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Senior onderzoeker/Apotheker/psycholoog

Lentis Research



Disclosure belangen spreker

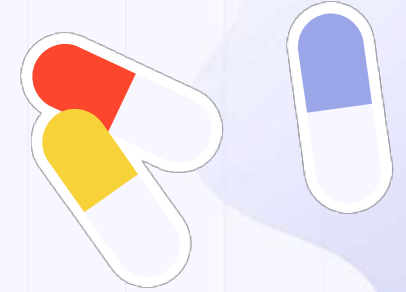
(potentiële) belangenverstremgeling	Geen
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Geen
<ul style="list-style-type: none">• Sponsoring of onderzoeksgeld• Honorarium of andere (financiële) vergoeding• Aandeelhouder• Andere relatie, namelijk ...	<ul style="list-style-type: none">•••• Geen

Als apotheker, wat vind jij
van antipsychotica
polyfarmacie?

Medicatiebewaking

	Code	Omschrijving	Relevantie
[CD] HYDROCHLOORTHIAZIDE TABLET 12,5MG 16 ST			
Dubbelmedicatie	8	CHLOORTALIDON TABLET 25MG - HYDROCHLOORTHIAZIDE TABLET 12,5MG	1
Dubbelmedicatie	2	HYDROCHLOORTHIAZIDE TABLET 12,5MG - HYDROCHLOORTHIAZIDE TABLET 12,5MG	1
Contra-indicatie	16	DIABETES MELLITUS: THIAZIDEN	1

Antipsychotica polyfarmacie



01

Hoe vaak komt
het voor?

04

Veiligheid en
bijwerkingen

02

De theorie

05

Rationeel/
irrationeel

03

Evidence based

06

Afbouwen

Bronnen

Eigen onderzoek +



Literatuur



Bjornestad J, Lavik KO, Davidson L, Hjeltnes A, Moltu C, Veseth M. Antipsychotic treatment—a systematic literature review and meta-analysis of qualitative studies. *J Ment Heal.* 2020;29(5):513-523. doi:10.1080/09638237.2019.1581352

Horowitz MA, Jauhar S, Natesan S, Murray RM, Taylor D. A Method for Tapering Antipsychotic Treatment That May Minimize the Risk of Relapse. *Schizophr Bull.* 2021;47(4):1116-1129. doi:10.1093/schbul/sbab017

Hui CLM, Honer WG, Lee EHM, et al. Long-term effects of discontinuation from antipsychotic maintenance following first-episode schizophrenia and related disorders: a 10 year follow-up of a randomised, double-blind trial. *The Lancet Psychiatry.* 2018;5(5):432-442. doi:10.1016/S2215-0366(18)30090-7

Taipale H, Tanskanen A, Tiihonen J. Safety of Antipsychotic Polypharmacy Versus Monotherapy in a Nationwide Cohort of 61,889 Patients With Schizophrenia. *Am J Psychiatry.* 2023;180(5):377-385. doi:10.1176/appi.ajp.20220446

Tiihonen J, Taipale H, Mehtälä J, Vattulainen P, Correll CU, Tanskanen A. Association of Antipsychotic Polypharmacy vs Monotherapy with Psychiatric Rehospitalization among Adults with Schizophrenia. *JAMA Psychiatry.* 2019;76(5):499-507. doi:10.1001/jamapsychiatry.2018.4320

Wunderink L, Nieboer RM, Wiersma D, Sytema S, Nienhuis FJ. Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation or maintenance treatment strategy long-term follow-up of a 2-year randomized clinical trial. *JAMA Psychiatry.* 2013;70(9):913-920. doi:10.1001/jamapsychiatry.2013.19

Bronnen



Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS)

- Routine outcome monitoring (ROM)
- Psychose (antipsychotica gebruikers)
- Noorden van NL (UCP, GGz Drenthe, GGz Friesland, Lentis)
- Dynamisch cohort=Mixed effect models
- 2009-2024

Polyfarmacie

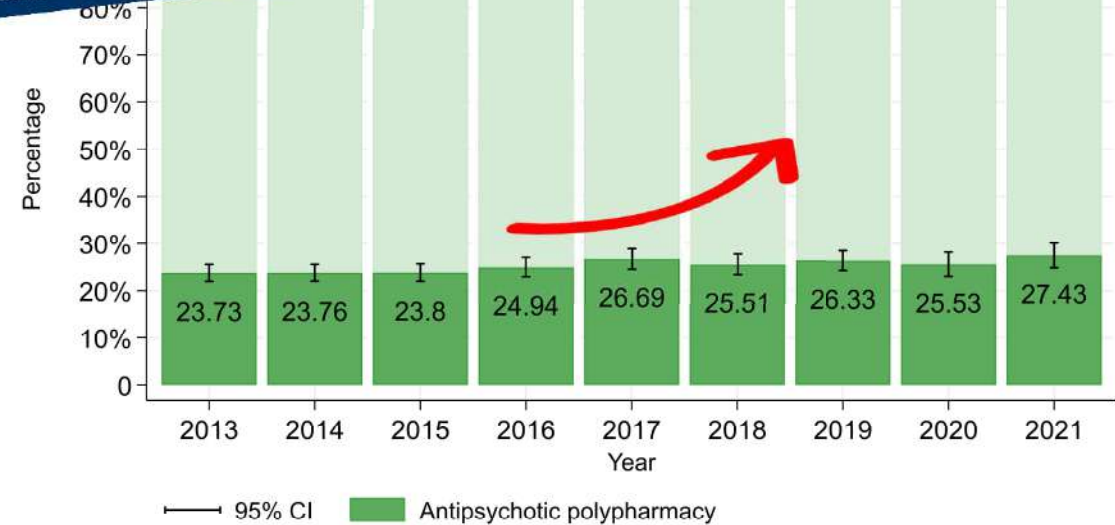
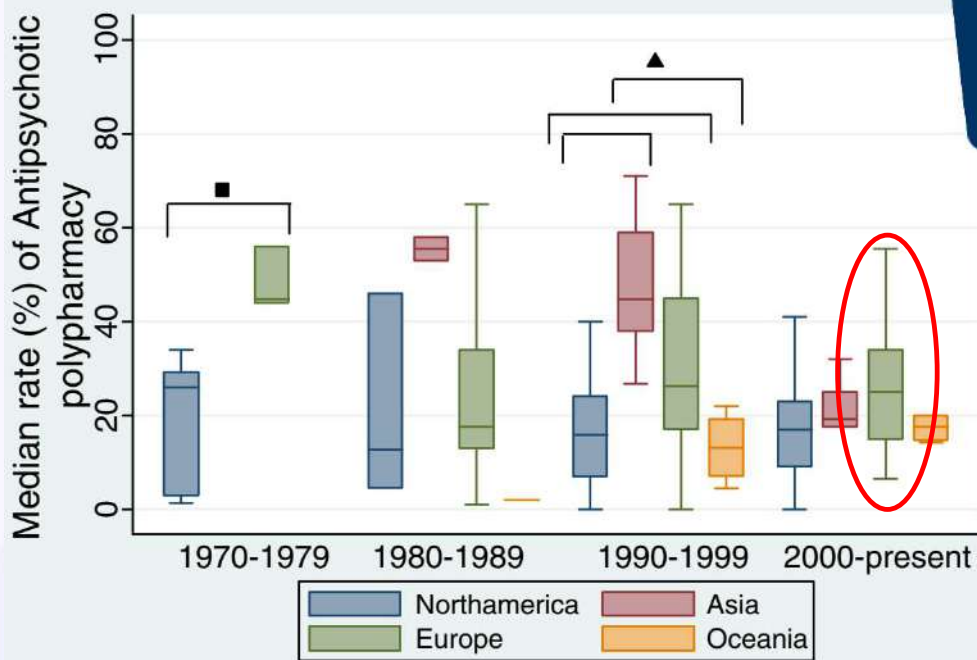
Richtlijnen

“Losse casus en enkele niet-gerepliceerde studies hebben bescheiden successen gemeld van het toevoegen van een middel aan clozapine, zoals een selectieve serotonine heropnameremmer, **een tweede antipsychoticum** of een antiepilepticum. Hiermee moet terughoudend worden omgegaan om onnodige polyfarmacie te voorkomen.”

Hoe vaak komt het voor?



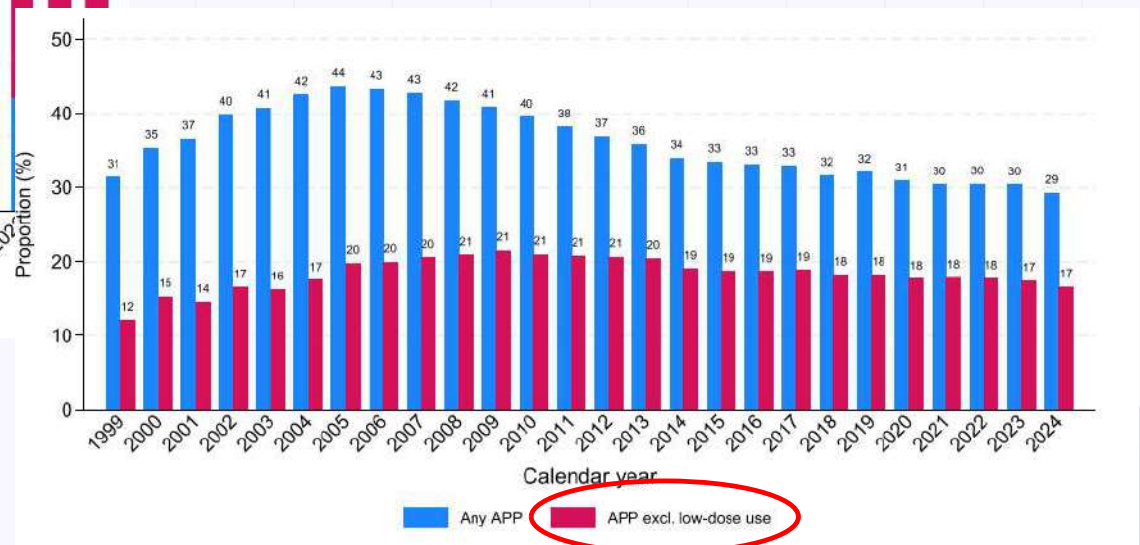
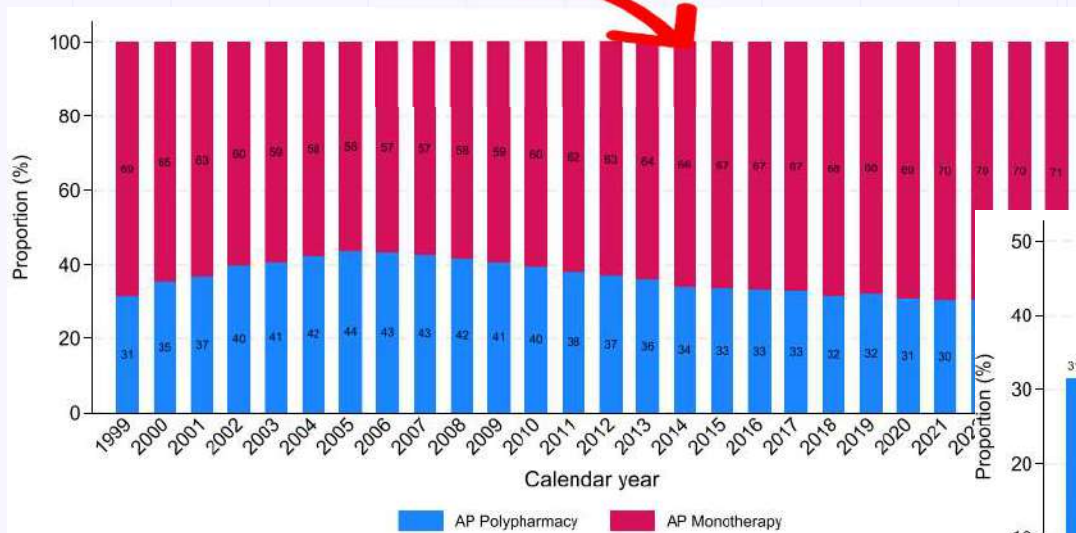
Ongeveer net zo vaak als depots of clozapine



Gallego JA, Bonetti J, Zhang J, Kane JM (2012) Prevalence and correlates of antipsychotic polypharmacy: A systematic review and meta-regression of global and regional trends from the 1970s to 2009. Schizophr Res 138:18–28. <https://doi.org/10.1016/j.schres.2012.03.018>

Crutzen S, Gangadin S, Hua KH, Visser E, Jörg F, van der Meer L, Pijnenborg GHM, Veling W, Castelein S. Trends in Antipsychotic Polypharmacy and Potential Overtreatment with Antipsychotics: A Naturalistic Cohort Study of People in Long-term Care. Schizophr Bull. 2026 Jan 16;52(1):sbafo41. doi: 10.1093/schbul/sbaf041. PMID: 40329432; PMCID: PMC12809800.

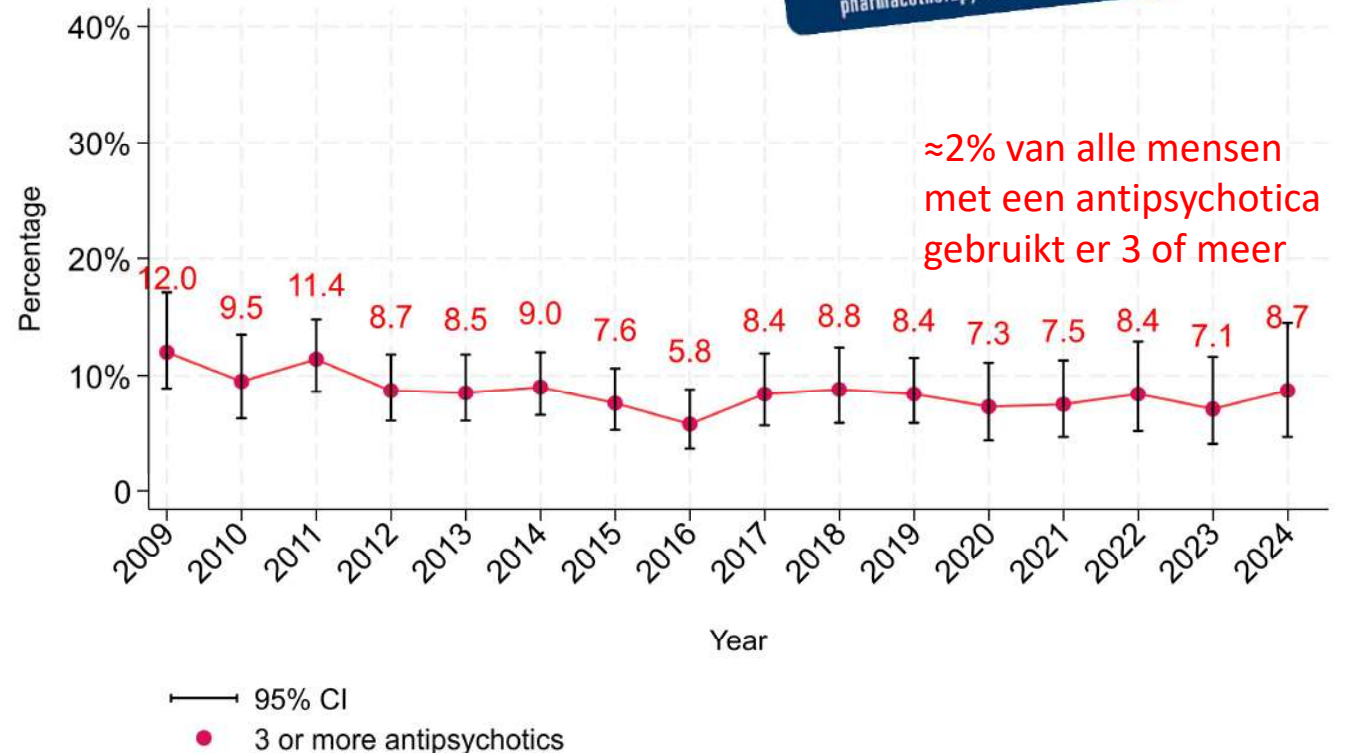
Polyfarmacie



Højlund M, Rohde C, Gasse C, Hallas J, Fink-Jensen A, Correll CU, Köhler-Forsberg O. Antipsychotic polypharmacy in patients with schizophrenia between 1999 and 2024 in Denmark: Prevalence, time trends, and combinations. *Eur Neuropsychopharmacol.* 2025 Nov;100:4-12. doi: 10.1016/j.euroneuro.2025.08.580. Epub 2025 Aug 28. PMID: 40882582.

Polyfarmacie

3 of meer antipsychotica van alle antipsychotica polyfarmacie



Højlund M, Rohde C, Gasse C, Hallas J, Fink-Jensen A, Correll CU, Köhler-Forsberg O. Antipsychotic polypharmacy in patients with schizophrenia between 1999 and 2024 in Denmark: Prevalence, time trends, and combinations. Eur Neuropsychopharmacol. 2025 Nov;100:4-12. doi: 10.1016/j.euroneuro.2025.08.580. Epub 2025 Aug 28. PMID: 40882582.

De theorie

Waarom 2 antipsychotica (therapieresistentie)

60-80% receptor
bezetting

	D ₁	D ₂	5HT _{1a}	5HT _{2a}	5HT _{2c}	α ₁	α ₂	H ₁	M ₁
Amisulpride	?	+++	0	0	0	0	0	0	?
<u>Aripiprazole^a</u>	+	++++	+++	++	++	++	++	++	0
Chlorpromazine	+	+++	0	+++	++	+++	?	+++	+
<u>Clozapine</u>	+	+	+	+++	++	+++	+	+++	+++
Haloperidol	++	+++	0	+	0	++	++	+	0
<u>Olanzapine</u>	++	++	0	+++	++	++	+	++++	+++
Paliperidone	+	+++	+	+++	++	+++	++	+++	+
Perphenazine	?	++++	+	+++	+	++	+	+++	0
Pimozide	0	+++	+	++	0	+	?	0	0
<u>Quetiapine</u>	+	+	+	+	0	++	+	++	+
Risperidone	++	+++	+	++++	++	+++	+++	+++	0
Sertindole	?	+++	++	++++	++++	+++	+	+	0
Thioridazine	++	++	+	++	++	+++	?	++	+
Ziprasidone	++	+++	++	++++	++	+++	+	+++	+

De uitzonderingen

Clozapine

	D ₁	D ₂	5HT _{1a}	5HT _{2a}	5HT _{2c}	α ₁	α ₂	H ₁	M ₁
Amisulpride	?	+++	0	0	0	0	0	0	?
Aripiprazole ^a	+	++++	+++	++	++	++	++	++	0
Chlorpromazine	+	+++	0	+++	++	+++	?	+++	+
Clozapine	+	+	+	+++	++	+++	+	+++	+++
Haloperidol	++	+++	0	+	0	++	++	+	0

Partiele agonist M4
 Net als:
 KarXT/Cobenfy
 (xanomeline en
 trospium)



De D2 uitzonderingen

Quetiapine en olanzapine

Kiss and run

	D ₁	D ₂	5HT _{1a}	5HT _{2a}	5HT _{2c}	α ₁	α ₂	H ₁	M ₁
Amisulpride	?	+++	0	0	0	0	0	0	?
Aripiprazole ^a	+	++++	+++	++	++	++	++	++	0
Chlorpromazine	+	+++	0	+++	++	+++	?	+++	+
Clozapine	+	+	+	+++	++	+++	+	+++	+++
Haloperidol	++	+++	0	+	0	++	++	+	0
Olanzapine	++	++	0	+++	++	++	+	++++	+++
Paliperidone	+	+++	+	+++	++	+++	++	+++	+
Perphenazine	?	++++	+	+++	+	++	+	+++	0
Pimozide	0	+++	+	++	0	+	?	0	0
Quetiapine	+	+	+	+	0	++	+	++	+

De D2 uitzonderingen

Aripiprazole (brexpiprazol of cariprazine)

Partiele agonist
30% agonist
70% antagonist

	D ₁	D ₂	5HT _{1a}	5HT _{2a}	5HT _{2c}	α ₁	α ₂	H ₁	M ₁
Amisulpride	?	+++	0	0	0	0	0	0	?
Aripiprazole ^a	+	++++	+++	++	++	++	++	++	0
Chlorpromazine	+	+++	0	+++	++	+++	?	+++	+
Clozapine	+	+	+	+++	++	+++	+	+++	+++
Haloperidol	++	+++	0	+	0	++	++	+	0
Olanzapine	++	++	0	+++	++	++	+	++++	+++
Paliperidone	+	+++	+	+++	++	+++	++	+++	+
Perphenazine	?	++++	+	+++	+	++	+	+++	0
Pimozide	0	+++	+	++	0	+	?	0	0
Quetiapine	+	+	+	+	0	++	+	++	+

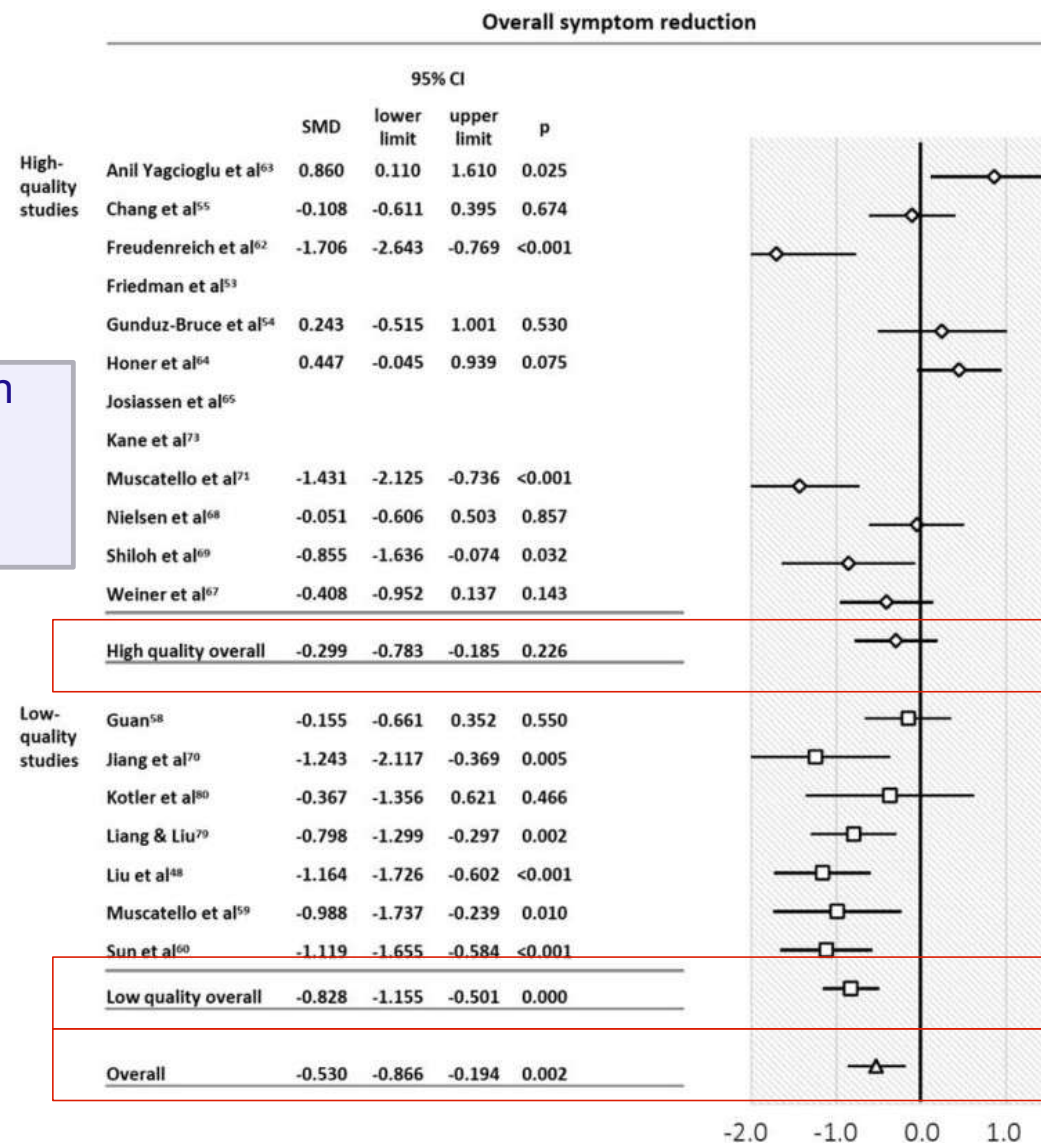
Bewijs

Verminderen van symptomen (RCT)

Negatieve symptomen



Toevoegen van een tweede antipsychotica (Augmentatie)



Galling B, Roldán A, Hagi K, et al (2017) Antipsychotic augmentation vs. monotherapy in schizophrenia: systematic review, meta-analysis and meta-regression analysis. *World Psychiatry* 16:77–89. <https://doi.org/10.1002/wps.20387>

Bewijs

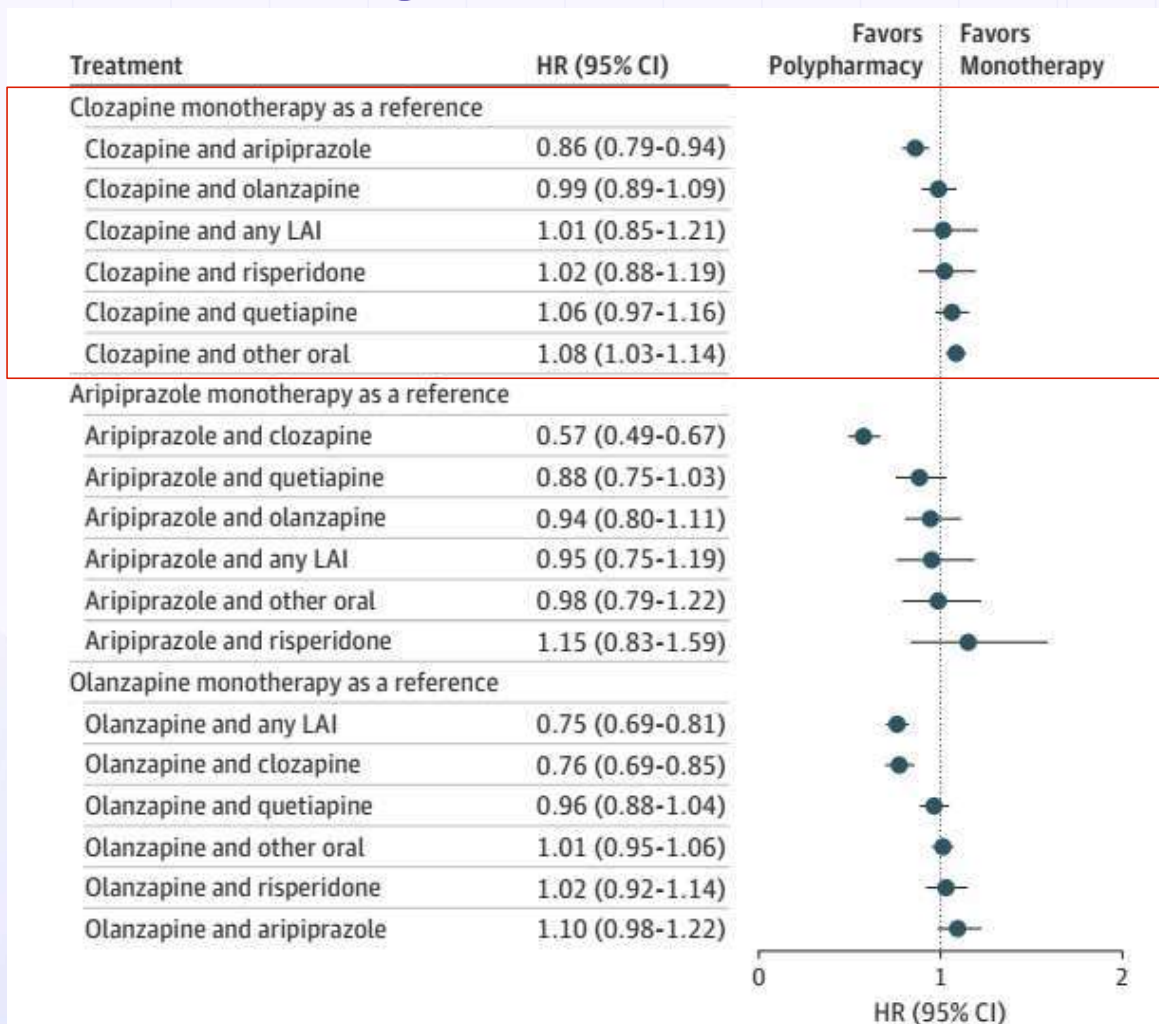
Psychiatrische heropname

Nationwide cohort study

Treatment	HR (95% CI)	Favors Use of Antipsychotics	Favors No Use of Antipsychotics
Clozapine and aripiprazole	0.42 (0.39-0.46)	●	
Any LAI and olanzapine	0.48 (0.44-0.51)	●	
Clozapine and olanzapine	0.49 (0.44-0.54)	●	
Clozapine monotherapy	0.49 (0.47-0.51)	●	
Clozapine and any LAI	0.50 (0.42-0.59)	●	
Clozapine and risperidone	0.50 (0.43-0.59)	●	
Clozapine and quetiapine	0.52 (0.48-0.57)	●	
Clozapine and other oral	0.53 (0.50-0.56)	●	
Any LAI and quetiapine	0.55 (0.50-0.60)	●	
Any LAI and other oral	0.55 (0.53-0.58)	●	
Any LAI monotherapy	0.56 (0.54-0.58)	●	
Other combination of multiple drugs	0.58 (0.56-0.60)	●	
Olanzapine and quetiapine	0.61 (0.56-0.66)	●	
Olanzapine monotherapy	0.64 (0.61-0.66)	●	

Tiihonen J, Taipale H, Mehtälä J, et al (2019) Association of Antipsychotic Polypharmacy vs Monotherapy with Psychiatric Rehospitalization among Adults with Schizophrenia. JAMA Psychiatry 76:499–507.
<https://doi.org/10.1001/jamapsychiatry.2018.4320>

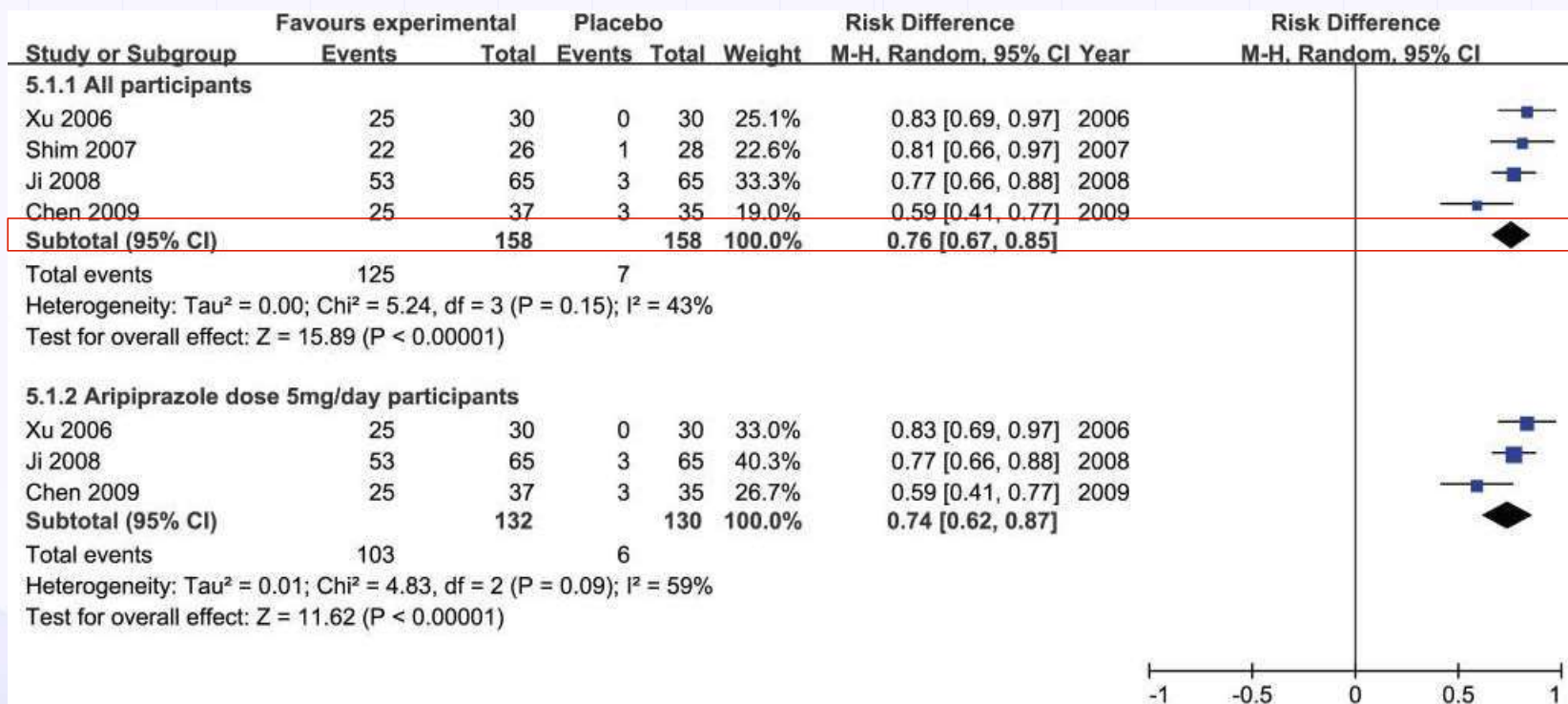
Bewijs Psychiatrische heropname



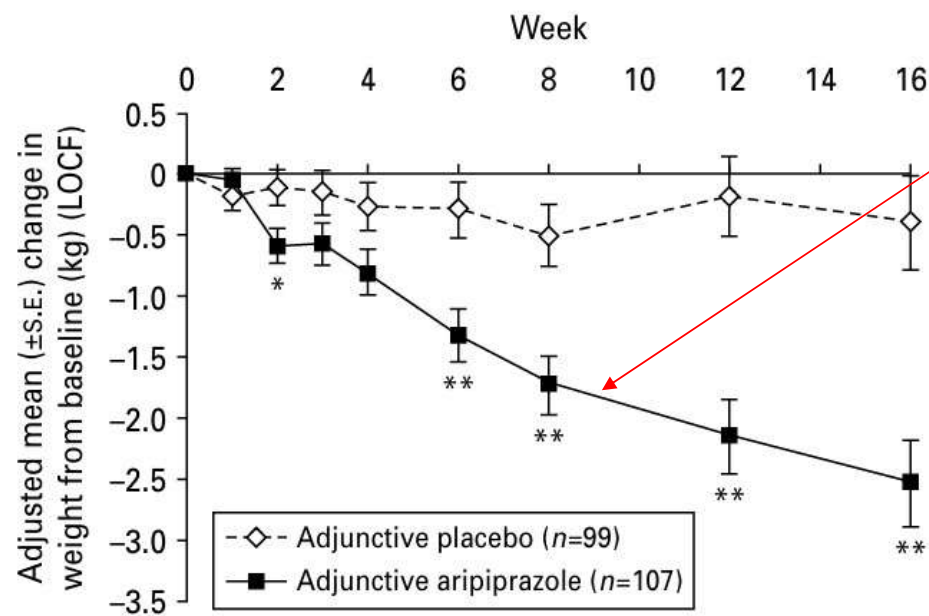
9 to <16.5 mg/dag
aripirazole

Tiihonen J, Tanskanen A, Mittendorfer-Rutz E, Howes OD, Correll CU, Siskind D, Taipale H. Effectiveness of clozapine augmentation with specific doses of other antipsychotics in schizophrenia: a meta-analysis from two nationwide cohorts. *World Psychiatry*. 2025 Jun;24(2):250-259. doi: 10.1002/wps.21316. PMID: 40371869; PMCID: PMC12079427.

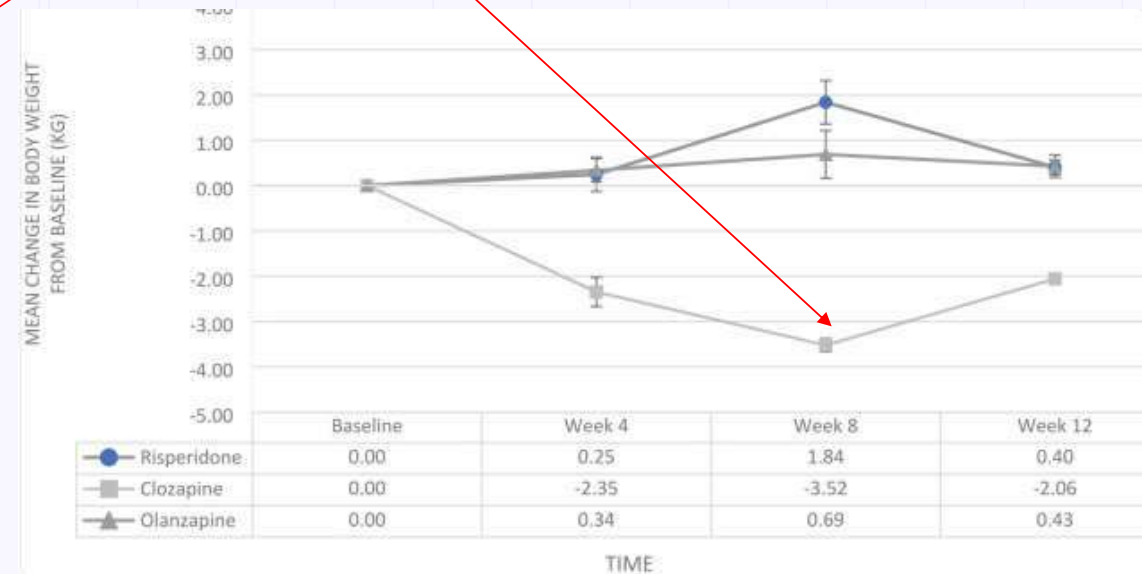
Bewijs Aripiprazole bij hyperprolactine



Bewijs Aripiprazole bij gewichtstoename



Clozapine



W. Wolfgang Fleischhacker, Martti E. Heikkinen, Jean-Pierre Olié, Wally Landsberg, Patricia Dewaele, Robert D. McQuade, Jean-Yves Loze, Delphine Hennicken, Wendy Kerselaers, Effects of adjunctive treatment with aripiprazole on body weight and clinical efficacy in schizophrenia patients treated with clozapine: a randomized, double-blind, placebo-controlled trial, *International Journal of Neuropsychopharmacology*, Volume 13, Issue 8, September 2010, Pages 1115-1125, <https://doi.org/10.1017/S1461145710000490>

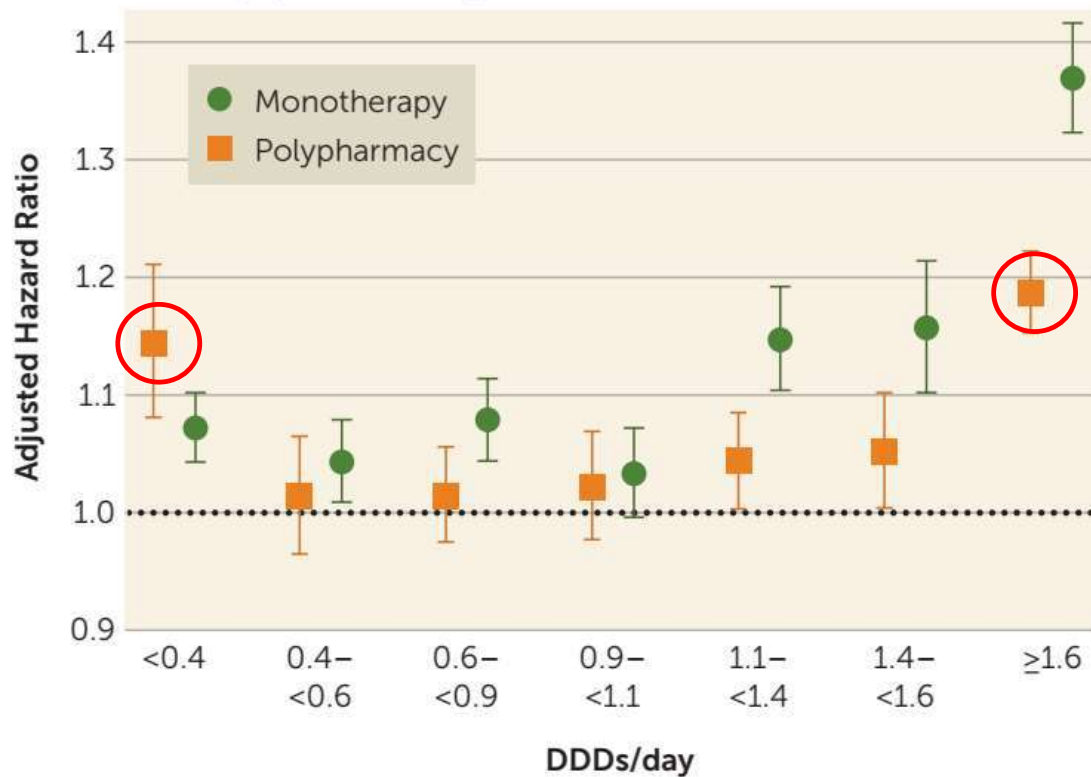
Gupta B, Chee KS, Neo LQ, et al. Effect of aripiprazole as an adjunct to atypical antipsychotics on weight and metabolic profile: a 12-week open-label trial. *Ther Adv Psychopharmacol*. 2021;11. doi:10.1177/20451253211046765

Veiligheid

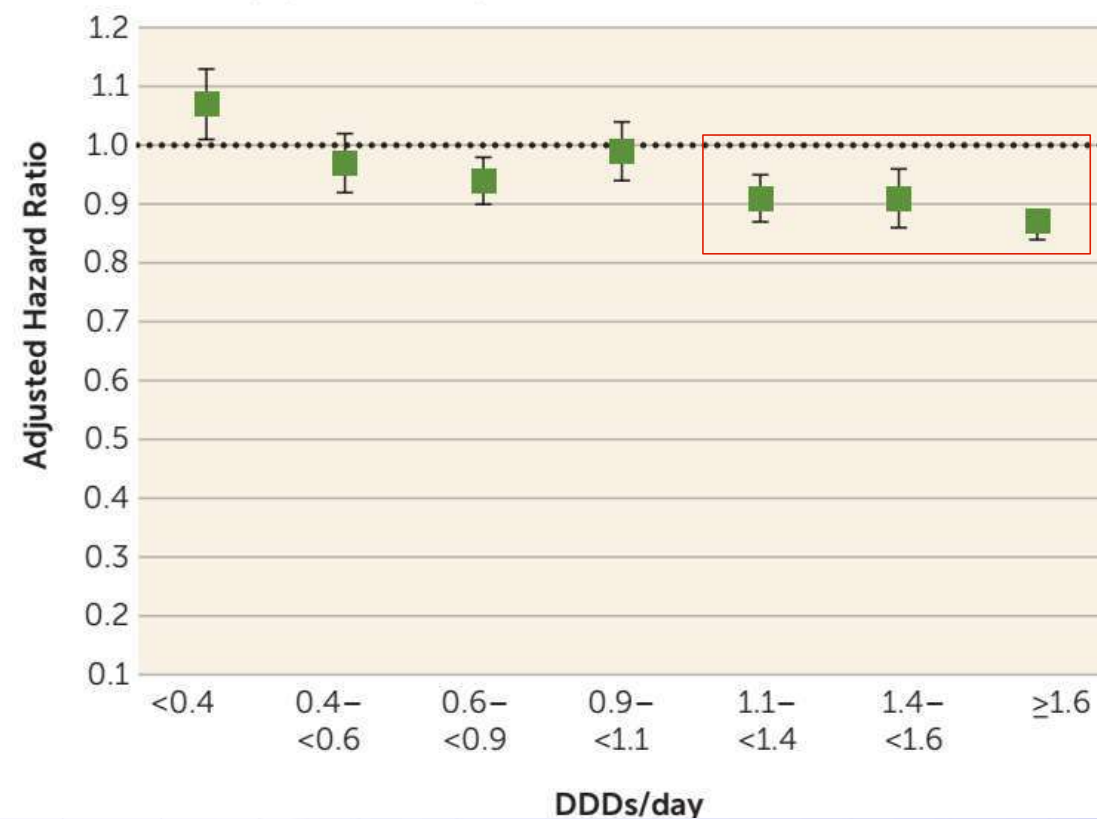
Non-psychiatrische ziekenhuisopname

Nationwide cohort study

A. Risk of Nonpsychiatric Hospitalization



A. Risk of Nonpsychiatric Hospitalization

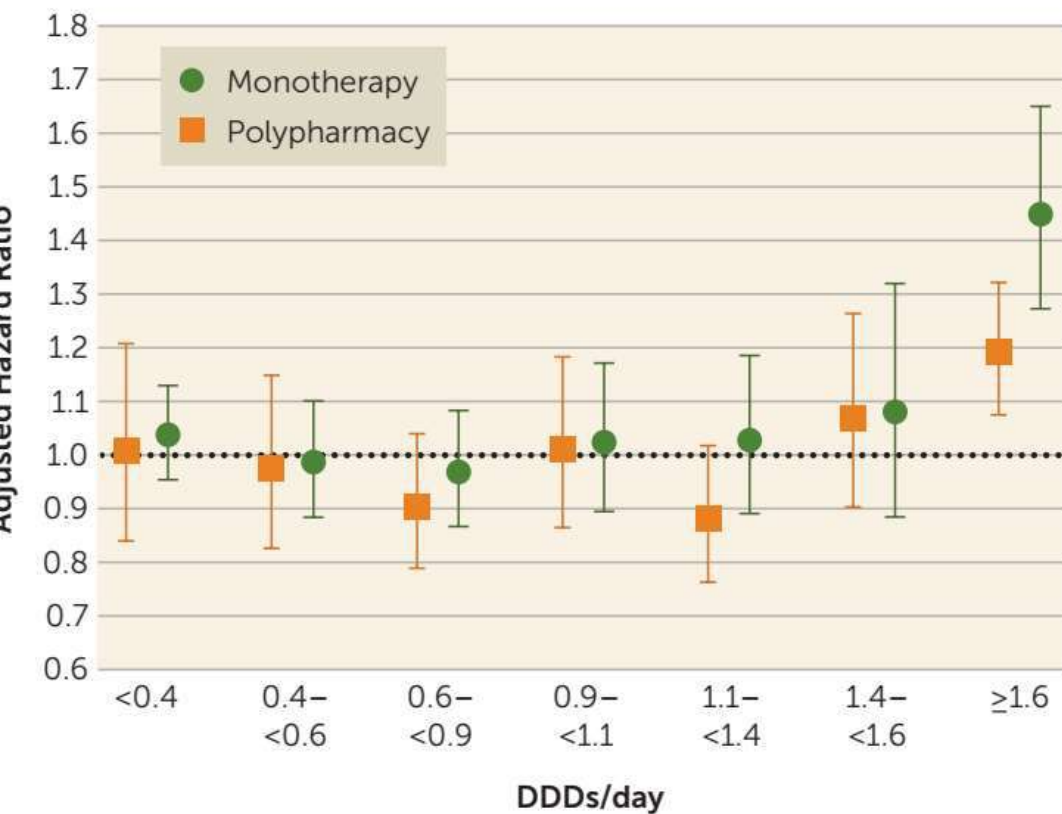


Taipale H, Tanskanen A, Tiihonen J (2023) Safety of Antipsychotic Polypharmacy Versus Monotherapy in a Nationwide Cohort of 61,889 Patients With Schizophrenia. *Am J Psychiatry* 180:377–385. <https://doi.org/10.1176/appi.ajp.20220446>

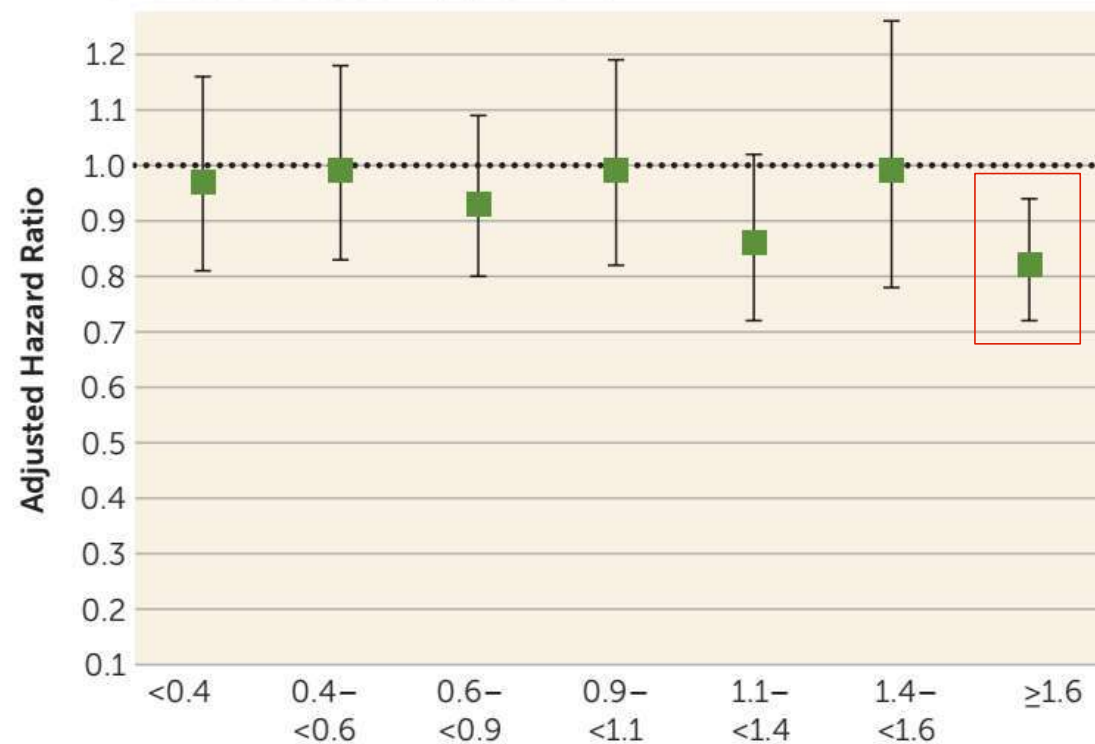
Veiligheid

Cardiovasculaire ziekenhuisopname

B. Risk of Cardiovascular Hospitalization



B. Risk of Cardiovascular Hospitalization



Taipale H, Tanskanen A, Tiihonen J (2023) Safety of Antipsychotic Polypharmacy Versus Monotherapy in a Nationwide Cohort of 61,889 Patients With Schizophrenia. *Am J Psychiatry* 180:377–385. <https://doi.org/10.1176/appi.ajp.20220446>

Ervaren bijwerkingen

tolerantie



	Beta coefficient	Standard error	P-value	95% CI
Total risperidone equivalent dose	0.0549	0.0210	.009	0.0138; 0.0959
Antipsychotic polypharmacy	1.28	0.229	<.001	0.838; 1.73
Female sex	2.18	0.293	<.001	1.60; 2.75
Age	-0.0111	0.0117	.243	-0.0340; 0.0118
Time	-0.0590	0.0326	.070	-0.123; 0.00493

Kikkert MJ, de Mooij L, de Koning M, Dekker J. Subjective Medication Satisfaction With Antipsychotic Polypharmacy in a Naturalistic Inpatient and Outpatient Sample. *J Clin Psychiatry*. 2021 Dec 21;83(1):20m13756. doi: 10.4088/JCP.20m13756. PMID: 34936243.

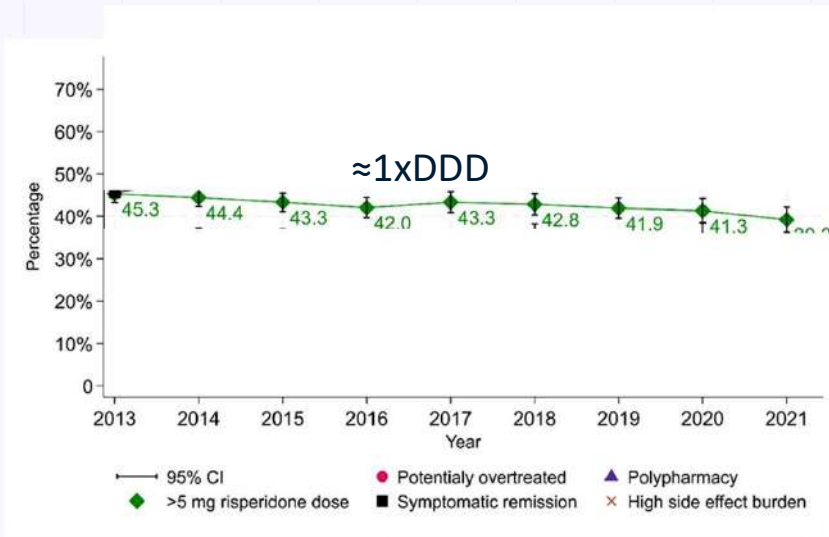
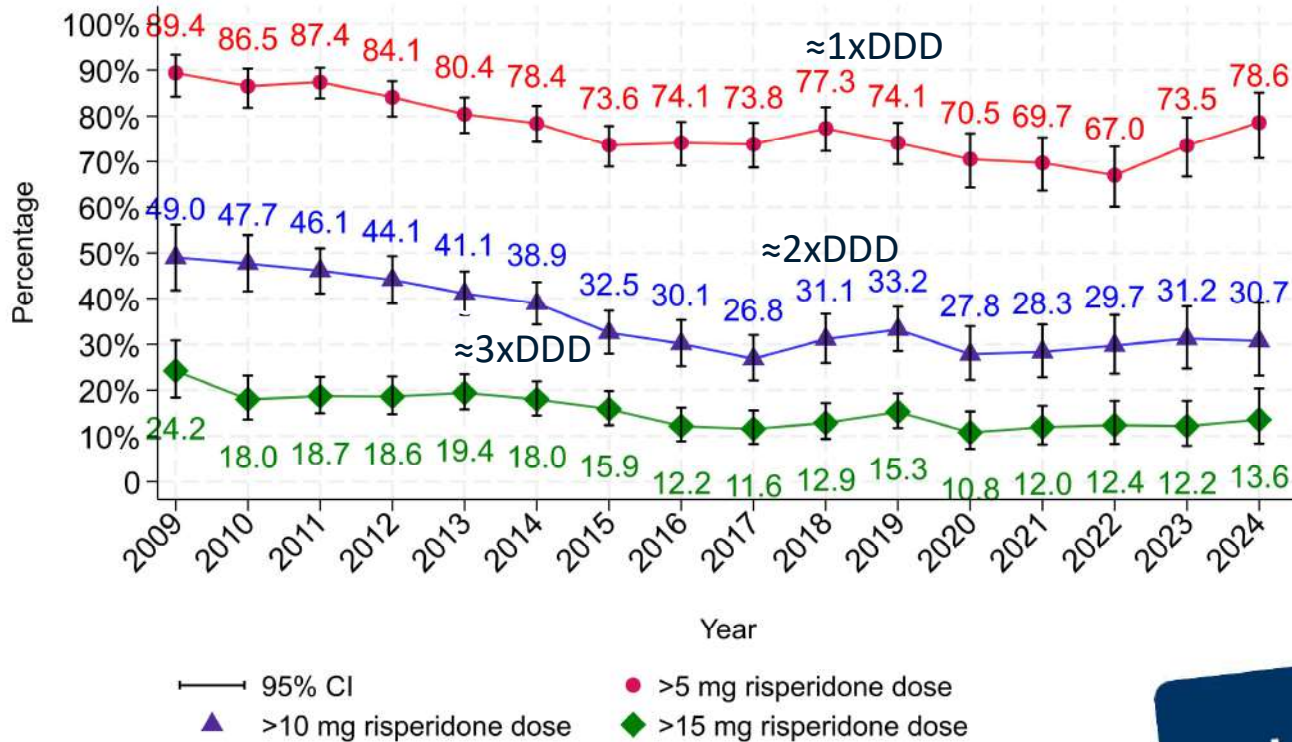
Table 3. Treatment Satisfaction Questionnaire for Medication (TSQM) Scores for Patients Receiving Antipsychotic Monotherapy and Polypharmacy

TSQM Subscale Score ^a	Antipsychotic Monotherapy (n=124)	Antipsychotic Polypharmacy (n=36)	t _{df}	P
Effectiveness	60.9 (19.9)	52.7 (19.8)	2.133 ₁₅₆	.034
Side effects	78.6 (24.9)	68.4 (30.5)	2.049 ₁₅₈	.042
Ease of use	64.0 (14.9)	61.9 (16.7)	0.714 ₁₅₆	.476
Overall satisfaction	59.8 (19.1)	54.6 (19.4)	1.418 ₁₆₃	.158

^aValues are shown as mean (SD). Subscale scores on the TSQM range between 0 and 100; higher scores indicate more satisfaction with medication.

Crutzen S, Gangadin S, Hua KH, Visser E, Jörg F, van der Meer L, Pijnenborg GHM, Veling W, Castelein S. Trends in Antipsychotic Polypharmacy and Potential Overtreatment with Antipsychotics: A Naturalistic Cohort Study of People in Long-term Care. *Schizophr Bull*. 2026 Jan 16;52(1):sbaf041. doi: 10.1093/schbul/sbaf041. PMID: 40329432; PMCID: PMC12809800.

Total dosering polyfarmacie

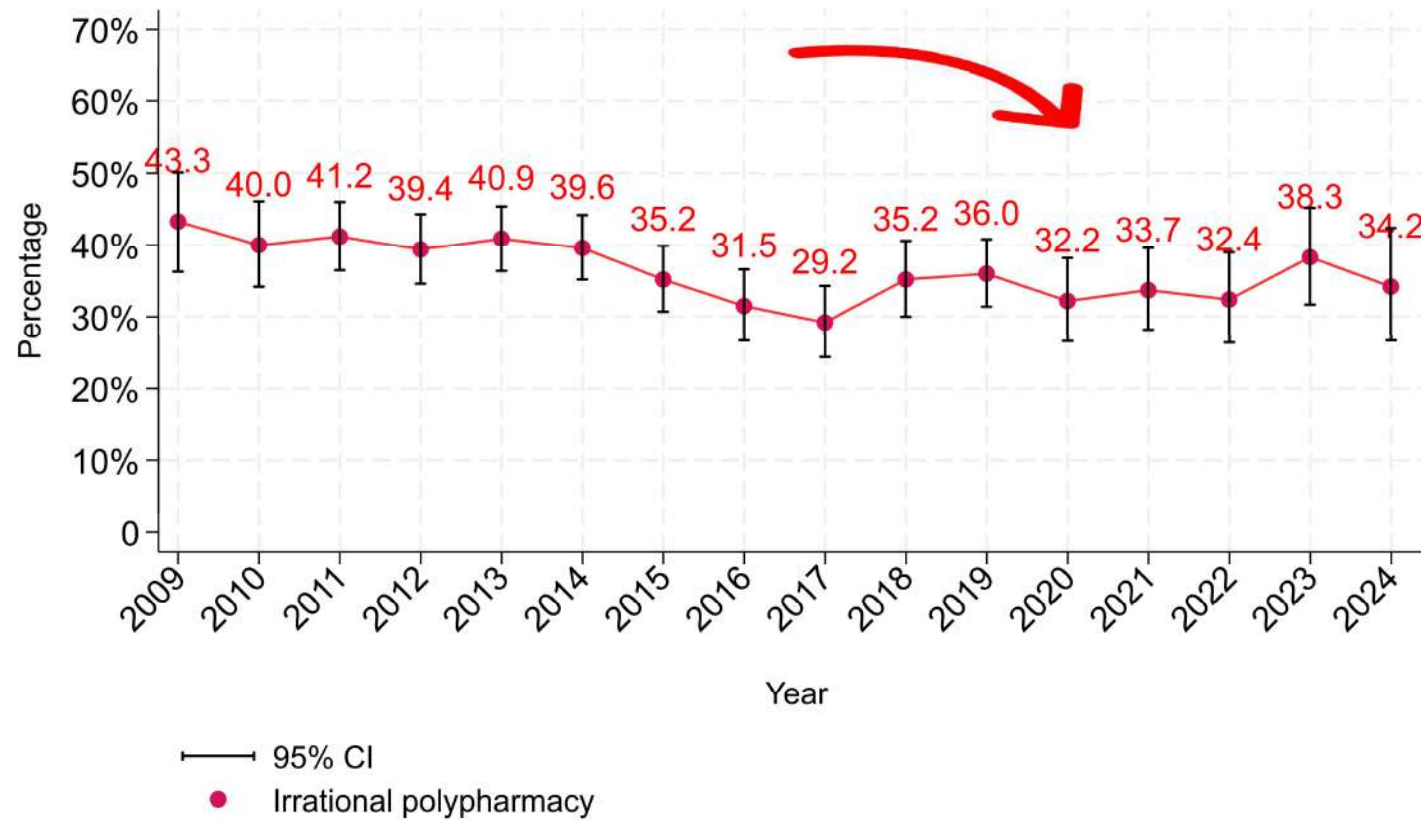


Onlogische combinaties

(In de meeste gevallen)

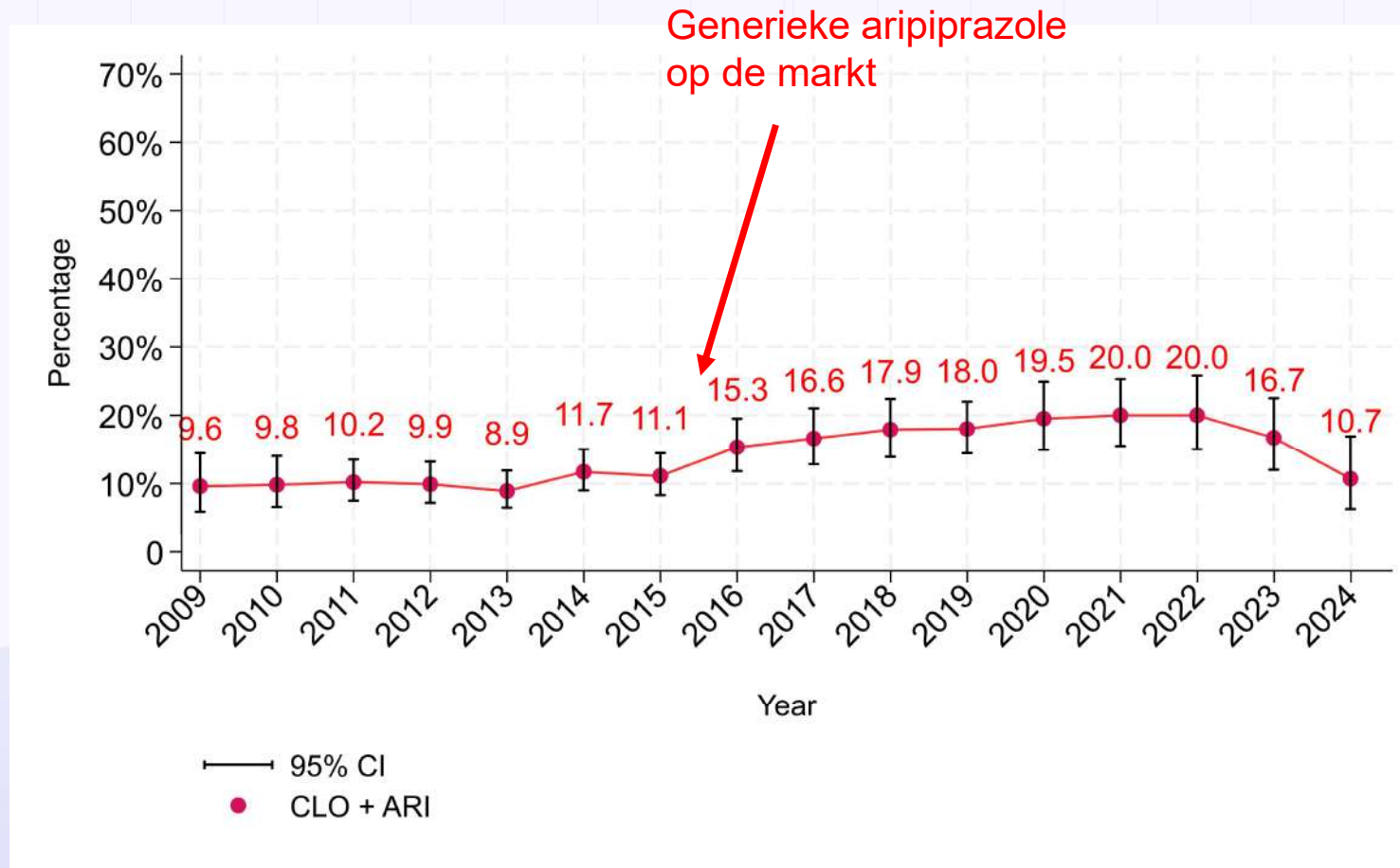
1. 2 sterke D2 antagonisten (Haloperidol, risperidon, amisulpride, Paliperidon, Zuclopentixol)
2. 2 "pines" (clozapine, quetiapine and olanzapine)
3. 3 verschillende antipsychotica
4. Augmentatie van clozapine met een hoog gedoseerde tweede antipsychoticum
5. Augmentatie met hoog gedoseerde aripirazole >16.5mg

Onlogische combinaties



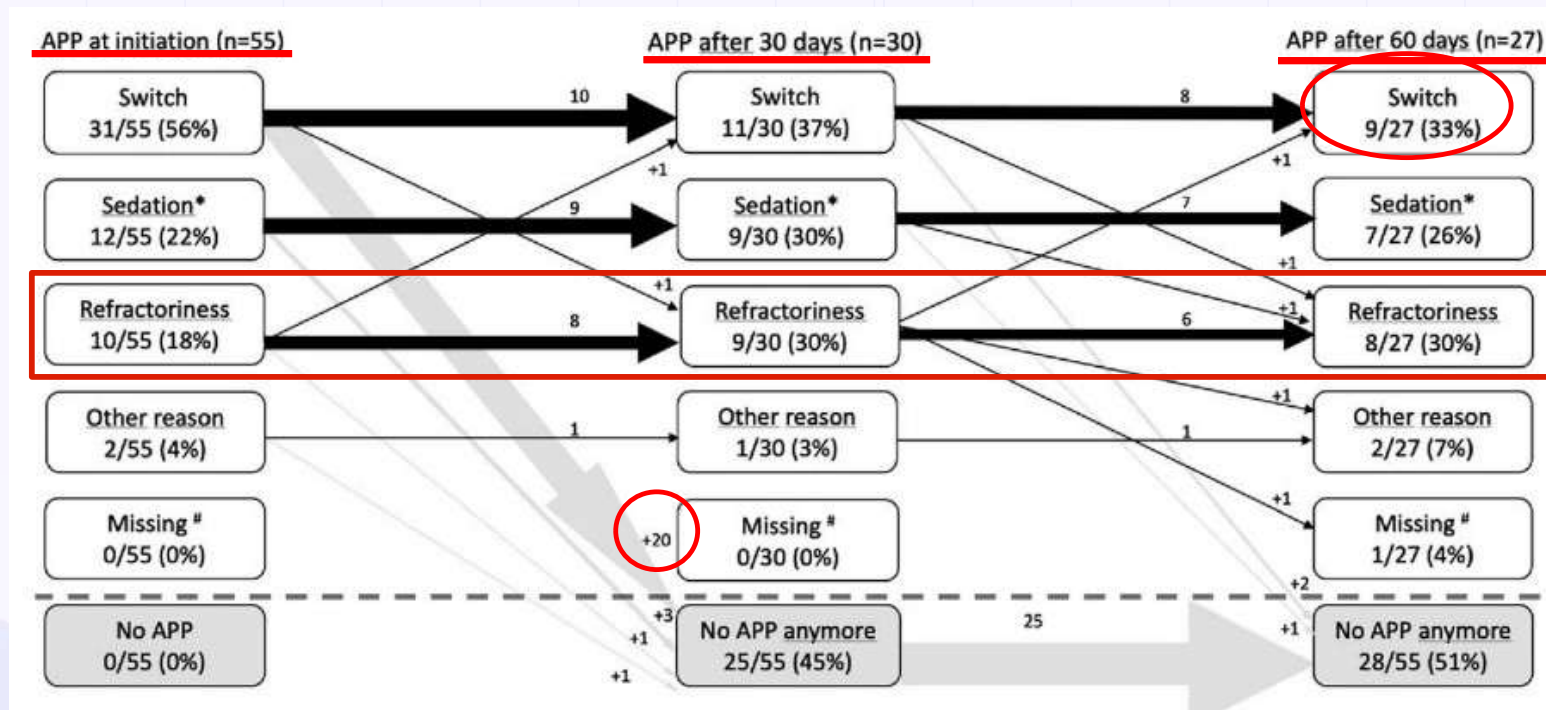
Evidence based combinaties

Clozapine plus aripiprazole



Rationeel gebruik

Cross-titration trap

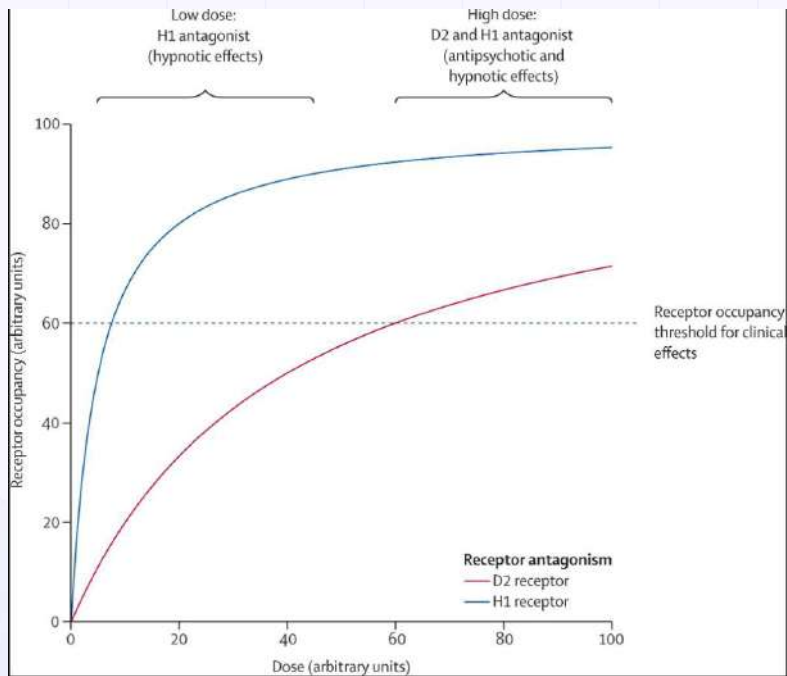


Post hoc ergo propter hoc

Off-label
Effectiviteit

Rationeel gebruik

Off-label



Sedatie
Activatie
prolactine verlagen
Gewichtsafname
Stemmingsklachten

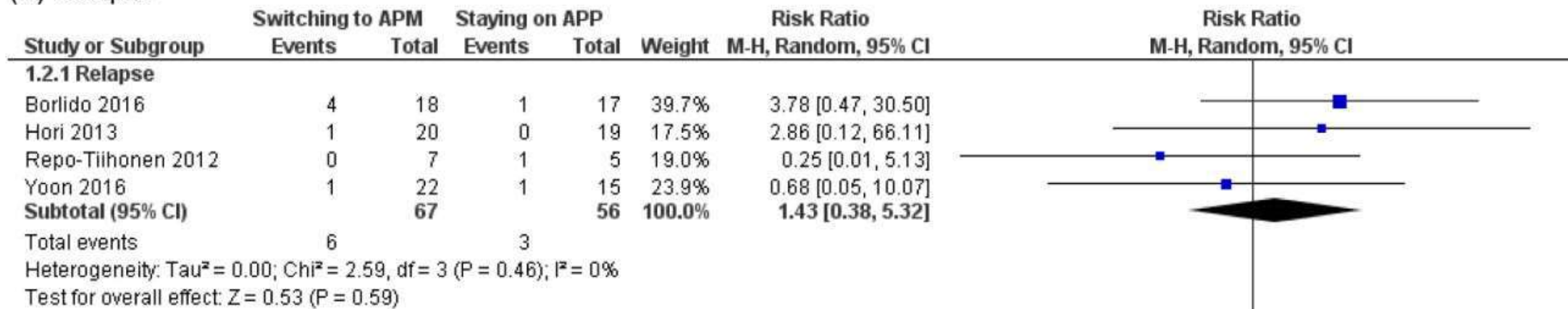
Zemach S, Zohar J, Correll CU, Stahl SM, Drago F, Goodwin GM, Moller HJ, Uchida H, Sifis S, Santos M, Blier P. Dose-dependent pharmacological mechanisms within the Neuroscience-based Nomenclature: a new concept to facilitate neuroscience-based prescribing. *Lancet Psychiatry*. 2026 Jan 14:S2215-0366(25)00338-4. doi: 10.1016/S2215-0366(25)00338-4. Epub ahead of print. PMID: 41547365.

Afbouwen polyfarmacie

Terugval (RCT)

Switchen naar
mono-therapie

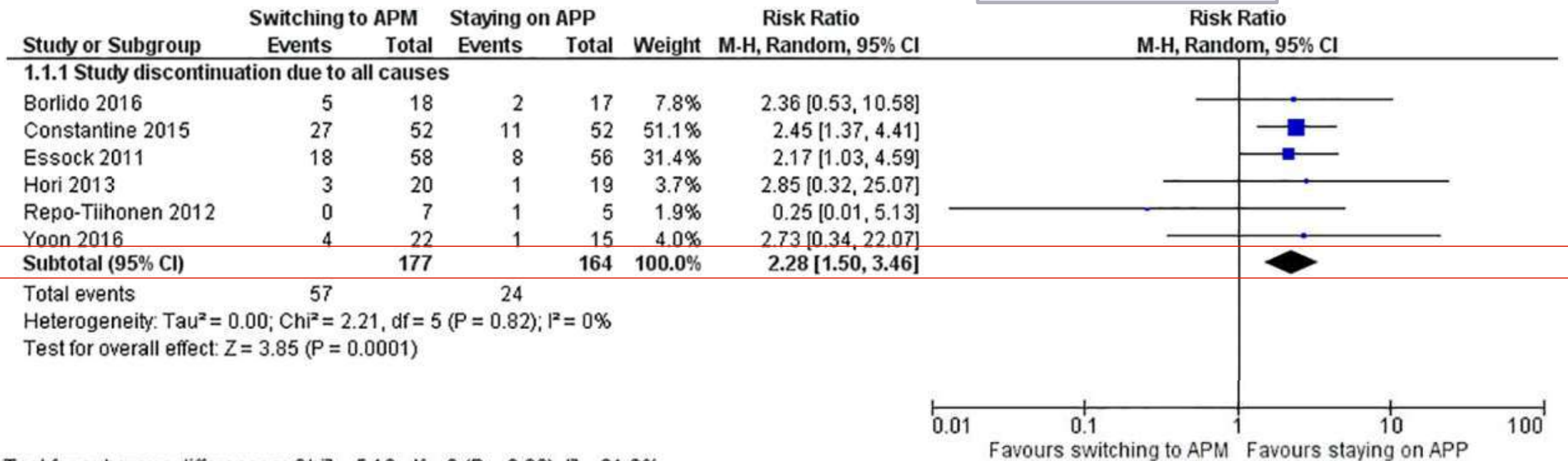
(A) Relapse



Afbouwen polyfarmacie

All cause discontinuation (RCT)

Switchen naar mono-therapie



Antipsychotica polyfarmacie

Samenvatting

- Logisch in theorie? = Ja op zich wel
- Effectiever? = Soms/misschien/in bepaalde contexten
- Evidence based? = Zelden
- Veiliger? = Ja, maar nee.....
- Minder bijwerkingen? = Eerder meer, behalve.....
- Kan je afbouwen? = Waarschijnlijk, maar let op

Clozapine + aripiprazole 9-16.5 mg

Take home message

Wees terughoudend!

Bedankt voor de aandacht!
s.crutzen@lentis.nl