

Diabetes Mellitus and Antipsychotics

Findings from A Retrospective Cohort Study

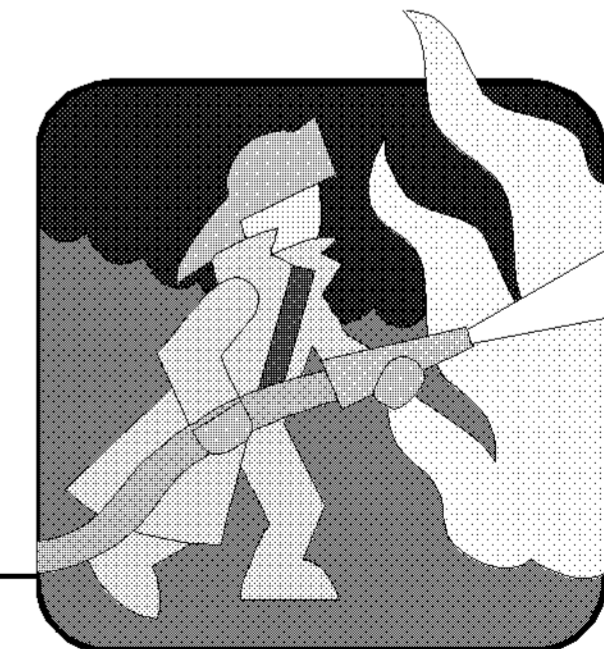
Introduction

- **A common perception of psychiatrists in US**

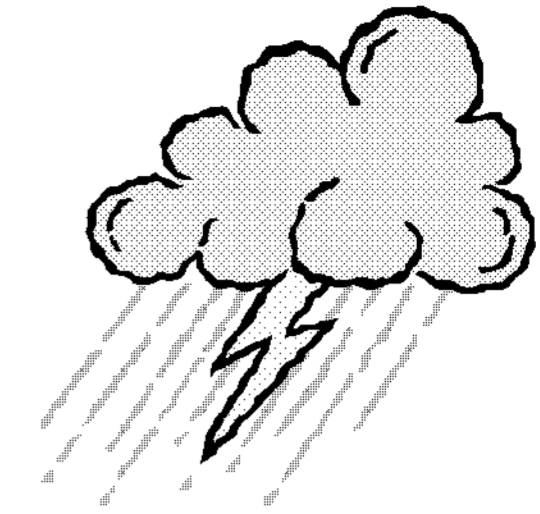
- that Zyprexa has a greater association with diabetes than most other antipsychotics

- **FDA request**

- Lilly to look into the possibility of conducting an epidemiology study to assess the diabetogenic potential of Zyprexa

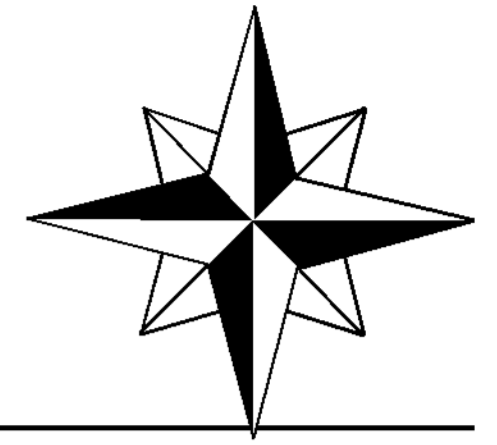


Introduction (con't)



- **Janssen Pharmaceutical Company claimed that in their epidemiology studies:**
 - Olanzapine had a greater association with diabetes than risperidone
 - Olanzapine was the only antipsychotic to demonstrate dose-dependent changes in the incidence of diabetes
 - Risperidone had no apparent diabetogenic effect

Diabetes Study in US

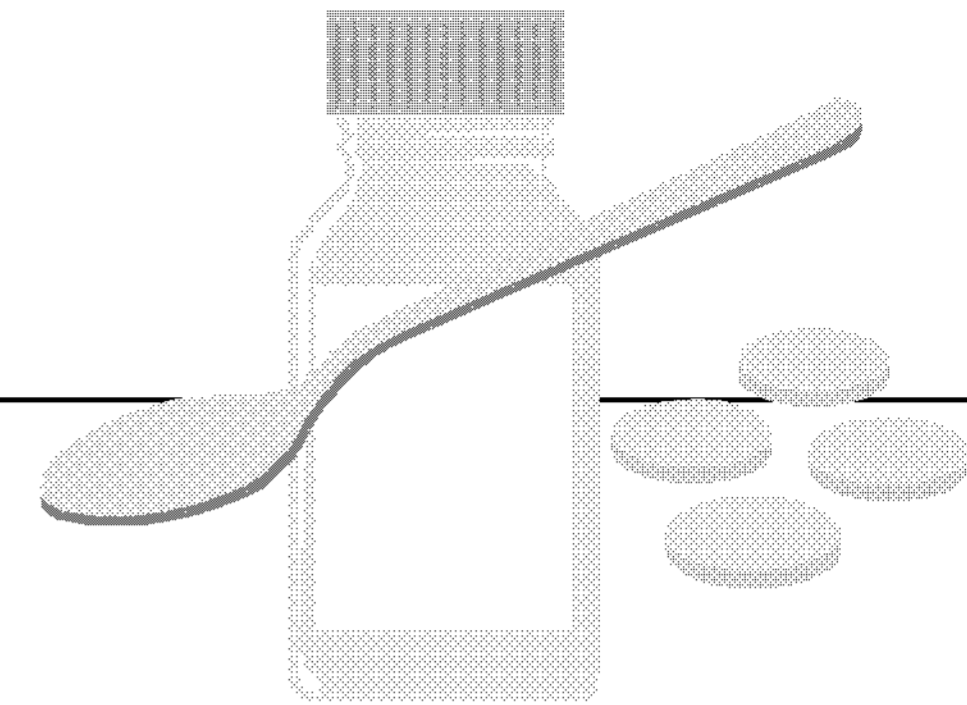


Objectives:

- **To compare the diabetogenic potential of**
 - Atypical vs conventional antipsychotics as a class
 - Olanzapine vs Risperidone

- **To determine whether the incidence of DM increased with the dosage of**
 - Olanzapine
 - Risperidone
 - Haloperidol

Method



- **Study Design**

- Retrospective cohort study

- **Database**

- AdvancePCS prescription claim database

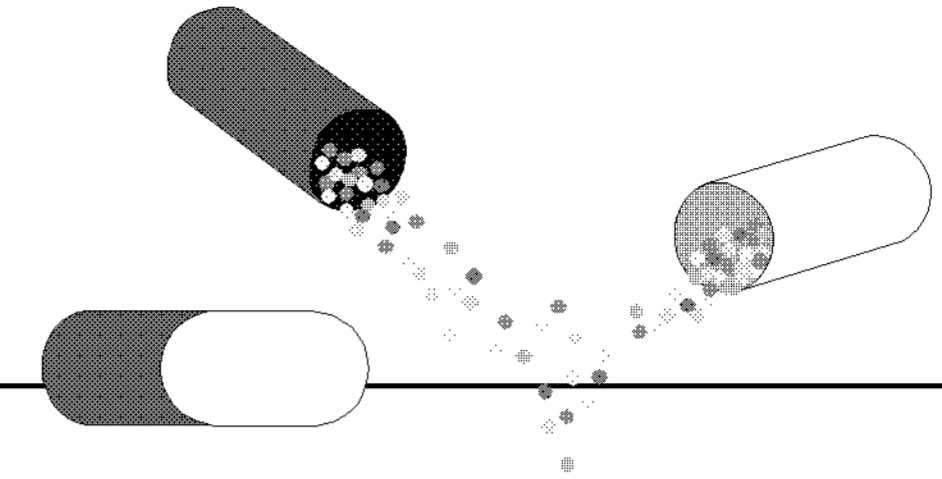
- **Onset of diabetes mellitus (DM) was identified by**

- Prescription claims for diabetes drugs for the first time during exposure to antipsychotics

- **Statistical method**

- Logistic regression model to estimate the odds of diabetes
- Age and gender as covariates

Cohorts Compared



Monotherapy Cohorts

- **All conventional antipsychotics** (N=19,782)
- Haloperidol (N= 8,476)
- **All atypical antipsychotics** (N= 38,735)
- Olanzapine (N= 13,863)
- Risperidone (N= 20,633)
- Seroquel (N= 4,196)
- Clozapine (N= 277)

General PCS patient cohort (N= 6 millions)

- Served as the reference group for comparison with antipsychotic cohorts in regression analysis

RESULTS

Odds of Developing Diabetes for the Conventional and Atypical Antipsychotics

Antipsychotic Cohort	Odds	95% Confidence Interval	
		Lower	Upper
Conventional	1.5*	1.3	1.7
Atypical	1.8*	1.6	1.9

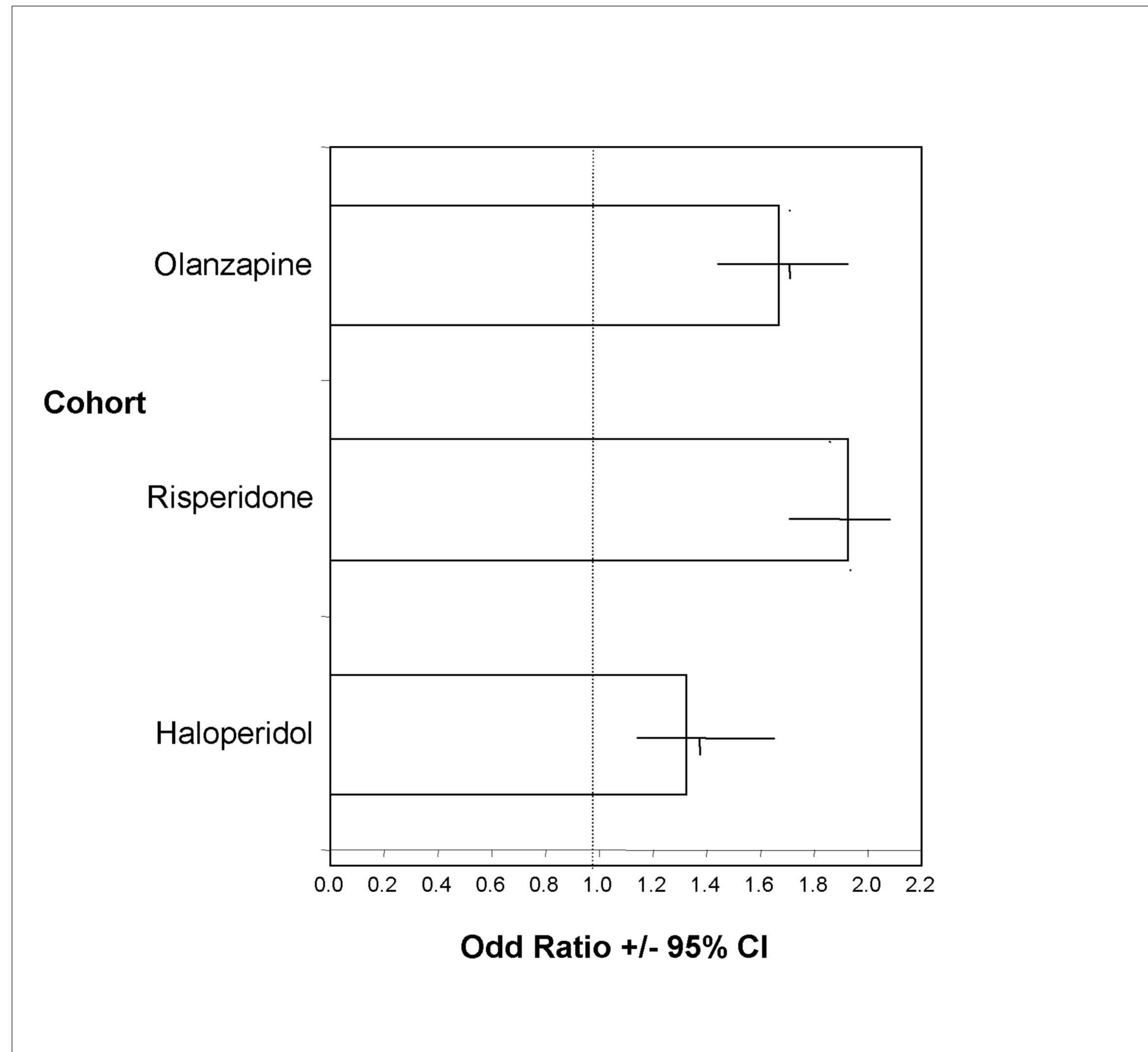
* Significantly different ($p < 0.05$) from the general patient population (odds = 1.0) after adjusting for age and gender difference.

Odds of Diabetes for individual Antipsychotic Cohorts (relative to general patient population)

COHORTS	Odds	95% Confidence Interval	
		Lower	Upper
Haloperidol	1.3*	1.1	1.6
Seroquel	1.1	0.8	1.5
Olanzapine	1.7*	1.4	1.9
Risperidone	1.9*	1.7	2.1
Clozapine	2.9*	1.2	5.6

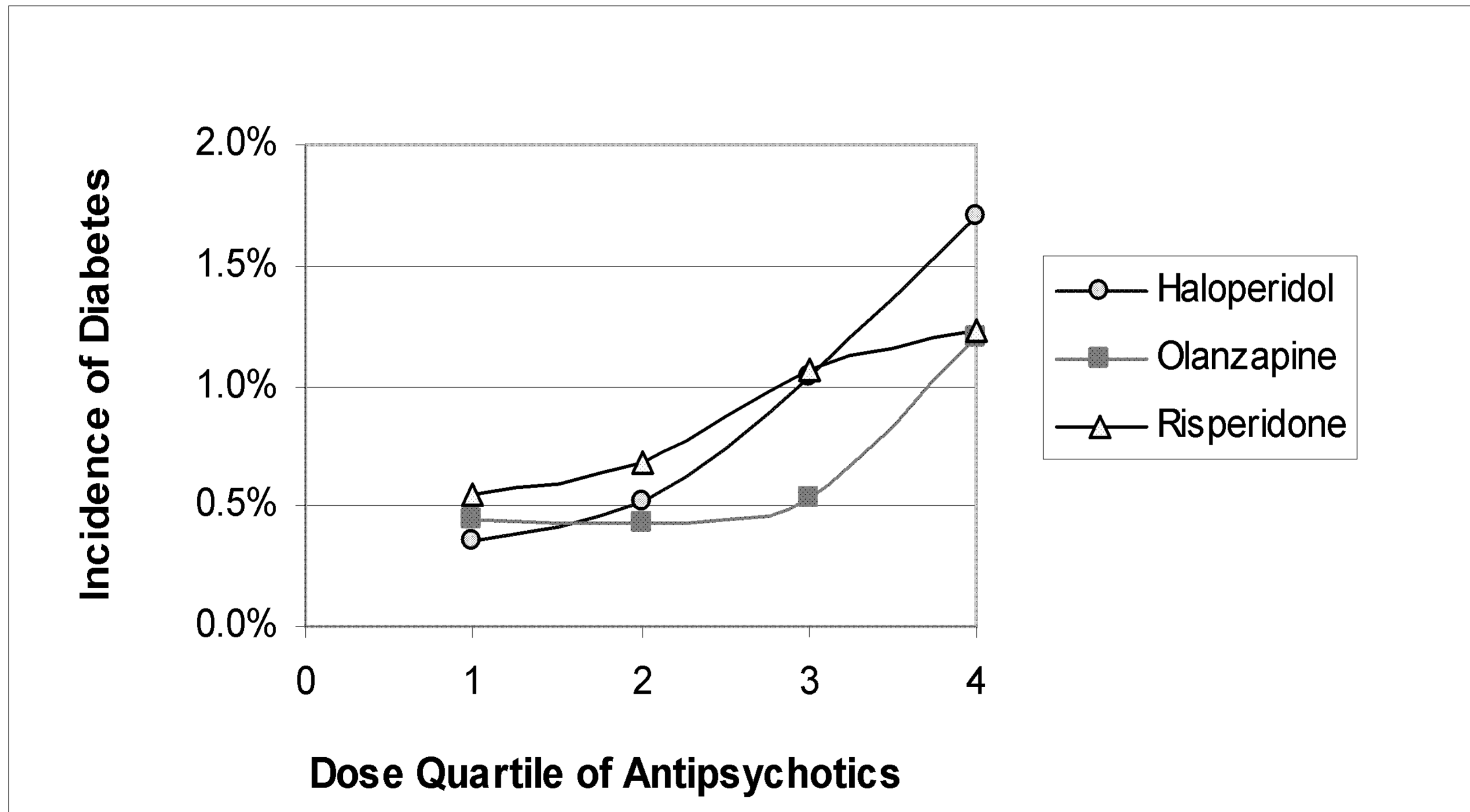
* Significantly different ($p < 0.05$) from the general patient population (odds = 1.0) after adjusting for age and gender difference.

The Odds of Developing Diabetes while taking Antipsychotics



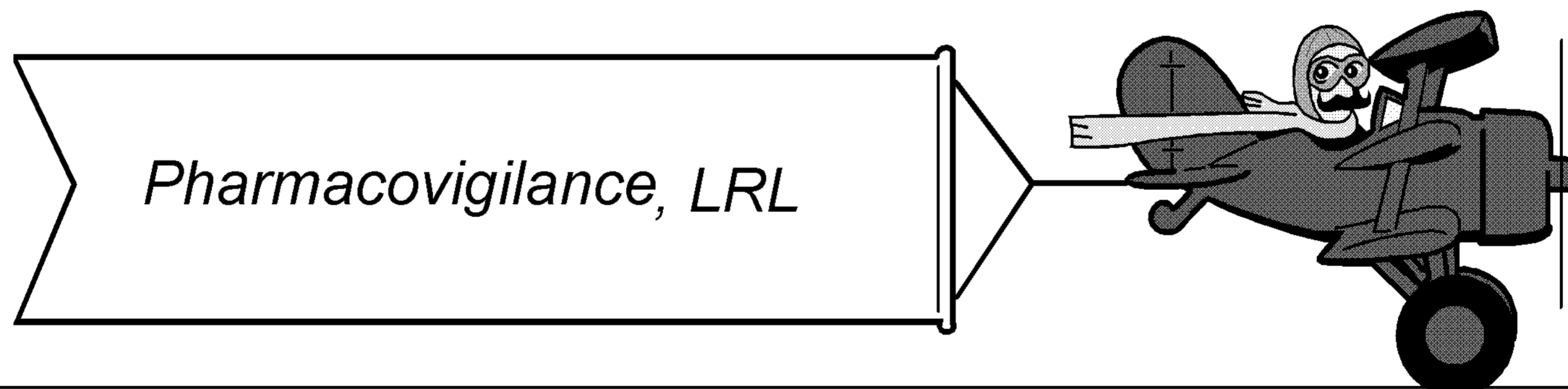
DOSE-INCIDENCE RELATIONSHIP

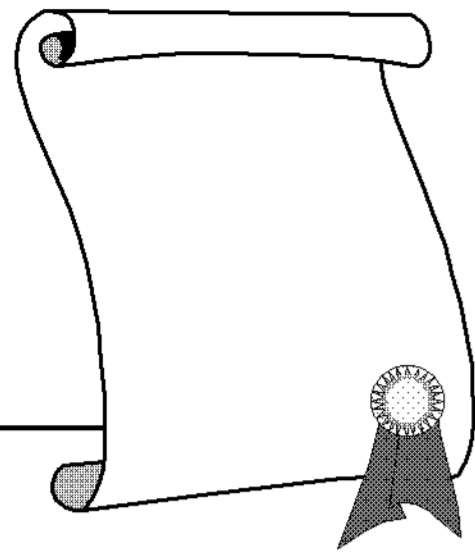
(between antipsychotics and diabetes)



CONCLUSIONS

- Hyperglycemia appears to be a class effect of both conventional and atypical antipsychotics
- Contrary to the claims of Janssens Pharmaceutical:
 - The diabetogenic potential of risperidone was comparable to that of olanzapine.
 - A dose-incidence relationship was suggested not only for olanzapine, but also for risperidone.





NEXT STEPS

- **To perform Cox regression analyses**
 - for direct comparisons between antipsychotic cohorts in their risk of diabetes development

- **To share our findings to**
 - Key regulatory agencies
 - Practitioners worldwide
 - * through publications, scientific conferences, and our marketing folks