

Effecten en bijwerkingen van 32 orale antipsychotica: een systematisch overzicht en netwerkmeta-analyse

C.A.J. BAAS, S.K. SPOELSTRA, H. KNEGTERING

Stephan Leucht en collega's publiceerden de laatste 15 jaar meerdere overzichten over de werkzaamheid en bijwerkingen van antipsychotica (Leucht e.a. 2013). Wij bespreken een sterk uitgebreid en geactualiseerd overzicht uit 2019 met Maximilian Huhn als eerste auteur. De belangrijkste conclusie is dat de verschillen in bijwerkingen groter zijn dan de verschillen in werkzaamheid (Huhn e.a. 2019).

De auteurs includeerden 402 studies met in totaal 53.463 deelnemers, allen met acute symptomen van schizofrenie of aanverwante stoornissen zoals schizoaffectieve stoornis, bij een gemiddelde ziekteduur van 12 jaar. 32 antipsychotica werden vergeleken op acht dimensies voor effectiviteit (algeheel beeld, positieve, negatieve en depressieve symptomen, levenskwaliteit, sociaal functioneren, stoppen vanwege gebrek aan werkzaamheid en stoppen om alle redenen) en acht dimensies voor bijwerkingen (parkinsonisme, akathisie, gewichtstoename in kg, gewichtstoename meer dan 7%, sedatie, prolactinestijging, otc-verlenging en anticholinerge bijwerkingen). Natuurlijk werden de verschillen in deze 16 uitkomstmaten tussen de 32 antipsychotica niet allemaal in direct vergelijkend onderzoek bepaald. Een netwerkanalyse maakt het mogelijk te schatten hoe middelen die niet direct met elkaar zijn vergeleken zich ten opzichte van elkaar verhouden. Met bayesiaanse statistiek is het mogelijk aan deze verhoudingen een geloofwaardigheid toe te kennen (credibility interval). Zo konden de auteurs voor elke uitkomstmaat een rangorde bepalen: deze gaven zij in 16 tabellen weer. De onderliggende 402 onderzoeken verschilden in methodologie, kwaliteit en gebruikte meet schalen, maar de rangordes in de tabellen bleven onveranderd na allerlei correcties (o.a. voor jaar van publicatie, placeborespons of percentage mannen). Daarom gaan de auteurs ervan uit dat hun resultaten redelijk betrouwbaar zijn.

Enkele opvallende bevindingen: in onderzoek naar oudere antipsychotica bleken er kleinere studies, kleinere placebo-effecten en meer publicatiebias te zijn geweest, waardoor hun werkzaamheid mogelijk werd overschat ten opzichte van nieuwere middelen. Hoge effectiviteit van amisulpride

en clozapine op 'algemene symptoomverandering' en 'positieve symptomen' contrasteerde met het grote risico op otc-verlenging bij amisulpride en de grote kans op gewichtstoename, anticholinerge effecten en sedatie bij clozapine. De hoge effectiviteit van clozapine bleek te berusten op tamelijk kleine onderzoeken en het geloofwaardigheidsinterval voor effect op positieve symptomen overlapte dan ook met dat van veel andere antipsychotica. Het in Nederland weinig bekende zotepine bleek op werking hoog te scoren, maar gaf een opvallend hoog risico op gewichtstoename en sedatie.

Dankzij de overzichtelijke tabellen van voor- en nadelen kan dit artikel helpen om samen met de patiënt een individuaaliserende en weloverwogen keus te maken voor een antipsychoticum.

Tegelijkertijd belichten de auteurs naar ons gevoel een belangrijk probleem onvoldoende. De onderliggende onderzoeken betreffen alle kortetermijneffecten (meestal 6 weken) op acute symptomen tijdens ziektebelopen van gemiddeld 12 jaar, waarbij steeds de patiënten met de

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Table of Contents Groepstherapie En Sensitivitraig Een Systematisch Overzicht

1. Understanding the eBook Groepstherapie En Sensitivitraig Een Systematisch Overzicht
 - The Rise of Digital Reading Groepstherapie En Sensitivitraig Een Systematisch Overzicht
 - Advantages of eBooks Over Traditional Books
2. Identifying Groepstherapie En Sensitivitraig Een Systematisch Overzicht
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Groepstherapie En Sensitivitraig Een Systematisch Overzicht
 - User-Friendly Interface
4. Exploring eBook Recommendations from Groepstherapie En Sensitivitraig Een Systematisch Overzicht
 - Personalized Recommendations
 - Groepstherapie En Sensitivitraig Een Systematisch Overzicht User Reviews and Ratings

- Groepstherapie En Sensitivitairng Een Systematisch Overzicht and Bestseller Lists
- 5. Accessing Groepstherapie En Sensitivitairng Een Systematisch Overzicht Free and Paid eBooks
 - Groepstherapie En Sensitivitairng Een Systematisch Overzicht Public Domain eBooks
 - Groepstherapie En Sensitivitairng Een Systematisch Overzicht eBook Subscription Services
 - Groepstherapie En Sensitivitairng Een Systematisch Overzicht Budget-Friendly Options
- 6. Navigating Groepstherapie En Sensitivitairng Een Systematisch Overzicht eBook Formats
 - ePub, PDF, MOBI, and More
 - Groepstherapie En Sensitivitairng Een Systematisch Overzicht Compatibility with Devices
 - Groepstherapie En Sensitivitairng Een Systematisch Overzicht Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Highlighting and Note-Taking Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Interactive Elements Groepstherapie En Sensitivitairng Een Systematisch Overzicht
- 8. Staying Engaged with Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Groepstherapie En Sensitivitairng Een Systematisch Overzicht
- 9. Balancing eBooks and Physical Books Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Groepstherapie En Sensitivitairng Een Systematisch Overzicht
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Setting Reading Goals Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Fact-Checking eBook Content of Groepstherapie En Sensitivitairng Een Systematisch Overzicht
 - Distinguishing Credible Sources

13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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