

#CHAIR2020

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Master Class for Neuroscience Professional Development

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Schizophrenia

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Chart Review: Charles

Background

54-year-old man whose first hospitalization was at age 21. Reports he was diagnosed with anxiety and depression. However, discharged after 1 month on fluphenazine, suggesting diagnosis and treatment for schizophrenia. Described as “reclusive” and discharged to live with family. Treated for years with fluphenazine, eventually as a depot.

Psychiatric History

Hospitalized 10 times over the last 30 years - last time was 2 months ago. Hospitalizations all due to non-adherence. Develops progressively odd behavior and beliefs followed by disorganization and hallucinations over several weeks.

Psychotropic Medications

Haloperidol 15 mg, risperidone 4 mg

Chart Review: Charles

2006

Did well on haloperidol with a pattern of recovery and stability, then followed by non-adherence due to loss of insight, leading to relapse every 3 years. Pattern persisted with non-adherence. It was thought that he would do better on depot medication. Failed risperidone but did well on fluphenazine. Since did well on haloperidol, switched to haloperidol decanoate 100/mo. You notified and mobilized family when he eventually missed shots.

2006-2012

Remained in treatment for 6 years. Worked in construction, lived in single-room occupancy buildings, moved frequently. Borrowed from loan sharks, often threatened. Refused depot and resumed oral prescription. Involuntary admission in 2009 following non-adherence. Three involuntary hospitalizations in 2012. When he last presented, he was lying on the highway encrusted in urine and feces.

Chart Review: Charles

Hospital Course

Anxious, disorganized, pacing, incoherent, with delusions. Good response to haloperidol. Discharged on oral medication to nursing homes.

Take-Home Points

History predicted clinical course. Patient had 36 months of good judgment before relapsing. Poor insight and treatment non-adherence led to devastating consequences including step-wise functional deterioration.

SMART GOALS

- Incorporate level of insight in to determining self report history and diagnosis
- Consider long term delivery options early in course of disease to attenuate trajectory
- Consider which treatments have long term delivery options when choosing initial therapy



Meta-Analysis of Randomized Trials of Depot Versus Oral Medication

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Schizophrenia Research

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Oral versus depot antipsychotic drugs for schizophrenia—A critical systematic review and meta-analysis of randomised long-term trials

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What Have We Learned About Long-term Delivery?



Depots Significantly Reduce Relapse (0.0009)

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Study or Subgroup	Depot		Oral		Weight	Risk Ratio	Risk Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
Arango 2005	10	26	6	20	5.2%	1.28 [0.56, 2.93]	
Barnes 1983	3	19	3	17	1.9%	0.89 [0.21, 3.85]	
Del Guidice 1975	21	27	30	31	22.8%	0.80 [0.65, 0.99]	
Falloon 1978	8	20	5	24	4.2%	1.92 [0.74, 4.95]	
Gaebel 2010	54	355	102	355	18.6%	0.53 [0.39, 0.71]	
Hogarty 1979	22	55	32	50	14.8%	0.63 [0.43, 0.92]	
Li 1996	32	155	52	137	15.1%	0.54 [0.37, 0.79]	
Potapov 2008	4	20	8	20	3.6%	0.50 [0.18, 1.40]	
Rifkin 1977	2	23	3	28	1.4%	0.81 [0.15, 4.45]	
Schooler 1979	26	143	35	147	12.4%	0.76 [0.49, 1.20]	
Total (95% CI)		843		829	100.0%	0.70 [0.57, 0.87]	

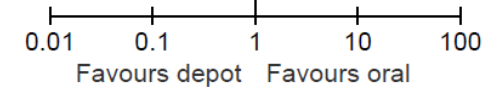
Total events

182

276

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 15.35$, $df = 9$ ($P = 0.08$); $I^2 = 41\%$

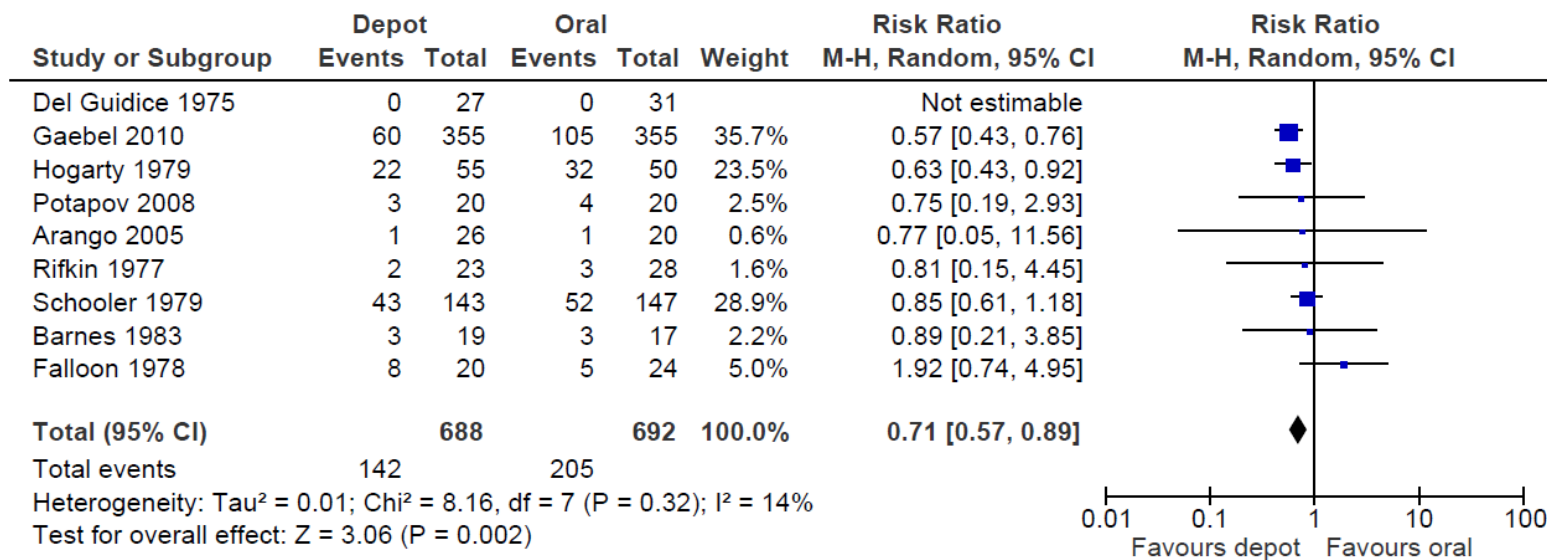
Test for overall effect: $Z = 3.32$ ($P = 0.0009$)





Depots Significantly Reduce Dropout Due to Efficacy (0.002)

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But no sig. differences in dropout due to side effects
 No diff. for hospitalization in controlled studies
 Save for Q&A – medical, academic and commercial concerns



Naturalistic Studies Also Support Long-Term Drug Delivery In Real World Situations

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- 10-yr retrospective/5-yr prospective study in West Africa
 - Reduction from 100 d/yr. oral to 5 d/yr. depot (de Jong, 2006)
- 2,588 patients on Finland over 7 yr.
 - 1/3rd hospitalizations on depot vs. oral (Tiihonen, 2011)
- Re-hospitalization significantly lower in German outpatients with depot after 24 & 36 mo ($p = .03$, $p = .03$, (Gutwinski et al., 2007))

Conclusion: Depots work better than oral medications

Challenge: How do we extend this approach for better care?



Part 2: Goals for Long-Term Antipsychotic Delivery System (Short Term Impact)

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- Career detour – from imaging to drug delivery
- 1 year of medication delivery
- Simple outpatient procedure done by Psychiatrists
- Biodegradable - no need for removal
- Protectable IP - 18 patents issued for antipsychotic and Parkinson's Dis. medications licensed to NuPathe / Teva
- Removable if necessary *
- Simple process & design using GRAS materials *
- Scalable and amenable to other APIs