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Longitudinal trajectory of the association between quality of life and depression among people living with HIV in China: a mixed effects model

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ABSTRACT

Although depression has been associated with low QOL, limited research has quantified the change of depression to improvement of QOL among naïve PLHIV using ART in Shanghai, China. This study examined the association between depression symptoms and QOL among Chinese PLWH in a six-month longitudinal study. Data were collected from 111 people living with HIV at baseline, 3rd month and 6th month after initiating ART, using the WHOQOL-HIV BREF and the Center for Epidemiologic Studies Depression Scale (CES-D), and analyzed using a mixed effects model. QOL is improved after initiating ART, while the symptoms of depression did not decrease significantly. The depression symptoms were strong and negatively associated with QOL and all domains of QOL, and the strength of this association decreased over time in the six months follow-up. ART had different impacts on depression symptoms and QOL. Besides, depression symptoms were strong and negatively associated with QOL among PLHIV over time. Mental health practitioners and nurses should consider the ART and time factors when designed interventions to improve QOL by targeting depression symptoms. Interventions designed to improve QOL and depression symptoms should be developed targeting both ART and self-management among PLHIV.

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KEYWORDS

HIV; depression; quality of life; longitudinal trajectory; China

Introduction

HIV epidemics have had a global impact, including on China. Approximately 849,602 people are living with HIV (PLWH) in China, with an approximately 14% increase in 2018 (NCAIDS, NCSTD & China CDC, 2018; UNAIDS, 2019), the free antiretroviral therapy (ART) provided by the Chinese government has been available since 2003 for all PLWH (Zhang et al., 2007). As a result, the life expectancy of PLWH has increased and HIV has become a manageable chronic condition (Teeraananchai et al., 2017). Improving the quality of life (QOL) among PLWH has become one of the main goals in HIV healthcare (Webster, 2017). Similar to other PLWH, Chinese PLWH suffer from HIV symptoms, side effects of ART, HIV-related stigma and psychological distress—all of which contribute to low QOL (Zhu et al., 2019; Hidru et al., 2016).

The World Health Organization (WHO) defines QOL as “the individuals’ perception of their position in life in the concept of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (WHO, 2003). This indicates that QOL is a subjective as well as a

multidimensional variable that includes physical, psychological and social factors (Ferrans et al., 2005). For PLWH, QOL is associated with some demographics, such as age, sex, income and employment (Jiang et al., 2019). ART has also had an impact on QOL among PLWH. Studies have demonstrated that the QOL of PLWH with ART is higher than among those who are ART naïve (Jaquet et al., 2013; Stangl et al., 2007), and adherence to ART is also associated with improved QOL (Wang et al., 2009). These studies indicate that the importance of QOL should be evaluated in every clinical setting where PLWH visit.

A total of 22% to 60% of PLWH suffer from depression worldwide (Rezaei et al., 2019) and it has become one of the most common psychological distresses among PLWH (Lu et al., 2018). PLWH experience depression symptoms due to their deteriorated health status, the side effects of ART, violence, and stigma (Effendy et al., 2019). Many studies have shown the association between depression symptoms and QOL among PLWH in China (Hidru et al., 2016; Li et al., 2015; Xiao et al., 2017) and have indicated that depression symptoms are negatively related to

QOL among Chinese PLWH (Shao et al., 2018; Xiaowen et al., 2018). Interestingly, one study conducted among newly diagnosed PLWH in China demonstrated that depression at baseline did not predict the QOL at the one-year follow-up (Huang et al., 2019). This converse finding indicates that the association between QOL and depression should be further explored.

The Wilson and Cleary health-related QOL model has been widely used in HIV populations (Vidrine et al., 2005; Wilson & Cleary, 1995). This model suggests that possible variables can affect psychological and physical symptoms, and significantly predicts the QOL by direct effects, or indirect effects through functional health and general health perceptions in patients with chronic disease (Wilson & Cleary, 1995). In addition, the Wilson and Cleary health-related QOL model indicates that depression symptoms have shown the highest magnitude of relative impact on health-related QOL (Ojelabi et al., 2017). Based on the literature, the present study is designed to explore the changes of QOL and depression among PLWH after initiating ART. We also focused on the association between depression symptoms and QOL among Chinese PLWH in a six-month longitudinal study. The findings from this study can provide an understanding of the changes in depression and QOL over time.

Methods

Sample, settings, and procedures

This was a longitudinal study that focused on QOL and depression among ART naïve PLWH. Recruitment occurred from May to August 2017, with the last follow-up assessment of the participants completed in February 2018. All participants were recruited from a designated hospital for all infectious disease care including HIV and which serves PLWHs in Shanghai and adjacent vicinities. The affiliated university and facilities' institutional ethical review boards approved this study. Inclusion criteria include the following: confirmed HIV serostatus, ART naïve, 18 years of age and above, and willing to participate in a series of three surveys. Demographics, depression and QOL data were collected at baseline, 3-month and 6-month follow-up.

A convenience sample method was used to recruit participants when PLWH came to the clinic during May to August 2017. During this time, of the 330 PLWH who initiated ART, 111 agreed to participate and completed the three surveys. All of the participants did not stop ART during the six months and no missing data in this study. Informed consent was secured before

implementing the study survey. All participants received a small reimbursement for their participation.

Measures

Demographics

Participants' gender, age, educational level, employment status, monthly income, marital status, potential HIV transmission routes, and baseline CD4+ T-cell counts were collected.

Quality of life

QOL was evaluated using the WHO Quality of Life HIV short version (WHOQOL-HIV BREF), a 31-item scale that assesses QOL of PLWH in six domains: physical, psychological, level of independence, social relationships, environment and personal beliefs (WHO, 2003, p. 2004). Each item uses a five-point Likert-type scale; higher scores denote better QOL. The Chinese version of the WHOQOL-HIV BREF has been tested and Cronbach's alpha reliability was 0.93 (Zhu et al. 2017).

Depression

The depression symptomology was assessed by the Center for Epidemiologic Studies Scale (CES-D) (Radoff, 1977). CES-D is a 20-item self-reported instrument; each has a response option of 0 = rarely or none of the time, less than one day, to 3 = most or all the time, 5–7 days. Scores over 16 indicate the presence of depression symptoms. CES-D has been translated into Chinese, has established reliability, and has been validated. As reported, the Chinese CES-D scale's Cronbach alpha was 0.87 (Jiang et al., 2019), and test-retest reliability was 0.91 (Chin et al., 2015).

Analysis

All analyses were performed with SPSS 24.0 (IBM, Chicago, IL); $p < 0.05$ was considered significant. Descriptive statistics were computed. The categorical variables, such as gender, education, employment, monthly income, marital status, and HIV transmission were expressed as percentages. The continuous variables, such as age and CD4+ T-cell count were expressed as mean and standard deviation (SD).

General linear model repeated measures analysis was used to assess the statistically significant difference in depression, QOL and all domains of QOL over time. The following parameters were used for the repeated measures general lineal model: the within-subject factor, referred to as "time point," included three levels for all variables (depression, QOL, physical, psychological, level of independence, social relationships,

environment, and personal beliefs). If the condition of sphericity (Mauchly's sphericity test) was not met, the Greenhouse-Geisser correction for tests of within-subjects' effects was interpreted.

The mixed effects model (Stram & Lee, 1994) was fitted to evaluate the six-month trend in depression and QOL scores from baseline and three-month to six-month follow-ups. In this model, we assessed seven interaction terms: depression and QOL, depression and physical, depression and psychological, depression and level of independence, depression and social relationships, depression and environment, depression and personal beliefs. The model included intercept and time as fixed terms.

Results

Descriptive analysis

Demographic characteristics are presented in Table 1. As shown in the Results section, 98.20% ($N=109$) were male, with a mean age of 32 years ($SD=8.18$, range=20-54). Three-fourths of the study participants (75.70%; $N=84$) had an educational level above diploma. Most participants were employed (82.9%; $N=92$), with high monthly income (84.70%; $N=94$); $\geq 3,000$ RMB ($\sim \$450$)/month. Most were unmarried (73.9%; $N=82$), and had contracted HIV via men who have sex with men (MSM) (83.8%; $N=93$). At baseline, the CES-D mean score for depression symptoms was 15.68 (range from 1 to 41). The total mean score of QOL was 81.31 (range from 50.60-110.90). The mean score for QOL

Table 1. Baseline demographic characteristics, depression and QOL.

Characteristics	N	Mean (SD) or %
Gender (%)	111	
Male	109	98.20
Education (%)	111	
Above diploma	84	75.70
Employment (%)	111	
Employed	92	82.90
Monthly income (RMB, %)	111	
$\geq 3,000$ ($\sim \$420$)	94	84.70
Marital status (%)	111	
Single	82	73.90
Married	27	24.30
Divorced/Widowed	2	1.80
Potential HIV transmission route (%)	111	
MSM	93	83.80
Heterosexual	18	16.20
Age (years, mean)	111	32.78.18
Baseline CD4 count (cells/ml, mean)	111	301.19 (196.26)
CES-D score (mean)*	111	15.68 (9.37)
≤ 16	66	59.46
16~23	25	22.52
≥ 23	20	18.02

*CES-D score cut off point is set at ≤ 16 . Less than 16 points indicative of or "mild" depressive symptomatology.

domains was separately calculated at 13.16 for physical, 13.56 for psychological, 14.81 for level of independence, 13.47 for social relationships, 13.68 for environment, and 12.63 for personal beliefs.

The general linear model repeated measures analysis

Table 2 shows the change in depression, QOL, and QOL domains during the six-months follow-up. There is no statistically significant difference in depression ($F=2.87$, $p > 0.05$), psychological domain ($F=2.97$, $p > 0.05$), level of independence domain ($F=2.35$, $p > 0.05$), or social relationships domain ($F=0.11$, $p > 0.05$); however, the change in total QOL ($F=5.86$, $p < 0.05$), physical domain ($F=10.50$, $p < 0.001$), environmental domain ($F=3.55$, $p < 0.05$), and personal beliefs domain ($F=18.73$, $p < 0.001$) was significant. The significant change in total QOL ($F=2.76$, $p < 0.05$), physical domain ($F=1.08$, $p < 0.001$), environmental domain ($F=0.37$, $p < 0.05$), and personal beliefs ($F=1.36$, $p < 0.001$) was discerned mainly in the first three-months follow-up. Details about the individual variations is shown in Figures 1-3.

As shown in Table 2 and Figures 1-3, during the six-months follow-up, the changes in total QOL and environmental domains were presented as a rising trend from baseline to the six-months follow-up. The significant changes in physical and personal beliefs domains were also found and presented as increasing then declining characteristics. As for depression, there was a statistically significant difference in depression from baseline to the three-month follow-up, but non-significant in the six-month follow-up. There is no statistically significant difference in other QOL domains, including psychological, level of independence, or social relationships domain ($p \leq 0.05$).

The mixed effects model

Table 3 shows the association between all domains of QOL and depression. Overall, depression symptoms were negatively associated with all domains of QOL ($p < 0.001$). In addition, this negative association was shown to be lasting to the six-month follow-up ($p < 0.001$).

The intercept effect between time and depression was significant. Generally, time has a moderate effect between depression symptoms and QOL ($p < 0.001$). Overall, the strength of the association between depression symptoms and QOL decreased over time in the six-months follow-up. Specifically, the strength decreased 0.265 in total QOL, 0.064 in the physical

Table 2. Changes in depression, QOL and all of domains of QOL during six-months follow-up.

	T ₀		T ₃		T ₆		T ₀₋₃		T ₃₋₆		T ₀₋₆	
	Mean	SD	Mean	SD	Mean	SD	F	P	F	P	F	P
Depression	15.68	9.37	14.05	9.87	13.33	8.70	-1.63	0.05*	-0.72	0.56	2.87	0.06 [§]
QOL	81.31	12.60	84.07	14.48	84.45	14.14	2.76	0.007*	0.39	0.63	5.86	0.004*
Physical	13.16	2.48	14.24	2.64	14.03	2.82	1.08	<0.001**	-0.22	0.27	10.50	<0.001**
Psychological	13.56	2.32	13.85	2.51	14.01	2.77	0.29	0.14	0.16	0.33	2.97	0.05*
Level of independence	14.81	2.76	14.95	2.67	15.25	2.56	0.14	0.56	0.31	0.09 [§]	2.35	0.10 [§]
Social relationship	13.47	2.43	13.38	2.82	13.45	2.87	-0.09	0.68	0.07	0.70	0.11	0.90
Environmental	13.68	2.20	14.05	2.54	14.14	2.52	0.37	0.04*	0.10	0.59	3.55	0.03*
Personal beliefs	12.63	3.45	13.99	3.14	13.18	3.39	1.36	<0.001**	-0.81	<0.001**	18.73	<0.001**

* $P \leq 0.05$; ** $P \leq 0.001$; $§ P \leq 0.1$; T₀₋₃: from the baseline to the 3-month follow-up, T₃₋₆: from the 3-month follow-up to the 6-month follow-up, T₀₋₆: from the baseline to the 6-month follow-up

domain, 0.043 in the psychological domain, 0.055 in the level of independence domain, 0.021 in the social relationships domain, 0.042 in the environmental domain, and 0.050 in the personal beliefs domain. For different QOL domains, the moderate effect of time was different in a period of follow-up. In the first three-months follow-up, the strength of association between depression symptoms and QOL decreased in total QOL, physical domain and personal beliefs domain, while increasing in the psychological domain, independence domain, social relationships domain, and environmental domain. In the last three-months follow-up, the strength of association between depression symptoms and QOL decreased in total QOL, physical domain, psychological domain, level of independence domain, social relationships domain, and environmental domain, while increasing in the personal beliefs domain.

Discussion

Depression plays a vital role in HIV care because it impacts health outcomes such as PLWH's QOL (Hidru et al., 2016; Xiao et al., 2017). Contrasting with previous studies (Shao et al., 2018; Xiaowen et al.,

2018), the present study is one of the initial reports to explore the relationship between depression and QOL among ART naive PLWH in a six-months period. We found the influence of depression on QOL through the time change. As such, healthcare providers can design and implement a culturally sensitive intervention to improve QOL by targeting depression in HIV health-care settings.

In the present study, 59% percent of PLWH presented no depression symptoms, which is higher than other cities in China (Wang et al., 2018). Also, the 18% of PLWH with major depression symptoms (CESD ≥ 23) was much lower than the percentage in Uganda and New Yorkers (47% vs. 39%, respectively) (Geoczze et al., 2010; Kaharuza et al., 2006). Interestingly, Shanghai's PLWH's QOL at baseline was also higher than PLWH in other cities in China (Tang et al., 2015; Xu et al., 2017). The findings of this study are different from other results obtained elsewhere in the world, and here are some potential explanations. Depression symptomatology and QOL among PLWH has regional differences and that Shanghai's PLWH present much less depression and experience better QOL than other PLWH in China and globally. Shanghai is metropolitan and has a well-established health system in China. With

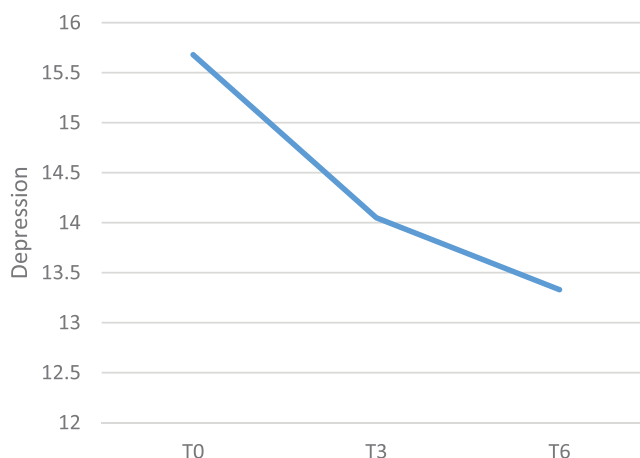


Figure 1. Changes in depression during three time points Note: T0- Baseline; T3- 3-month follow-up; T6- 6-month follow-up.

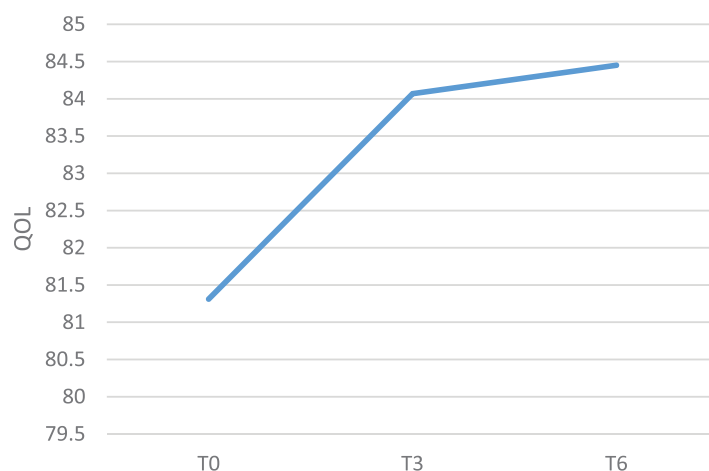


Figure 2. Changes in QOL at three time points Note: T0- Baseline; T3- 3-month follow-up; T6- 6-month follow-up.

better access to healthcare systems, PLWH are more likely to report higher QOL (Krause et al., 2013). Additionally, the more MSM PLWH in this study might be one of the reasons for the result of lower levels of depression. Echoing other studies, the prevalence of depression in MSM PLWH is lower than in other PLWH populations (Wang et al., 2018).

The results of the changes in depression and QOL during the two follow-up assessments demonstrated

the different longitudinal trajectories of these variables. In the first three months after starting ART, PLWH in Shanghai showed decreased depression symptoms and better QOL (Table 2); however, after three months of ART, those positive effects decreased and were no longer significant. Overall, QOL was significantly improved during this study. ART is a key to maintaining QOL in PLWH (Jaquet et al., 2013; Stangl et al., 2007); however, it does not directly impact the depression

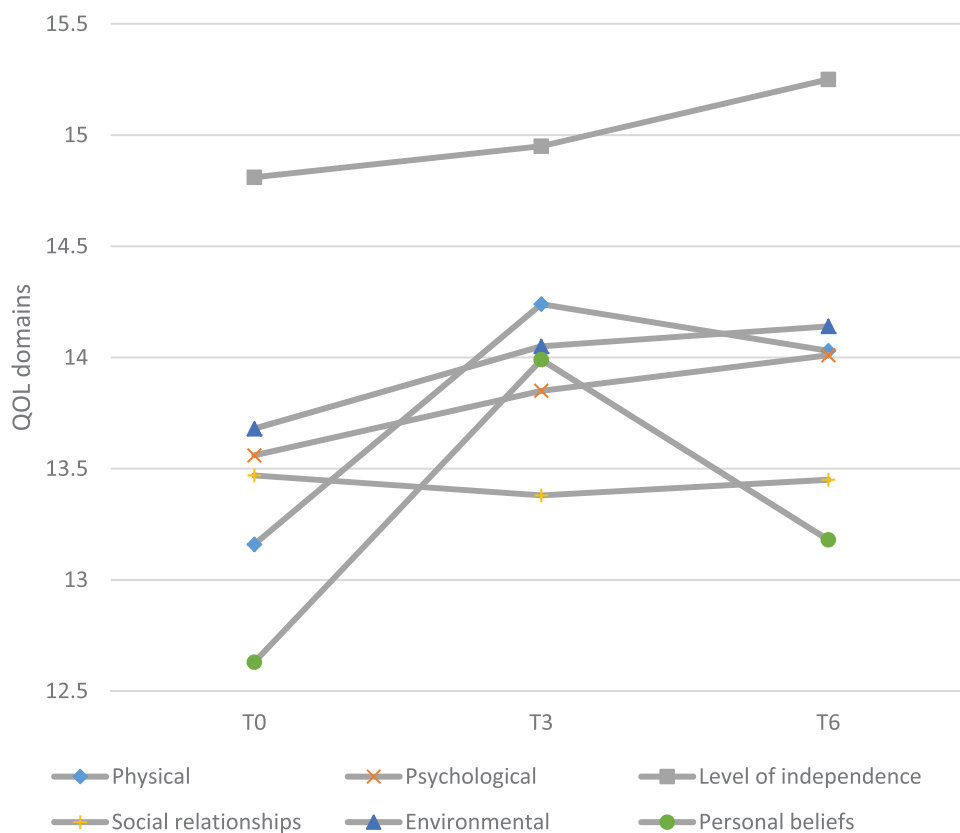


Figure 3. Changes in all domains of QOL at three time points Note: T0- Baseline; T3- 3-month follow-up; T6- 6-month follow-up.

Table 3. Associations between depression, QOL and time using Mixed Effects Model.

Depression	T ₀		T ₃		T ₆		T P
	β_0	P ₀	β_3	P ₃	β_6	P ₆	
Total QOL	-0.936	<0.001**	-0.906	<0.001**	-0.671	<0.001**	<0.001**
Physical	-0.159	<0.001**	-0.129	<0.001**	-0.095	<0.001**	<0.001**
Psychological	-0.154	<0.001**	-0.164	<0.001**	-0.111	<0.001**	<0.001**
Level of independence	-0.120	<0.001**	-0.136	<0.001**	-0.065	0.02*	<0.001**
Social relationships	-0.128	<0.001**	-0.152	<0.001**	-0.107	<0.001**	<0.001**
Environment	-0.118	<0.001**	-0.121	<0.001**	-0.076	<0.001**	<0.001**
Personal beliefs	-0.231	<0.001**	-0.177	<0.001**	-0.181	<0.001**	<0.001**

* $P < 0.05$; ** $P < 0.001$; Independent variable: Depression; Dependent variables: QOL, Physical, Psychological, Level of independence, Social relationships, Environment, Personal beliefs.

symptoms (Ciasca et al., 2018). This may due to good ART; PLWH can live as normal persons, especially in Shanghai, where ART is provided continuously. Therefore, future interventions on depression reduction among PLWH in Shanghai should focus on the non-treatment factors, such as stigma and social support. Similar to the depression symptoms, the QOL domains of psychological, level of independence, and social relationships did not show significant improvement within six months. These different changes demonstrate the different impacts of ART on the QOL domains. QOL is a multidimensional variable, which means a comprehensive intervention should be designed and tested to enhance the self-management of PLWH, including physical symptoms, mental health, social relationships, and overall QOL.

The results in the present study show that depression symptoms are negatively associated with QOL and with all domains of QOL over time, which is consistent with other studies (Bengtson et al., 2015; Garfin et al., 2019). Although the depression symptoms and QOL changed differently in the first six months of initiating ART, a strong correlation was presented between the depression symptoms and QOL. This study highlights that depression symptoms are highly correlated to QOL among PLWH. Also, the trend of the association decreased in PLWH in Shanghai after using ART for six months. This confirmed that the association between depression and QOL changes over time with ART. After starting ART, PLWH may experience the side effects of ART, which can cause depression symptoms and affect their QOL. Several studies have shown that the side effects were positively associated with depression symptoms and low QOL (Chen et al., 2013; Liu et al., 2018). In the meantime, more studies have shown that achieving ART adherence has a positive impact on QOL and decreases depression symptoms (Aragónés-López et al., 2012; Ghiasvand et al., 2019; Wang et al., 2009). As such, the importance of ART adherence becomes one of the most important factors to decrease depression symptoms and to enhance the QOL in PLWH.

Therefore, comprehensive interventions targeting ART adherence should be encouraged.

Limitations

There are several limitations in the present study. First, as this study was based on a purposive recruitment, the representation of the study to other PLWH is limited. Second, the small sample size from one clinic in Shanghai limited the generalizability of this study, and the majority of male study participants may bring potential bias to this study. Thus, future research should expand to other sites to ensure the replication of the study results. Last, we used only three time points to collect the depression symptoms and QOL of treatment naïve PLWH. This might not reflect the true change in depression and QOL among PLWH in the HIV disease trajectory. Therefore, a longer study design should be deployed to explore depression symptoms and QOL over time among PLWH.

Conclusions

QOL is an important outcome for PLWH. In this longitudinal study, we explored the changes of depression symptoms and QOL in ART naïve PLWH in Shanghai. This study shows that depression symptoms are associated with total QOL during the first six months of initiating ART; however, each of the QOL domains changed the association between the QOL domains over time. Future interventions should be designed to decrease symptoms of depression and improve QOL.

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In this collaboration, Wei-Ti Chen and Hongzhou Lu are responsible for designing, guiding, organizing and planning this study. Wenxiu Sun is responsible for data collection, analysis and manuscript writing. Feifei Huang and Chengshi Shiu are responsible for quantitative data analysis. Ling Zhang are responsible for organizing this study. We gratefully acknowledge all the study participants; without them, it would not have been possible to complete this project.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Ethical conduct of research

This research was approved by the Shanghai public health clinical center (2015-S043-01).

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