POTENTIAL COST SAVINGS OF HAVING ACCESS TO ANTIPSYCHOTIC PLASMA LEVELS AT THE POINT OF CARE FOR PATIENTS WITH SCHIZOPHRENIA

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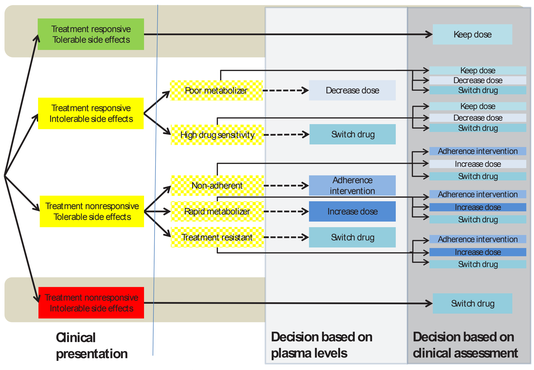
Background & Objective

- Pharmacological management of schizophrenia remains a challenge, as only about half of patients respond well to the initial regimen and can tolerate it. The remaining patients either do not respond, or experience intolerable side effect or both.
- Prescribers lack tools to determine the root cause of treatment failure for these complicated courses and respond accordingly. (Figure 1)
  - **Management based on clinical presentation alone is only unambiguous for patients with intolerable side effects and lack of response as they need to be switched to another drug.**
- The objective of the project is to estimate potential cost savings of point-of-care testing of antipsychotic plasma levels as a possible solution to guide treatment decisions.

Figure 1: Decision tree under current state of care (solid lines) and with access to plasma level information (dotted lines)



Note: Yellow cells denote constellations for which clinical presentation alone does not allow prescriber to identify and address the root cause for a complicated treatment course.

Methods

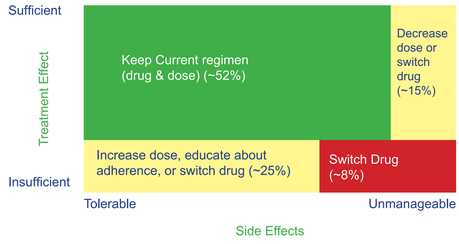
- Literature review to obtain frequency estimates for root causes of nonresponse and intolerable side effects
- Literature review to obtain estimates for the excess healthcare cost of schizophrenia care for non-adherent and poorly controlled patients
  - Expressed in annual cost in 2015 US$
- Simulation model to estimate annual excess cost of schizophrenia care assuming treatment decisions based on knowledge of plasma levels compared to current state of care assuming that prescribers use one of the following three hypothetical decisions strategies
  - Treatment based on published estimates of actual decisionmaking
  - Treatment of all cases based on the most common root cause
  - Treatment based on applying the underlying distribution of causes randomly

Results

Based on literature estimates, about 52% of patients respond to the initially selected regimen and are able to tolerate the drug (Figure 2).

- ~25%[1-5] of patients do not respond
- ~15% [6] have intolerable side effects
- ~8%[1-5] experience both.

Figure 2: Estimated frequency distribution of responses to initial treatment regimen



Note: Yellow cells denote constellations for which clinical presentation alone does not allow prescriber to identify and address the root cause for a complicated treatment course.

Table 1: Estimated frequency of underlying causes for inadequate treatment response

Clinical Presentation		Underlying Cause		
	% of population		% of population	% of non-responders
Inadequate response	25%	Non-adherent	20%	80%
		Treatment Resistant	4%	16%
		Rapid Metabolizer	1%	4%

Table 2: Estimated frequency of underlying causes for patients with treatment response but intolerable side effects.

Clinical Presentation		Underlying Cause		
	% of population			% of those with intolerable side effects
Treatment response but intolerable side effects	15%	High Sensitivity	4%	27%
		Poor Metabolizer	11%	73%

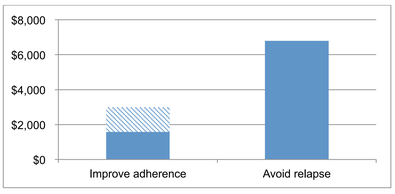
Table 3: Estimation of risk of incorrect treatment assignment in the balance of access to plasma levels

Percent of patients incorrectly treated if actual treatment decision follows					
Clinical Presentation	Underlying Cause	Actual Frequency	Published Estimates	Most Common Cause	Random Assignment
Inadequate response	Non-Adherent Treatment resistant	80% 16%	52% 56%	0% 16%	16% 13%
	Rapid Metabolizer	4%	4%	4%	4%
Intolerable side effects	High sensitivity Poor Metabolizer	27% 73%	N/A N/A	27% 0%	20% 20%

Note: We use the following sources or assumptions to estimate rates of patients incorrectly treated in the absence of plasma level information:

1. ***Published estimates** for decisions. Based on data from Stephenson et al. (2012), who showed that prescribers overestimate the percentage of patients who are adherent. Data for incorrect assessment of the root cause of side effects were not available.*
2. ***Most common cause:** We assume that prescribers treat all patients with complicated courses according to the most common root cause of their presentation.*
3. ***Random assignment:** We assume that prescribers are aware of the underlying distribution of the root causes of complicated treatment courses, but lack the information to decide which root cause is present in which specific patient. They then assign treatment decisions at random based on the underlying distribution.*

Figure 3: Estimated potential savings in cost of schizophrenia care per patient-year (in 2015 US$)



Calculations:
"Improve adherence" – the lower bound was the estimated potential savings from improving adherence (from Predmore, Mattke, Horvitz-Lennon 2015). The upper bound for savings from improved adherence was calculated by taking a weighted average of published data on increased hospital costs in nonadherent patients (Gilmer et al. 2004).
"Avoid relapse" – this estimate was produced by multiplying the excess cost associated with a relapse (The costs from the "NR" patient group ["patients with no prior relapse but with subsequent relapse"] minus the costs of the "NN" patient group ["patients who did not relapse during either time period"] from Ascher-Svanum et al. 2010) by the 63% of patients with uncontrolled schizophrenia who have a relapse (Almond et al. 2004).

Table 4: Estimated cost impact of incorrect treatment (in 2015 US$)

Cost if actual treatment decision follows			
Clinical Presentation	Published Estimates	Most Common Cause	Random Assignment
Average excess cost per patient-year of incorrect treatment decision - inadequate response lower bound	$801	$43	$239
Average excess cost per patient-year of incorrect treatment decision - inadequate response upper bound	$1,512	$81	$450
Average excess cost per patient-year of incorrect treatment decision - intolerable side effects	N/A	$489	$1,328

Conclusions

Without information on antipsychotic plasma levels, prescribers are estimated to make incorrect decisions in 10-18% of the approximately 40% of patients with schizophrenia and complicated treatment courses, i.e., patients that do not respond to initial treatment or experience intolerable side effects to it. For patients with lack of treatment response, the incorrect decision would lead to avoidable annual cost of $81 to $1,512, and for patients with intolerable side effects of $489 to $1,383. **The findings imply that plasma level testing in patients with complicated treatment courses would be at least cost-neutral, if the cost of a single test were between $81 and $1512.**

Limitations

- As in all modeling studies, we combined parameter estimates derived from studies of different populations, which may have introduced errors and even bias.
- We assume that correct determination of the root cause of non-response and intolerable side effects allows managing the patient properly. This may lead us to overestimate the savings from plasma level monitoring.
- The number of high-quality studies that allocate excess cost of care for patients with complicated treatment courses is limited.

Implications

Access to point of care antipsychotic plasma levels **would help avoid incorrect management decisions in 10-18% of the complicated treatment courses** and has the potential to improve disease management and reduce healthcare costs.

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References

1. Mortimer A, Singh P, Shepherd C, Puthiryackal J. Clozapine for Treatment-Resistant Schizophrenia: National Institute of Clinical Excellence (NICE) Guidance in the Real World. Clinical Schizophrenia & Related Psychoses. 2010;4(1):49-55. 2. Kane J, Honigfeld G, Singer J, Meltzer H. Clozapine for the treatment-resistant schizophrenic. A double-blind comparison with chlorpromazine. Arch Gen Psychiatry. 1988;45(9):789-796. 3.Kennedy JL, Altar CA, Taylor DL, Degtiar I, Hornberger JC. The social and economic burden of treatment-resistant schizophrenia: a systematic literature review. Int. Clin. Psychopharmacol. 2014;29(2):63-76. 4.Conley RR, Kelly DL. Management of treatment resistance in schizophrenia. Biol. Psychiatry. 2001;50(11):898-911. 5. McCutcheon R, Howes, O, et al. Treatment Resistant or Resistant to Treatment? Antipsychotic plasma levels in patients with poorly controlled psychotic symptoms. Psychopharm 2015; 1-6. 6. Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. N. Engl. J. Med. 2005;353(12):1209-1223. (CATIE) 7. Predmore Z, Mattke S, Horvitz-Lennon M. Improving Antipsychotic Adherence Among Patients With Schizophrenia: Savings for States. Psych. Serv. 2015;66(4):343-345 8. Ascher-Svanum H, Zhu B, Faries DE, et al. The cost of relapse and the predictors of relapse in the treatment of schizophrenia. BMC Psychiatry. 2010;10(2). 9. Almond S, Knapp M, Francois C, et al. Relapse in schizophrenia: costs, clinical outcomes and quality of life. The British Journal of Psychiatry. 2004;184(4):346-351.10. Stephenson J, Tuncelli O, Gu T, et al. Adherence to oral second□generation antipsychotic medications in patients with schizophrenia and bipolar disorder: physicians' perceptions of adherence vs. pharmacy claims. Int J Clin Pract. 2012;66:565-573. 11. Gilmer TP, Dolder CR, Lacro JP, et al. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. American Journal of Psychiatry. 2004; 1616(4):692-699.