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Influencing factors of multiple adverse outcomes among schizophrenia patients using count regression models: a cross-sectional study

Lichang Chen^{1†}, Wenyan Tan^{2†}, Xiao Lin¹, Haicheng Lin², Junyan Xi¹, Yuqin Zhang¹, Fujun Jia^{2*} and Yuantao Hao^{1,3,4*}

Abstract

Background: Schizophrenia patients have increased risks of adverse outcomes, including violent crime, aggressiveness, and suicide. However, studies of different adverse outcomes in schizophrenia patients are limited and the influencing factors for these outcomes need clarification by appropriate models. This study aimed to identify influencing factors of these adverse outcomes by examining and comparing different count regression models.

Methods: This study included schizophrenia patients who had at least one follow-up record in the Guangdong Mental Health Center Network Medical System during 2020. Three types of adverse outcomes were included: a) aggressiveness with police dispatch or violent crime, b) aggressiveness without police dispatch, and c) self-harm or suicide attempts. The incidence density of these adverse outcomes was investigated using the Poisson, negative binomial (NB), zero-inflated Poisson (ZIP), and zero-inflated negative binomial (ZINB) models, accordingly. The best model was chosen based on goodness-of-fit tests. We further analyzed associations between the number of occurrences of adverse outcomes and sociodemographic, clinical factors with the best model.

Results: A total of 130,474 schizophrenia patients were enrolled. Adverse outcomes rates were reported to be less than 1% for schizophrenia patients in 2020, in Guangdong. The NB model performed the best in terms of goodness-of-fit and interpretation when fitting for the number of occurrences of aggressiveness without police dispatch, whereas the ZINB models performed better for the other two outcomes. Age, sex, and history of adverse outcomes were influencing factors shared across these adverse outcomes. Higher education and employment were protective factors for aggressive and violent behaviors. Disease onset aged ≥ 18 years served as a significant risk factor for aggressiveness without police dispatch, and self-harm or suicide attempts. Family history of mental diseases was a risk factor for self-harm or suicide attempts individually.

Conclusions: NB and ZINB models were selected for fitting the number of occurrences of adverse outcomes among schizophrenia patients in our studies. Influencing factors for the incidence density of adverse outcomes included both

[†]Lichang Chen and Wenyan Tan are authors contributed equally to this work.

*Correspondence: jiafujun@126.com; haoyt@bjmu.edu.cn

¹ Department of Medical Statistics, School of Public Health, Sun Yat-sen University, Guangzhou 510080, Guangdong, China

² Guangdong Mental Health Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou 510080, Guangdong, China

Full list of author information is available at the end of the article



those shared across different types and those individual to specific types. Therefore, comprehensive and customized tools in risk assessment and intervention might be necessary.

Keywords: Schizophrenia, Aggressiveness, Violent crime, Suicide attempt, Influencing factor, Count model

Background

Schizophrenia is a severe mental disorder characterized by delusions, hallucinations, impaired motivation, reduction in spontaneous speech, and social withdrawal [1]. According to the Global Burden of Disease Study 2019, the worldwide prevalence of schizophrenia was 0.32% whereas China's prevalence was slightly higher, reaching 0.4% [2]. Besides prevalence burden, schizophrenia was associated with a weighted average of 14.5 years of potential life lost [3]. Schizophrenia patients are at an increased risk of several adverse outcomes, such as aggression, crime, suicide attempt, and suicide. The odds ratio of violent crime, suicide, and premature mortality for patients with schizophrenia and related disorders was over 7.5 when compared with the general population [4]. The prevalence of any aggression assessed by MOAS (Modified Overt Aggression Scale) in schizophrenia patients was above 30% [5, 6]. In terms of aggression that have more public health and public safety importance, the rate of physical violence was about 3% in China [7], whereas the rate of violent offence was 0.8% among women patients in Sweden [4]. The frequency of experiencing physical violence in their primary caregivers was 75.8% [8], while the lifetime risk of suicide attempts was 40–50% [9, 10]. Therefore, these adverse outcomes represent an essential public health issue and pose a great challenge to clinical treatment and patients' health. Fortunately, these adverse events are considered to be preventable if intervention towards relevant influencing factors is carefully tailored. Thus, there remains a need and it is necessary to develop effective assessment methods for revealing influencing factors among schizophrenia patients with an inclination of adverse outcomes.

Many studies investigated the influencing factors for these adverse outcomes among schizophrenia patients. Being male and early in age were the common risk factors [11–13]. Other socio-demographic characteristics also serve as the risk factors for violence, including unemployment, lower levels of education, single status, and lower income [11, 14, 15]. Previous studies suggested that these adverse outcomes were also associated with a history of adverse outcomes, drug use, and a family history of psychiatric illness [13–15]. Other significant clinical factors including hospitalizations, lower satisfaction, and treatment adherence had been proposed in previous

studies [12, 14, 16]. However, to the best of our knowledge, these studies only provided limited evidence concerning influencing factors for different types of adverse outcomes within the same population. Investigation of individual and shared influencing factors for the occurrences of adverse outcomes may contribute to risk assessment for these mental patients and shed a light on the prevention and treatment of schizophrenia.

In addition, patients may suffer from these events several times during the specified period, which means re-occurrence of outcomes within the same individual should be considered as count data. However, most studies treated these outcomes as dichotomous data. For instance, the MOAS score has been used as the dichotomous data for comparison between those reporting no aggressiveness (MOAS score equals 0) and those reporting aggressiveness (MOAS score greater than 0) without thinking about the re-occurrence of aggression behaviors. However, the re-occurrence of aggression behaviors indicates the level of aggressiveness, and previous studies suggested that higher aggressive levels were associated with severer psychiatric symptoms, thereby influencing the treatment and management of schizophrenia patients [15, 17]. Treating the variable as a simple dichotomous variable may result in loss of information and a decrease in statistical power. Therefore, treating the number of adverse outcomes as a count data, and identifying important factors of the incidence density of these events in patients with schizophrenia is necessary.

The Poisson regression model is commonly used to model count data, but its assumption of equal mean and variance is not reasonable in some cases. For over-dispersed count data (greater variance compared with mean), the negative binomial regression is more appropriate [18, 19]. However, the above models cannot handle count data with excess zeros. The zero-inflated regression models considered the data as a mixture of a "zero" subset and another "non-zero" subset following specific distribution to address excess zeros [20, 21]. There are few studies investigating and empirically comparing the performance of different count models in terms of modeling adverse events among schizophrenia patients. In this study, we aimed to identify influencing factors that lead to different types of adverse outcomes, whether they are shared or individual related to these outcomes, by examining and comparing different count regression models.

Methods

Study participants

The study participants were enrolled from the Guangdong Mental Health Center Network Medical System (GDMHS), which was a disease registration report system based on the community mental health service network in Guangdong, China. GDMHS covered over 99% of schizophrenia patients in the province. There were over 348,000 patients registered in GDMHS during the periods from 2010 to 2019 in Guangdong, one of the biggest provinces in China [22]. Patient profile, clinical characteristics, and treatment information were recorded and maintained into GDMHS. Psychiatrist doctors and chief physicians were responsible for the data validation. To ensure data reliability, the Guangdong Health Commission conducted verification on the dataset annually by sampling surveys. The present study included schizophrenia patients with International Classification of Diseases, Tenth Revision code F20* in GDMHS. Other inclusion criteria were as follows: (1) the age of onset between 6–65 years of age; (2) having at least one follow-up during the period from January 1, 2020, to December 31, 2020; (3) no missing or implausible data. Patients with psychiatric comorbidities (including intellectual disabilities, alcohol or substance abuse, major depressive disorder, bipolar disorder) or other severe neurological diseases (including neurodegenerative diseases, cerebrovascular diseases, neurological tumors, neurological infectious diseases) were not included in the present study.

Measures

We classified adverse outcomes according to different characteristics of behaviors, victim objects, interventions as well as services. The first outcome is the aggressiveness with police dispatch or violent crime, which is aggression or violence against others and leads to police dispatch or violation of Chinese law. The public security department was responsible for identifying aggressiveness with police dispatch and violent crime. The second outcome is aggressiveness without police dispatch, which is aggression or violence against others but does not lead to police dispatch. The third outcome is self-harm or suicide attempts. Aggressiveness without police dispatch, self-harm, and suicide attempts were reported by patients or their caregivers and assessed by community public health service workers. The total numbers of each outcome in 2020 were considered as the dependent variables.

Independence variables included sex, age, register type, education level, employment status, marital status, residential type, economic status, other medical history, family history of mental diseases, duration of illness, psychosis treatment status, duration of untreated psychosis,

onset age, history of adverse outcomes. Information regarding independence variables was collected at the time of patient registration in GDMHS. All the categorical variables were entered into the models as the dummy variables.

Analysis methods

The adverse outcome and independent variables were analyzed using descriptive analysis. Then, the Poisson regression, negative binomial (NB) regression, zero-inflated Poisson (ZIP) regression, and zero-inflated negative binomial (ZINB) regression were used to fit the data without covariates for each adverse outcome. The Likelihood Ratio test was used to identify overdispersion. The Vuong test was used for the non-nested model to determine whether there were excess zeros. In addition, the fitting goodness of each regression was evaluated by the difference between predicted and observed probabilities, log-likelihood, and Akaike information criterion (AIC). We selected the best fit model for multivariate regression for all adverse outcomes. We used backward stepwise selection as the variable selection method in our study. The logit part of ZIP and ZINB regression included intercept and the non-zero part included the same covariates as the Poisson and NB regression. Statistical significance was defined as $p < 0.05$. All analyses were conducted using R, version 4.0.

Results

As shown in Table 1, a total number of 130,474 schizophrenia patients was enrolled in this study, and the adverse outcomes were reported by less than 1% of schizophrenia patients in 2020, in Guangdong, China. The majority of schizophrenia patients have not reported any adverse events in 2020. Only about 0.2%, 0.7%, and 0.1% of schizophrenia patients reported aggressiveness with police dispatch or violent crime, aggressiveness without police dispatch, and self-harm or suicide attempts, respectively.

Table 2 shows the distribution of independent variables. The mean age in schizophrenia patients was 47.6 ± 13.9 years with a range from 9.25 years to 99.8 years. Compared with all enrolled patients, those who had adverse events were early in age. Schizophrenia patients who reported self-harm or suicide attempts had the lowest age (35.9 ± 13.4 years). Among schizophrenia patients, 54.0% were males and larger proportions of males were found in all adverse outcomes. Most of the patients (87.7%) were registered. Among these patients, 85.5% had education levels of junior high school education or below. About 43.7% of the patients were unemployed. Aggressiveness with police dispatch or violent crime cases had a lower proportion of unemployment

Table 1 Number and proportion of adverse outcomes

Number of adverse outcomes	Aggressiveness with police dispatch or violent crime	Aggressiveness without police dispatch	Self-harm or suicide attempts
0	130,219 (99.805)	129,502 (99.255)	130,400 (99.943)
1	179 (0.137)	640 (0.491)	63 (0.048)
2	35 (0.027)	154 (0.118)	6 (0.005)
3	13 (0.010)	58 (0.044)	2 (0.002)
4	5 (0.004)	28 (0.021)	2 (0.002)
≥ 5	23 (0.018)	92 (0.071)	1 (0.001)
total	130,474(100)	130,474(100)	130,474(100)

Data are n (%)

(40.4%), while aggressiveness without police dispatch cases (47.0%) and self-harm or suicide attempts cases (60.8%) had a higher proportion. Among schizophrenia patients, 51.3% of them were married, 64.3% of them lived in rural areas, and 41.3% of them had personal income lower than the local poverty level. Compared with total patients, those reporting aggressiveness with police dispatch or violent crime (74.5%), and aggressiveness without police dispatch cases (66.4%) were more likely to live in rural areas. Aggressiveness with police dispatch or violent crime cases had a lower proportion of living with poverty (29.0%) compared with overall patients. Only a small proportion of patients had a medical history (3.0%), and a family history of mental diseases (6.4%). Aggressiveness with police dispatch or violent crime cases had the lowest proportion of other medical history (0.4%), whereas self-harm or suicide attempts cases had the highest proportion of family history of mental diseases (17.6%). The majority of patients (82.9%) had their age at onset of schizophrenia at ≥ 18 years, but the cases of three outcomes had less proportion, with 79.6%, 80.3%, and 74.3% respectively. The mean duration of untreated psychosis was 4.17 ± 7.78 years (range 0–73 years), while the mean duration of illness was 19.2 ± 11.1 years (range 0.2–89.3 years). All types of adverse events cases had a shorter duration of illness as well as a shorter duration of untreated psychosis. Most of the patients received treatment (99.7%) and had adverse outcomes history (86.1%). However, patients reporting adverse outcomes had less proportion of adverse outcomes history, with 65.1%, 62.8%, and 60.8% respectively.

Figure 1 shows the difference between the predicted and observed probabilities for each intercept-only model fitted to the number of adverse outcomes. It suggested that the Poisson model was a poor fit for all three outcomes. This model underestimated the probabilities of zeros and overestimated the probabilities of ones. The ZIP model performed better than the Poisson model,

but the ZIP model predicted less 1 s and more > 1 s when fitting for the number of occurrences of aggressive and violent behaviors. The NB and ZINB models produced better fit when compared to the ZIP model, for the outcome of aggressiveness without police dispatch. The NB model overestimated the probabilities of zeros and underestimated the probabilities of ones in fitting the number of occurrences of aggressiveness with police dispatch or violent crime as well as in fitting the number of occurrences of self-harm or suicide attempts, while the ZINB model gave the best fit. The significant likelihood ratio test ($p < 0.001$, Table 3) showed that the number of counts of events was overdispersed. The Vuong test indicated that the ZIP model was favored over the Poisson ($p < 0.001$) when fitting for the number of occurrences of aggressive and violent behaviors. It also indicated that the ZINB model was favored over the NB model ($p < 0.05$) when fitting for the number of occurrences of aggressiveness with police dispatch or violent crime and for self-harm or suicide attempts. In addition, the value of Log-likelihood and AIC showed similar results. Taking the goodness-of-fit and model interpretation into account, the ZINB model was the best choice in modeling the number of occurrences of aggressiveness with police dispatch or violent crime, and the number of occurrences of self-harm or suicide attempts, while the NB model was the final model for fitting the number of occurrences of aggressiveness without police dispatch.

The results of multivariate count regression models are shown in Fig. 2. Sex, age, and adverse outcomes history were associated with all types of adverse outcomes. The number of occurrences of aggressiveness with police dispatch or violent crime and the number of occurrences of aggressiveness without police dispatch for female patients was lower than that for males patients, with incidence rate ratios (IRR) being 0.52 (95% CI: 0.33,0.82; $p = 0.005$) and 0.45 (95% CI: 0.35,0.58; $p < 0.001$) respectively. On the other hand, being female was a risk factor

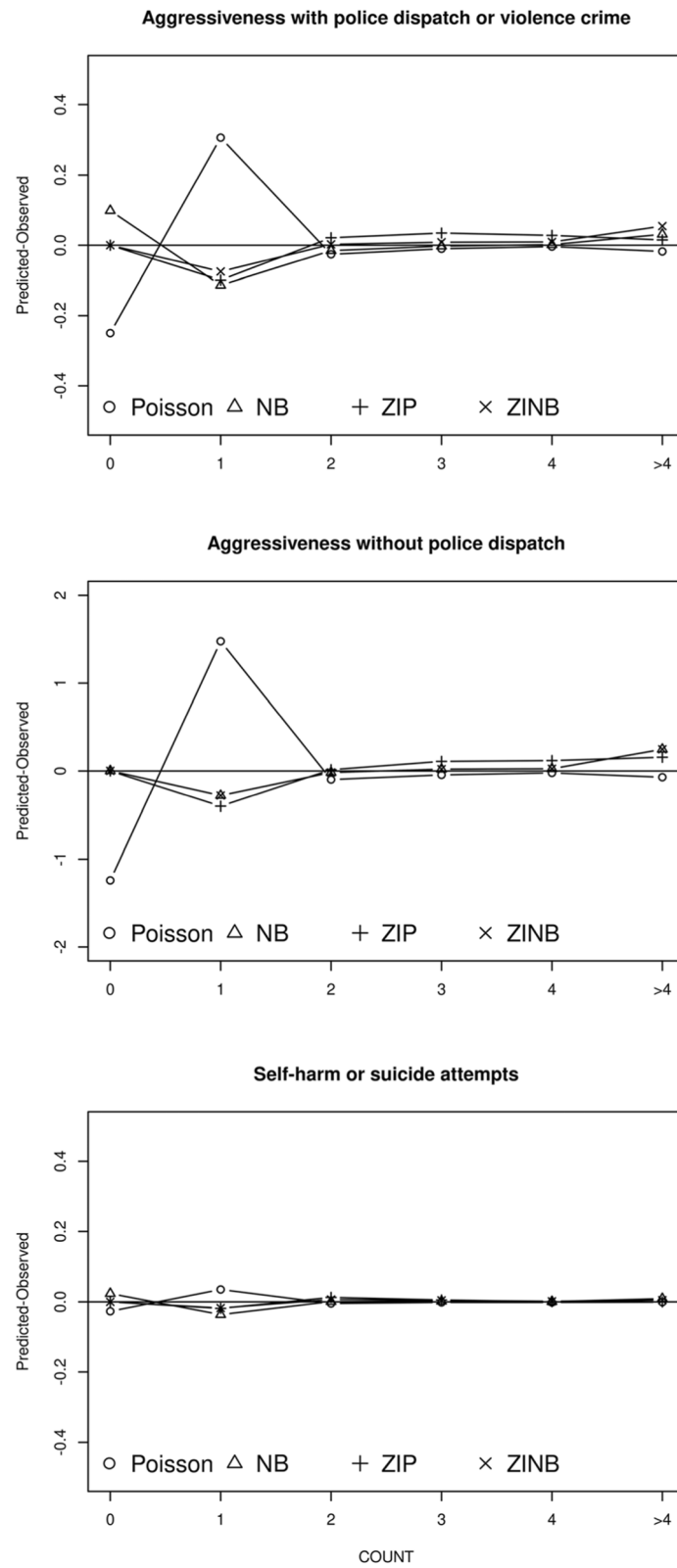


Fig. 1 Predicted minus observed probabilities for four intercept-only models. NB, negative binomial; ZIP, zero-inflated Poisson; ZINB, zero-inflated negative binomial

Table 2 Descriptive statistics for the characteristics of schizophrenia patients, grouped by each adverse outcome

Variable	Total Patients (n = 130,474)	Aggressiveness with police dispatch or violent crime cases (n = 255)	Aggressiveness without police dispatch cases (n = 972)	Self-harm or suicide attempts cases (n = 74)
Age(years)	47.6 ± 13.9	42.0 ± 12.5	42.9 ± 12.9	35.9 ± 13.4
Duration of untreated psychosis (years)	4.17 ± 7.78	2.84 ± 5.05	3.29 ± 6.34	2.54 ± 5.32
Duration of illness (years)	19.2 ± 11.1	15.7 ± 9.46	17.0 ± 10.1	13.6 ± 9.75
Sex				
Male	70,441 (54.0)	175 (68.6)	671 (69.0)	42 (56.8)
Female	60,033 (46.0)	80 (31.4)	301 (31.0)	32 (43.2)
Register type				
Register	114,390 (87.7)	228 (89.4)	857 (88.2)	58 (78.4)
Non-register	16,084 (12.3)	27 (10.6)	115 (11.8)	16 (21.6)
Educational level				
No education	19,933 (15.3)	35 (13.7)	92 (9.5)	6 (8.1)
Primary education	47,181 (36.2)	89 (34.9)	290 (29.8)	19 (25.7)
Junior high school education	44,329 (34.0)	93 (36.5)	408 (42.0)	31 (41.9)
High school education	11,180 (8.6)	26 (10.2)	102 (10.5)	8 (10.8)
Higher education	7851 (6.0)	12 (4.7)	80 (8.2)	10 (13.5)
Employment status				
Unemployment	57,007 (43.7)	103 (40.4)	457 (47.0)	45 (60.8)
Employment	73,467 (56.3)	152 (59.6)	515 (53.0)	29 (39.2)
Marital status				
Single	53,400 (40.9)	136 (53.3)	522 (53.7)	47 (63.5)
Married	66,990 (51.3)	93 (36.5)	364 (37.4)	23 (31.1)
Widowed	3786 (2.9)	2 (0.8)	21 (2.2)	1 (1.4)
Divorced	6298 (4.8)	24 (9.4)	65 (6.7)	3 (4.1)
Residential type				
Urban	46,555 (35.7)	65 (25.5)	327 (33.6)	28 (37.8)
Rural	83,919 (64.3)	190 (74.5)	645 (66.4)	46 (62.2)
Economic status				
Non-poverty	76,546 (58.7)	181 (71.0)	549 (56.5)	35 (47.3)
Poverty	53,928 (41.3)	74 (29.0)	423 (43.5)	39 (52.7)
Medical history				
Yes	3925 (3.0)	1 (0.4)	37(3.8)	2 (2.7)
No	126,549 (97.0)	254 (99.6)	935 (96.2)	72 (97.3)
Family history of mental diseases				
Yes	8533 (6.6)	20 (7.8)	94 (9.7)	13 (17.6)
No	120,697 (93.4)	235 (92.2)	878 (90.3)	61 (82.4)
Onset age(years)				
< 18 years	22,364 (17.1)	52 (20.4)	191 (19.7)	19 (25.7)
≥ 18 years	108,110 (82.9)	203 (79.6)	781 (80.3)	55 (74.3)
Psychosis treatment				
Yes	130,030 (99.7)	255 (100)	968 (99.6)	74 (100)
No	444 (0.3)	0 (0)	4 (0.4)	0 (0)
Adverse outcomes history				
Yes	112,329 (86.1)	166 (65.1)	610 (62.8)	45 (60.8)
No	18,145 (13.9)	89 (34.9)	362 (37.2)	29 (39.2)

Data are mean ± SD for continuous variables

n(%) for categorical variables

Table 3 The results of goodness-of-fit statistics and tests for four intercept-only models

Models	Log likelihood	AIC	The likelihood ratio test (p-Value) ^a	The Vuong test (p-Value) ^b
Aggressiveness with police dispatch or violent crime				
Poisson	-4827.2	9656.4	4893.7(<0.001)	-4.2(<0.001)
NB	-2380.3	4764.7	—	-4.1(<0.001)
ZIP	-2870.0	5744.1	1121.8(<0.001)	—
ZINB	-2309.1	4624.3	—	—
Aggressiveness without police dispatch				
Poisson	-18,726.1	37,454.2	22,152.0(<0.001)	-8.6(<0.001)
NB	-7650.2	15,304.4	—	-0.002 (= 0.499)
ZIP	-10,786.3	21,576.6	6272.2(<0.001)	—
ZINB	-7650.2	15,306.4	—	—
Self-harm or suicide attempts				
Poisson	-990.9	1983.7	513.4(<0.001)	-1.6(= 0.054)
NB	-734.2	1472.4	—	-1.7(= 0.046)
ZIP	-762.7	1529.3	92.8(<0.001)	—
ZINB	-716.3	1438.6	—	—

NB negative binomial, ZIP zero-inflated Poisson, ZINB zero-inflated negative binomial

^a the likelihood ratio test for overdispersion (Poisson vs. NB and ZIP vs. ZINB)

^b the Vuong test for excess zeros (Poisson vs. ZIP and NB vs. ZINB)

for self-harm or suicide attempts (IRR = 2.20; 95% CI: 1.14, 4.25; $p = 0.019$). Elderly patients and patients having adverse outcomes history showed less risk in three adverse outcomes. Patients who had higher educational levels exhibited a lower likelihood of aggressiveness with police dispatch or violent crime. Having higher education (IRR = 0.48; 95% CI: 0.27, 0.89; $p = 0.010$) also decreased the number of occurrences of aggressiveness without police dispatch compared to those who had received no education. There was an association between unemployment and an increased number of occurrences of aggressiveness with police dispatch or violent crime, and that of occurrences of aggressiveness without police dispatch. Living in rural (IRR = 0.44; 95% CI: 0.33, 0.57; $p < 0.001$) and poverty (IRR = 0.28; 95% CI: 0.17, 0.49; $p < 0.001$) was associated with reduced risk of aggressiveness without police dispatch, and aggressiveness with police dispatch or violent crime respectively. Having medical history was significantly associated with a higher risk of aggressiveness without police dispatch (IRR = 2.62; 95% CI: 1.39, 5.42; $p = 0.002$), and significantly associated with lower risk of aggressiveness with police dispatch or violent crime (IRR = 0.28; 95% CI: 0.17, 0.47; $p < 0.001$). Longer duration of illness (IRR = 1.02; 95% CI: 1.01, 1.04; $p = 0.002$) and adult-onset schizophrenia (onset age ≥ 18 years) (IRR = 1.78; 95% CI: 1.20, 2.64; $p = 0.001$) significantly increased the risk of aggressiveness without

police dispatch. Adult-onset schizophrenia (IRR = 2.82; 95% CI: 1.24, 6.42; $p = 0.002$) and having family history of mental diseases (IRR = 6.55; 95% CI: 2.78, 15.43; $p < 0.001$) were risk factors for self-harm or suicide attempts.

Discussion

To the best of current knowledge, though count models have been implemented in many epidemiological and public health studies, our study is the first of its kind to utilize count regression models to analyze the incidence density of the adverse outcomes in schizophrenia patients [23–26]. Moreover, it is crucially important to select the best-fitted model for the data since there is no model fitted well for all data. Here, we used four count regression models to fit the incidence density of the adverse outcomes in schizophrenia patients and investigated influencing factors associated with the number of occurrences of adverse outcomes by the best-fitted model. In our study, about 1% of schizophrenia patients have reported adverse outcomes in 2020. Traditional Poisson regression had the worst fit to this study data for all types of outcomes because of the overdispersion and excess zeros in the present study. To solve the zero-inflated problem, the ZIP model was used which was an obvious choice over Poisson regression. To deal with the overdispersion problem, the NB model was used and also fitted the data better than the Poisson model. However, the NB model can not yet solve the zero-inflated issue. Hence, the ZINB model was used, which took both overdispersion and the excess zeroes into account. The ZINB model can also provide a similar fit compared to the NB model because no zero-inflated issue was depicted when using the NB model for aggressiveness without police dispatch. Therefore, the NB model was selected to be the simplest and first choice to fit the number of aggressiveness without police dispatch because of no zero-inflated issue, whereas the ZINB model was preferred for the other two outcomes to account for both overdispersion and the excess zeroes.

Investigation of influencing factors for adverse outcomes is of benefit to intervention and prevention of schizophrenia. Specifically, epidemiological knowledge may translate into clinical practice by developing clinically feasible assessment tools to predict risk and support the clinical judgement. Interventions, as well as preventions, can be targeted at those likely to have a risk of adverse outcomes. In our study, a wide range of sociodemographic and clinical factors were assessed. Our finding indicated that being early in age increased the risk of all outcomes, including aggressiveness with police dispatch or violent crime, aggressiveness without police dispatch, and self-harm or suicide attempts. These results are consistent with the results of previous

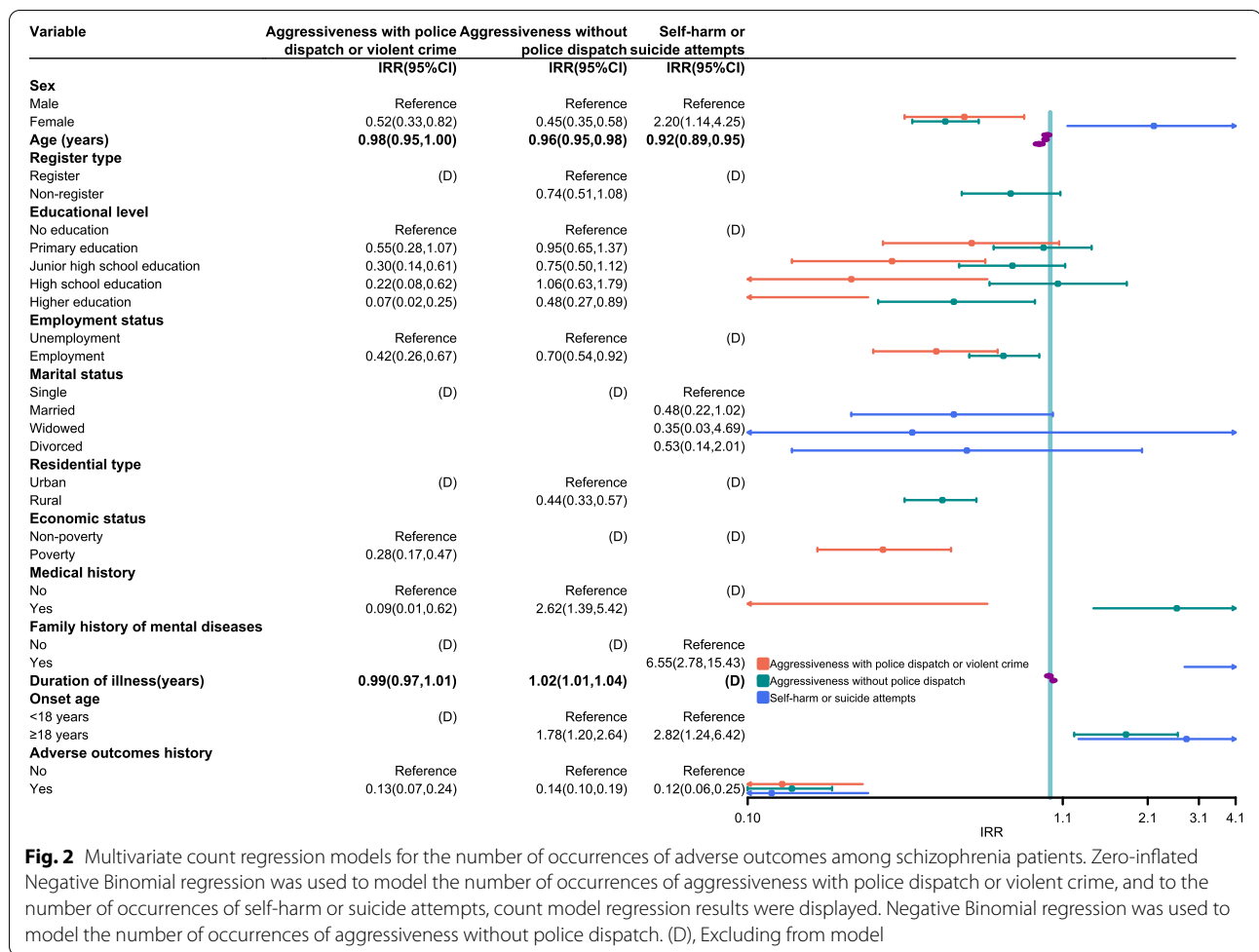


Fig. 2 Multivariate count regression models for the number of occurrences of adverse outcomes among schizophrenia patients. Zero-inflated Negative Binomial regression was used to model the number of occurrences of aggressiveness with police dispatch or violent crime, and to the number of occurrences of self-harm or suicide attempts, count model regression results were displayed. Negative Binomial regression was used to model the number of occurrences of aggressiveness without police dispatch. (D), Excluding from model

studies that have explored risk factors with binomial response [11, 12, 27, 28]. The risk of adverse events for violence against others is increased for males, being consistent with those conducted by Fazel et al. [29]. When self-harm or suicide attempts are strictly defined as physical violence against oneself, the risk of self-harm or suicide attempts is increased for females, which is also consistent with previous studies [30, 31].

In addition, our findings revealed that having history of adverse outcomes significantly decreases the likelihood of all three outcomes. It is contrary to the finding of previous studies [15, 30, 32, 33]. It is worth noting that the schizophrenia patients in our study were all provided with primary public health care freely offered by the Chinese government [34]. They received regular follow-up and intervention by community mental health professionals. Patients who had the previous report of adverse outcomes had higher scores of risk assessments, and thus received more frequent follow-up services [22]. Moreover, patients' information about adverse outcomes can be shared with public security departments, by which the

occurrences of adverse outcomes can be prevented from having a negative impact on the social harmony and stability. Therefore, not only their caregivers, but also public security personnel may take on a more active role in helping schizophrenia patients with behavioral issues to prevent the recurrence of adverse outcomes. Besides, their psychiatrists may adjust drug doses or modify treatment regimens according to the mental health condition, thereby leading to remission. Therefore, having a history of adverse outcomes may decrease the risk of adverse events because of the above intervention. However, our inference for the relationship between the above-mentioned intervention and each adverse outcome may still need further exploration in the future study.

However, results from our study showed that many risk factors were not shared across the adverse outcomes. It suggests that it is distinct for mechanism between violence and self-harm or suicide attempts, and customized tools in risk assessment and intervention for specific events are necessary. It also provides a priori knowledge for risk assessment in clinical practice. For example,

educational level, employment status, and medical history were related to violence against others but not to self-harm and suicide attempts. Our findings were in concordance with the results of previous studies which reported unemployment status and low educational level as risk factors for violence [17, 35, 36]. Employment status and educational level should be one of the most important factors considered by clinicians when assessing the risk of violence. Whiting et al. reported that having medical history increases the risk of violence [37]. However, our study found a negative relationship between medical history and aggressiveness with police dispatch or violent crime. The possible reasons may be similar to the association between history of adverse outcomes and violence. Having medical history may increase the risk of adverse effects [38–40]. When patients had an adverse effect, he or she may be evaluated as having an unstable mental condition and thus received more intensive follow-up services and symptomatic treatment, thereby contributing to the decreases of their occurrence of violence.

Having a family history of mental disease increased the risk of self-harm or suicide attempts but did not affect violent behaviors. Several previous research found that family history of mental disease was a significant risk factor for self-harm or suicide attempts [13, 41–43], but suggested no conclusive finding in terms of violence [44]. Our findings, consistent with many others, support that self-harm or suicide attempts may be affected by genetic factors [45, 46]. Although previous studies found that earlier age of onset was a risk factor of violence and suicide, we found that adult-onset schizophrenia increases the risk of aggressiveness without police dispatch and the risk of self-harm or suicide attempts. This is in line with previous studies, suggesting that adult-onset patients are more susceptible to schizophrenia and may have more traits for passive as well as aggressive personality disorder compared with early-onset patients [30, 47, 48]. Further studies are warranted to address the relationship between the density of events and the age of illness onset.

In our study, patients who had a longer duration of illness were more likely to conduct aggressiveness without police dispatch, but were unlikely to lead to other outcomes. However, schizophrenia patients with a history of severe violence or with suicide attempts had a longer duration of illness in other studies [31, 49, 50]. It is possible that, for patients with a longer duration of illness, the caregivers, as well as community mental health professionals, may have a better awareness of their much more serious outcomes (for example, suicide attempts and violent crime). Based on these notions, we argue that the caregivers and the other relevant stakeholders may be in a more active role in preventing occurrences of more

serious outcomes. Further studies are needed to clarify the relationship between the duration of illness and different types of adverse outcomes.

Additionally, the residential type was another individual influencing factor for aggressiveness without police dispatch, in which living in rural was found to be a protective factor. A possible explanation is that rural schizophrenia patients are much more inclined to receive primary public health care and have better access to primary medical institutions in China, which may contribute to achieving effective control and decreasing the risk of violence [51, 52]. The different clinical strategies of treatment of schizophrenia between urban and rural areas may be another possible explanation. A previous study in China found that rural patients were more likely to receive anticholinergics compared to urban patients [53]. Similarly, poverty was an individual protective factor for aggressiveness with police dispatch or violent crime. This may be attributed to the higher rate of receiving regular follow-ups and increasing demand and utilization of health services among patients under the poverty lines [51, 54].

In our study, some factors were not significantly associated with the number of occurrences of adverse outcomes. For instance, psychosis treatment status showed an insignificant association with the number of occurrences of these outcomes. The fact that there were too few untreated patients in our study resulted in insufficient statistical power to detect the differences. Other factors, such as marital status, register type, were not related to the number of occurrences of adverse outcomes. It may be attributed to the different statistical analysis methods. In the count regression model, the exponentiated regression coefficient of the count model is the ratio of expected counts instead of the odds ratio in the logistic regression model. In other words, the exponentiated coefficient represents the IRR for each unit change in the predictor, while the other predictors in the model are held constant. Another possible reason for the non-significance is the differences in the definition of these adverse outcomes and the research population. Further studies should be needed to assess the impact of varying covariates on the incidence density of these events among schizophrenia patients.

Several limitations should be noted. First, the inclusion and exclusion criteria of patients may introduce selection bias, but the demographics distribution of enrolled patients in our study was similar to that of the schizophrenia patients followed up in 2020. Secondly, moderate correlation between some given independent variable would generally not result in severe multicollinearity, and thus there is no need for additional attention for such groups of covariates in terms of our regression problem.

Finally, our results were limited due to the definition of adverse outcomes and the lack of variables that may contribute to adverse outcomes (for example, scales, antipsychotic drugs, drug adherence, parental abuse, and clinical symptoms).

Conclusions

Count regression model not only assesses the presence or absence of adverse outcomes but also the incidence density of it. We compared the model performance of the Poisson, NB, ZIP, and ZINB regression models to investigate the distributed nature of three types of adverse outcomes in schizophrenia patients and selected the NB and ZINB as the best models. Several shared influencing factors across different adverse outcomes were detected, such as age, sex, and history of adverse events. However, many factors were specific only to some adverse outcomes, which suggests that risk assessment and intervention might have to be tailored for specific outcomes. Moreover, some influencing factors were inconsistent with previous studies because of the different analysis models, study population, definition and measurement of adverse outcome, and intervention of community public health. It is necessary to translate epidemiological knowledge into comprehensive and customized tools to assess and manage the risk of adverse outcomes, thereby improving medical care and public safety.

Abbreviations

GDMHS: Guangdong Mental Health Center Network Medical System; NB: Negative binomial; ZIP: Zero-inflated Poisson; ZINB: Zero-inflated negative binomial; AIC: Akaike information criterion.

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Authors' contributions

LC conceived and designed the research, performed the analyses, and drafted the manuscript. WT designed the research, collected the data, and drafted the manuscript. XL, HL, JX, YZ, FJ, and YH contributed to the visualization and investigation of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data that support the findings of this study are available from Guangdong Mental Health Center but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Guangdong Mental Health Center.

Declarations

Ethics approval and consent to participate

Ethics approval was obtained for the study from the research ethics committee of the Guangdong Mental Health Center in China (authorization

No.GDMHR2019201H). All participants (or their parent or legal guardian in the case of children under 16, or their legally authorized representative in the case of illiterate participants) signed informed consent after receiving oral and written information about the study. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Medical Statistics, School of Public Health, Sun Yat-sen University, Guangzhou 510080, Guangdong, China. ²Guangdong Mental Health Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou 510080, Guangdong, China. ³Sun Yat-sen Global Health Institute, Sun Yat-sen University, Guangzhou 510080, Guangdong, China. ⁴Center for Public Health and Epidemic Preparedness & Response, Peking University, Beijing 100191, China.

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