Michael Hoefer
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Epi 105.3 Final Research Protocol

Title: Financial Incentives and Treatment Adherence in Schizophrenic Patients on Depot Antipsychotics

Investigators: Michael Hoefer, MD and Steven Hamilton MD, PhD

Abstract:
Schizophrenia is a chronic debilitating disease and antipsychotic medications have proven efficacy for psychotic symptomatology and improving functional outcomes in medication adherent patients. Unfortunately, medication adherence is major barrier clinical response and there is a paucity of interventions with proven efficacy in increasing adherence in patients with schizophrenia. The proposed study will involve a clinical trial with historical controls to determine whether a financial incentive, in the form of a $50 credit voucher, can increase adherence to the depot antipsychotic haldol decanote and improve functional outcomes (rates of inpatient Psychiatric hospitalizations, emergency room visits, arrests, incarceration, suicide attempts, and quality of life scale (QLS)) over a 1 yr time period. The study will recruit 76 schizophrenic participants currently prescribed the depot antipsychotic haldol decanoate by a San Francisco Community Mental Health Clinic provider and exhibiting low medication adherence (receiving < 50% prescribed injections). Baseline values will be calculated from historical data for each participant over the 3 yr period prior to enrollment in the study. Baseline values will be compared to prospective data collected for the entire cohort while receiving the financial incentive for adherence with each monthly administration of haldol decanoate over 1 yr time period. If effective, a randomized controlled trial with an economic cost analysis will be conducted to further explore the potential benefit of this intervention in clinical practice.

Specific Aims:
To determine the effects of a financial incentive, in the form of $50 credit voucher, on adherence to the depot antipsychotic medication haldol decanoate in schizophrenic patients
To explore the effects of a financial incentive given for medication adherence on rates of inpatient Psychiatric hospitalizations, emergency room visits, arrests, incarceration, suicide attempts, and quality of life scale (QLS) in schizophrenic patients on haldol decanoate

Significance:
Schizophrenia is a chronic debilitating disease characterized by auditory hallucinations, delusional thinking, disorganized behavior, cognitive deficits, negative affective symptom, and significant morbidity and mortality (Goff et al., 2005). Antipsychotic medications have demonstrated efficacy for schizophrenic symptomatology and functional outcomes in clinical trials (Miyamoto et al., 2005). However, medication adherence is a major barrier to clinical response and lower rates of adherence result in

higher annual treatment costs (Lieberman etl al., 2011; Thieda et al., 2003). Unfortunately, there is a paucity of interventions with proven efficacy in increasing antipsychotic adherence in schizophrenic patients (Fenton et al., 1997).

Monthly depot injections of antipsychotic medications can improve adherence in select schizophrenic populations, but overall compliance remains low (Kane et al., 1998)**.** Financial incentives have been show to increase treatment adherence in substance abusers (Prendergast et al., 2006; Higgins et al., 1994) and dual diagnosis patients (have diagnosis of both schizophrenia and substance abuse) (Leontieva et. al, 2008), although there has been minimal research exploring incentive efficacy in non-substance abusing schizophrenics.

In the present proposal, a clinical trial will be conducted to determine whether a financial incentive, in the form of a $50 credit voucher, can increase adherence to the depot antipsychotic haldol decanoate and decrease inpatient psychiatric hospitalizations, emergency room visits, arrests, incarceration, suicide attempts, and improve quality of life over a 1 year time period in schizophrenic patients. If effective, further studies including a randomized controlled trial with an economic cost analysis will be conducted to explore the potential benefit of this intervention in clinical practice.

Methods:

Study Design**:** A clinical trial with historical controls of 76 schizophrenic participants currently prescribed haldol decanoate by a San Francisco Community Mental Health Clinic provider exhibiting low medication adherence rates (receiving < 50% prescribed injections). All participants will receive a financial incentive, in the form of a $50 credit voucher, for each administered dose of haldol decanoate in addition to standard care over a 1 yr period. Standard care in this population consists of monthly meetings with an Outpatient Psychiatrist, monthly injections of haldol decanoate, and twice monthly meetings with a Case Manager. All outcomes will be compared to participant's baseline measures from the 3 yr period prior to enrollment in the study (ie each pt is their own control). Outcome measures will be pooled from multiple sources including admission/discharge records of inpatient psychiatric units in county of San Francisco, SFGH Psychiatric Emergency Service electronic records, medical records at San Francisco Community Health Clinics, relevant police/county jail databases, and participant self-report.

The depot antipsychotic haldol decanote was chosen because it requires monthly injections (as opposed to q 2 wk or q 3 wk injections), is relatively inexpensive, is on formulary for most health plans, and is commonly used in the community. A $50 credit voucher was selected in accordance with incentive value used in previous studies (Higgins et al., 1994; Leontieva et al., 2008; Prendergast et al., 2006) and to strike a balance between what may be conceivably motivating in this population and economically/clinically feasible.

Study Mechanics: A $50 credit voucher will be given to each participant after intramuscular administration of haldol decanoate in the gluteus, quadriceps, or triceps

muscle at their monthly clinic appointment. Perfect attendance will correspond with a maximum possible value of 12 injections (ie 1 per month) and $600. Patients may receive their antipsychotic injection and voucher if they present within 4 business days on either side of their appointment. The flexibility in dates is to address the cognitive impairment and disorganization present in this patient population without compromising the pharmacodynamic and pharmacokinetic effects of the antipsychotic medications (ie maintenance of steady-state). At the end of each appointment, all patients will receive a card stating time and date of their next appointment, but will receive no additional reminders or researcher initiated contact. If a patient does not present to their appointment within this time-frame, they may still receive their antipsychotic injection, but will not receive the voucher for that particular assessment point. Patients may be switched to oral antipsychotics at any time point due to side effects or personal preference.

Study Subjects

Target Population: Schizophrenic patients with low adherence to depot antipsychotics (ie receive < 50% prescribed doses)

Accessible Population: Schizophrenic patients with low adherence to haldol decanoate receiving care in the San Francisco Community Mental Health Clinics.

Inclusion Criteria:

Demographic characteristics- > 18 yo, male, all gender identities, all races/ethnicities

Clinical characteristics- Diagnosis of schizophrenia established by clinical interview utilizing DSM-IV-R criteria, currently prescribed a depot antipsychotic medication, history of noncompliance to monthly antipsychotic injections (receive less than < 50% of prescribed injections)

Exclusion Criteria:

1. Severe medical illness that limits patient's ability to transport self to appointments or with high likelihood of passing away from medical causes during study period.
2. Impending court date or legal issues with a high likelihood of incarceration for majority of study period**.**
3. Comorbid mental retardation, dementia, or cognitive deficits that render patient unable to appreciate relevance of financial incentives or provide informed consent.
4. Medical: history of hypersensitivity reaction, intolerable side effects, agranulocytosis, dystonic reaction compromising respiratory status, or neuroleptic malignant syndrome from haldol or haldol decanoate. Diagnosis of Parkinson's Disease, participant attempting to become pregnant, or QTc > 500 msec

Sampling Design: A consecutive convenience sampling approach will be implemented till recruitment goals are reached using all San Francisco Community Health Clinic schizophrenic patients currently prescribed haldol decanoate exhibiting low adherence (ie receiving less than <50 % prescribed doses) with their medication.

Recruitment: Participants will be recruited via direct collaboration with mental health providers at the San Francisco Community Mental Health Clinics. Flyers will also be placed in the clinics waiting rooms.

Retention: During the intake appointment, researchers will collect all available contact information from participants including address, home phone #, cell phone #, email, PMD, SSN, medicare #, and also contact information for 2 friends. Repeated efforts will be made to contact participants and their mental health providers to prevent drop-out.

Measurements
Predictor Variable**:** Financial incentive provided for adherence to monthly haldol decanoate injection in the form of a $50 credit voucher.

Primary Outcome: Change in adherence to treatment (ie # haldol decanoate injections received / # prescribed) for 1 year after introduction of a financial incentive compared to baseline adherence measures (annual adherence averaged over 3 yrs prior to enrollment in the study).

Secondary Outcome: Changes in rates of inpatient Psychiatric hospitalizations, emergency room visits, arrests, incarceration, suicide attempts, and quality of life scale (QLS) compared to participants baseline measures.

Statistics:
Null assumption: there is no difference in adherence to monthly haldol decanoate injections and functional outcomes in patients receiving a financial incentive compared to baseline measures.
Alternative hypothesis: there is a difference in adherence to monthly haldol decanoate injections and functional outcomes in patients receiving a financial incentive compared to baseline measures.

Statistical Tests- Historical data will be used for up to 3 yrs prior to intervention to calculate baseline medication adherence and secondary outcome rates. Paired t-tests will be used to assess changes in adherence (ie # haldol decanoate injections received / # prescribed) before and after introduction of the financial incentive. Secondary outcomes of changes in rates of inpatient Psychiatric hospitalization, emergency room visits, arrests/incarceration, suicide attempts, and QLS scores before and after intervention will also be compared with paired t-tests.

Effect size= 0.166. An effect size of increase in 2 monthly depot antipsychotic injections out of 12 possible during the post-intervention year ie 2/12= 0.166 was chosen because it may represent a meaningful clinical response and could reveal differences in functional outcomes. Meta-analyses in substance abusers given financial incentives have shown effect sizes .25-.49. However, these studies typically involved higher value of vouchers and complicated reinforcement schedules which may not feasible in clinical practice. Schizophrenic participants may also have a lower response to incentives secondary to the cognitive difficulties and behavioral disorganization characteristic of the disorder.

Variability (std deviation) = .333. A study by Leontieva et al. (2008), which utilized vouchers in dual diagnosed pts with schizophrenia and alcohol abuse showed a standard

deviation 0.26 for adherence to oral naltrexone therapy (ie # appointments attended over 34 wk time period). In the present, study due to increased variability in this patient population a standard deviation of 4 out of 12 depot antipsychotic injections (.333) was chosen as a conservative estimate.

Standardized effect size= 0.166/0.333= .498
Alpha (two-sided) = 0.05 Beta= 0.20 Power= 80%
Sample size estimate= 75.6 participants (value includes correction for estimated 20% participant drop-out)

Quality Control, Data Management and Administrative Considerations
Pretest plans: Research staff will be oriented to the structure of San Francisco Community Health Clinics and correct utilization of data sources (ie clinic medical records, SFGH PES database, police/county jail databases, etc…) prior to commencing study. Sample ID numbers will also be generated and Microsoft Access database tested prior to beginning of study.

Quality Control and Data Management: Research staff will undergo standardized orientation to the operations manual, relevant data sources, and research databases. All research data will be stored in a Microsoft Access Database on a password protected labtop stored in a locked cabinet. Participants will be assigned arbitrary study ID numbers, personal info will be removed, and the identity key will be stored in a locked cabinet to preserve anonymity. Data will be analyzed using SPSS.

Personnel: PI- Steven Hamilton MD, PhD; project director, clinic coordinator, data manager, programmer/analyst- Michael Hoefer, MD, two research assistants who will also work as recruiters and administrative assistants, 1 statistician.

Time-table: 1. Six month period to establish procedures, orient research staff, create databases, and develop collaborative relationship with San Francisco Community Mental Health Clinics. 2. Enrollment for study will occur over 2 yr period and participants will be followed for 1 year following enrollment 3. Data analysis and manuscript preparation will occur over 6 month period after completion of study.

Ethical Considerations:
All participants will take part in a standardized informed consent process and protocol will be reviewed by the UCSF IRB. Participants will be instructed that not participating in study will not have any affect on their medical care and if choose to participate, they are free to withdraw from study at any time. Concern has been previously expressed for the coercive potential of financial incentives and a relatively low value incentive (ie $50 credit voucher) was chosen in the present study to minimize this risk. In addition, all participants involved will have been prescribed haldol decanoate by their mental health provider prior to enrollment in the study. Thus, the financial incentive will be implement to attempt to improve adherence to a treatment they are already receiving.

References

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Research Question: Does a financial incentive, in the form of a $50 credit voucher, increase adherence to depot antipsychotic medication regimens and improve functional outcomes among patients with schizophrenia?