

Cost-Utility Analysis of Blister Packaging vs. Dispensing as Usual All Medications for Veterans with Conditions Associated with Suicide Risk: Results from a Pragmatic Randomized Controlled Trial

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Disclosures

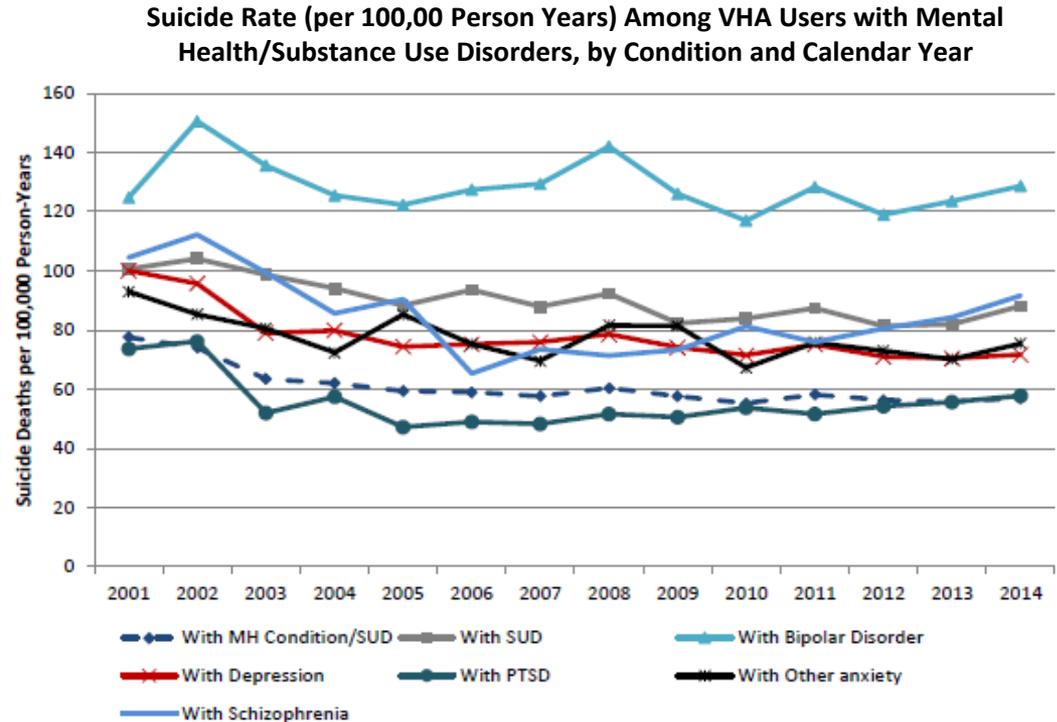
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Suicide and Veterans

- Nearly 43,000 people die by suicide annually.
- Serious mental illnesses are associated with increased suicide risk.
- Suicide is a top 10 cause of death in the US – with Veterans and Service members at increased risk.



VA Office of Mental Health and Suicide Prevention. *Suicide Among Veterans and Other Americans 2001-2014*. US Department of Veterans Affairs, Washington, DC. 2016



Blister Packaging

- Medications prescribed to treat conditions associated with suicide risk may be used as means in suicide attempts
- UK regulatory change in the packaging of paracetamol, from bulk packaging to blister packaging, was associated with reduced suicide incidence in the UK.
- Studies also show increased medication adherence with blister packaging.





Previous Studies

- Effects of Blister Packaging on Adherence
- Bhattacharya D, Aldus CF, Barton G, et al.(2016).
 - Patients (aged 75+).
 - No differences in adherence after 8 weeks.
 - Neither patients nor caregivers reported increased confidence nor increased feeling of autonomy



Background

Few studies with mixed results:

- Von Korff, et al. (1998) – RCT of primary care patients (n=322) with major depressive disorder (MDD) treated initiating MDD enhanced pharmacotherapy management and education interventions
 - found ICER of \$1,592/patient vs. usual care
 - Patients observed at months 1, 4, and 7.
- Bosmans, et al. (2007) -Economic evaluation was conducted alongside a 6-month RCT in the Netherlands
 - 89 pharmacy patients initiating non-tricyclic antidepressant therapy at 19 different pharmacies (urban and rural settings) were randomized into education/coaching by pharmacist vs. usual care
 - Mean difference -0.15; 95% CI -.54, 0.23



Poll Question #1

- What is your primary role in VA?
 - Student, trainee, or fellow
 - Clinician
 - Researcher
 - Manager or policy-maker
 - Other





Poll Question #2

- What is your area of expertise?
 - Suicide prevention or Mental health
 - Pharmacy
 - Academia
 - Primary care/internal medicine
 - Other





Design: Subjects, Setting, Location

- Trial results are described in Gutierrez P, et al. (2017).
- Subjects
 - 303 Veterans aged ≥ 18
 - discharged from inpatient psychiatric units or receiving care in outpatient mental health, substance abuse, or post-traumatic stress disorder (PTSD) clinics
 - In Denver, CO between September 2011 and January 2014.
 - Inclusion criteria: ≥ 1 of: major affective disorder, bipolar affective disorder, post-traumatic stress disorder, or schizophrenia.



Design: Randomization & Follow-up

- After giving informed consent, subjects returned with all of their medications. Research pharmacy staff randomized subjects to intervention or control.
- 243 (80.2%) completed the 12 month trial with at least two assessments
- No significant differences between those who dropped out and those who did not.



Subject Characteristics

Subject Characteristics			
	Blister Pack n=119	DAU N=123	p-value
Age (Mean, SD)	54.2 (9.2)	54.5 (11.0)	0.82
Male	99 (83%)	112 (91%)	0.07
Service Connected Disability Rating (Mean, SD) (2 subjects had invalid data values)	25.1% (35.7)	37.2 (40.3)	0.02
Alcohol Abuse	53 (44%)	38 (31%)	0.03
Alcohol Dependence	40 (33%)	26 (21%)	0.03



Treatment Alternatives

Blister Packaging

- Cold-sealed blister cards with 28, 31 or 90 blisters
- Each blister contained only one dose of one medication labelled with the day, date and time of the dose.
- Medications to be taken as needed (TPN) were each packaged on a single card, one pill per blister, and labelled accordingly.
- If tablets were required to be split by prescription, a manual splitter routinely provided to patients was used to halve tablets prior to blister packaging only.

Dispensing as Usual

- In vials with lids, 1 per prescription.



Time Horizon and Discounting

- Costs and outcomes were evaluated over the same time period at the trial.
- Costs and outcomes were not discounted because follow-up was to 12 months only.
- All costs are expressed in 2016 dollars (i.e., were adjusted using the Consumer Price Index).



Measurement of QALYs

- All subjects survived the trial.
- Utility was calculated from the SF-6D, a health state classification system based on 6 dimensions of the SF-36 (Brazier, et al, 2008).
- Subjects completed the SF-36 v. 2 at baseline and then monthly. Cumulative QALYs were calculated as the area under the preference score curve plotted against time (Glick H, et al. 2014, pp. 84-85).



Evaluation of QALYs

- Willingness to pay for an additional QALY is \$50,000 to \$300,000 in the US (Glick, et al, 2014; Neumann PJ, Cohen & Weinstein, 2014).
- The minimally important difference (MID) for the SF-6D is 0.033 (Walters & Brazier, 2003).
- Under the economic MID definition (any difference that we are willing to pay to modify), this value may be 0.005 (if it is associated with a cost of treatment of 1.0 as defined by the study data (Glick, et al, 2014, p. 70).



Estimating Costs: Intervention

- The VHA Corporate Data Warehouse (CDW) Pharmacy dataset itemizes ingredients (drugs) and dispensing (packaging, labor) costs.
- Based on expert opinion, we estimated the blister pack dispensing at 5% more than DAU (sensitivity analysis range: 0 to 10%).
- Use of expert opinion follows VA guidelines for micro-costing and VA recommendations for economic analyses of healthcare interventions (Smith et al, 2010).



Costs of the Blister Packaging Intervention

Units and Unit Costs (2016 US \$) per Dispensed Prescription*		
	Unit Cost (\$, 2016)	Source
Blister Packaging, per prescription		
Filling blister card, Labor only (per 31 count card)	1.05 X bulk dispensing cost	Expert opinion
Memory Pac® 31 Count Blister Card	\$0.46	VA RCT purchasing records, 2012
Memory Pac® 28 Count Weekly Blister Card	\$0.48	VA RCT purchasing records, 2012
Memory Pac® 90 Count Blister Card	\$0.52	VA RCT purchasing records, 2012
Bulk Dispensing, per prescription		
Dispensing, Labor only (per 30 day fill)	7.92	Decision Support System
Bottle & cap (Friendly and Safe Vial with Child Resistant Cap Attached, 16 Dram)	\$0.02	http://www.gohcl.com/ accessed 1.5.17



Total VA Costs

- Total healthcare costs for 12-month trial period
- Estimated using the Decision Support System (DSS) and included cost of medication (ingredients and dispensing), inpatient and outpatient costs.
- The intervention included every medication regardless of indication, therefore all healthcare utilization and cost was included.



Total VA Healthcare Cost

- Mean costs/subject ranged from \$157 (DAU) to \$181,412 (intervention)
- We found no statistically significant differences by study arm.

Mean Cost of VA Health Services During 12-months of Follow-up (\$ 2016)		
	Blister Pack, mean (SD) (n=119)	DAU, mean (SD) (n=123)
Total Inpatient	5,946 (17,324)	6,738 (17,337)
Total Outpatient	21,173 (16,651)	22,402 (20,921)
Behavioral Health	9,710 (9,205)	11,194 (12,163)
Emergency Department	524 (760)	602 (1,068)
Total Pharmacy		
Ingredient Cost	1,473 (1,703)	1,592 (2,390)
Dispensing Cost (labor, packaging)	275 (202)	316 (249)



Modeling Total VA Healthcare Cost

- Trial arms had significantly different baseline numbers of prescription medications.
- Generalized linear model (GLM) with gamma family (Modified Parks Test) and log link function:
 - Blister packaging was not significant.
 - Significant explanatory factors: older AND male, total inpatient days 12 months prior to enrollment, and drug abuse or bipolar disorder or major affective disorder dx.



Mortality and Quality of Life

- All subjects survived the study period
- 2,242 SF-36 forms were completed by the 243 participants
- Summary preference scores (utilities) for each completed survey ranged from 0.30 to 1.0
- QALYs for the 12-month trial period did not vary by study arm.

Mean Utilities Derived from SF-6D and Associated Mean QALYs*		
	Blister Pack, mean (SD)	DAU Mean (SD)
SF-6D Utilities		
Baseline	0.575 (0.112)	0.573 (0.093)
Month 3	0.590 (0.107)	0.590 (0.103)
Month 6	0.598 (0.109)	0.577 (0.099)
Month 9	0.597 (0.094)	0.590 (0.084)
Month 12	0.597 (0.051)	0.586 (0.036)
Mean QALY	0.591 (0.120)	0.580 (0.108)
Mean differential QALY (95% CI)	0.011 (-0.008 – 0.031)	



Incremental Cost-Utility Ratio (ICER)

- ICER was calculated as follows:

$$\frac{\text{Mean Cost}_A - \text{Mean Cost}_B}{\text{Mean QALYs}_A - \text{Mean QALYs}_B}$$

Where A is the intervention (blister pack) group and B is the control (dispense as usual) group.

- Bootstrapping was used to create an acceptability curve to illustrate the probability that the ICER falls below the cost per QALY threshold.



Cost-Utility Analysis

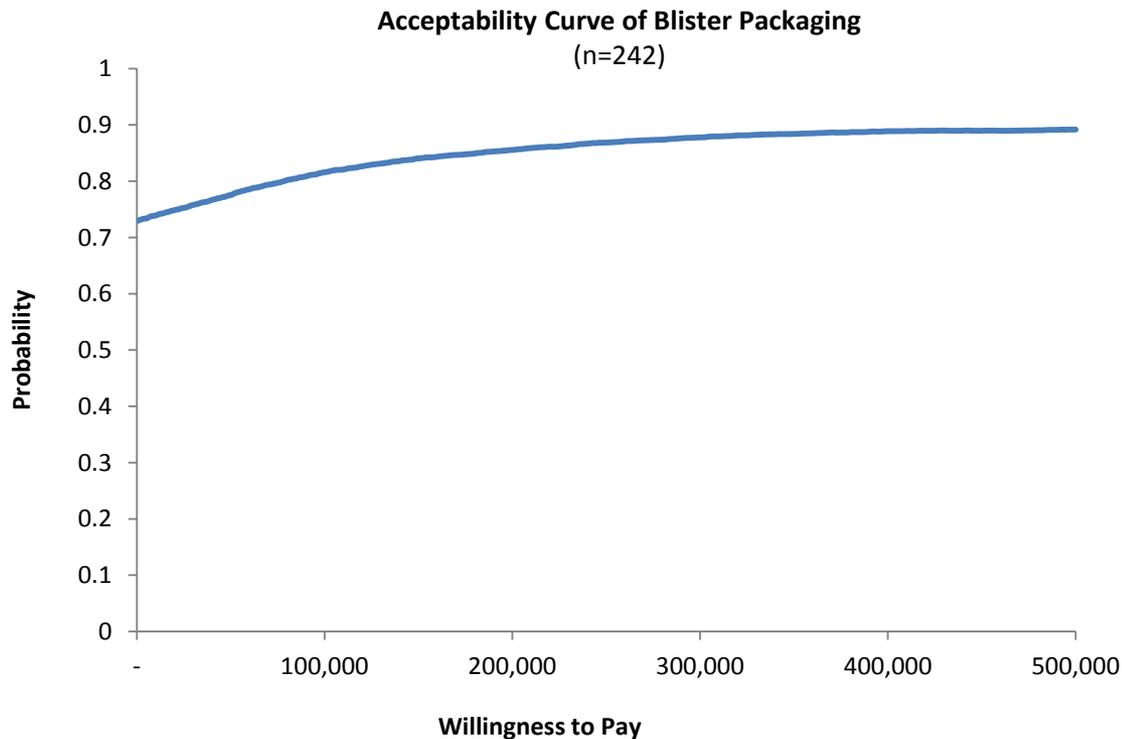
Costs, Outcomes and the Incremental Cost-Utility Ratio						
Group	Mean Total Cost (\$ 2016)	Cumulative QALY, mean	ICER	P(CE) at \$50,000 (WTP)	P(CE) at \$300,000 (WTP)	Ceiling Ratio at P(CE)=0.95
Blister Pack (n=119)	28,591	0.59		0.775	0.878	NA
DAU (n=123)	30,732	0.58				
Difference (% CI)	-2,140 (-9,053 – 4,773)	0.04 (-0.01 – 0.03)	Blister Dominant (not stat sig)			

- Cost and QALY point estimates suggest that blister packaging was dominant (less expensive and more effective), however, differences were not statistically significant.
- As previously noted, costs and QALYs were not significantly different across study arms.



Probabilistic Sensitivity Analysis

- At both low and high thresholds of willingness to pay (\$50,000/QALY and \$300,000/QALY), blister pack and DAU demonstrate similar treatment value .





Sensitivity Analyses

Mean total costs were similar across the intervention and control groups during the study period even after conducting sensitivity and subgroup analyses:

1. Among only subjects who were not hospitalized during the study.
2. Among only subjects with the worst baseline adherence (difference from perfect adherence to their baseline score using the BARS.)



Conclusion

In this pragmatic randomized controlled trial of 303 Veterans discharged from inpatient psychiatric units or receiving care in outpatient mental health, substance abuse, or post-traumatic stress disorder (PTSD) clinics between September 2011 and January 2014 in Denver Colorado for treatment of major affective disorder, bipolar affective disorder, post-traumatic stress disorder, or schizophrenia, **blister packaging all medications had no significant effect on quality adjust life-years or total VA healthcare costs compared to dispensing as usual.**



Discussion

- This trial included Veterans with a relatively high burden of illness
 - Utilities were relatively low in both groups (0.60 versus 0.59)
 - 1/3 were hospitalized during their 12-months of follow-up.
- Blister packaging effectiveness was likely affected by subject morbidity
 - Intervention exposure was interrupted during hospitalizations.
 - Medications are often changed after hospitalization, introducing new variables affecting adherence.
- Reasons other than cost-effectiveness (patient preference) may justify blister packaging. Economies of scale and technology reduce costs significantly.



Pharmacy Dispensing Technologies and Cost to Dispense

- Cost of bulk dispensing is well-established, while costs of tablet splitting and blister packaging are not
- Small changes in dispensing methods may significantly change costs
 - 30-day vs. 14-day dispensing cycles
 - Median per prescription cost would decrease
 - Semi-fixed and fixed costs would nearly double
 - Median cost to dispense does not control for days supply



Limitations

- Intervention costs were estimated by the study pharmacist, but may vary by setting and technology
 - Robots and mail order could likely reduce unit cost
- Only VA-filled medications were included



Questions/Comments?

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