A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO SCHIZOPHRENIA –

some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – PRIMARY CARE PROVIDERS' ROLE IN THE CARE OF PATIENTS WITH SCHIZOPHRENIA

Viron M, Baggett T, Hill M, Freudenreich O. Schizophrenia for primary care providers: how to contribute to the care of a vulnerable patient population. Am J Med. 2012 Mar;125(3):223-30. doi: 10.1016/j.amjmed.2011.05.002. Review. PubMed PMID: 22340915.

URL: http://www.sciencedirect.com/science/article/pii/S0002934311003858 -- payment required

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Comment in Am J Med. 2012 Mar;125(3):219-20.

ABSTRACT

Patients with schizophrenia represent a vulnerable population with high medical needs that are often missed or undertreated. Primary care providers have the potential to reduce health disparities experienced by this population and make a substantial difference in the overall health of these patients. This review provides primary care providers with a general understanding of the psychiatric and medical issues specific to patients with schizophrenia and a clinically practical framework for engaging and assessing this vulnerable patient population and assisting them in achieving optimal health. Initial steps in this framework include conducting a focused medical evaluation of psychosis and connecting patients with untreated psychosis to psychiatric care as promptly as possible. Given the significant contribution of cardiovascular disease to morbidity and mortality in schizophrenia, a top priority of primary care for patients with schizophrenia should be cardiovascular disease prevention and treatment through regular risk factor screening, appropriate lifestyle interventions, and other indicated therapies.

 PMID: 22340915 [PubMed - indexed for MEDLINE]

READING 2 – COMPULSORY COMMUNITY TREATMENT ORDERS MIGHT REDUCE MORTALITY AMONG PATIENTS WITH PSYCHIATRIC DISORDERS

Kisely S, Preston N, Xiao J, Lawrence D, Louise S, Crowe E. Reducing all-cause mortality among patients with psychiatric disorders: a population-based study. CMAJ. 2013 Jan 8;185(1):E50-6. doi: 10.1503/cmaj.121077. Epub 2012 Nov 12. PubMed PMID: 23148054; PubMed Central PMCID: PMC3537812.

URL: http://www-ncbi-nlm-nih-gov/pmc/articles/PMC3537812/pdf/1850e50.pdf - Free full text

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ABSTRACT

BACKGROUND: Among patients with psychiatric disorders, there are 10 times as many preventable deaths from physical disorders as there are from suicide. We investigated whether compulsory community treatment, such as community treatment orders, could reduce all-cause mortality among patients with psychiatric disorders.

METHODS: We conducted a population-based survival analysis of an inception cohort using record linking. The study period extended from November 1997 to December 2008. The cohort included patients from all community-based and inpatient psychiatric services in Western Australia (state population 1.8 million). We used a 2-stage design of matching and Cox regression to adjust for demographic characteristics, previous use of health services, diagnosis and

length of psychiatric history. We collected data on successive cohorts for each year for which community treatment orders were used to measure changes in numbers of patients, their characteristics and outcomes. Our primary outcome was 2-year all-cause mortality. Our secondary outcomes were 1-and 3-year all-cause mortality.
RESULTS: The study population included 2958 patients with community treatment orders (cases) and 2958 matched controls (i.e., patients with psychiatric disorders who had not received a community treatment order). The average age for cases and controls was 36.7 years, and 63.7% (3771) of participants were men. Schizophrenia and other nonaffective psychoses were the most common diagnoses (73.4%) among participants. A total of 492 patients (8.3%) died during the study. Cox regression showed that, compared with controls, patients with community treatment orders had significantly lower all-cause mortality at 1, 2 and 3 years, with an adjusted hazard ratio of 0.62 (95% confidence interval 0.45-0.86) at 2 years. The greatest effect was on death from physical illnesses such as cancer, cardiovascular disease or diseases of the central nervous system. This association disappeared when we adjusted for increased outpatient and community contacts with psychiatric services.
INTERPRETATION: Community treatment orders might reduce mortality among patients with psychiatric disorders. This may be partly explained by increased contact with health services in the community. However, the effects of uncontrolled confounders cannot be excluded.
PMCID: PMC3537812 PMID: 23148054 [PubMed - in process]

READING 3 – COST EFFECTIVE STRATEGIES

Chisholm D, Saxena S. Cost effectiveness of strategies to combat neuropsychiatric conditions in sub-Saharan Africa and South East Asia: mathematical modelling study. BMJ. 2012 Mar 2;344:e609. doi: 10.1136/bmj.e609. PubMed PMID: 22389339; PubMed Central PMCID: PMC3292519.

URL: http://www-ncbi-nlm-nih-gov/pmc/articles/PMC3292519/pdf/bmj.e609.pdf - full free text

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ABSTRACT
OBJECTIVE: To assess the comparative costs and effects of interventions to combat five neuropsychiatric conditions (schizophrenia, bipolar disorder, depression, epilepsy, and heavy alcohol use). DESIGN: Cost effectiveness analysis based on an epidemiological model.
SETTING: Two epidemiologically defined World Health Organization sub-regions of the world: countries in sub-Saharan Africa with very high adult and high child mortality (AfrE); and countries in South East Asia with high adult and high child mortality (SearD).
DATA SOURCES: Published studies, costing databases.
MAIN OUTCOME MEASURES: Cost per capita and cost per disability adjusted life year (DALY) averted, expressed in international dollars ($Int) for the year 2005.
RESULTS: Across 44 assessed intervention strategies for the five neuropsychiatric conditions, cost effectiveness values differed by as much as two orders of magnitude (from $Int100-250 to $Int10,000-25,000 for a year of healthy life gained). In both sub-regions, inpatient based treatment of schizophrenia with newer antipsychotic drugs was the most costly and least cost effective strategy. The most cost effective strategies in the African sub-region related to population based alcohol control, while in the South East Asian sub-region the most cost effective intervention was drug treatment of epilepsy in primary care. The cumulative cost per capita of the most cost effective set of interventions covering all five conditions was estimated at $Int4.90-5.70. This package comprises interventions for epilepsy (older first line antiepileptic drugs); depression (generically produced newer antidepressants and psychosocial treatment); bipolar disorder (mood stabiliser drug lithium); schizophrenia (neuroleptic antipsychotic drugs and psychosocial treatment); and heavy alcohol use (increased taxation and its enforcement, reduced access, and, in the African sub-region, advertising bans and brief advice to heavy drinkers in primary care).
CONCLUSIONS: Reallocation of resources to cost effective intervention strategies would increase health gain, save money and help implement much needed expansion of services for neuropsychiatric conditions in low resource settings.
PMCID: PMC3292519 PMID: 22389339 [PubMed - indexed for MEDLINE]

READING 4 – TREATMENT OF HALLUCINATIONS IN SCHIZOPHRENIA SPECTRUM DISORDERS

Sommer IE, Slotema CW, Daskalakis ZJ, Derks EM, Blom JD, van der Gaag M. The treatment of hallucinations in schizophrenia spectrum disorders. Schizophr Bull. 2012 Jun;38(4):704-14. doi: 10.1093/schbul/sbs034. Epub 2012 Feb 24. Review.
PubMed PMID: 22368234.

URL: http://schizophreniabulletin.oxfordjournals.org/content/38/4/704.full.pdf+html – payment required

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ABSTRACT
This article reviews the treatment of hallucinations in schizophrenia. The first treatment option for hallucinations in schizophrenia is antipsychotic medication, which can induce a rapid decrease in severity. Only 8% of first-episode patients still experience mild to moderate hallucinations after continuing medication for 1 year. Olanzapine, amisulpride, ziprasidone, and quetiapine are equally effective against hallucinations, but haloperidol may be slightly inferior. If the drug of first choice provides inadequate improvement, it is probably best to switch medication after 2-4 weeks of treatment. Clozapine is the drug of choice for patients who are resistant to 2 antipsychotic agents. Blood levels should be above 350-450 μg/ml for maximal effect. For relapse prevention, medication should be continued in the same dose. Depot medication should be considered for all patients because nonadherence is high. Cognitive-behavioral therapy (CBT) can be applied as an augmentation to antipsychotic medication. The success of CBT depends on the reduction of catastrophic appraisals, thereby reducing the concurrent anxiety and distress. CBT aims at reducing the emotional distress associated with auditory hallucinations and develops new coping strategies. Transcranial magnetic stimulation (TMS) is capable of reducing the frequency and severity of auditory hallucinations. Several meta-analyses found significantly better symptom reduction for low-frequency repetitive TMS as compared with placebo. Consequently, TMS currently has the status of a potentially useful treatment method for auditory hallucinations, but only in combination with state of the art antipsychotic treatment. Electroconvulsive therapy (ECT) is considered a last resort for treatment-resistant psychosis. Although several studies showed clinical improvement, a specific reduction in hallucination severity has never been demonstrated.
PMID: 22368234 [PubMed - indexed for MEDLINE]

READING 5 – COMPARING EFFICACY AND SAFETY OF INDIVIDUAL SECOND GENERATUIB ANTIPSYCHOTICS VS FIRST GENERATION ANTIPSYCHOTICS

Zhang JP, Gallego JA, Robinson DG, Malhotra AK, Kane JM, Correll CU. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: a systematic review and meta-analysis. Int J Neuropsychopharmacol. 2012 Dec 3:1-14. [Epub ahead of print] PubMed PMID: 23199972.

URL: http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=8768990 – payment needed

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ABSTRACT
Because early treatment choice is critical in first-episode schizophrenia-spectrum disorders (FES), this meta-analysis compared efficacy and tolerability of individual second-generation antipsychotics (SGAs) with first-generation antipsychotics (FGAs) in FES. We conducted systematic literature search (until 12 December 2010) and meta-analysis of acute, randomized trials with ≥1 FGA vs. SGA comparison; patients in their first episode of psychosis and

diagnosed with schizophrenia-spectrum disorders; available data for psychopathology change, treatment response, treatment discontinuation, adverse effects, or cognition. Across 13 trials (n = 2509), olanzapine (seven trials) and amisulpride (one trial) outperformed FGAs (haloperidol: 9/13 trials) in 9/13 and 8/13 efficacy outcomes, respectively, risperidone (eight trials) in 4/13, quetiapine (one trial) in 3/13 and clozapine (two trials) and ziprasidone (one trial) in 1/13, each. Compared to FGAs, extrapyramidal symptom (EPS)-related outcomes were less frequent with olanzapine, risperidone and clozapine, but weight gain was greater with clozapine, olanzapine and risperidone. Pooled SGAs were similar to FGAs regarding total psychopathology change, depression, treatment response and metabolic changes. SGAs significantly outperformed FGAs regarding lower treatment discontinuation, irrespective of cause, negative symptoms, global cognition and less EPS and akathisia, while SGAs increased weight more ($p < 0.05$-0.01). Results were not affected by FGA dose or publication bias, but industry-sponsored studies favoured SGAs more than federally funded studies. To summarize, in FES, olanzapine, amisulpride and, less so, risperidone and quetiapine showed superior efficacy, greater treatment persistence and less EPS than FGAs. However, weight increase with olanzapine, risperidone and clozapine and metabolic changes with olanzapine were greater. Additional FES studies including broader-based SGAs and FGAs are needed.
PMID: 23199972 [PubMed - as supplied by publisher]

READING 6 – RELAPSE PREVENTION IN SCIZOPHRENIA

Kishimoto T, Agarwal V, Kishi T, Leucht S, Kane JM, Correll CU. Relapse prevention in schizophrenia: a systematic review and meta-analysis of second-generation antipsychotics versus first-generation antipsychotics. Mol Psychiatry. 2013 Jan;18(1):53-66. doi: 10.1038/mp.2011.143. Epub 2011 Nov 29. PubMed PMID: 22124274; PubMed Central PMCID: PMC3320691.

URL: http://www.nature.com/journal/v18/n1/pdf/mp2011143a.pdf -- payment required

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ABSTRACT
Few controlled trials compared second-generation antipsychotics (SGAs) with first-generation antipsychotics (FGAs) regarding relapse prevention in schizophrenia. We conducted a systematic review/meta-analysis of randomized trials, lasting more than 6 months comparing SGAs with FGAs in schizophrenia. Primary outcome was study-defined relapse; secondary outcomes included relapse at 3, 6 and 12 months; treatment failure; hospitalization; and dropout owing to any cause, non-adherence and intolerability. Pooled relative risk (RR) (±95% confidence intervals (CIs)) was calculated using random-effects model, with numbers-needed-to-treat (NNT) calculations where appropriate. Across 23 studies (n=4504, mean duration=61.9±22.4 weeks), none of the individual SGAs outperformed FGAs (mainly haloperidol) regarding study-defined relapse, except for isolated, single trial-based superiority, and except for risperidone's superiority at 3 and 6 months when requiring ≥3 trials. Grouped together, however, SGAs prevented relapse more than FGAs (29.0 versus 37.5%, RR=0.80, CI: 0.70-0.91, P=0.0007, I(2)=37%; NNT=17, CI: 10-50, P=0.003). SGAs were also superior regarding relapse at 3, 6 and 12 months (P=0.04, P<0.0001, P=0.0001), treatment failure (P=0.003) and hospitalization (P=0.004). SGAs showed trend-level superiority for dropout owing to intolerability (P=0.05). Superiority of SGAs regarding relapse was modest (NNT=17), but confirmed in double-blind trials, first- and multi-episode patients, using preferentially or exclusively raw or estimated relapse rates, and for different haloperidol equivalent comparator doses. There was no significant heterogeneity or publication bias. The relevance of the somewhat greater efficacy of SGAs over FGAs on several key outcomes depends on whether SGAs form a meaningful group and whether mid- or low-potency FGAs differ from haloperidol. Regardless, treatment selection needs to be individualized considering patient- and medication-related factors. PMCID: PMC3320691 [Available on 2013/7/1] PMID: 22124274 [PubMed - in process]

READING 7 – PHARMACOLOGIC TREATMENT OF FIRST EPISODE SCHIZOPHRENIA

Thomas SP, Nandhra HS, Singh SP. Pharmacologic treatment of first-episode schizophrenia: a review of the literature. Prim Care Companion CNS Disord. 2012;14(1). doi:pii: PCC.11r01198. 10.4088/PCC.11r01198. Epub 2012 Jan 5. PubMed PMID: 22690369; PubMed Central PMCID: PMC3357581.

URL: http://www-ncbi-nlm-nih-gov/pmc/articles/PMC3357581/ - full free text

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ABSTRACT

OBJECTIVE: To review the evidence base for the efficacy and tolerability of antipsychotic medication for the treatment of the first episode of schizophrenia.

DATA SOURCE: MEDLINE databases were searched for published articles in English over the last 25 years, from January 1986 to January 2011, on choice of antipsychotic treatment for the first episode of schizophrenia, with an emphasis on efficacy and tolerability of antipsychotic drugs in the acute phase of psychotic illness.

STUDY SELECTION: The keywords antipsychotic drugs and schizophrenia were used in combination with drug treatment, pharmacologic treatment, efficacy, and tolerability in addition to atypical antipsychotics, first-generation antipsychotics, second-generation antipsychotics, first-episode psychosis, and acute psychotic episode.

DATA SYNTHESIS: At present, there is no convincing evidence to guide clinicians in choosing a single first-line antipsychotic that is effective in treating the positive and negative symptoms of the first episode of schizophrenia. Even though second-generation antipsychotic drugs offer potential benefits in terms of less extrapyramidal side effects and some benefits in treating negative, affective, and cognitive symptoms, these drugs are not without their own side effects.

CONCLUSIONS: With the introduction of a number of second-generation antipsychotic drugs there have been significant advances in antipsychotic drug treatment over the last decade. Despite these advances, there are still a number of limitations in continued use of some antipsychotic medications due to their efficacy and tolerability issues in the acute and early maintenance phases of psychosis. Active research in this area would provide more promising results of improved efficacy and tolerability of antipsychotic medication.

PMCID: PMC3357581 PMID: 22690369 [PubMed - in process]

READING 8 – ORAL VS LONG ACTING INJECTABLE ANTIPSYCHOTICS

Zhornitsky S, Stip E. Oral versus Long-Acting Injectable Antipsychotics in the Treatment of Schizophrenia and Special Populations at Risk for Treatment Nonadherence: A Systematic Review. Schizophr Res Treatment. 2012;2012:407171. doi: 10.1155/2012/407171. Epub 2012 Feb 15. PubMed PMID: 22966436; PubMed Central PMCID: PMC3420751.

URL: http://www.hindawi.com/journals/sprt/2012/407171/ - free full text

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ABSTRACT

Long-acting injectable antipsychotics (LAIs) should offer better efficacy and tolerability, compared to oral antipsychotics due to improved adherence and more stable pharmacokinetics. However, data on LAIs has been mixed, with some studies finding that they are more effective and tolerable than oral antipsychotics, and others finding the contrary. One possibility for the disparate results may be that some studies administered different

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antipsychotics in the oral and injectable form. The present systematic review examined the efficacy and tolerability of LAIs versus their oral equivalents in randomized and naturalistic studies. In addition, it examined the impact of LAIs on special populations such as patients with first-episode psychosis, substance use disorders, and a history of violence or on involuntary outpatient commitment. Randomized studies suggest that not all LAIs are the same; for example, long-acting risperidone may be associated with equal or less side effects than oral risperidone, whereas fluphenazine decanoate and enanthate may be associated with equal or more side effects than oral fluphenazine. They also suggest that LAIs reduce risk of relapse versus oral antipsychotics in schizophrenia outpatients when combined with quality psychosocial interventions. For their part, naturalistic studies point to a larger magnitude of benefit for LAIs, relative to their oral equivalents particularly among first-episode patients.
PMCID: PMC3420751 PMID: 22966436 [PubMed]

READING 9 – MAINTENANCE PHASE ANTIPSYCHOTIC TREATMENT

Takeuchi H, Suzuki T, Uchida H, Watanabe K, Mimura M. Antipsychotic treatment for schizophrenia in the maintenance phase: a systematic review of the guidelines and algorithms. Schizophr Res. 2012 Feb;134(2-3):219-25. doi: 10.1016/j.schres.2011.11.021. Epub 2011 Dec 10. Review. PubMed PMID: 22154594.

URL: http://www.sciencedirect.com.libproxy1.nus.edu.sg/science/article/pii/S0920996411006190 - payment required

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ABSTRACT
OBJECTIVE: Antipsychotic treatment strategy for the maintenance phase of schizophrenia has been inconsistent in the literature. The purpose of this systematic review is to overview recommendations in various guidelines and algorithms.
METHODS: The guidelines and algorithms for schizophrenia that were published or updated in English after 2000 were searched, using Medline, PubMed, EMBASE, and PsycINFO with the following key words: guideline, algorithm, schizophrenia, and psychosis (last search: July 2011). The reference lists of the relevant reports were also examined.
RESULTS: Fourteen guidelines and algorithms were identified; only five of them clearly defined terms about the maintenance phase and treatment. Ten of 11 guidelines and algorithms did not recommend discontinuation of antipsychotics within five years; six of them partially recommended antipsychotic discontinuation for patients with first-episode schizophrenia exclusive. All nine guidelines and algorithms that referred to intermittent or targeted antipsychotic strategy endorsed against this strategy. Although being a hot topic of controversy, dose reduction of antipsychotics or lower dose therapy in the maintenance phase compared to the acute dosage is not recommended on the whole concerning atypical antipsychotics, whereas dose reduction appears sometimes considered acceptable for typical antipsychotics.
CONCLUSION: What constitutes maintenance phase and its treatment in schizophrenia has not yet been established in the literature. While discontinuation and intermittent or targeted strategies are not generally recommended, there is controversy regarding dose reduction or lower dose therapy, especially with regards to atypical antipsychotics. Further evidence is needed in order to derive treatment recommendations on antipsychotics in this critical treatment phase of schizophrenia.
 PMID: 22154594 [PubMed - indexed for MEDLINE]

READING 10 – ANTICHOLINERGIC MEDICATION DISCONTINUATION IN PATIENTS RECEIVING ANTIPSYCHOTICS

Desmarais JE, Beauclair L, Margolese HC. Anticholinergics in the era of atypical antipsychotics: short-term or long-term treatment? J Psychopharmacol. 2012 Sep;26(9):1167-74. doi: 10.1177/0269881112447988. Epub 2012 May 31. Review. PubMed PMID: 22651987.

URL: http://jop.sagepub.com/cgi/pmidlookup?view=long&pmid=22651987 – payment required

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ABSTRACT

Anticholinergic agents are usually prescribed to prevent or treat antipsychotic-induced extrapyramidal symptoms. Their long-term benefits are questionable and they carry diverse adverse effects, including cognitive impairment and worsening of tardive dyskinesia. This literature review explores the impact of anticholinergic medication discontinuation on movement disorders, cognition and psychopathology in patients receiving antipsychotics. Medline, Embase and PsycInfo were searched from 1950 to July 2011 using "cessation /withdrawal /discontinuation /stopping" with "anticholinergic*" or "antiparkinson*" and "neuroleptic*" or "antipsychotic*". Additional articles were obtained by searching the bibliographies of relevant references. Earlier studies of anticholinergic agent discontinuation in patients receiving first-generation antipsychotics reported relapse rates of extrapyramidal symptoms between 4% and 80%, reflecting the heterogeneity of the studies. Two recent studies of patients prescribed second-generation antipsychotics obtained relapse rates of 4% and 33%. Some studies suggest improvement in tardive dyskinesia with cessation of anticholinergics. Four studies examined the effects of anticholinergic agent discontinuation on cognition and all observed an improvement post-discontinuation. Changes in symptoms of schizophrenia with anticholinergic discontinuation are conflicting, with more recent studies suggesting an improvement. Given their questionable benefit with continued use, clinicians should consider a gradual withdrawal of anticholinergic agents in stable patients receiving antipsychotics.

PMID: 22651987 [PubMed - indexed for MEDLINE]