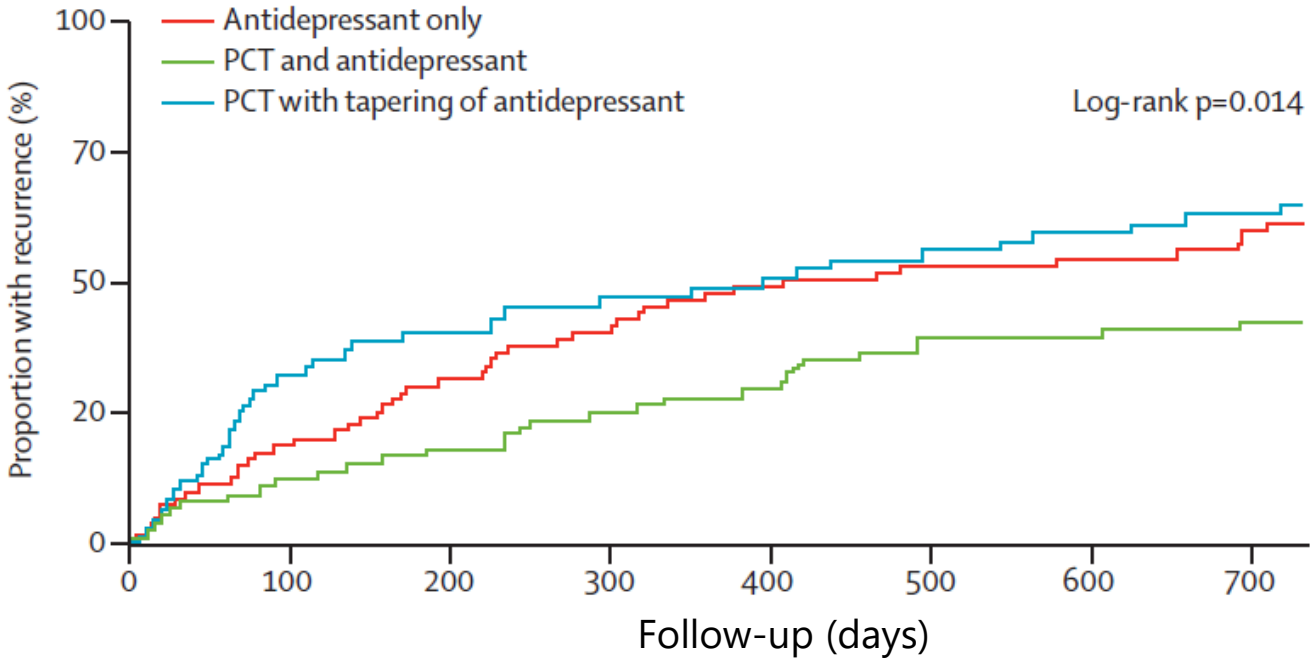
Preventive cognitive therapy (PCT)

- N = 289 Pat. mit mind. 2 depressiven Episoden
- Ansprechen auf AD-Behandlung seit mind. 6 Mten
- Randomisierung:
  - PCT & AD
  - Nur AD
  - Nur PCT (Ausschleichen des AD)

Hauptinhalte PCT:

- Evaluation dysfunktionaler Haltungen
- Aktivierung von Schemata, welche positive Gefühle aktivieren
- Verstärkung positiver Erfahrungen in der Vergangenheit
- Formulierung präventiver Strategien

Bockting et al., Lancet Psych 2018



«Adding eight sessions of PCT to antidepressant treatment after recovery yielded substantial protective effects compared with antidepressants alone (and PCT alone). Therefore, ***PCT should be offered to individuals with recurrent depression on maintenance antidepressant treatment and to individuals who wish to stop antidepressant treatment after recovery****.»*

Bockting et al., Lancet Psych 2018

Effectiveness and Acceptability of Cognitive Behavior Therapy Delivery Formats in Adults With Depression
A Network Meta-analysis

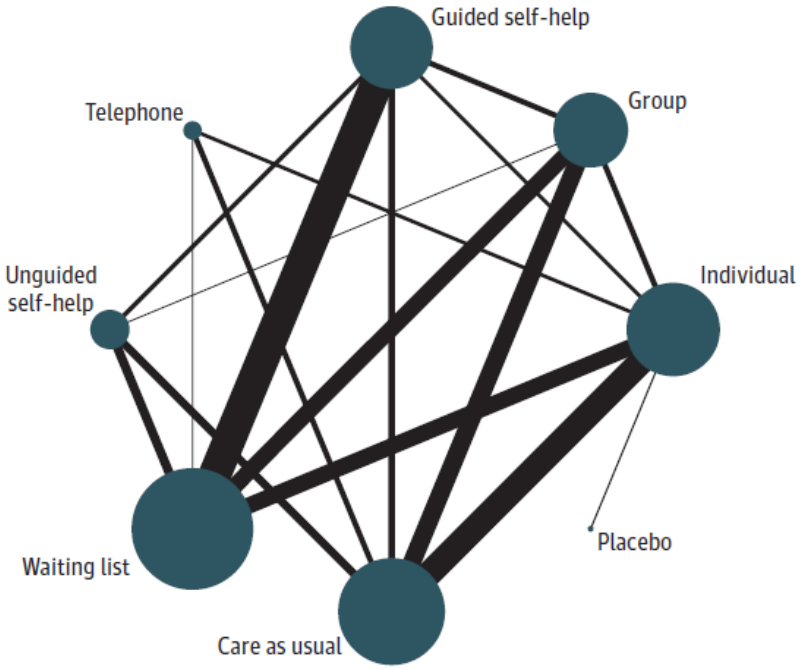
Pim Cuijpers, PhD; Hisashi Noma, PhD, MD; Eirini Karyotaki, PhD; Andrea Cipriani, PhD, MD; Toshi A. Furukawa, PhD, MD

Netzwerk-Metaanalyse: 155 Studien mit 15'191 Teilnehmern

Acceptability = Dropout aus irgendeinem Grund

- **5 Formate von KVT**
  - Einzeltherapie individuell
  - Einzeltherapie telefonisch
  - Gruppentherapie
  - Geführte Selbsthilfe
  - Ungeführte Selbsthilfe
- **Vergleichsinterventionen**
  - Warteliste
  - TAU

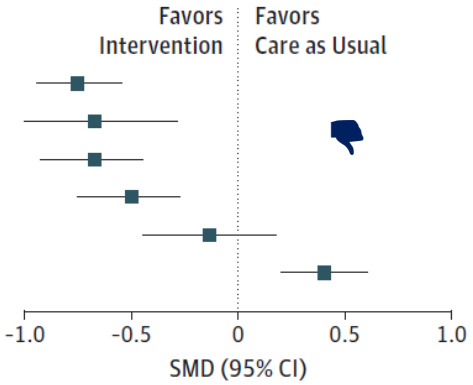
Figure 1. Network Plot of Meta-analysis



Cuijpers et al., JAMA Psych 2019

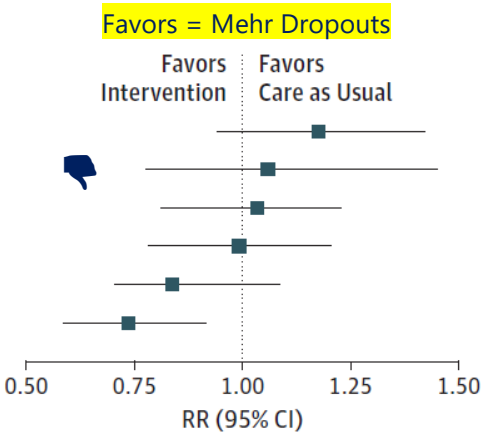
A Effectiveness

CBT format	SMD (95% CI)
Group	-0.72 (-0.92 to -0.52)
Telephone	-0.63 (-1.00 to -0.27)
Individual	-0.63 (-0.80 to -0.45)
Guided self-help	-0.47 (-0.70 to -0.25)
Unguided self-help	-0.13 (-0.39 to 0.13)
Waiting list	0.39 (0.18 to -0.60)



B Acceptability (Dropout rate)

CBT format	RR (95% CI)
Waiting list	1.14 (0.92 to 1.42)
Telephone	1.06 (0.77 to 1.45)
Individual	1.03 (0.85 to 1.24)
Group	0.99 (0.80 to 1.22)
Unguided self-help	0.86 (0.69 to 1.08)
Guided self-help	0.72 (0.57 to 0.90)



*"This study suggests that **group, telephone, and guided selfhelp treatments are effective interventions that may be considered as alternatives to individual CBT**. Applying effective and acceptable CBT in a range of different formats will make CBT easier to implement, disseminate, and deliver across different settings and diverse patient populations.»*

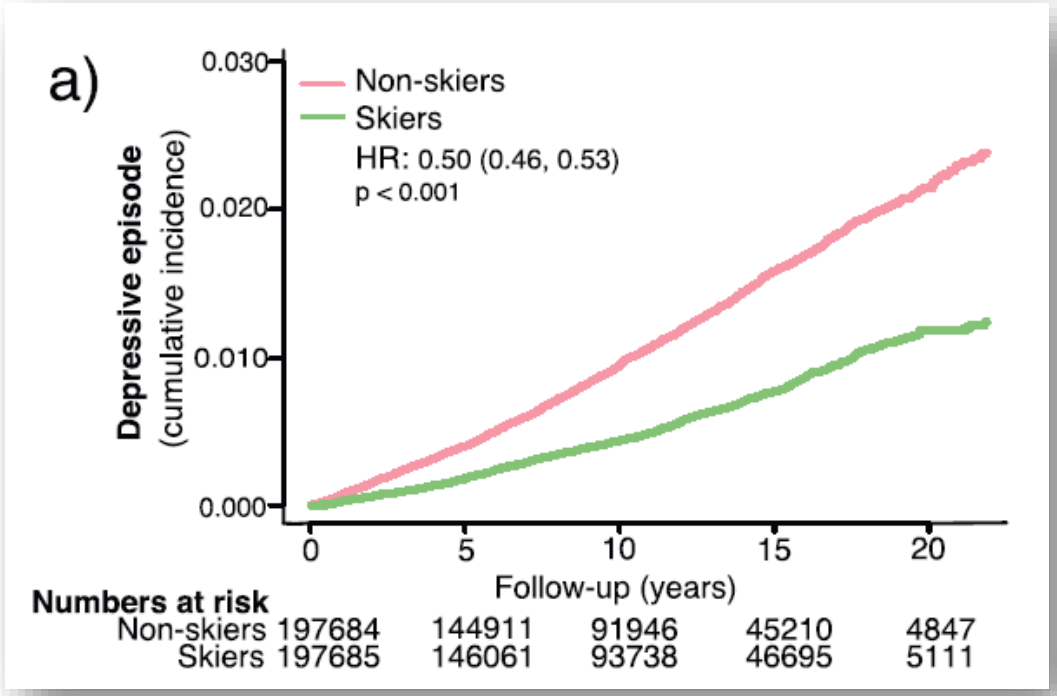
Cuijpers et al., JAMA Psych 2019

Sport & Depression

Bewegung (Langlauf) und Depressionsrisiko

Vasaloppet: Grösstes Skirennen der Welt

- Beobachtungsstudie über 21 Jahre
- N=395’369
  - 30-60km Langlaufrennen
  - Matched controls
- Swedish National Patient Registry

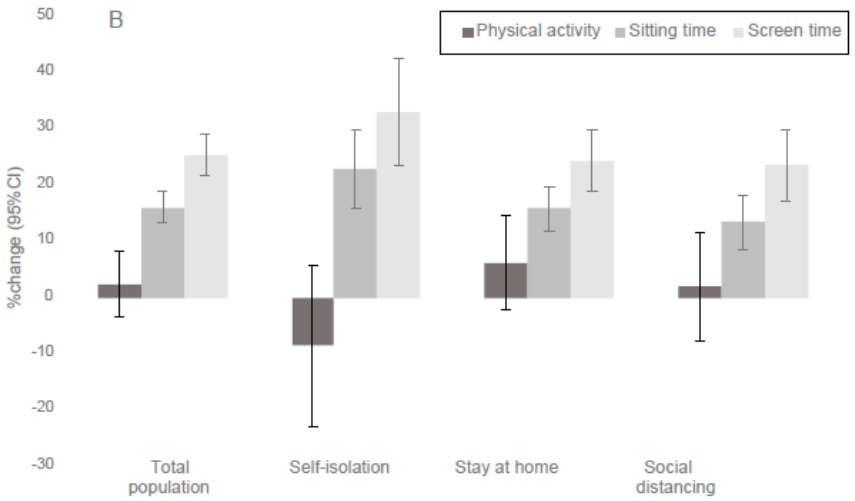


Svensson et al., Psychiatry Research 2019

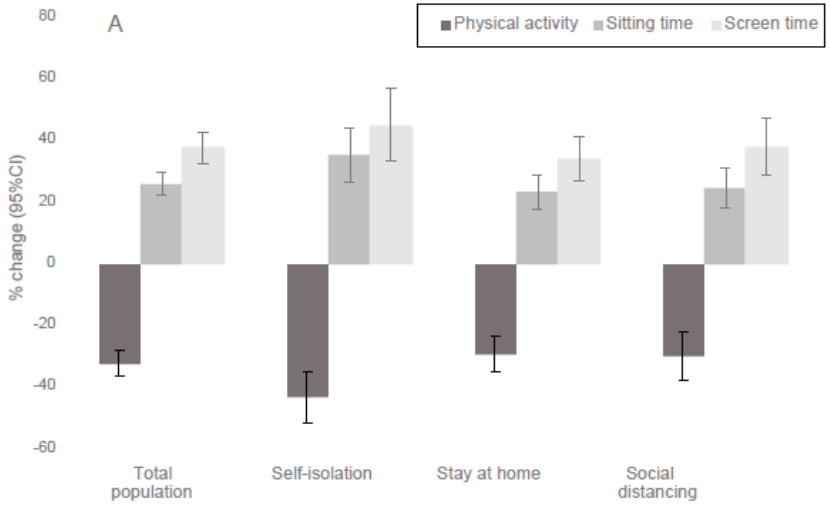
Changes in Physical Activity and Sedentary Behavior in Response to COVID-19 and Their Associations with Mental Health in 3052 US Adults

Jacob Meyer [1,*], Cillian McDowell [2], Jeni Lansing [1], Cassandra Brower [1], Lee Smith [3], Mark Tully [4] and Matthew Herring [5]

Not meeting PA-guidelines (pre-COVID-19)



meeting PA-guidelines (pre-COVID-19)



mean change: -32.3% [95% CI: -36.3%, -28.1%]

Cross-sectional
N = 3'052, online-survey via mass emails
Self report

- Pre and post-COVID-19 PA, sitting-, screen-time
- Stress, depressive & anxiety symptoms

«***No longer meeting PA guidelines and increased screen time*** *were associated with* ***worse depression, loneliness, stress [...](p < 0.001)"***

Meyer et al., Int. J. Environ. Res. Public Health 2020

Bouldering psychotherapy is more effective in the treatment of depression than physical exercise alone: results of a multicentre randomised controlled intervention study

Nina Karg[1*], Lisa Dorscht[1], Johannes Kornhuber[2] and Katharina Luttenberger[1]

N = 133 Ambulante Pat. mit Depression

10 Wochen Programm:

- Bouldering Psychotherapy (BPT)
  10x 2h Session
- Supervidiertes Sportprogramm (EP)
  3x20' / Woche
- Kognitive VT in Gruppe (CBT)

Per protocol Analyse (n = 198)

Table 1 Overview of sessions of the BPT [37]

Session	Topic
1	Introduction to bouldering and mindfulness
2	Physical feeling and body's centre of gravity
3	Healthy handling of limitations
4	Expectations and standards
5	Self-efficacy, achievements, and pride
6	Self-esteem
7	Fear and trust I
8	Fear and trust II
9	Social relationships
10	Problem solving, reflecting on lessons learned, and transfer to daily life

Karg et al., BMC Psychiatry 2020

175 JAHRE
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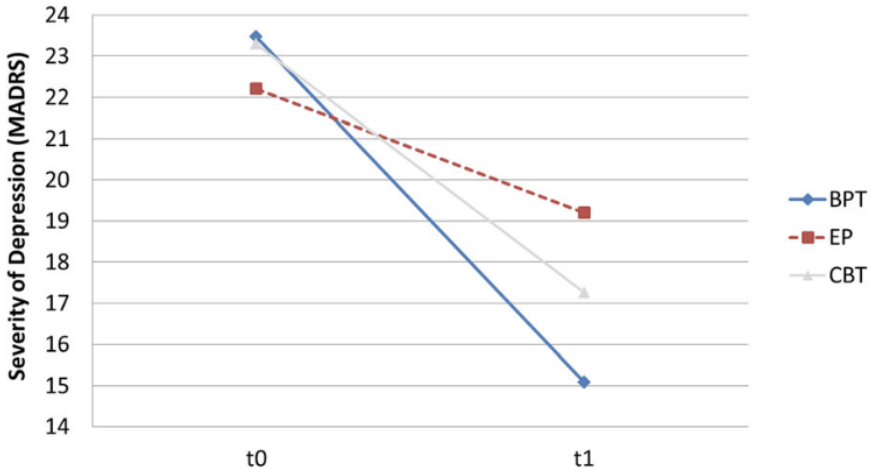


Fig. 3 Change in Depression Scores between t0 and t1 on the MADRS. *Notes.* BPT: Bouldering psychotherapy, CBT: cognitive behavioural therapy, EP: exercise programme

Table 3 Group Differences between the BPT and the EP Group for Change Scores between t0 and t1

Scale	BPT ($n = 64$) ΔM (SD)	EP ($n = 69$) ΔM (SD)	Cohen's d	*Independent t*-test p	*U*-test p
Primary outcome					
Depression (MADRS)	−8.4 (10.4)$^{+}$	−3.0 (9.3)$^{+}$	0.55	.002*	.001*
Secondary outcomes					
Anxiety (GAD-7)	−3.4 (4.3)$^{+}$	−2.0 (4.0)$^{+}$	0.35	.046*	.079†
Body Image (FKB-20)	3.5 (6.6)$^{+}$	1.0 (5.3)	0.42	.018*	.010*
Global self-esteem (R-SES)	3.6 (4.2)$^{+}$	1.7 (4.3)$^{+}$	0.45	.011*	.007*
Active and passive coping (FERUS)	3.2 (7.2)$^{+}$	1.3 (6.4)	0.28	.115	.130
Interpersonal sensitivity (SCL-90)	−3.5 (6.2)$^{+}$	−3.0 (5.8)$^{+}$	0.09	.591	.880
Additional measure					
Depression (PHQ-9)	−4.7 (6.3)$^{+}$	−2.6 (5.2)$^{+}$	0.36	.041*	.043*

Note. Differences between t0 and t1 (t1-t0): Negative values on the MADRS, PHQ-9, GAD-7, and SCL-90 indicate improvements in symptoms, positive values on the FKB-20, GSE, R-SES, and FERUS indicate positive effects

$^{+}$ indicates a significant difference between t0 and t1 within the group; † $p \leq .10$; * $p \leq .05$

Depression & Demenz

RESEARCH ARTICLE

The association of depression with subsequent dementia diagnosis: A Swedish nationwide cohort study from 1964 to 2016

Sofie Holmquist[1,2], **Anna Nordström**[1,3], **Peter Nordström**[4]*

1 Department of Public Health and Clinical Medicine, Occupational and Environmental Medicine, Umeå University, Umeå, Sweden, **2** Department of Applied Educational Science, Umeå University, Umeå, Sweden, **3** Department of Community Medicine, Arctic University of Norway, Tromsø, Norway, **4** Department of Community Medicine and Rehabilitation, Geriatric Medicine, Umeå University, Umeå, Sweden

2 Kohorten ≥50 Jahre alt per 31.12.2005

1. N = 119'386 Probanden mit Dg Depression, matched 1:1 mit Kontrollen ohne Depression
2. N = 50'644 gleichgeschlechtliche Geschwisterpaare mit Diskordanz bezüglich der Dg einer Depression

- Endpunkt: Diagnose eine Demenz während Follow-up
- *Angepasste Modelle:* Geschlecht, Alter bei Einschluss, Nationalität, Zivilstatus, Haushaltseinkommen, Diagnosen bei Einschluss

Holmquist et al., PLOS Medicine 2020

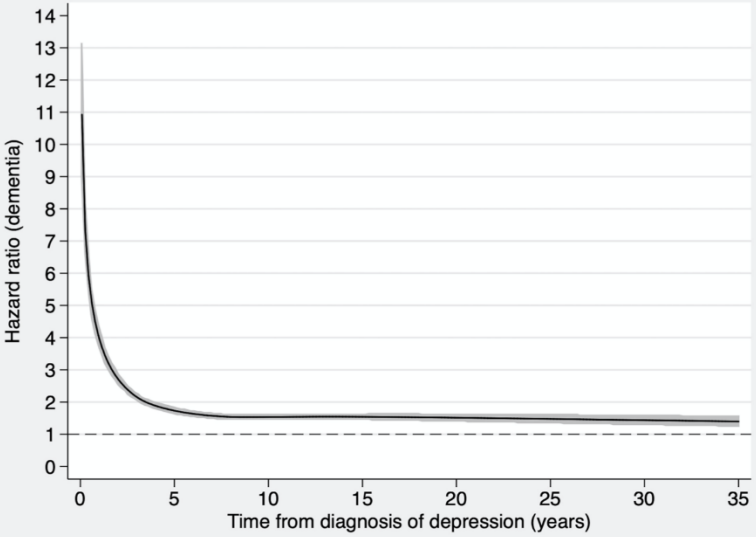
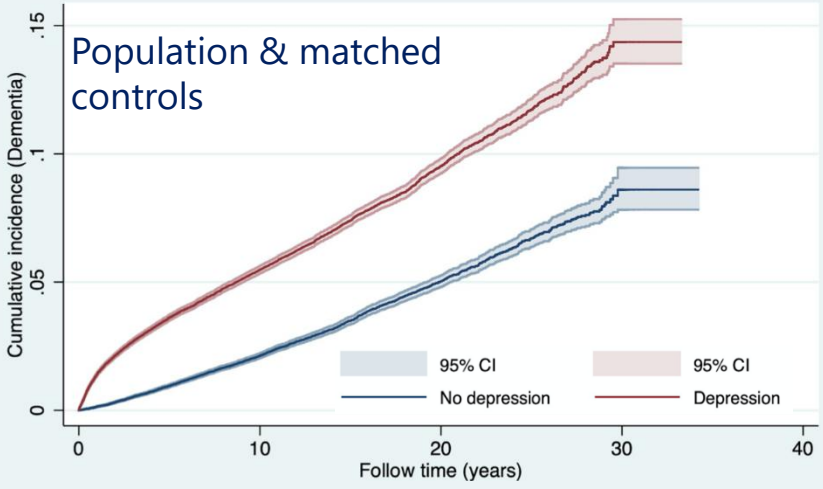
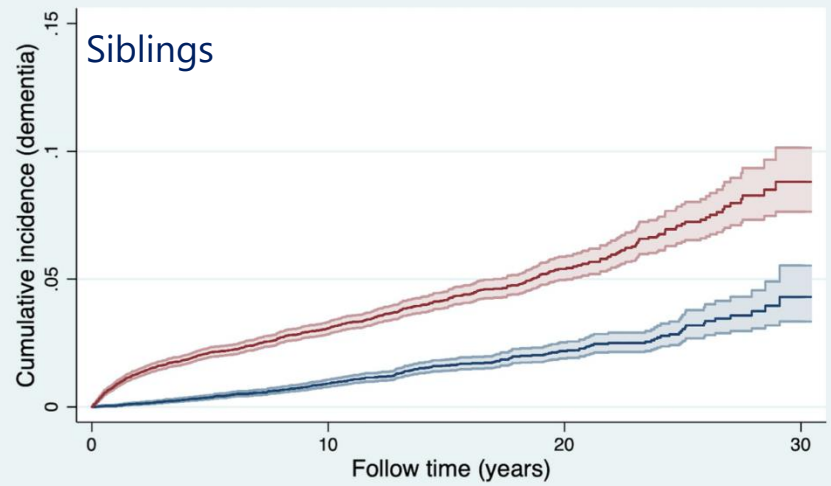


Fig 1. Association between depression and the risk of dementia during follow-up for 238,772 individuals. Individuals with follow-up time of less than 1 month were excluded. The figure was constructed using a flexible parametric model with 5 degrees of freedom and knots in default positions. The black line represents the hazard ratio, and the grey areas represent 95% confidence intervals.





- Deutliche Risikosteigerung in den ersten Jahren nach Dg
- Bei schwerer Depression höheres RR

Holmquist et al., PLOS Medicine 2020

Danke für Ihre Aufmerksamkeit

christian.imboden@pkwyss.ch

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SEIT 1845