Cost and Cost-Effectiveness in a Randomized Trial of Long-Acting Risperidone for Schizophrenia

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ABSTRACT

Objective: The effect of long-acting injectable (LAI) risperidone on health care costs was determined in a multisite clinical trial.

Method: Veterans Health Administration patients with unstable schizophrenia or schizoaffective disorder established by the Structured Clinical Interview for *DSM-IV* (N = 369) were randomized between 2006 and 2009 to long-acting risperidone or physician's choice of oral antipsychotic. Health care utilization and cost were tracked in administrative data. Medication administered by the trial was recorded on case report forms. Medication cost was based on unit costs to the US Medicaid program. Economic outcomes were assessed with the Quality of Well-Being instrument.

Results: Participants randomized to LAI risperidone (n = 187) incurred \$14,916 per quarter in total health care costs, which was not significantly different from the \$13,980 cost incurred by the control group (P = .732) (n = 182). The LAI group incurred \$3,028 per guarter in medication cost, significantly more than the \$1,913 incurred by the control group (P=.003). Hospitalization costs were \$7,088 in the experimental group and \$6,891 in the control group (P = .943); outpatient costs were \$11,888 in the experimental group and \$12,067 in the control group (P=.639). LAI risperidone did not result in better outcomes as evaluated by a measure of schizophrenia symptoms or an assessment of health related quality of life and incurred more adverse events.

Conclusions: Patients with unstable schizophrenia were randomized in a practical trial of LAI risperidone. This antipsychotic significantly increased medication costs but did not reduce hospital or total health care cost or improve outcomes and was thus not cost-effective.

Trial Registration: ClinicalTrials.gov identifier: NCT00132314

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Corresponding author: Paul G. Barnett, PhD, Health Economics Resource Center, VA Cooperative Studies Program, VA Palo Alto Health Care System, 795 Willow Rd (152), Menlo Park, CA 94025 (paul.barnett@va.gov). S chizophrenia symptoms can be managed with antipsychotic medications, but poor adherence to prescribed medication is associated with symptomatic exacerbations, hospitalizations, and high health care costs.^{1,2} To overcome this limitation of short-acting oral medications, long-acting injectable (LAI) formulations of antipsychotics have been advocated as a way to achieve sustained medication coverage, improve outcomes, and reduce hospitalization.³

Long-acting injectable risperidone is the first LAI formulation of a second-generation antipsychotic to become available in the United States. Economic models of LAI risperidone have reported that the substantial cost of this drug may be offset by reductions in the cost of hospitalization.⁴⁻⁶ In the absence of data from clinical trials, these models were based on expert opinion about the likely effect of LAI risperidone on adherence. A recent review noted the need for data on the cost-effectiveness of LAI second-generation antipsychotics.⁷

Some observational studies noted an association between prescription of LAI risperidone and reduced psychiatric hospitalization. Patients starting on LAI risperidone had greater reduction in hospital use than those who began oral antipsychotics.⁸ Reduced hospital use was also observed in patients who switched from an oral agent to LAI risperidone,^{9–11} but the switch to LAI risperidone has also been reported to be associated with increased hospital use and greater overall health care costs.¹²

Randomized trials of LAI risperidone have not yet reported rates of hospitalization, health care utilization, or cost. Trials in stable patients^{13,14} and patients with a recent exacerbation^{15,16} did not find a significant advantage of LAI risperidone relative to oral agents in other measures of outcome. One trial in stable patients found fewer relapses in patients assigned to LAI risperidone.¹⁷

We evaluated the health care utilization and cost incurred by participants in a recently completed trial of LAI risperidone.¹⁸ Unstable patients were randomized to receive LAI risperidone or psychiatrist's choice of oral antipsychotic therapy. This article provides the first trial-based estimates of the effect of LAI risperidone on psychiatric hospitalization and total health care cost.

METHOD

Clinical Trial

This comparative effectiveness clinical trial used a naturalistic design to measure the impact of the intervention in real-world clinical practice. Patients were randomized to biweekly (every 2 weeks) administration of 25–50 mg of LAI risperidone or psychiatrist's choice of oral antipsychotic medication. Because steady state levels of LAI risperidone are achieved slowly, previous oral antipsychotics were to be continued for at least 3 weeks.

The trial enrolled patients receiving care in the Veterans Health Administration (VHA) who had a diagnosis of schizophrenia or schizoaffective disorder as assessed with the Structured Clinical Interview based on the Fourth Edition of the *Diagnostic and Statistical Manual of Mental Disorders*.¹⁹ Because unstable patients have frequent psychiatric hospital stays,

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they might benefit the most from a long-acting medication, and they represent the group in which the hypothesis of cost offset is most likely to prove true. The trial enrolled patients at risk for psychiatric hospitalization, including those hospitalized within the previous 2 years and those whose use of mental health services to prevent relapse was increasing. Inclusion of patients in the latter group was adjudicated by the study chairpersons.

Participants provided informed consent under a human subjects' protocol approved by an Institutional Review Board at each of the 19 sites. Participants provided separate authorization for the release of their health care utilization and cost records under the privacy provisions of the Health Insurance Portability and Accountability Act of 1996. Approval to extract these health care data sets was obtained from the Institutional Review Board of Stanford University. The trial was registered with the National Institutes of Health Clinical Trials Registry (http://clinicaltrials.gov) and assigned number NCT00132314.

Cost and Utilization Data

We obtained information from the VHA Decision Support System on the cost and utilization of hospital, residential care, outpatient services, and pharmacy, including prescriptions for antipsychotic medications. The Decision Support System employs an activity-based cost allocation system, a method of finding cost that is regarded as more accurate than cost-adjusted charges.²⁰ We included information on all VHA care from the date of randomization until the end of follow-up. We included only partial costs of hospital stays that were underway at randomization.

Trial case report forms were used to obtain information on LAI risperidone administered by trial personnel and to document health services utilized outside of the VHA health care system in the 30 days prior to each quarterly assessment. When the patient reported that their first psychiatric hospitalization was at a facility not operated by the US Department of Veterans Affairs (VA), the hospital was asked to confirm admission. Reports of other non-VA health care utilization were not independently verified.

We analyzed costs from the perspective of the health care sponsor. Compared to the societal perspective, this approach neglected costs incurred by patients, including the cost of traveling to the clinic to receive injectable antipsychotic medication. We adopted the payor perspective over concern that findings might be driven by the assumptions needed to value patient time and travel cost.

The VHA pays less for medications than other US health care sponsors.²¹ To have a more generalizable finding, we used the medication cost of the US Medicaid program, which is the predominant payor for schizophrenia care in the United States.²² Medication cost was estimated as 64% of the Average Wholesale Price, the net cost of brand name medications to Medicaid.²³ For each administration of LAI risperidone, we included \$20.92, the average reimbursement for administration of an injectable drug (CPT code 90782) paid by Medicare under the Resource Based Relative Value System.²⁴

- Long-acting injectable (LAI) risperidone was compared to oral agents in unstable schizophrenia.
- LAI risperidone added \$4,060 annual pharmacy costs without a significant clinical benefit.
- Excluding LAI risperidone from formularies would save drug cost without affecting patient welfare.

We assigned cost and utilization to quarterly periods that were defined starting with the date of randomization and each 91 days thereafter. Inpatient care was assigned to 1 of 3 categories: acute psychiatric, acute medical-surgical, and all other, a category that included inpatient substance abuse treatment, nursing home, and other residential care. Costs were expressed as 2009 US dollars, using the Consumer Price Index for all goods to adjust for inflation.²⁵

Outcomes

Blinded video-conference assessments were completed every 3 months to record symptoms of schizophrenia using the Positive and Negative Syndrome Scale (PANSS).²⁶ Healthrelated quality of life was assessed with the Self-Administered Quality of Well-Being (QWB) Scale.²⁷ QWB responses are assigned to the range of 0 to 1, with the highest score reflecting perfect health. It employs community-rated preference weights that allow outcomes to be expressed as qualityadjusted life-years, the standard measure recommended for cost-effectiveness analysis.²⁸ The QWB has been found to be valid and responsive to differences in the health status of patients with schizophrenia.²⁹

Statistical Methods

We used a count model, negative binomial regression, to compare differences in health care utilization by treatment group, including days of inpatient stay and number of outpatient visits. Generalized linear model regressions were used to compare group differences in health care cost.³⁰ We used a Box-Cox test to determine that the appropriate link function was log for all cost variables with the exception of square root for the cost of other hospital stays, other outpatient medications, and all outpatient medications. A modified Park test was used to determine the appropriate distributional assumption. This was the γ distribution (for most cost variables), the Poisson distribution (for cost of stays underway at randomization, LAI risperidone, oral atypical medications, conventional long-acting antipsychotics, total outpatient medication), or the normal distribution (cost of acute psychiatric stay, other stays, other psychiatric visits, medical visits, atypical antipsychotic medications, and total cost).

The trial used a rolling enrollment scheme, in which participants were enrolled throughout the study and followed for 24 months or until study close-out, whichever came first.

Table 1. Baseline Characteristics of Patients With Schizophrenia or Schizoaffective Disorder by Randomized Assignment to Standard Care or LAI Risperidone

	Standard	
	Care (oral	LAI
	antipsychotic),	Risperidone,
Characteristic	n=182	$n = 187^{a}$
Age, mean (SD)	51.3 (8.8)	50.7 (9.7)
Sex, male, %	91.2	92.0
Race/ethnicity, %		
White	45.1	46.5
Black	47.8	43.3
Hispanic	3.3	8.0**
Asian/American Indian	3.8	1.6
Unknown	0.0	0.5
Single/never married, %	86.8	84.5
QWB score (n = 364), mean (SD) ^b	0.598 (0.16)	0.595 (0.16)
VA health services utilization during year		
prior to randomization		
At least 1 acute psychiatry stay, %	80.2	83.0
No. of acute psychiatry stays, mean (SD)	1.5 (1.3)	1.5 (1.3)
Days in acute psychiatry stay, mean (SD)	25.7 (50.6)	20.9 (36.5)**
Patients with acute care stays	35.2	45.5*
underway at randomization, %		
At least 1 acute medical/surgical stay, %	11.5	7.0
Days in acute medical/surgical stay, mean (SD)	0.42 (1.63)	0.32 (1.73)
At least 1 other inpatient stay, %	23.1	15.0**
Days in other inpatient stay, mean (SD)	17.4 (53.4)	8.5 (26.7)*
MHICM visits, mean (SD)	7.7 (20.9)	5.6 (18.1)*
All outpatient visits, mean (SD)	54.7 (60.5)	51.7 (61.8)
VA health care cost during year prior to		
randomization in 2009 US dollars, mean		
Acute psychiatry hospital stays	25,391	20,846
Acute medical/surgical stays	1,341	554
Other hospital stays	7,476	4,272
Outpatient care	11,061	11,054
Antipsychotic medication	1,751	1,500
Total cost	47,020	38,225**
Days of follow-up, mean (SD)	506.8 (223.8)	476.1 (236.4)

^aSignificantly different from participants receiving standard care: *P value < .01; **P value < .05.

^bFive patients did not receive baseline QWB assessments.

Abbreviations: LAI = long-acting injectable, MHICM = Mental Health

Intensive Case Management, QWB = Quality of Well-Being Scale,

VA = US Department of Veteran Affairs.

This design maximized the power of the study, but resulted in fewer observations to represent time periods that were more distant from randomization. We corrected for this administrative censoring by applying an inverse probability weight, with the probability estimated as the Kaplan-Meier estimator for the observation being excluded by administrative censoring.³¹ We analyzed quarterly costs by treatment group, using a random effects model so that standard errors were corrected for the correlation of observations from the same trial participant.

RESULTS

Characteristics of Study Participants

The 369 trial participants were randomized between 2006 and 2009. The characteristics of the experimental and control groups are compared in Table 1. Almost all (95%) of the trial participants had a history of hospitalization within the prior 2 years. There were few significant differences by treatment group assignment. The LAI risperidone group had

Table 2. Health Services Utilization by Treatment Group, Mean Quantity Per Quarter of Follow-Up

	Standard Care		
	(oral antipsychotic)	LAI Risperidone	
	(no. of	(no. of	Р
Type of Utilization	quarters = 1,109)	quarters = 1,074)	Value ^a
Acute medical/surgical	0.2 (0.05)	0.2 (0.08)	.764
hospital stays, total days, mean (SE)			
Acute psychiatry hospital stays, mean (SE)			
Days in stay underway at randomization	0.3 (0.1)	1.0 (0.6)	.021**
Days in subsequent stays	2.5 (0.6)	2.2 (0.8)	.714
Total days	2.8 (0.6)	3.2 (0.9)	.730
Residential and other inpatient hospitalization, total days, mean (SE)	3.3 (0.9)	2.1 (0.7)	.303
Outpatient visits, mean (SE)			
Individual psychiatry	8.0 (0.8)	6.8 (0.7)	.280
Group psychiatry	2.6 (0.6)	2.6 (0.7)	.943
Other psychiatry	1.2 (0.2)	1.1 (0.2)	.614
Medical/surgical	2.3 (0.4)	2.3 (0.4)	.939
Other ancillary care	3.0 (0.3)	3.2 (0.6)	.733
^a Significantly different from	natients receiving st	andard care	

*P value < .01, **P value < .05.

Abbreviation: LAI = long-acting injectable.

significantly fewer days of psychiatric inpatient stay in the year before baseline, but patients in this group were more likely to be in an acute psychiatric hospital when they were randomized. The LAI risperidone group had fewer visits to a Mental Health Intensive Case Management (MHICM) clinic during the baseline year. MHICM is intensive communitybased care provided with a goal of reducing hospitalization of patients who are seriously ill. Patients were followed for a mean of 16.2 months (range 1-29 months).

Utilization of Health Services and Medication

Differences in health care utilized by treatment group are presented in Table 2. The table reports the mean quantity of health services used during 1,109 quarters of follow-up of patients assigned to standard care and 1,074 quarters of follow-up of the experimental group. There were no significant differences between the treatment groups in the number of days of inpatient stay or in the number of outpatient visits. Trial participants randomized to LAI risperidone had a mean of 3.2 days of acute psychiatric hospital stay per quarter, compared to 2.8 days in the control group, a difference that was not significant. The only significant difference between groups was in the number of days of stay in hospitalizations that were underway at the time of randomization. The LAI risperidone group had a mean of 1.0 days of stays in psychiatric hospitalizations that were already underway at the time of randomization, compared to 0.3 days in the control group (P = .021).

At quarterly follow-up assessments, respondents reported on care received in the preceding 30 days from providers outside the VA health care system (data not shown in a table). The LAI risperidone group reported having spent a mean of 0.08 nights in non-VA hospitals, compared to 0.13 in the

Table 3. Outpatient Medications by Treatment Group, Mean Quantity per Quarter of Follow-Up

	Standard Care		
	(oral antipsychotic)	LAI Risperidone	
Outpatient Medication	(no. of quarters $=$ 1,109)	(no. of quarters = 1,074)	P Value ^a
No. of injections administered, mean (SE)			
LAI risperidone	0.4 (0.1)	3.4 (0.3)	<.001*
Other LAI antipsychotic medications	0.02 (0.02)	0.02 (0.02)	.974
No. of days supply dispensed, mean (SE)			
Oral atypical antipsychotic medications	61.5 (5.4)	38.6 (4.0)	.001*
Oral conventional antipsychotic	5.3 (1.5)	5.0 (1.8)	.886
medications			
Other oral psychiatric medications	94.5 (8.7)	81.5 (9.9)	.329
^a Significantly different from patients receiv Abbreviation: LAI = long-acting injectable.	ing standard care: *P value	e<.01.	

Table 4. Costs by Treatment Group, Mean (SD) Cost per Quarter of Follow-Up in 2009 US Dollars

Type of Cost	Standard Care (oral antipsychotic) (no. of quarters = 1,109)	LAI Risperidone (no. of quarters = 1,074)	P Value ^a
Inpatient			
Acute medical/surgical hospital stays	569 (236)	475 (181)	.747
Acute psychiatric hospital stays	4,335 (1,122)	5,441 (2,333)	.650
Psychiatric stays underway at	364 (87)	1,087 (518)	.040**
randomization			
Subsequent psychiatric stays	3,971 (1,115)	4,354 (2,315)	.878
Other hospital stays	1,987 (637)	1,172 (338)	.220
Subtotal inpatient stays	6,891 (1,501)	7,088 (2,325)	.943
Outpatient			
Individual psychiatry	3,116 (413)	2,383 (316)	.152
Group psychiatry	386 (84)	545 (170)	.365
Other psychiatry	240 (54)	230 (49)	.884
Medical/surgical	858 (142)	1,067 (215)	.405
Other ambulatory care	576 (71)	577 (113)	.994
Subtotal outpatient	5,176 (482)	4,801 (628)	.639
Total inpatient and outpatient	12,067 (1,565)	11,888 (2,302)	.949
Outpatient medication			
Atypical antipsychotic medications (oral and LAI)	1,157 (219)	1,919 (186)	.017**
LAI risperidone	152 (41)	1,425 (170)	<.001*
Oral atypical antipsychotic medications	1,005 (219)	495 (73)	.007*
Conventional antipsychotic medications	20 (10)	16 (9)	.780
LAI convention medications	0.2 (0.1)	0.3 (0.2)	.517
Oral conventional medications	20 (10)	16 (9)	.773
Other outpatient medication	735 (110)	1,092 (149)	.051
Other oral psychiatric medications	260 (28)	265 (30)	.887
Other nonpsychiatric medications	476 (98)	826 (135)	.035**
Subtotal, outpatient medication	1,913 (231)	3,028 (299)	.003*
Total cost	13,980 (1,514)	14,916 (2,321)	.732
^a Significantly different from patients receiv	ing standard care: *P value	<.01, ** <i>P</i> value < .05.	

Abbreviation: LAI = long-acting injectable.

oral treatment group (not significant, P=.21). The LAI risperidone group reported receiving a mean of 0.25 visits to non-VA psychiatric providers, compared to 0.49 visits in the oral treatment group (not significant, P=.59).

The mean quantity of antipsychotic medications dispensed to study participants per quarter is provided in Table 3. The control group, which was randomized to the psychiatrist's choice of oral medications, received a mean of 61.5 days of atypical antipsychotic medications and 5.3 days of conventional antipsychotics per quarter. The LAI risperidone group received significantly less oral atypical antipsychotic medications (P=.001). Some of the oral agents received by

the experimental group were per protocol, which specified that oral medication should be continued during the initial period of LAI treatment, while others represent off protocol, naturalistic use. The LAI risperidone group received 3.4 injections per quarter, compared to 0.4 injections provided to control group members who crossed over to the experimental treatment (P < .001). These means include all medications recorded on case report forms and in administrative data. The control group mean reflects a preponderance of quarters in which no LAI risperidone was received. There were 41 individuals (22.5%) in the control group who crossed over to receive at least one LAI risperidone injection during the trial.

Health Care Cost

Table 4 compares cost incurred in the VHA system by treatment group. The table reports the cost of inpatient stays, outpatient visits, and medications. The costs of care within these categories are reported. The indented items in the table are subcategories of cost within the categories of psychiatric hospitalization, atypical antipsychotic medication, conventional antipsychotic medication, and other types of medication. Participants randomized to LAI risperidone incurred a mean of \$14,916 per quarter in health care costs, which was not significantly different from the mean of \$13,980 incurred by the control group (P = .732). The experimental group incurred a mean of

\$3,028 per quarter in outpatient medication cost, significantly more than the \$1,913 incurred by the control group (P < .003). The mean cost of atypical antipsychotic medications, both oral and long-acting, was significantly greater in the LAI risperidone group (\$1,919 versus \$1,157, P = .017).

Inpatient costs averaged \$7,088 in the experimental group and \$6,891 in the control group, a difference that was not statistically significant (P=.943). Outpatient costs were \$4,801 in the experimental group and \$5,176 in the control group (P=.639).

We considered whether findings about the difference in cost by treatment group were attributable to differences in



baseline characteristics. We estimated multivariate models that included treatment group assignment and baseline covariates: the number of days of psychiatric stay, the number of MHICM visits during the year before randomization, and an indicator that the participant was randomized during an acute psychiatric hospital stay. Inclusion of these covariates had no effect on the statistical significance of the differences in cost between treatment groups and only very small effect on the point estimate of the difference.

We considered whether there was any trend in health care cost over time, and whether there were differences between the treatment groups in the trend in health care cost. We estimated multivariate models that included treatment group assignment, time (number of quarters since randomization), and the interaction of time and group assignment. There was no trend in the total health care cost incurred by participants over time, and no significant differences between treatment groups in the trend in total health care costs. The lack of trend over time is illustrated in Figure 1. This figure presents the cumulative total cost incurred by each treatment group. All available data were used to create the figure, that is, the cost added in each quarter to the cumulative total is the mean cost of participants still in the study.

Outcomes

A mixed model was used to compare trial participants' outcomes through 18 months (data not shown in a table). Among those randomized to LAI risperidone, the mean value of the total PANSS score was 74.1 (SD = 0.91), which was not significantly different from the mean of 74.7 (SD = 0.92) in the oral medication group (P=.65). The LAI risperidone

group had a mean QWB value of 0.66 (SD = 0.02), which was not significantly different from 0.67 (SD = 0.02) in the oral medication group (P=.63).

DISCUSSION

Health care interventions are considered to be costeffective if they yield sufficient improvement in outcomes to justify their cost. Compared to the physician's choice of oral antipsychotic, LAI risperidone resulted in no significant improvement in health-related quality of life or several other outcomes; patients receiving the medication reported more adverse events at the injection site and more neurologic symptoms.¹⁸ The average preference weight (utility) was 0.67 for LAI risperidone compared to 0.66 for oral agents.

Patients randomized to LAI risperidone incurred significantly more pharmaceutical cost than those who were randomized to oral agents; their mean drug costs were \$1,015 per quarter greater (or \$4,060 per year). There was no significant reduction in their use of the psychiatric hospital or in the total cost of their care, with the LAI risperidone group incurring a mean cost of \$14,916 per quarter versus \$13,980 for oral agents. Because neither outcomes nor cost were significantly different, we did not estimate the incremental cost-effectiveness ratio, as any point estimate would be bracketed by very large uncertainty. There was no evidence that LAI risperidone yielded sufficient value to be regarded as cost-effective.

Previous observational studies estimated that LAI risperidone reduced hospital use and improved outcomes. Data from this study show that these estimates were excessively optimistic and may be methodological artifacts. Previous "mirror" studies used patients as their own control. They compared rates of hospitalization in the period in which patients used oral agents to the rate after they switched to LAI risperidone. Most of these studies found an advantage to LAI risperidone,⁹⁻¹¹ with one exception.¹² Mirror studies have been reported to be subject to a number of biases, including regression to the mean.³² Regression to the mean would occur if patients who enrolled in these studies had a higher than average rate of hospital use and were subsequently hospitalized at a lower rate that is more typical in all patients with schizophrenia.

In this trial, we found that participants randomized to the LAI risperidone group were hospitalized for a mean of 20.9 days in the year before randomization and an average of 12.7 days per year during the trial. Using the methodology of a "mirror study," one might conclude that LAI risperidone reduced hospitalization. Yet there was also a decline in hospital use by patients randomized to oral agents. They were hospitalized for 25.7 days in the year prior to randomization and 11.2 days per year during the trial. There was no significant difference in the decline in the 2 groups. We thus observed similar degrees of regression to the mean in both groups.

This study has several limitations. We did not include costs incurred by patients, for example, the time and travel cost of attending clinic appointments, but these are likely to have been small in comparison to the large health care expenditures.

We did not include costs incurred outside the VHA health care system. We gathered information on this care for the month preceding each follow-up visit and found no difference between treatment groups.¹⁸ These self-reports suggest that trial participants received 90% or more of their health care from VHA. Exclusion of the cost incurred outside VHA is unlikely to affect the conclusions about the effect of LAI risperidone on cost.

The trial was conducted in VA and this may limit its generalizability. VA patients with schizophrenia are older and have higher incomes, but are similar to those treated in non-VA settings in their clinical presentation, symptom distress, and community adjustment.³³ VA has relied more heavily on hospitalization and made less use of community-based services than non-VA providers, but this difference has undoubtedly eroded with the increased emphasis on ambulatory care by VA. The quality of pharmacotherapy provided by VA was found to be comparable to that of the private sector.³⁴

Veterans Health Administration health care costs may be similar or somewhat less than those of other providers, with the largest part of the difference attributable to lower medication cost.³⁵ For this reason, we used the medication costs of the US Medicaid program to make the study cost findings relevant to other payers.

The trial randomized 369 participants, and found no greater reduction in cost for LAI risperidone compared to psychiatrist choice of oral agent. It is possible that a larger

number of participants would have allowed greater precision in estimating the incremental effect of LAI risperidone; however, 4 previous trials found that this medication was not superior to oral agents.^{13–16} One recently published study did find less relapse and hospitalization in stable patients with schizophrenia who were randomly assigned to LAI risperidone,¹⁷ but dosage of the comparison oral medication may have been less than optimal.

This trial differed from the earlier trials because it enrolled patients with poor medication adherence, high rates of psychiatric hospitalization, and significant comorbidities and randomized them in a practical study of effectiveness that measured their health care utilization and cost. LAI risperidone did not reduce hospitalization use, decrease total cost, improve the outcomes, or reduce adverse effects of these patients.

Antipsychotics are the most costly therapeutic class of medications to the US Medicaid program, accounting for more than \$3 billion in spending in 2006.³⁶ That cost is now shifting to Medicare under the Part D drug benefit. Although expiration of patents on atypical antipsychotic drugs will reduce the cost of some oral medications in the next few years, adoption of new patented drugs would result in cost increases that can be justified only if there is a substantial therapeutic benefit. This study found that adoption of long-acting risperidone would increase pharmaceutical costs without any improvement in outcomes. These programs could avoid a substantial new drug cost by excluding LAI risperidone from their formulary, without any evident loss to patient welfare.

Drug names: risperidone (Risperdal Consta).

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Cost-Effectiveness of Long-Acting Injectable Risperidone

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testimony for the plaintiffs in UFCW Local 1776 and Participating Employers Health and Welfare Fund, et al v Eli Lilly and Company; for the respondent in Eli Lilly Canada Inc vs Novapharm Ltd and Minister of Health; and for the Patent Medicines Prices Review Board, Canada, in the matter of Janssen Ortho Inc and Risperdal Consta. **Dr Barnett** and **Ms Scott** have no competing interests.

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