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Sexual behavior changes and HIV infection among men who have sex with men: evidence from an open cohort in China, 2011-2019

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Abstract

Background- In a long-term cohort, how the complex behavior pattern changed and the association with the HIV risk were unclear at present.

Methods- Using three indicators (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners), participants with 0, 1, and 2 or 3 risk indicators were categorized as behavior type of “protective”, “moderate”, and “fragile”. Change in behavior type between baseline and each visit was considered.

Results- Of 2029 MSM include in the study, 127 had seroconversion. The overall incidence rate was 3.36 per 100 person-years. The percentage of “protective” and “moderate” behavior type had a conspicuous growth trend as the follow-up. Furthermore, the HIV incidence rate in each visit among different behavior transition types showed a general downward trend as the number of total follow-up times increased. Individual who remained in “fragile” (aHR, 25.86 [95%CI, 6.92-96.57]) or changed from “protective” to “moderate”, (aHR, 4.79 [95%CI, 1.18-19.47]) “protective” to “fragile” (aHR, 23.03 [95%CI, 6.02-88.13]), “moderate” to “fragile” (aHR, 25.48 [95%CI, 6.79-95.40]) between baseline and the last follow-up had a higher HIV risk. Gained risk indicators were associated with the increase of HIV risk (gained 1 indicator, aHR: 2.67,95%CI: 1.68-4.24; gained 2 or 3 indicators, aHR, 4.99, [95%CI, 3.00-8.31]) while lost just one risk indicator could halve the risk (aHR, 0.43, [95%CI, 0.21-0.90]).

Conclusions- Among MSM in Tianjin, it was necessary to get timely behavior change for those with risky sexual behavior patterns while sustaining for those with protective patterns.

Keyword: Men who have sex with men; HIV; Behavior change; Cohort study

Article summary

Strengths and limitations of this study

- In this study, sexual behavior changes are collectively defined by three indicators (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) related to participants' sexual behavior in the past six months. Behavior changes from 2011-2019 and ensuing HIV infection risk are calculated.
- Long-term sexual behavior patterns of MSM keep changing and gradually have a tendency to be less risky during the study period. The proportion of high-risk behavior pattern is 30.70% at baseline. This number decline to 14.77% at visit 6 and more. This result demonstrates the effectiveness of community-based HIV/AIDS interventions.
- Transition from low-risk behavior to high-risk behavior is associated with a higher risk of HIV infection than continuing high-risk behavior. Futher strategies are needed to promote the low-risk change.
- MSM should sustain low-risk behavior patterns otherwise would undergo higher HIV infection risk.
- Future HIV interventions should focus not only on those MSM who have high-risk sexual behaviours, but also on those MSM who have temporarily low-risk sexual behavior but are at risk of switching to high-risk sexual behaviours.

Introduction

The epidemic of the human immunodeficiency virus (HIV) was a significant public health issue of worldwide concern(1-4). The prevalence of HIV had been low among the general population over the past three decades. However, the burden of HIV was disproportionately concentrated among men who have sex with men (MSM)(5-7). China's HIV epidemic began in the early 1990s among injecting drug users(8, 9). The main route of transmission was needle-sharing(10, 11). Due to China's effective legal control and intensive regulations on drugs(12, 13), the main spread route of HIV inevitably turned into sexual contact since the 21st century, especially homosexual sexual contact(7, 14, 15). Corresponding studies aimed to ascertain the pattern of sexual behaviors among MSM had important practical significance though sexual behaviors between men were taboo both politically and by cultural tradition in China(16, 17).

Effective intervention and behavior change had been responsible for the HIV prevention successes to date(18, 19). HIV interventions typically concentrate on unprotected anal intercourse (UAI)(20), multiple sex partners(21), alcohol and drug use(13, 22), pre-exposure prophylaxis (PrEP)(23, 24) or post-exposure prophylaxis (PEP)(25, 26) utilization and adherence to antiretroviral therapy (ART)(27). It was well established from a variety of studies that timely behavior change and biomedical intervention can reduce HIV transmission. However, most studies used a single measurement to describe behavior change. In a long-term cohort, how the complex behavior pattern changed and the association with the HIV risk was largely unknown

at present.

This study was based on an open cohort among MSM in Tianjin, China, 2011-2019. Three indicators (condom use in last anal sex(28), frequency of condom use during anal sex(21), and the number of sexual partners(29)) were used to define the pattern of sexual behavior type. Behavior change was described by the change of behavior type (or the number of indicators) in each visit. The aims of the present study were the following: (1) to describe the HIV incidence rate over the cohort; (2) to quantify the behavior changes over the follow-up and to address the association between behavior change and the risk of HIV infection; and (3) to explore influencing factors for progression to behavior change.

Methods

Study Design

The men who have sex with men health encouragement longitudinal project (MSMHELP) was a longitudinal cohort study among MSM launched in Tianjin, China, designed to establish HIV prevention service stations aimed at the key population, improve the accessibility and utilization of HIV testing and prevention services, and provide ART support services for those infected HIV. The organizations involved in the project included US Centers for Disease Control and Prevention (CDC); National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and prevention (NCAIDS/STD); Tianjin City CDC and Tianjin Shenlan Community-Based Organization (CBO). This study was registered with the Chinese Clinical Trials Registry (Identifier: ChiCTR2000039500).

Data Collection and Participants

Tianjin Shenlan CBO was a formally community-based organization that provided community-based HIV voluntary counseling & testing (VCT) support services (including HIV testing, counseling, and psychological support) for MSM. Participants were mobilized to get tested for HIV in Shenlan's public health advisory service center. When participants came to the center for testing or counseling, experienced MSM investigators would conduct a face-to-face interview with participants in a private room. During this period, a structured questionnaire (included demographics and sexual behaviors information) was completed by the participants under the guidance of the investigators. The investigators of the organization mostly were also MSM. All investigators had undergone training before entering work, which would be a benefit for smooth unhindered communication with participants and could ensure the reliability of the results. After the interview, every participant would get several condoms and lubricant for free. Information collection adopted a real-name registration system (ID card number, mobile phone number and fingerprint information were collected). Enrolled participants were encouraged to routine HIV test every three months (90 days). The entire research process was supervised and coordinated by Tianjin City CDC.

The snowball sampling method was used to recruit participants. Participants were recruited from gay bars, gay bathhouses, social network sites (WeChat, QQ, gay chat website), gay apps and peer referrals. The initial enrollment took place on October 1, 2011, and follow-up ended up on December 31, 2019. Inclusion criteria were: (1) had

at least two visits during the cohort period and HIV serological test was negative when they first registered, (2) ≥ 16 years old, (3) biologically male, (4) reported anal intercourse with another man in the past six months. The participants of the cohort change dynamically, the original participants could drop out continuously, and the new participants could join at any time. Of 6565 MSM captured in this study, 4096 were excluded for having only one visit, 432 for having HIV seropositive result at baseline, and 8 for lack of behavioral information. 2029 MSM met the eligibility criteria and were included in the study eventually. The comparison of baseline characteristics between included and excluded MSM were listed in sTable 1 in the Supplement.

Definitions of Behavior Changes

In this study, behavior changes include the change in the number of risk indicators and change in sexual behavior type. Sexual behavior type was used to represent different patterns of sexual behavior characteristics. It was collectively defined by three indicators related to participants' sexual behavior in the past six months. The three indicators included variables of condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners. These three variables were related to the HIV infection (sTable 2 in the Supplement). Participants had the information of the three variables in each follow-up. Each indicator was divided into two levels: "ideal level" and "risk level" (sTable 3 in the Supplement). Among the three variables mentioned above, if one participant had one variable of "risk level" then meant the participant had one risk indicator, and so on. The number of risk indicators was in the range of zero to three.

Behavior type was defined based on the risk indicators. Behavior type was categorized as “protective” if the participant had no risk indicator; as “moderate” if the participant had one risk indicator; as “fragile” if the participant had more than two risk indicators (two or three risk indicators). The behavior type and the number of risk indicators could change as time varying (during the follow-up period).

Change in the number of risk indicators was defined as the difference of risk indicators between any two follow-ups. Behavior transition type was defined as the change of behavior type between any two visits. Then the behavior transition type yielded nine possible combinations of behavior types: consistently protective, protective to moderate, protective to fragile, moderate to protective, consistently moderate, moderate to fragile, fragile to protective, fragile to moderate, consistently fragile.

HIV Laboratory Test

Before testing, MSM would choose to collect blood or saliva. Patrons’ oral mucosal exudate test (Mano Bio-Pharmaceutical Co., Ltd, Beijing, China) was used for the former and a blood rapid detection reagent (Wan Fu Biotechnology Co., Ltd, Guangzhou, China) for the latter. In addition, 5ml of blood sample was collected from those who get any positive tests above. Then, the blood sample was sent to Tianjin CDC to perform enzyme-linked immunosorbent (ELISA; Wan Tai Biological Pharmaceutical Co., Ltd, Beijing, China). HIV infection was by confirmed Western blot (WB) assay (MP Biomedical Asia Pacific Pte Ltd, Singapore). As the exact seroconversion time was hard to affirm, for the chronic infections, the seroconversion

time was defined as the mid-point between last negative test date and first positive test time while the acute and early infection was the time diagnosed as HIV infection.

Statistical Methods

Category variables were described by frequencies and percentages. For the general demographic characteristics, differences were calculated using Pearson's chi-squared test or Fisher's exact test.

HIV incidence rates were estimated within each year and among subgroups of different behavior transition types in each visit, with person-year (PY) over the follow-up time as the denominator.

Change in behavior type was calculated in each visit (according to baseline behavior type). Univariate and multivariate time-varying Cox models were performed to evaluate (1) risk of HIV infection among different behavior type subgroups over each follow-up (all records of the participants were included in the model in counting process format) (2) behavior changes and association with the risk of HIV infection (two time points were opted to define the behavior change, baseline, and the last follow-up). Hazard ratios (HR), adjusted hazard ratios (aHR) and 95% confidence interval (95%CI) of the variables were estimated. The logistic regression model was applied to investigate the influencing factors for progression to behavior type of "fragile" or "moderate" in the last follow-up among baseline behavior type subgroups. Odds ratios (OR), adjusted odds ratios (aOR) and 95% confidence interval (95%CI) were estimated. In addition, all models were adjusted for baseline covariates. All the data analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC).

Patient and public involvement

This study was mainly completed by Tianjin CDC, with Tianjin Shenlan CBO as the specific implementor of the study. Patients or the public were not directly involved in the design and implementation of the study. But the findings could influence the design of other subsequent studies, such as specific studies targeting drug users or male sex workers in the MSM population.

Results

Characteristics of the Participants

A total of 2029 MSM met the eligibility criteria and were included in the study eventually. The total follow-up person time was 3772.03 PY. The median total follow-up time was 1.28 years (interquartile range [IQR], 0.57 to 2.72; range, 8 days to 8.13 years) starting from baseline. Confirmed by the laboratory test, 127 participants had HIV seroconversion (i.e., were diagnosed as HIV infection). 63 were classified as acute and early HIV infected and 64 were chronic infected.

The characteristics of the participants when they first registered (baseline) were shown in Table 1. Among all the participants, the mean age was 35.7 $\pm$ 12.3 years (ranging from 16 to 79 years); 53.33% were unmarried; 57.76% had a high school degree; 39.48% had a college degree or above; 71.87% had been lived in Tianjin for more than 2 years while 19.96% had been lived in Tianjin for less than 3 months; 76.39% used condom in last anal sex; 38.69% had a condom consistent use during anal sex over past six months; 84.23% had less than 10 sexual partners over past six months; 3.35% had STI over past six months; 46.23% had received HIV health service over past

one year; 5.03% had been worked as MSW.

The total number of follow-up times of each participant were listed in sTable 4 in the Supplement. The mean follow-up times were 4.39 $\pm$ 3.96 times (range from 2 to 34, median: 3). 41.01% of participants had 2 follow-up times; 78.46% had follow-up times no more than 5 times. Participants with a total number of follow-up times more than 10 times was 7.15%

HIV Incidence Rate

Among the whole study population, the overall HIV incidence rate was 3.36 per 100 PY (95%CI, 2.83-3.99).

Figure 1 and sTable 5 in the Supplement showed the HIV incidence rates by years. The rates were relative higher in 2013 (4.57 per 100 PY [95%CI, 3.31-6.31]), 2015 (4.65 per 100 PY [95%CI, 3.53-6.12]) and 2019 (5.51 per 100 PY [95%CI, 3.97-7.66]), though the rates did not show a liner trend significance over 2011-2019. Among age subgroups, incidence rates were <45, 3.83 per 100 PY (95%CI, 3.24-4.52); 45-60, 2.81 per 100 PY (95%CI, 2.14-3.69); >60, 2.08 per 100 PY (95%CI, 0.95-4.55) (sTable 6 in the Supplement).

To compare the HIV incidence rate among different behavior transition types, participants were divided into subgroups according to their number of total follow-up times. The calculation of the HIV incidence rate was done within each subgroup. Stratified by the behavior type categories at baseline, the overall HIV incidence rates were: “protective”, 3.14 per 100 PY (95%CI, 2.30-4.29); “moderate”, 2.92 per 100 PY

(95%CI, 2.13-3.99); “fragile”, 4.02 per 100 PY (95%CI, 3.07-5.26) (sTable 7 in the Supplement). On the whole, HIV incidence rate shown a general downward trend as the number of total follow-up times increased (2 times: 4.88 [95%CI, 3.65-6.53]; 3 times: 4.49 [95%CI, 3.06-6.59]; 4 times: 2.89 [95%CI, 1.72-4.84]; 5 times: 3.21 [95%CI, 1.74-5.91]; 6 times and more: 2.27 [95%CI, 1.64-3.15]). MSM who had more visits showed a low risk of infection in comparison with those who had fewer visits. Within each subgroup, the HIV incidence rate tended to concentrate towards the lower right corner of the heatmap (i.e., concentrate towards behavior type of “fragile”) (Figure 2).

Time-varying behavior type and risk of HIV infection

The risk of HIV infection was evaluated through Cox models with time-varying behavior types. Compared with “protective” behavior type, “moderate” behavior type (aHR, 2.22 [95%CI, 1.05-4.71]) and “fragile” behavior type (aHR, 16.53 [95%CI, 8.57-31.88]) were associated with a greater risk of HIV infection. Likewise, there was a significant and linear increase in the risk of HIV infection for each additional time-varying risk indicator (aHR, 3.37 [95%CI, 2.76-4.11]) (Table 2).

Behavior Types in Each Visit

The percentage of each behavior type (“protective”, “moderate”, and “fragile”) at baseline were: 31.69% (643/2029), 37.60% (763/2029), and 30.70% (623/2029), respectively. As the number of follow-up visits increased, the percentage of “protective” and “moderate” had a growth trend (35.06% and 50.18% at 6th and more, respectively) while the percentage of “fragile” was declined (14.77% at 6th and more)

(Figure 3).

Behavior Changes and Association with the Risk of HIV Infection from Baseline to the Last Follow-Up

The behavior types of baseline and the last follow-up was selected to evaluate the behavior changes (change in risk indicators: difference in risk indicators between baseline and the last follow-up; change in behavior type: "behavior types at baseline" to "behavior types in the last follow-up") and the association with the risk of HIV infection. The choice of two time points was based on a main argument: the pattern of behavior changes from baseline to each follow-up was relatively stable (details in sTable 8 and sFigure 1 in the Supplement). The first and the last visit were good surrogates for behavior changes during follow-up.

In multivariable analysis, "no change in indicators" as the reference level, lost one risk indicator could decline the risk at 0.43 (95%CI: 0.21-0.90). While gained indicators were related to the increasing risk of HIV infection (gained one risk indicator: aHR, 2.67 [95%CI, 1.68-4.24]; gained two or three risk indicators: aHR, 4.99 [95%CI, 3.00-8.31]).

As for the different behavior transition types, the risk of HIV infection was not statistically different from that of the consistently protective group (reference level) in the moderate to protective group (aHR, 0.65 [95%CI, 0.08-5.16]), the consistently moderate group (aHR, 1.52 [95%CI, 0.31-7.41]), the fragile to protective group (aHR, 2.87 [95%CI, 0.66-12.46]), and the fragile to moderate group (aHR, 2.66 [95%CI, 0.61-11.53]). Instead, the risk of HIV infection was distinctly greater in the protective to

moderate group (aHR, 4.79 [95%CI, 1.18-19.47]), the protective to fragile group (aHR, 23.03 [95%CI, 6.02-88.13]), the moderate to fragile group (aHR, 25.48 [95%CI, 6.79-95.40]), and the consistently fragile group (aHR, 25.86 [95%CI, 6.92-96.57]) (Table 3 and sFigure2 in the Supplement).

Influencing Factors for Progression to Behavior Type of "fragile" or "moderate" in the Last Follow-Up

We also investigated which influencing factors were related to the progression of behavior transition type of "fragile" or "moderate" by the end of follow-up among baseline behavior type subgroups.

Within age subgroups, the younger participants had a higher likelihood of progression to behavior type of "fragile" or "moderate" by the end of follow-up.

Notably, the likelihood of progression to behavior type of "fragile" or "moderate" was weakened as the number of total follow-up times increasing (per 1-time increase in the total follow-up times, aOR, 0.95 [95CI%, 0.91-0.99]) among participants "fragile" at baseline.

Compared with participants who lived in Tianjin less than three months, participants who lived in Tianjin for more than two years had a lower likelihood of progression to behavior type of "fragile" or "moderate" by the end of follow-up (aOR, 0.65 [95CI%, 0.37-0.87]) (sTable 9).

Discussion

The characteristics of MSM were mainly high mobility and concealment. It was a challenge to ensure long-term cohort retention and sustain routine HIV test programs

among this population. Therefore, we conducted an open cohort study among MSM in Tianjin, China. 2029 MSM were included in the study eventually from 2011-2019. Among the whole study population, the overall HIV incidence rate was 3.36 per 100 PY (95%CI, 2.83-3.99). The incidence rate was at a lower level. Previous studies conducted in other cities in China had shown a pretty high HIV incidence among MSM, 6.6 per 100 PY in Hangzhou(30), 6.78 per 100 PY in Yangzhou, 5.77 per 100 PY in Guangzhou(31), 5.3 per 100 PY in Shenyang(32), 5.12 per 100 PY in Nanjing(33), 3.5 per 100 PY in Yunnan(34) and 7.1 per 100 PY in Beijing(35). In this study, the percentage of "protective" and "moderate" behavior types had a conspicuous growth trend as the follow-up. Furthermore, the HIV incidence rate in each visit among different behavior transition types showed a general downward trend as the number of total follow-up times increased. The evidence mentioned above indicated the effectiveness of the community-based VCT project in reducing HIV incidence. However, challenges still existed and need to be addressed. The incidence rate in 2019 was much higher than in other years (5.51 per 100 PY [95%CI, 3.97-7.66]). We speculated that the reason might be the publicity and promotion of PrEP/PEP started in 2018 among the MSM population in Tianjin. PrEP/PEP were effective biomedical strategies to prevent the further transmission of HIV(23, 24). Although the utilization of PrEP/PEP was not widespread among MSM in Tianjin, this might promote the cognitive concepts of "treatment optimism" about HIV(36). MSM might rationalize their risk behavior before (or after) engaging in sexual behaviors(37), which promoted the generate of risk behaviors(38, 39).

Previous studies concentrate on using one stand-alone indicator to describe the behavior change. For example, one study in China(40) used the percentage of unprotected anal intercourse (UAI) occurrence to describe the behavior change. However, this study evaluated behavior change with greater precision (behavior changes were collectively defined by three indicators and divided into two patterns: change in the number of risk indicators and behavior transition type) among a great sample size (N=2029) in a long-term follow-up (2011-2019). What's more, this study quantified the behavior changes and association with the risk of HIV infection from baseline to the last follow-up. The results of this study showed, individual who remained "fragile" or changed from "protective" to "moderate", "protective" to "fragile", "moderate" to "fragile" between baseline and the last follow-up had a higher HIV risk as compared with individuals with persistently "protective". When this analysis was conducted in risk indicators, similar results were found. Gained risk indicators were associated with the increase of HIV risk while lost just one risk indicator could halve the risk (aHR:0.43). This study demonstrated the importance of maintaining protective sexual practices and timely behavior changes in high-risk groups could help reduce the risk of HIV infection.

Limitations

This research has several limitations. First, in our study, the snowball sampling method was used to recruit participants, which may have certain tendentiousness. However, we recruited participants in a variety of ways (gay bars, gay bathhouses, social network sites, gay apps and peer referrals) to increase the representativeness.

Second, our data lacked information on the use of addictive substances related to sexual behavior. The presence of these substances might affect the sexual behavior of participants, which should be addressed in future research. Further, our data collection adopted a real-name registration system (ID card number, mobile phone number and fingerprint information were involved). Due to the privacy of some questions (such as whether you had ever had STI), the participants might have concealed the actual situation which may result in social expectation bias. We conducted an interview-style questionnaire collection to avoid this. Besides, all MSM investigators had received professional training to ensure the authenticity of the data.

Contributorship

ZY, CL, ZC, YL, and JM contributed to the conception of the study. HH, TZ and DS contributed to the framework of the study. MY and JY collected the data. QC and XW cleared the raw data. HH and HZ helped perform the analysis with constructive discussions. TZ and ZY analyzed the data and wrote the manuscript. ZC revised the manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethics approval

This study was reviewed and approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, China CDC [IRB approve number: X130205267].

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Data sharing

No additional data available

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Table1. Characteristics and sexual behaviors at baseline for MSM with HIV infection or negative HIV test

Variables at Baseline	Total N (%)	HIV Infection N (%)	HIV Negative N (%)
Age			
<45	1504 (74.13)	96 (75.59)	1408 (74.03)
45-60	464 (22.87)	27 (21.16)	437 (22.98)
>60	61 (3.01)	4 (3.15)	57 (3.00)
Marital status			
Married	947 (46.67)	70 (55.12)	877 (46.11)
Unmarried	1082 (53.33)	57 (44.88)	1025 (53.89)
Education			
Below high school	56 (2.76)	5 (3.94)	51 (2.68)
High school	1172 (57.76)	90 (70.87)	1082 (56.89)
College or more	801 (39.48)	32 (25.20)	769 (40.43)
Residence time in Tianjin			
<3 months	405 (19.96)	41 (32.28)	364 (19.14)
3-7 months	39 (1.92)	2 (1.57)	37 (1.74)
7-12 months	41 (2.02)	5 (3.94)	36 (1.89)
1-2 years	86 (4.24)	2 (1.57)	84 (72.61)
>2 years	1458 (71.86)	77 (60.63)	1381 (72.61)
Condom use in last anal sex			
Yes	1550 (76.39)	78 (61.42)	1472 (77.39)
No	479 (23.61)	49 (38.58)	430 (22.61)
Frequency of condom use during anal sex[ab]			
Consistent use	785 (38.69)	43 (33.86)	742 (39.01)
Inconsistent use	1244 (61.31)	84 (66.14)	1160 (60.99)
Number of Sexual partners[b]			
<10	1709 (84.23)	116 (91.34)	1593 (83.75)
More than 10	320 (15.77)	11 (8.66)	309 (16.25)
STI[b]			
Yes	68 (3.35)	2 (1.57)	66 (3.47)
No	1961 (96.65)	125 (98.43)	1836 (96.53)
Inject drugs[b]			
Yes	22 (1.08)	2 (1.57)	20 (1.05)
No	2007 (98.92)	125 (98.43)	1882 (98.94)
Accept health service[c]			
Yes	938 (46.23)	53 (41.73)	885 (46.50)
No	1091 (53.77)	74 (58.27)	1017 (53.50)
MSW[db]			
Yes	102 (5.03)	5 (3.94)	97 (5.10)
No	1927 (94.97)	122 (96.06)	1805 (94.90)

Abbreviations: STI, sexually transmitted infections; MSW, male sex workers.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

Table2. Univariate and multivariate Cox proportional hazard model with time-varying covariates for HIV infection

HIV infection risk models[a]	Per 1-risk indicator increase[b]	Categories of sexual behavior type		
		Protective	Moderate	Fragile
HR (95%CI)	3.68 (3.03-4.46)	REF	2.38 (1.12-5.02)	19.74 (10.28-37.91)
adjusted HR (95%CI)[c]	3.37 (2.76-4.11)	REF	2.22 (1.05-4.71)	16.53 (8.57-31.88)

Abbreviations: HR, hazard ratio; 95%CI, 95% confidence interval; REF, reference level.

[a] All follow-up records of each participants were included into the model in counting process format.

[b] The number of risk indicators were in range of 0 to 3. Per 1-risk indicator increase meant the number of indicators were included into the model as a continuous variable.

[c] Multivariable Cox regression analysis was adjusted for age, education, marital status, residence time in Tianjin, MSW.

Table3. Behavior changes and association with the risk of HIV infection between baseline and the last follow-up

Behavior changes[a]	HIV infection status (N, %)		Univariate Cox regression analysis			Multivariable Cox regression analysis[b]		
	Negative	HIV	HR	95%CI	*P* value	aHR	95%CI	*P* value
Change in risk indicators								
Lost 2-3 indicators	236 (12.4)	7 (5.5)	0.56	0.25-1.27	0.1680	0.57	0.25-1.29	0.1822
Lost 1 indicator	525 (27.6)	9 (7.1)	0.41	0.19-0.86	0.0182	0.43	0.21-0.90	0.0251
No change in indicators	725 (38.1)	30 (23.6)	REF			REF		
Gained 1 indicator	325 (17.1)	48 (37.8)	2.82	1.78-4.46	0.0001	2.67	1.68-4.24	0.0001
Gained 2-3 indicators	91 (4.8)	33 (26.0)	6.13	3.73-10.08	0.0001	4.99	3.00-8.31	0.0001
Behavior transition type								
Consistently Protective	318 (16.7)	2 (1.6)	REF			REF		
Protective to Moderate	210 (11.0)	11 (8.7)	4.78	1.18-19.26	0.0275	4.79	1.18-19.47	0.0283
Protective to Fragile	77 (4.0)	25 (19.7)	28.76	7.66-108.05	0.0001	23.03	6.02-88.13	0.0001
Moderate to Protective	301 (16.0)	1 (0.8)	0.64	0.08-5.03	0.6703	0.65	0.08-5.16	0.6912
Consistently Moderate	315 (16.6)	4 (3.1)	1.62	0.33-7.84	0.5449	1.52	0.31-7.41	0.6019
Moderate to Fragile	109 (5.7)	33 (26.0)	34.32	9.27-127.06	0.0001	25.48	6.79-95.40	0.0001
Fragile to Protective	219 (11.5)	7 (5.5)	2.95	0.68-12.67	0.1457	2.87	0.66-12.46	0.1590
Fragile to Moderate	237 (12.5)	7 (5.5)	3.06	0.71-13.17	0.1316	2.66	0.61-11.53	0.1906
Consistently Fragile	116 (6.1)	37 (29.1)	31.43	8.53-115.75	0.0001	25.86	6.92-96.57	0.0001
Total	1902	127						

Abbreviation: HR, hazard ratio; CI: confidence interval; REF, reference level.

[a] Two time points (baseline and the last follow-up) were opted to evaluate behavior changes.

[b] Multivariable Cox regression analysis was adjusted for age, education, marital status, residence time in Tianjin, MSW.

Figure legends:

Figure1. HIV Incidence rates by year

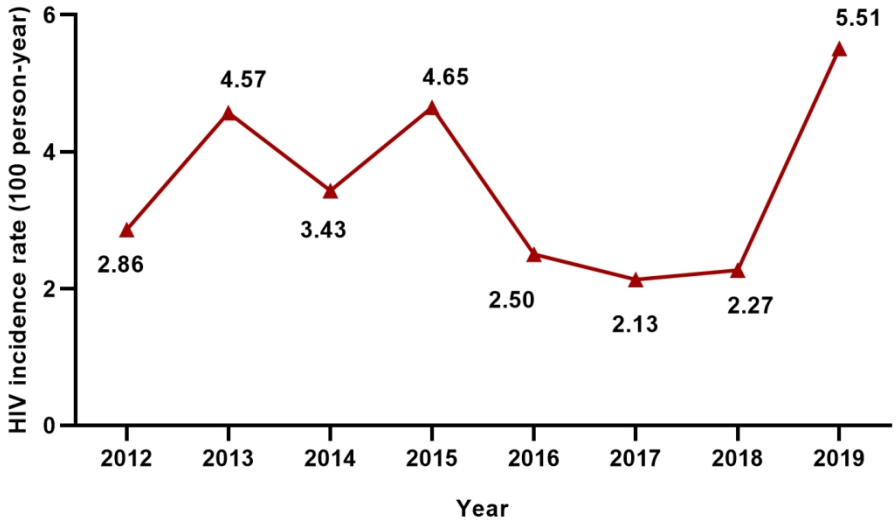
Figure legend 1: When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participants in this year. The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

Figure2. Heatmap of HIV incidence rates among MSM with different follow-up times

Figure legend 2: MSM with 2 follow-up times times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup. Values and colors indicated HIV incidence rate per 100 PY (for example, in Figure 2A, 0.37 represented the HIV incidence rate in "protective" to "protective" group was 0.37 per 100 PY). A lighter color indicates that the HIV incidence rate was lower for MSM in that subgroup, whereas a darker color indicated a higher incidence rate in that subgroup.

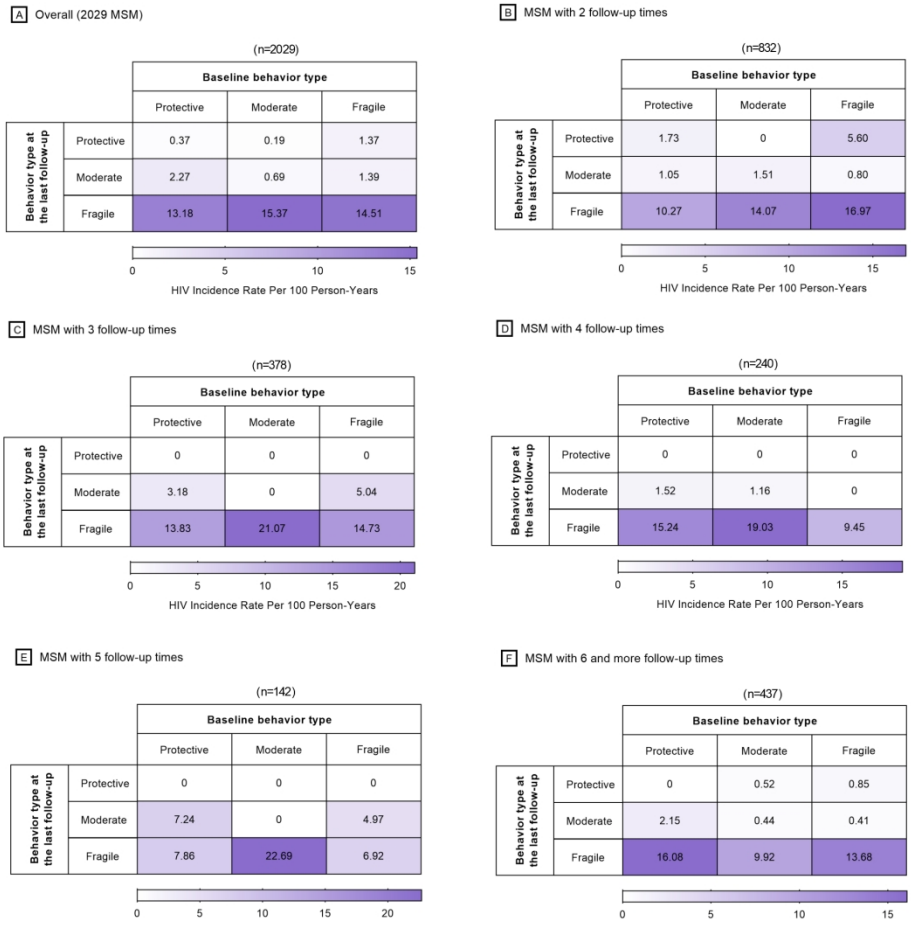
Figure3. Percentage of behavior type in each visit

Figure legend 3: Values and area of the rectangles indicated percentage of behavior type in each visit (for example, in Figure 3, 31.69 represented the percentage of "protective" behavior type was 31.69% at baseline).



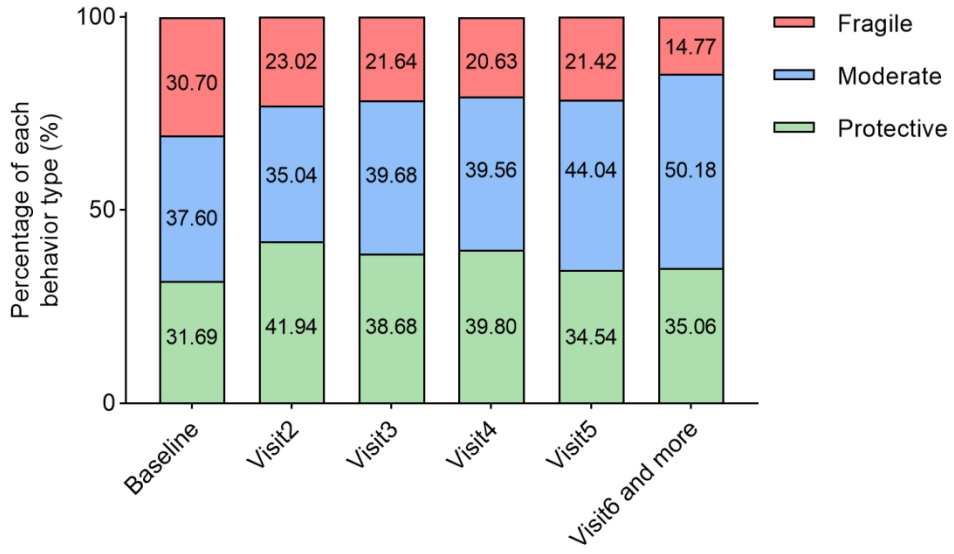
When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participants in this year. The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

135x79mm (300 x 300 DPI)



MSM with 2 follow-up times times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup. Values and colors indicated HIV incidence rate per 100 PY (for example, in Figure 2A, 0.37 represented the HIV incidence rate in "protective" to "protective" group was 0.37 per 100 PY). A lighter color indicates that the HIV incidence rate was lower for MSM in that subgroup, whereas a darker color indicated a higher incidence rate in that subgroup.

540x514mm (96 x 96 DPI)



Values and area of the rectangles indicated percentage of behavior type in each visit (for example, in Figure 3, 31.69 represented the percentage of "protective" behavior type was 31.69% at baseline).

130x80mm (300 x 300 DPI)

sTable1. Characteristics of excluded and included study participants at baseline

Variables at Baseline	Included (N=2029) N (%)	Excluded (N=4096) N (%)	*P*
Age			0.1555
<45	1504(74.13)	3098(75.63)	
45-60	464(22.87)	856(20.90)	
>60	61(3.01)	142(3.47)	
Marital status			0.0198
Married	947(46.67)	1783(43.53)	
Unmarried	1082(53.33)	2313(56.47)	
Education			0.6467
Below high school	56(2.76)	125(3.05)	
High school	1172(57.76)	2322(56.69)	
College or more	801(39.48)	1649(40.26)	
Residence time in Tianjin			0.0001
<3 months	405(19.96)	1154(28.17)	
3-7 months	39(1.92)	125(3.05)	
7-12 months	41(2.02)	85(2.08)	
1-2 years	86(4.24)	166(4.05)	
>2 years	1458(71.86)	2566(62.65)	
Condom use in last anal sex			0.1283
Yes	1550(76.39)	3056(74.61)	
No	479(23.61)	1040(23.39)	
Frequency of condom use during anal sex[ab]			0.6946
Consistent use	785(38.69)	1606(39.21)	
Inconsistent use	1244(61.31)	2490(60.79)	
Number of Sexual partners[b]			0.4535
<10	1709(84.23)	3480(84.96)	
More than 10	320(15.77)	616(15.04)	
STI[b]			0.7909
Yes	68(3.35)	132(3.22)	
No	1961(96.65)	3963(96.78)	
Inject drugs[b]			0.7625
Yes	22(1.08)	41(1.00)	
No	2007(98.92)	4053(99.00)	
Accept health service[c]			0.0001
Yes	938(46.23)	1681(41.04)	
No	1091(53.77)	2415(58.96)	
MSW[db]			0.0369
Yes	102(5.03)	159(3.88)	
No	1927(94.97)	3936(96.12)	

Abbreviations: STI, sexually transmitted infections; MSW, male sex workers.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

sTable2. Univariate and multivariate cox proportional hazard model with time-varying covariates for HIV infection risk

Variables	Univariate cox regression analysis			Multivariate cox regression analysis[e]		
	HR	95%CI	P value	HR	95%CI	P value
Age						
<45	REF					
45-60	1.14	0.78-1.69	0.4819			
>60	0.94	0.38-2.32	0.8956			
Marital status						
Married	REF			REF		
Unmarried	4.73	2.90-7.71	0.0001	4.72	2.86-7.78	0.0001
Education						
Below high school	REF			REF		
High school	0.51	0.24-1.06	0.0719	0.93	0.43-2.01	0.7619
College or more	0.29	0.13-0.63	0.0018	0.47	0.20-1.07	0.0574
Residence time in Tianjin						
<3 months	REF			REF		
3-7 months	0.52	0.12-2.19	0.3804	0.66	0.16-2.83	0.5718
7-12 months	1.71	0.72-4.05	0.2195	1.14	0.48-2.78	0.7572
1-2 years	0.27	0.06-1.14	0.0770	0.27	0.06-1.13	0.0727
>2 years	0.50	0.34-0.74	0.0005	0.68	0.46-1.07	0.0748
Condom use in last anal sex						
Yes	REF			REF		
No	12.39	8.53-17.99	0.0001	5.10	3.19-8.13	0.0001
Frequency of condom use during anal sex[ab]						
Consistent use	REF			REF		
Inconsistent use	10.13	6.14-16.69	0.0001	3.66	1.97-6.82	0.0001
Number of Sexual partners[b]						
<10	REF			REF		
More than 10	1.33	0.93-1.92	0.1173	1.53	1.05-2.24	0.0266
STI[b]						
Yes	REF					
No	0.88	0.36-2.15	0.7831			
Inject drugs[b]						
Yes	REF					
No	1.81	0.25-13.01	0.5512			
Accept health service[c]						
Yes	REF			REF		
No	1.55	0.96-2.49	0.0687	1.20	0.74-1.94	0.4501
MSW[db]						
Yes	REF			REF		
No	0.66	0.34-1.27	0.2183	1.39	0.71-2.72	0.3340

Abbreviation: STI, sexually transmitted infections; MSW, male sex workers; HR, hazard ratio; CI: confidence interval; REF, reference level.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

[e] Multivariate cox regression analysis included marital status, education, residence time in Tianjin, condom use during last sex, condom use

during anal sex, number of sexual partners, health service utilization, MSW.

sTable3. Definition of sexual behavior indicator levels

Variables	Ideal level	Risky level
Condom use in last anal sex	Yes	No
Frequency of condom use during anal sex	Consistent use	Inconsistent use
Number of sexual partners	<10	More than 10

sTable4. Total number of follow-up times among MSM in Tianjin from 2011-2019

Number of Follow-Up Times[a]	**Number of MSM** (%)	**Cumulative Percentage** (%)
2	832 (41.01)	41.01
3	378 (18.63)	59.64
4	240 (11.83)	71.46
5	142 (7.00)	78.46
6	111 (5.47)	83.93
7	67 (3.30)	87.24
8	56 (2.76)	90.00
9	25 (1.23)	91.23
10	33 (1.63)	92.85
>10	145 (7.15)	100.00
Total	2029 (100.00)	

[a] Represented the total number of follow-ups for each participant within the period from first enrollment to the last follow-up. Mean: 4.39 times; Standard Deviation: 3.96; Median: 3 times; P_{25}: 2 times; P_{75}: 5 times.

sTable5. HIV Incidence rates by year

Year	Number of MSM	HIV seroconversion	Incidence Rate (95%CI)[a]
2012[b]	454	8	2.86 (1.59-5.14)
2013	589	20	4.57 (3.31-6.31)
2014	702	18	3.43 (2.35-4.98)
2015	794	27	4.65 (3.53-6.12)
2016	860	16	2.50 (1.63-3.83)
2017	823	12	2.13 (1.29-3.53)
2018	776	10	2.27 (1.32-3.93)
2019	518	16	5.51 (3.97-7.66)

[a] When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participants in this year.

[b] The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

sTable6. HIV incidence rate among age subgroups

Age subgroup	Number of MSM	HIV seroconversion	Incidence Rate (95%CI)
<45	1504	85	3.83 (3.24-4.52)
45-60	464	37	2.81 (2.14-3.69)
>60	61	5	2.08 (0.95-4.55)

sTable7. Incidence rates for HIV infection among MSM with different follow-up times

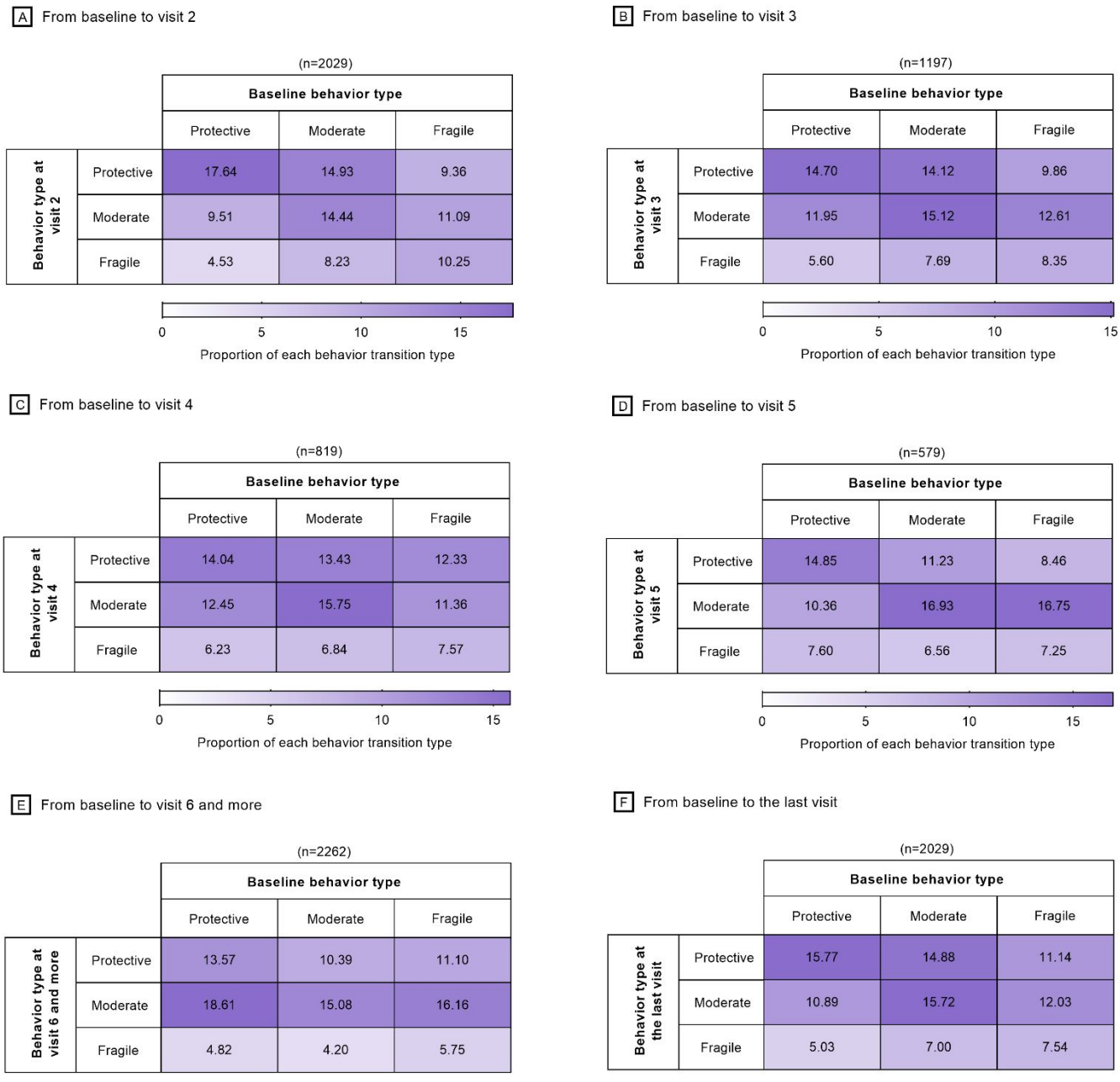
Behavior transition type		Incidence Rate Per 100 Person-Years (95%CI)			Total
		Baseline			
		Protective	Moderate	Fragile	
2 Times[a]	Protective	1.73 (0.44-6.83)	0 (0.00-0.00)	5.6 (2.39-13.12)	4.88 (3.65-6.53)
	Moderate	1.05 (0.15-7.38)	1.51 (0.38-5.97)	0.8 (0.11-5.63)	
	Fragile	10.27 (4.06-25.99)	14.07 (7.92-24.99)	16.97 (11.14-25.85)	
3 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	4.49 (3.06-6.59)
	Moderate	3.18 (0.81-12.44)	0 (0.00-0.00)	5.04 (1.67-15.18)	
	Fragile	13.83 (6.58-29.07)	21.07 (10.91-40.69)	14.73 (7.43-29.19)	
4 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	2.89 (1.72-4.84)
	Moderate	1.52 (0.22-10.63)	1.16 (0.17-8.14)	0 (0.00-0.00)	
	Fragile	15.24 (5.38-43.19)	19.03 (9.77-37.06)	9.45 (2.53-35.33)	
5 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	3.21 (1.74-5.91)
	Moderate	7.24 (1.91-27.51)	0 (0.00-0.00)	4.97 (1.29-19.19)	
	Fragile	7.86 (2.08-29.73)	22.69 (8.39-61.37)	6.92 (1.04-45.85)	
6 times And more	Protective	0 (0.00-0.00)	0.52 (0.07-3.67)	0.85 (0.21-3.38)	2.27 (1.64-3.15)
	Moderate	2.15 (0.90-5.12)	0.44 (0.06-3.11)	0.41 (0.06-2.9)	
	Fragile	16.08 (9.11-28.37)	9.92 (4.64-21.2)	13.68 (7.46-25.1)	
Overall	Protective	0.37 (0.09-1.48)	0.19 (0.03-1.35)	1.37 (0.66-2.86)	3.36 (2.83-3.99)
	Moderate	2.27 (1.27-4.07)	0.69 (0.26-1.83)	1.39 (0.67-2.9)	
	Fragile	13.18 (9.15-18.99)	15.37 (11.23-21.04)	14.51 (10.77-19.55)	
Total		3.14 (2.30-4.29)	2.92 (2.13-3.99)	4.02 (3.07-5.26)	

[a] 2 times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup.

sTable8. Behavior transition type from baseline to each visit

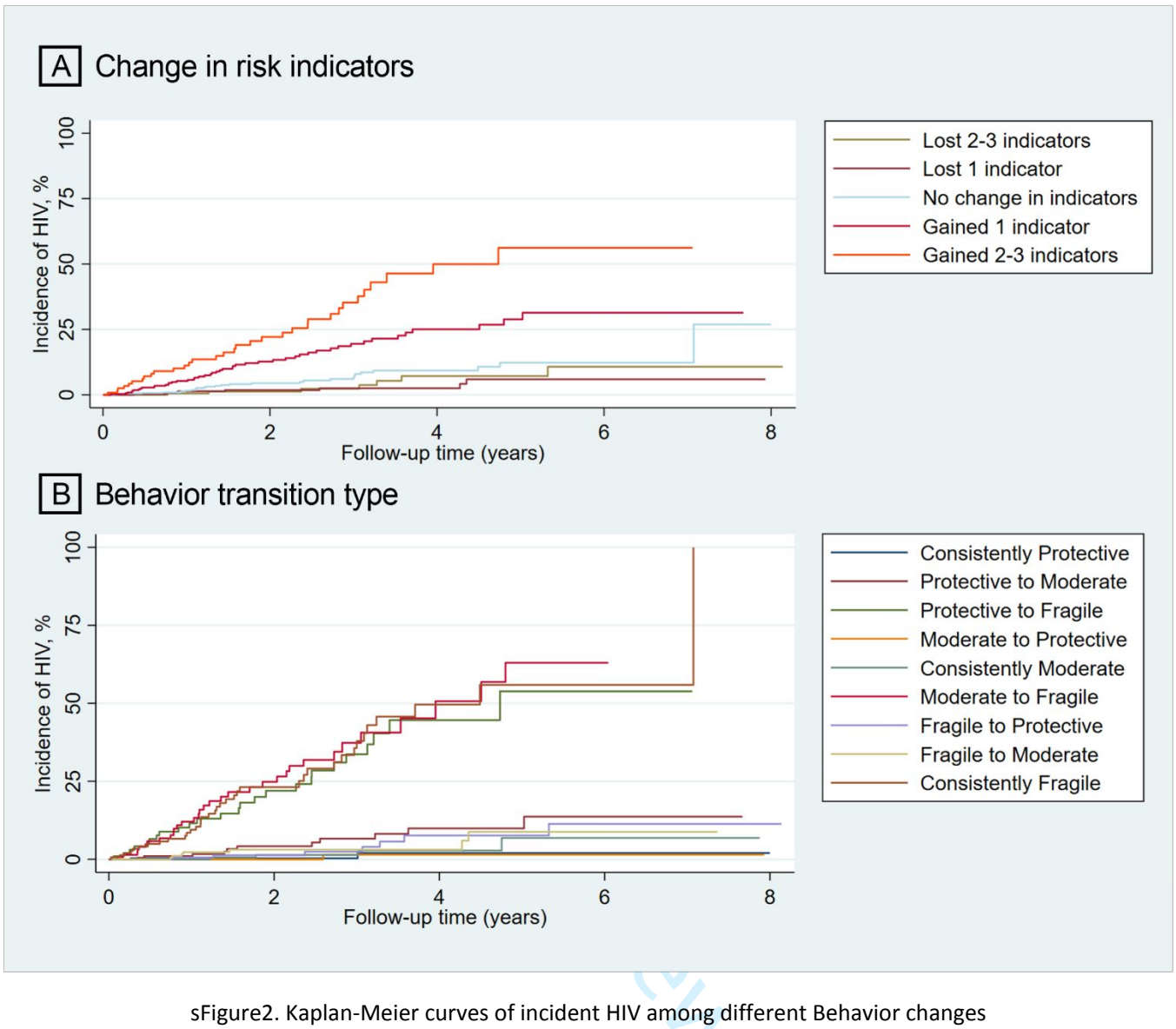
Behavior transition type in each visit[a] N (%)		Baseline			Total
		Protective	Moderate	Fragile	
2nd	Protective	358 (17.64)	303 (14.93)	190 (9.36)	851 (41.94)
	Moderate	193 (9.51)	293 (14.44)	225 (11.09)	711 (35.04)
	Fragile	92 (4.53)	167 (8.23)	208 (10.25)	467 (23.02)
3rd	Protective	176 (14.70)	169 (14.12)	118 (9.86)	463 (38.68)
	Moderate	143 (11.95)	181 (15.12)	151 (12.61)	475 (39.68)
	Fragile	67 (5.60)	92 (7.69)	100 (8.35)	259 (21.64)
4th	Protective	115 (14.04)	110 (13.43)	101 (12.33)	326 (39.80)
	Moderate	102 (12.45)	129 (15.75)	93 (11.36)	324 (39.56)
	Fragile	51 (6.23)	56 (6.84)	62 (7.57)	169 (20.63)
5th	Protective	86 (14.85)	65 (11.23)	49 (8.46)	200 (34.54)
	Moderate	60 (10.36)	98 (16.93)	97 (16.75)	255 (44.04)
	Fragile	44 (7.60)	38 (6.56)	42 (7.25)	124 (21.42)
6th And More	Protective	307 (13.57)	235 (10.39)	251 (11.10)	793 (35.06)
	Moderate	421 (18.61)	341 (15.08)	373 (16.16)	1135 (50.18)
	Fragile	109 (4.82)	92 (4.20)	130 (5.75)	334 (14.77)
Total		643 (31.69)	763 (37.60)	623 (30.70)	8915 (100.00)

[a] listed the number (proportion) of each behavior type in each visit.



sFigure1. Heatmap of percentage of each behavior transition type in each visit

Figure legends 1: Values and colors indicated the percentage of each behavior transition type in each visit (for example, in Figure 1A, 17.64 represented the percentage of "protective" to "protective" was 17.64% from baseline to visit2). A lighter color indicates that the percentage was lower for MSM in that subgroup, whereas a darker color indicated a higher percentage in that subgroup.



sFigure2. Kaplan-Meier curves of incident HIV among different Behavior changes

sTable9. OR and 95% CI for behavior transition-type of "fragile" or "moderate" in the last follow-up stratified by the behavior type categories at baseline

Behavior changes	"Fragile" or "Moderate" at the last follow-up as the dependent variable, OR (95% CI)[a]		
	Protective at baseline	Moderate at baseline	Fragile at baseline
Per 1-time increase in the total follow-up times	1.02 (0.98-1.06)	0.99 (0.95-1.03)	0.95 (0.91-0.99)
Age			
<45	REF	REF	REF
45-60	0.57 (0.37-0.87)	0.45 (0.29-0.68)	0.52 (0.35-0.78)
>60	0.48 (0.16-1.39)	0.23 (0.10-0.54)	0.71 (0.25-2.05)
Residence time in Tianjin			
<3 months	REF	REF	REF
3-7 months	0.51 (0.11-2.32)	1.31 (0.40-4.30)	3.54 (0.75-16.63)
7-12 months	1.06 (0.36-3.12)	1.53 (0.30-7.78)	1.76 (0.53-5.86)
1-2 years	1.93 (0.75-4.97)	0.89 (0.40-1.96)	1.88 (0.72-4.85)
>2 years	0.92 (0.59-1.43)	0.65 (0.45-0.99)	1.10 (0.73-1.66)

Abbreviation: OR, odds ratio; CI: confidence interval; REF, reference level.

[a] Multivariate logistic regression analysis included total follow-up times, age, marital status, education, residence time in Tianjin, health service utilization

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7, 8
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N/A
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sexual behavior changes and HIV infection among men who have sex with men: evidence from an open cohort in China

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Abstract

Background- The HIV epidemic in key population such as MSM is a public health issue of worldwide concern. China has seen an increasing in newly diagnosed HIV infections through male-male sexual contact in the past decade. In a long-term cohort, how the complex behavior pattern of MSM changed and the association with the HIV risk are unclear at present.

Methods- This study was conducted from October 2011 to December 2019 in Tianjin. MSM were recruited by snowball sampling through online and offline ways. Demographic and sexual behavioral data were collected for analysis. Using three indicators (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) to define the behavior change. Participants with 0, 1, and 2 or 3 risk indicators were categorized as behavior type of “protective”, “moderate”, and “fragile”. Change in behavior type between baseline and each visit was considered. Time-varying Cox models were performed to evaluate HIV infection risk.

Results- Of 2029 MSM include in the study, 127 were new HIV diagnoses. The overall incidence rate was 3.36 per 100 person-years. The percentage of “protective” and “moderate” behavior type had a conspicuous growth trend as the follow-up. Furthermore, the HIV incidence rate in each visit among different behavior transition types showed a general downward trend as the number of total follow-up times increased. Individual who remained in “fragile” (aHR, 25.86 [95%CI, 6.92-96.57]) or changed from “protective” to “moderate”, (aHR, 4.79 [95%CI, 1.18-19.47]) “protective”

to “fragile” (aHR, 23.03 [95%CI, 6.02-88.13]), “moderate” to “fragile” (aHR, 25.48 [95%CI, 6.79-95.40]) between baseline and the last follow-up had a higher HIV risk. Gained risk indicators were associated with the increase of HIV risk (gained 1 indicator, aHR: 2.67,95%CI: 1.68-4.24; gained 2 or 3 indicators, aHR, 4.99, [95%CI, 3.00-8.31]) while lost just one risk indicator could halve the risk (aHR, 0.43, [95%CI, 0.21-0.90]).

Conclusions- Among MSM in Tianjin, it is necessary to get timely behavior change for those with high-incidence behavior patterns while sustaining for those with low-incidence patterns.

Keyword: Men who have sex with men; HIV; Behavior change; Cohort study

Article summary

Strengths and limitations of this study

- This study was based on an open MSM cohort in China with long time span (2011-2019).
- Three indicators related to participants' sexual behaviors (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) were used to define the behavior change jointly.
- Associations between behavior change and risk of HIV infection were estimated through Cox models.
- Sexual behaviors were self-reported and measured retrospectively, and may have been misremembered or otherwise misreported.

Introduction

The epidemic of the human immunodeficiency virus (HIV) is a significant public health issue of worldwide concern(1-4). The prevalence of HIV have been low among the general population over the past three decades. However, the burden of HIV is disproportionately concentrated among men who have sex with men (MSM)(5-7). China's HIV epidemic began in the early 1990s among injecting drug users(8, 9). The main route of transmission was needle-sharing(10, 11). Due to China's effective legal control and intensive regulations on drugs(12, 13), the main spread route of HIV inevitably turned into sexual contact since the 21st century, especially male-to-male sexual contact(7, 14, 15). Corresponding studies aimed to ascertain the pattern of sexual behaviors among MSM had important practical significance though sexual behaviors between men were taboo both politically and by cultural tradition in China(16, 17).

Effective intervention and behavior change had been responsible for the HIV prevention successes to date(18, 19). HIV interventions typically concentrate on unprotected anal intercourse (UAI)(20), multiple sex partners(21), alcohol and drug use(13, 22), pre-exposure prophylaxis (PrEP)(23, 24) or post-exposure prophylaxis (PEP)(25, 26) utilization and adherence to antiretroviral therapy (ART)(27). It was well established from a variety of studies that timely behavior change and biomedical intervention can reduce HIV transmission(28-30). However, most studies used a single measurement to describe behavior change. In a long-term cohort, how the complex behavior pattern changed and the association with the HIV risk was largely unknown

at present.

This study was based on an open cohort among MSM in Tianjin, China, 2011-2019. The study collected each MSM's sexual behavior and HIV infection status at each visit. The aims of the present study were the following: (1) to describe the HIV incidence rate over the cohort; (2) to quantify the behavior changes over the follow-up and to address the association between behavior change and the risk of HIV infection; and (3) to explore influencing factors for progression to behavior change.

Methods

Study Design

The men who have sex with men health encouragement longitudinal project (MSMHELP) was a longitudinal cohort study among MSM launched in Tianjin, China. The main objectives of the project include: (1) establish community-based HIV prevention service stations aimed at the key population, (2) improve the accessibility and utilization of HIV testing and prevention services, (3) provide ART support services for people living with HIV. The organizations involved in the project included US Centers for Disease Control and Prevention (CDC); National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and prevention (NCAIDS/STD); Tianjin City CDC and Tianjin Shenlan Community-Based Organization (CBO). This study was registered with the Chinese Clinical Trials Registry (Identifier: ChiCTR2000039500).

Data Collection and Participants

Tianjin Shenlan CBO was a formally community-based organization that provided

community-based HIV voluntary counseling & testing (VCT) support services (including HIV testing, counseling, and psychological support) for MSM. Participants were mobilized to get tested for HIV in Shenlan's public health advisory service center. When participants came to the center for testing or counseling, experienced MSM investigators would conduct a face-to-face interview with participants in a private room. During this period, a structured questionnaire (included demographics and sexual behaviors information) was completed by the participants under the guidance of the investigators. The investigators of the organization mostly were also MSM. All investigators had undergone training before entering work, which would be a benefit for smooth unhindered communication with participants and could ensure the reliability of the results. After the interview, every participant would get several condoms and lubricant for free. Information collection adopted a real-name registration system (ID card number, mobile phone number and fingerprint information were collected). Prior to the interviews, all participants signed a written informed consent, including the objective, procedures, confidentiality and participants' rights. Enrolled participants were encouraged to routine HIV test every three months (90 days). The entire research process was supervised and coordinated by Tianjin City CDC.

The snowball sampling method was used to recruit participants. Participants were recruited from gay bars, gay bathhouses, social network sites (WeChat, QQ, gay chat website), gay apps and peer referrals. The initial enrollment took place on October 1, 2011, and follow-up ended up on December 31, 2019. Inclusion criteria were: (1) had

at least two visits during the cohort period and HIV serological test was negative when they first registered, (2) ≥ 16 years old, (3) biologically male, (4) reported anal intercourse with another man in the past six months. The participants of the cohort change dynamically, the original participants could drop out continuously, and the new participants could join at any time. Of 6565 MSM captured in this study, 4096 were excluded for having only one visit, 432 for having HIV seropositive result at baseline, and 8 for lack of behavioral information. 2029 MSM met the eligibility criteria and were included in the study eventually. The flow diagram of the study was listed in sFigure 1 in the Supplement. The comparison of baseline characteristics between included and excluded MSM were listed in sTable 1 in the Supplement.

Definitions of Behavior Changes

In this study, behavior changes include the change in the number of risk indicators and change in sexual behavior type. Sexual behavior type was used to represent different patterns of sexual behavior characteristics. It was collectively defined by three indicators related to participants' sexual behavior in the past six months. The three indicators included variables of condom use in last anal sex(31), frequency of condom use during anal sex(21), and the number of sexual partners(32). These three variables were related to the HIV infection (sTable 2 in the Supplement). Participants had the information of the three variables in each follow-up. Each indicator was divided into two levels: "ideal level" and "risk level" (sTable 3 in the Supplement). Among the three variables mentioned above, if one participant had one variable of "risk level" then meant the participant had one risk indicator, and so on. The number

of risk indicators was in the range of zero to three.

Behavior type was defined based on the risk indicators. Behavior type was categorized as “protective” if the participant had no risk indicator; as “moderate” if the participant had one risk indicator; as “fragile” if the participant had more than two risk indicators (two or three risk indicators). The behavior type and the number of risk indicators could change as time varying (during the follow-up period).

Change in the number of risk indicators was defined as the difference of risk indicators between any two follow-ups. Behavior transition type was defined as the change of behavior type between any two visits. Then the behavior transition type yielded nine possible combinations of behavior types: consistently protective, protective to moderate, protective to fragile, moderate to protective, consistently moderate, moderate to fragile, fragile to protective, fragile to moderate, consistently fragile.

HIV Laboratory Test

Before testing, MSM would choose to collect blood or saliva. Patrons’ oral mucosal exudate test (Mano Bio-Pharmaceutical Co., Ltd, Beijing, China) was used for the former and a blood rapid detection reagent (Wan Fu Biotechnology Co., Ltd, Guangzhou, China) for the latter. In addition, 5ml of blood sample was collected from those who get any positive tests above. Then, the blood sample was sent to Tianjin CDC to perform enzyme-linked immunosorbent (ELISA; Wan Tai Biological Pharmaceutical Co., Ltd, Beijing, China). HIV infection was by confirmed Western blot (WB) assay (MP Biomedical Asia Pacific Pte Ltd, Singapore). As the exact infection time

was hard to affirm, for the chronic infections (infection time over 6 months), the infection time was defined as the mid-point between last negative test date and first positive test time while the acute and early infection (<6 months) was the time diagnosed as HIV infection(33).

Statistical Methods

Category variables were described by frequencies and percentages. For the general demographic characteristics, differences were calculated using Pearson's chi-squared test or Fisher's exact test.

HIV incidence rates were estimated within each year and among subgroups of different behavior transition types in each visit, with person-year (PY) over the follow-up time as the denominator.

Change in behavior type was calculated in each visit (according to baseline behavior type). Considering that the total number of each participant was unequal, the proportion of each behavior type at each visit and the proportion of behavior transition type from baseline to each visit were calculated.

Univariate and multivariable time-varying Cox models were performed to evaluate (1) risk of HIV infection among different behavior type subgroups over each follow-up (all records of the participants were included in the model in counting process format) (2) behavior changes and association with the risk of HIV infection (two time points were opted to define the behavior change, baseline, and the last follow-up). Hazard ratios (HR), adjusted hazard ratios (aHR) and 95% confidence interval (95%CI) of the variables were estimated. The logistic regression model was applied to investigate the

influencing factors for progression to behavior type of “fragile” or “moderate” in the last follow-up among baseline behavior type subgroups. Odds ratios (OR), adjusted odds ratios (aOR) and 95% confidence interval (95%CI) were estimated. In addition, all models were adjusted for baseline covariates. All the data analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC).

Patient and public involvement

This study was mainly completed by Tianjin CDC, with Tianjin Shenlan CBO as the specific implementor of the study. Patients or the public were not directly involved in the design and implementation of the study. But the findings could influence the design of other subsequent studies, such as specific studies targeting drug users or male sex workers in the MSM population.

Results

Characteristics of the Participants

A total of 2029 MSM met the eligibility criteria and were included in the study eventually. The total follow-up person time was 3772.03 PY. The median total follow-up time was 1.28 years (interquartile range [IQR], 0.57 to 2.72; range, 8 days to 8.13 years) starting from baseline. Confirmed by the laboratory test, 127 participants were new HIV diagnoses. 63 were classified as acute and early HIV infected and 64 were chronic infected.

The characteristics of the participants when they first registered (baseline) were shown in Table 1. Among all the participants, the median age was 34 years old (P_{25},25; P_{75},45); 53.33% were unmarried; 57.76% had a high school degree; 39.48% had a

college degree or above; 71.87% had been lived in Tianjin for more than 2 years while 19.96% had been lived in Tianjin for less than 3 months; 76.39% used condom in last anal sex; 38.69% had a condom consistent use during anal sex over past six months; 84.23% had less than 10 sexual partners over past six months; 3.35% had STI over past six months; 46.23% had received HIV health service over past one year; 5.03% had been worked as MSW.

The total number of follow-up times of each participant were listed in sTable 4 in the Supplement. The median follow-up times were 3 times (range from 2 to 34, P_{25},2; P_{75},5). 41.01% of participants had 2 follow-up times; 78.46% had follow-up times no more than 5 times. Participants with a total number of follow-up times more than 10 times was 7.15%.

HIV Incidence Rate

Among the whole study population, the overall HIV incidence rate was 3.36 per 100 PY (95%CI, 2.83-3.99).

Figure 1 and sTable 5 in the Supplement showed the HIV incidence rates by years. The rates were relative higher in 2013 (4.57 per 100 PY [95%CI, 3.31-6.31]), 2015 (4.65 per 100 PY [95%CI, 3.53-6.12]) and 2019 (5.51 per 100 PY [95%CI, 3.97-7.66]), though the rates did not show a liner trend significance over 2011-2019. Among age subgroups, incidence rates were <45, 3.83 per 100 PY (95%CI, 3.24-4.52); 45-60, 2.81 per 100 PY (95%CI, 2.14-3.69); >60, 2.08 per 100 PY (95%CI, 0.95-4.55) (sTable 6 in the Supplement).

To compare the HIV incidence rate among different behavior transition types, participants were divided into subgroups according to their number of total follow-up times. The calculation of the HIV incidence rate was done within each subgroup. Stratified by the behavior type categories at baseline, the overall HIV incidence rates were: “protective”, 3.14 per 100 PY (95%CI, 2.30-4.29); “moderate”, 2.92 per 100 PY (95%CI, 2.13-3.99); “fragile”, 4.02 per 100 PY (95%CI, 3.07-5.26) (sTable 7 in the Supplement). On the whole, HIV incidence rate shown a general downward trend as the number of total follow-up times increased (2 times: 4.88 [95%CI, 3.65-6.53]; 3 times: 4.49 [95%CI, 3.06-6.59]; 4 times: 2.89 [95%CI, 1.72-4.84]; 5 times: 3.21 [95%CI, 1.74-5.91]; 6 times and more: 2.27 [95%CI, 1.64-3.15]). MSM who had more visits showed a low risk of infection in comparison with those who had fewer visits. Within each subgroup, the HIV incidence rate tended to concentrate towards the lower right corner of the heatmap (i.e., concentrate towards behavior type of “fragile”) (Figure 2).

Time-varying behavior type and risk of HIV infection

The risk of HIV infection was evaluated through Cox models with time-varying behavior types. Compared with “protective” behavior type, “moderate” behavior type (aHR, 2.22 [95%CI, 1.05-4.71]) and “fragile” behavior type (aHR, 16.53 [95%CI, 8.57-31.88]) were associated with a greater risk of HIV infection. Likewise, there was a significant and linear increase in the risk of HIV infection for each additional time-varying risk indicator (aHR, 3.37 [95%CI, 2.76-4.11]) (Table 2).

Behavior Types in Each Visit

The percentage of each behavior type ("protective", "moderate", and "fragile") at baseline were: 31.69% (643/2029), 37.60% (763/2029), and 30.70% (623/2029), respectively. As the number of follow-up visits increased, the percentage of "protective" and "moderate" had a growth trend (35.06% and 50.18% at 6th and more, respectively) while the percentage of "fragile" was declined (14.77% at 6th and more) (Figure 3).

Behavior Changes and Association with the Risk of HIV Infection from Baseline to the Last Follow-Up

The behavior types of baseline and the last follow-up was selected to evaluate the behavior changes (change in risk indicators: difference in risk indicators between baseline and the last follow-up; change in behavior type: "behavior types at baseline" to "behavior types in the last follow-up") and the association with the risk of HIV infection. The choice of two time points was based on a main argument: the pattern of behavior changes from baseline to each follow-up was relatively stable (details in sTable 8 and sFigure 2 in the Supplement). The first and the last visit were good proxy for behavior changes during follow-up.

In multivariable analysis, "no change in indicators" as the reference level, lost one risk indicator could decline the risk at 0.43 (95%CI: 0.21-0.90). While gained indicators were related to the increasing risk of HIV infection (gained one risk indicator: aHR, 2.67 [95%CI, 1.68-4.24]; gained two or three risk indicators: aHR, 4.99 [95%CI, 3.00-8.31]).

As for the different behavior transition types, the risk of HIV infection was not

statistically different from that of the consistently protective group (reference level) in the moderate to protective group (aHR, 0.65 [95%CI, 0.08-5.16]), the consistently moderate group (aHR, 1.52 [95%CI, 0.31-7.41]), the fragile to protective group (aHR, 2.87 [95%CI, 0.66-12.46]), and the fragile to moderate group (aHR, 2.66 [95%CI, 0.61-11.53]). Instead, the risk of HIV infection was distinctly greater in the protective to moderate group (aHR, 4.79 [95%CI, 1.18-19.47]), the protective to fragile group (aHR, 23.03 [95%CI, 6.02-88.13]), the moderate to fragile group (aHR, 25.48 [95%CI, 6.79-95.40]), and the consistently fragile group (aHR, 25.86 [95%CI, 6.92-96.57]) (Table 3 and sFigure3 in the Supplement).

Influencing Factors for Progression to Behavior Type of "fragile" or "moderate" in the Last Follow-Up

We also investigated which influencing factors were related to the progression of behavior transition type of "fragile" or "moderate" by the end of follow-up among baseline behavior type subgroups.

Within age subgroups, the younger participants had a higher likelihood of progression to behavior type of "fragile" or "moderate" by the end of follow-up.

Notably, the likelihood of progression to behavior type of "fragile" or "moderate" was weakened as the number of total follow-up times increasing (per 1-time increase in the total follow-up times, aOR, 0.95 [95CI%, 0.91-0.99]) among participants "fragile" at baseline.

Compared with participants who lived in Tianjin less than three months, participants who lived in Tianjin for more than two years had a lower likelihood of

progression to behavior type of “fragile” or “moderate” by the end of follow-up (aOR, 0.65 [95CI%, 0.37-0.87]) (sTable 9).

Discussion

The characteristics of MSM are mainly high mobility and concealment. It was a challenge to ensure long-term cohort retention and sustain routine HIV test programs among this population. Therefore, we conducted an open cohort study among MSM in Tianjin, China. 2029 MSM were included in the study eventually from 2011-2019. Among the whole study population, the overall HIV incidence rate was 3.36 per 100 PY (95%CI, 2.83-3.99). The incidence rate was at a lower level. Previous studies conducted in other cities in China had shown a pretty high HIV incidence among MSM, 6.6 per 100 PY in Hangzhou(34), 6.78 per 100 PY in Yangzhou, 5.77 per 100 PY in Guangzhou(35), 5.3 per 100 PY in Shenyang(36), 5.12 per 100 PY in Nanjing(37), 3.5 per 100 PY in Yunnan(38) and 7.1 per 100 PY in Beijing(39). The incidence is also at a low level compared with related studies in other regions (sub-Saharan Africa(40), Latin American(41), and United States(42-44)). In this study, the percentage of “protective” and “moderate” behavior types had a conspicuous growth trend as the follow-up. Furthermore, the HIV incidence rate in each visit among different behavior transition types showed a general downward trend as the number of total follow-up times increased. The evidence mentioned above indicated the effectiveness of the community-based VCT project in reducing HIV incidence. However, challenges still existed and need to be addressed. The incidence rate in 2019 was much higher than in other years (5.51 per 100 PY [95%CI, 3.97-7.66]). We speculated that the reason might be the publicity and promotion of PrEP/PEP started in 2018 among the MSM population in Tianjin. PrEP/PEP were effective biomedical strategies to prevent the

further transmission of HIV(23, 24). Although the utilization of PrEP/PEP was not widespread among MSM in Tianjin, this might promote the cognitive concepts of "treatment optimism" about HIV(45). MSM might rationalize their risk behavior before (or after) engaging in sexual behaviors(46), which promoted the generate of risk behaviors(47, 48).

Previous studies concentrate on using one stand-alone indicator to describe the behavior change. For example, one study in China(49) used the percentage of unprotected anal intercourse (UAI) occurrence to describe the behavior change. However, this study evaluated behavior change with greater precision (behavior changes were collectively defined by three indicators and divided into two patterns: change in the number of risk indicators and behavior transition type) among a great sample size (N=2029) in a long-term follow-up (2011-2019). What's more, this study quantified the behavior changes and association with the risk of HIV infection from baseline to the last follow-up. The results of this study showed, individual who remained "fragile" or changed from "protective" to "moderate", "protective" to "fragile", "moderate" to "fragile" between baseline and the last follow-up had a higher HIV risk as compared with individuals with persistently "protective". When this analysis was conducted in risk indicators, similar results were found. Gained risk indicators were associated with the increase of HIV risk while lost just one risk indicator could halve the risk (aHR:0.43). This study demonstrated the importance of maintaining protective sexual practices and timely behavior changes in high-incidence population could help reduce the risk of HIV infection.

The cohort had a high rate of loss to follow-up (for 4096 MSM only one visit record), which may have biased the results. Indeed, the complexity of the MSM population made maintaining a long-term follow-up cohort difficult. This study was based on an open cohort whose main purpose was to cover as many MSM as possible. Whether or not a participant will proceed to the next visit is entirely driven by their personal endogenous motivation, although messages were sent to MSM 90 days after their testing to remind them to perform another HIV testing. In the future, plans of following research including recruit more staff are under consideration. Special staff will conduct regular return visits and urge MSM to carry out routine HIV testing.

Limitations

This research has several limitations. First, in our study, the snowball sampling method was used to recruit participants, which may have selection bias. However, we recruited participants in a variety of ways (gay bars, gay bathhouses, social network sites, gay apps and peer referrals) to increase the representativeness. Second, our data lacked information on the use of alcohol, recreational drugs and PrEP usage. The presence of these substances might affect the sexual behavior of participants, which should be addressed in future research. Further, our data collection adopted a real-name registration system (ID card number, mobile phone number and fingerprint information were involved). Due to the privacy of some questions (such as whether you had ever had STI), the participants might have concealed the actual situation which may result in social expectation bias. We conducted an interview-style questionnaire collection to avoid this. Besides, all MSM investigators had received

professional training to ensure the authenticity of the data.

Conclusion

In this study, sexual behavior changes are collectively defined by three indicators (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) related to participants' sexual behavior in the past six months. Behavior changes from 2011-2019 and ensuing HIV infection risk are calculated. Long-term sexual behavior patterns of MSM keep changing and gradually have a tendency to be less risky during the study period. The proportion of high-risk behavior pattern is 30.70% at baseline. This number decline to 14.77% at visit 6 and more. This result may provide clues for the effectiveness of community-based HIV/AIDS interventions.

Transition from low-incidence population to high- incidence is associated with a similar risk of HIV infection than continuing high- incidence. Further strategies are needed to promote the low-incidence change.

MSM should sustain low-incidence behavior patterns otherwise would undergo higher HIV infection risk. Future HIV interventions should prioritize not only to those MSM who were high-incidence population, but also to those MSM who have temporarily low-incidence but are at risk of switching to high-incidence population.

Contributorship

Zeyang Yu (ZY), Changping Li (CL), Zhuang Cui (ZC), Yuanyuan Liu (YL), and Jun Ma (JM) contributed to the conception of the study. Huijie Huang (HH), Tiantian Zhang (TZ) and Desheng Song (DS) contributed to the framework of the study. Maohe Yu (MY) and Jie Yang (JY) collected the data. Qinxue Chang (QC) and Xiaomeng Wang (XW) cleared the raw data. HH and Honglu Zhang (HZ) helped perform the analysis with constructive discussions. TZ and ZY analyzed the data and wrote the manuscript. ZC revised the manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethics approval

This study was reviewed and approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, China CDC [IRB approve number: X130205267].

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Data sharing

No additional data available

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Table1. Characteristics and sexual behaviors at baseline for MSM with HIV infection or negative HIV test

Variables at Baseline	Total N (%)	HIV Infection N (%)	HIV Negative N (%)
Age			
<45	1504 (74.13)	96 (75.59)	1408 (74.03)
45-60	464 (22.87)	27 (21.16)	437 (22.98)
>60	61 (3.01)	4 (3.15)	57 (3.00)
Marital status			
Married	947 (46.67)	70 (55.12)	877 (46.11)
Unmarried	1082 (53.33)	57 (44.88)	1025 (53.89)
Education			
Below high school	56 (2.76)	5 (3.94)	51 (2.68)
High school	1172 (57.76)	90 (70.87)	1082 (56.89)
College or more	801 (39.48)	32 (25.20)	769 (40.43)
Residence time in Tianjin			
<3 months	405 (19.96)	41 (32.28)	364 (19.14)
3-7 months	39 (1.92)	2 (1.57)	37 (1.74)
7-12 months	41 (2.02)	5 (3.94)	36 (1.89)
1-2 years	86 (4.24)	2 (1.57)	84 (72.61)
>2 years	1458 (71.86)	77 (60.63)	1381 (72.61)
Condom use in last anal sex			
Yes	1550 (76.39)	78 (61.42)	1472 (77.39)
No	479 (23.61)	49 (38.58)	430 (22.61)
Frequency of condom use during anal sex[ab]			
Consistent use	785 (38.69)	43 (33.86)	742 (39.01)
Inconsistent use	1244 (61.31)	84 (66.14)	1160 (60.99)
Number of Sexual partners[b]			
<10	1709 (84.23)	116 (91.34)	1593 (83.75)
More than 10	320 (15.77)	11 (8.66)	309 (16.25)
STI[b]			
Yes	68 (3.35)	2 (1.57)	66 (3.47)
No	1961 (96.65)	125 (98.43)	1836 (96.53)
Inject drugs[b]			
Yes	22 (1.08)	2 (1.57)	20 (1.05)
No	2007 (98.92)	125 (98.43)	1882 (98.94)
Accept health service[c]			
Yes	938 (46.23)	53 (41.73)	885 (46.50)
No	1091 (53.77)	74 (58.27)	1017 (53.50)
MSW[db]			
Yes	102 (5.03)	5 (3.94)	97 (5.10)
No	1927 (94.97)	122 (96.06)	1805 (94.90)

Abbreviations: STI, sexually transmitted infections; MSW, male sex workers.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

Table2. Univariate and multivariable Cox proportional hazard model with time-varying covariates for HIV infection

HIV infection risk models[a]	Per 1-risk indicator increase[b]	Categories of sexual behavior type		
		Protective	Moderate	Fragile
HR (95%CI)	3.68 (3.03-4.46)	REF	2.38 (1.12-5.02)	19.74 (10.28-37.91)
adjusted HR (95%CI)[c]	3.37 (2.76-4.11)	REF	2.22 (1.05-4.71)	16.53 (8.57-31.88)

Abbreviations: HR, hazard ratio; 95%CI, 95% confidence interval; REF, reference level.

[a] All follow-up records of each participants were included into the model in counting process format.

[b] The number of risk indicators were in range of 0 to 3. Per 1-risk indicator increase meant the number of indicators were included into the model as a continuous variable.

[c] Multivariable Cox regression analysis was adjusted for age, education, marital status, residence time in Tianjin, MSW.

Table3. Behavior changes and association with the risk of HIV infection between baseline and the last follow-up

Behavior changes[a]	HIV infection status (N, %)		Univariate Cox regression analysis			Multivariable Cox regression analysis[b]		
	Negative	HIV	HR	95%CI	*P* value	aHR	95%CI	*P* value
Change in risk indicators								
Lost 2-3 indicators	236 (12.4)	7 (5.5)	0.56	0.25-1.27	0.1680	0.57	0.25-1.29	0.1822
Lost 1 indicator	525 (27.6)	9 (7.1)	0.41	0.19-0.86	0.0182	0.43	0.21-0.90	0.0251
No change in indicators	725 (38.1)	30 (23.6)	REF			REF		
Gained 1 indicator	325 (17.1)	48 (37.8)	2.82	1.78-4.46	0.0001	2.67	1.68-4.24	0.0001
Gained 2-3 indicators	91 (4.8)	33 (26.0)	6.13	3.73-10.08	0.0001	4.99	3.00-8.31	0.0001
Behavior transition type								
Consistently Protective	318 (16.7)	2 (1.6)	REF			REF		
Protective to Moderate	210 (11.0)	11 (8.7)	4.78	1.18-19.26	0.0275	4.79	1.18-19.47	0.0283
Protective to Fragile	77 (4.0)	25 (19.7)	28.76	7.66-108.05	0.0001	23.03	6.02-88.13	0.0001
Moderate to Protective	301 (16.0)	1 (0.8)	0.64	0.08-5.03	0.6703	0.65	0.08-5.16	0.6912
Consistently Moderate	315 (16.6)	4 (3.1)	1.62	0.33-7.84	0.5449	1.52	0.31-7.41	0.6019
Moderate to Fragile	109 (5.7)	33 (26.0)	34.32	9.27-127.06	0.0001	25.48	6.79-95.40	0.0001
Fragile to Protective	219 (11.5)	7 (5.5)	2.95	0.68-12.67	0.1457	2.87	0.66-12.46	0.1590
Fragile to Moderate	237 (12.5)	7 (5.5)	3.06	0.71-13.17	0.1316	2.66	0.61-11.53	0.1906
Consistently Fragile	116 (6.1)	37 (29.1)	31.43	8.53-115.75	0.0001	25.86	6.92-96.57	0.0001
Total	1902	127						

Abbreviation: HR, hazard ratio; CI: confidence interval; REF, reference level.

[a] Two time points (baseline and the last follow-up) were opted to evaluate behavior changes.

[b] Multivariable Cox regression analysis was adjusted for age, education, marital status, residence time in Tianjin, MSW.

Figure legends:

Figure1. HIV Incidence rates by year

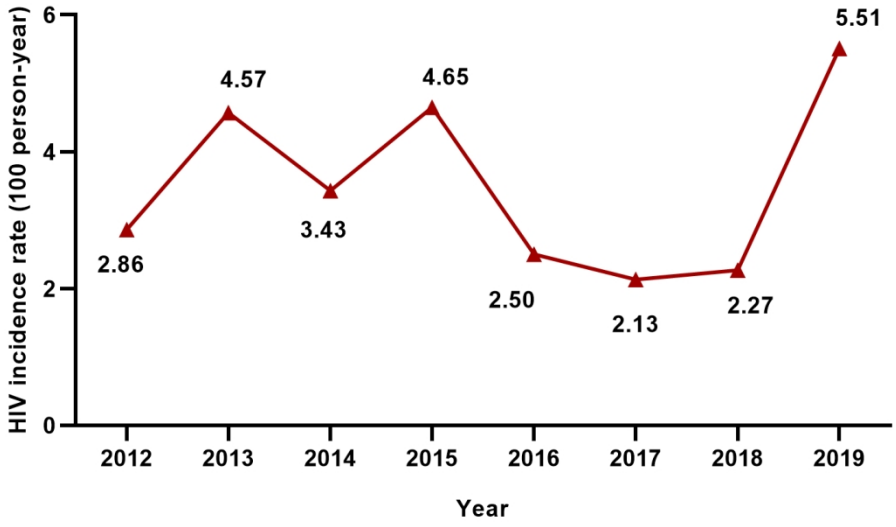
Figure legend 1: When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participant in this year. The first people newly diagnosed with HIV occurred in 2012, though the study started in 2011.

Figure2. Heatmap of HIV incidence rates among MSM with different follow-up times

Figure legend 2: MSM with 2 follow-up times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup. Values and colors indicated HIV incidence rate per 100 PY (for example, in Figure 2A, 0.37 represented the HIV incidence rate in "protective" to "protective" group was 0.37 per 100 PY). A lighter color indicates that the HIV incidence rate was lower for MSM in that subgroup, whereas a darker color indicated a higher incidence rate in that subgroup.

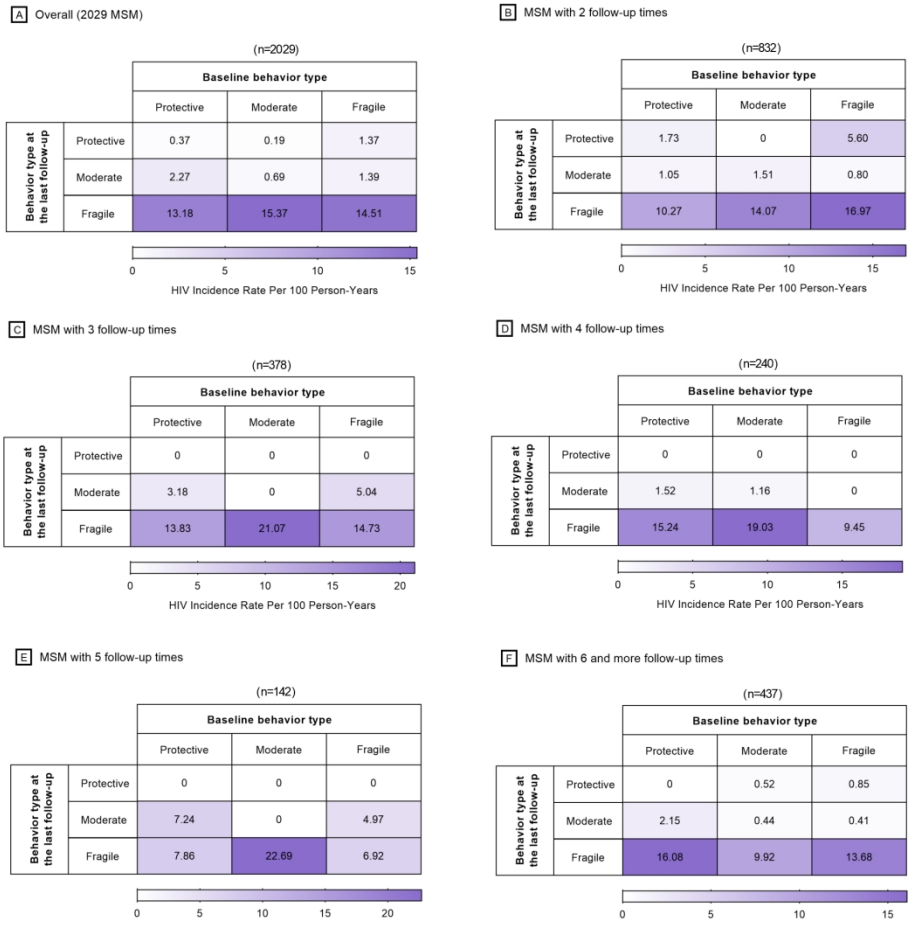
Figure3. Percentage of behavior type in each visit

Figure legend 3: Values and area of the rectangles indicated percentage of behavior type in each visit (for example, in Figure 3, 31.69 represented the percentage of "protective" behavior type was 31.69% at baseline).



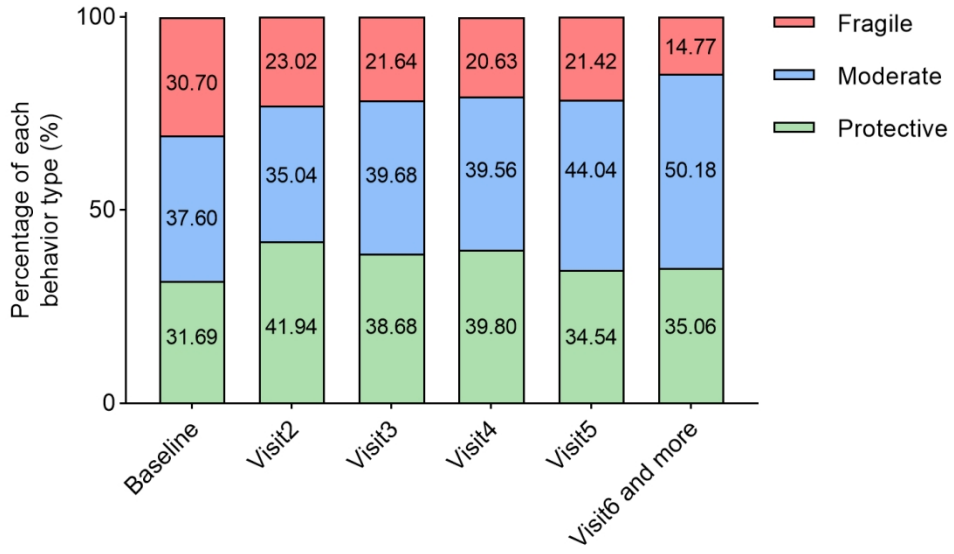
When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participants in this year. The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

135x79mm (300 x 300 DPI)



MSM with 2 follow-up times times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup. Values and colors indicated HIV incidence rate per 100 PY (for example, in Figure 2A, 0.37 represented the HIV incidence rate in "protective" to "protective" group was 0.37 per 100 PY). A lighter color indicates that the HIV incidence rate was lower for MSM in that subgroup, whereas a darker color indicated a higher incidence rate in that subgroup.

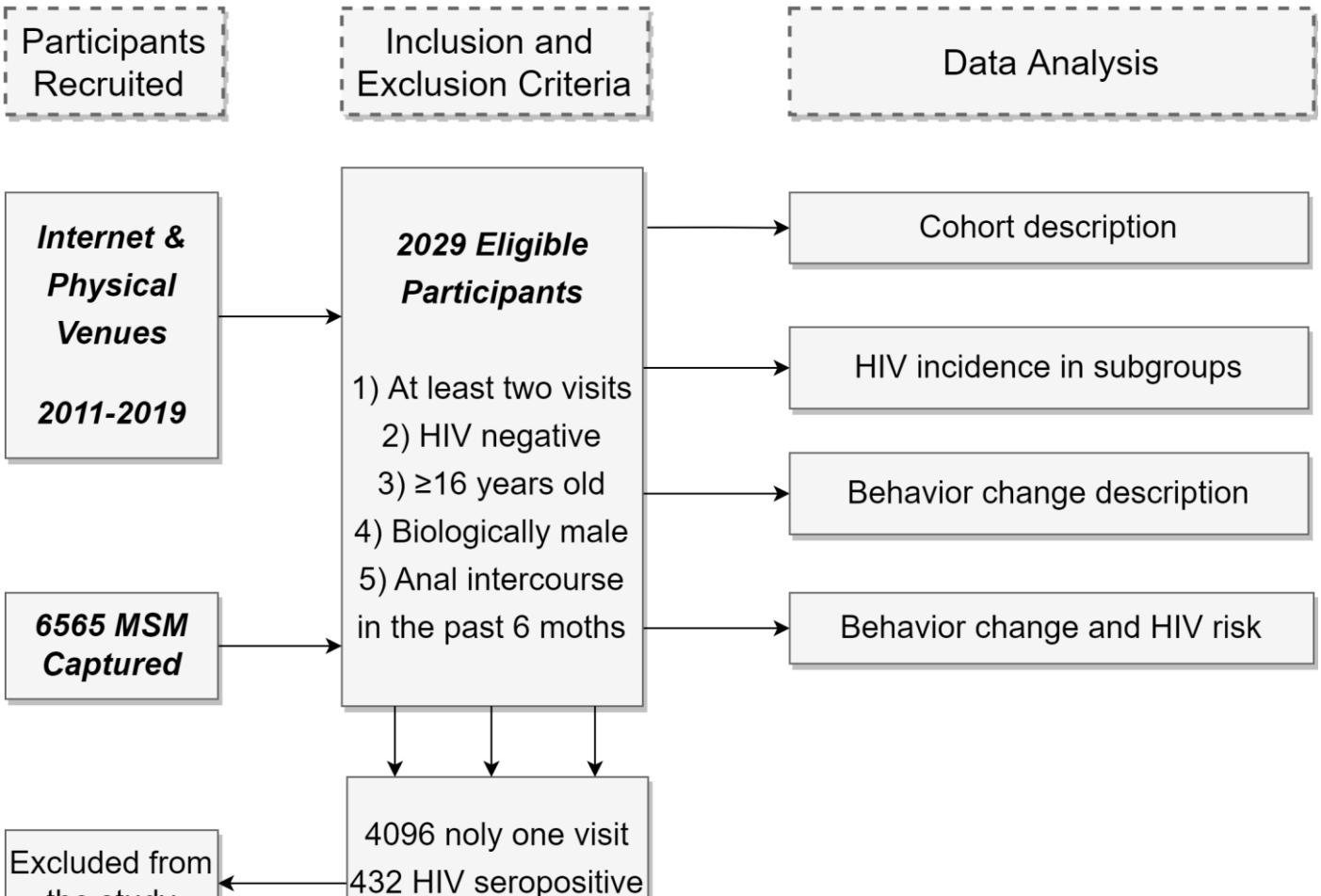
540x514mm (96 x 96 DPI)



Values and area of the rectangles indicated percentage of behavior type in each visit (for example, in Figure 3, 31.69 represented the percentage of "protective" behavior type was 31.69% at baseline).

130x80mm (300 x 300 DPI)

Contents



sFigure1. Flow diagram of the study

sTable1. Characteristics of excluded and included study participants at baseline

Variables at Baseline	Included (N=2029) N (%)	Excluded (N=4096) N (%)	*P*
Age			0.1555
<45	1504(74.13)	3098(75.63)	
45-60	464(22.87)	856(20.90)	
>60	61(3.01)	142(3.47)	
Marital status			0.0198
Married	947(46.67)	1783(43.53)	
Unmarried	1082(53.33)	2313(56.47)	
Education			0.6467
Below high school	56(2.76)	125(3.05)	
High school	1172(57.76)	2322(56.69)	
College or more	801(39.48)	1649(40.26)	
Residence time in Tianjin			0.0001
<3 months	405(19.96)	1154(28.17)	
3-7 months	39(1.92)	125(3.05)	
7-12 months	41(2.02)	85(2.08)	
1-2 years	86(4.24)	166(4.05)	
>2 years	1458(71.86)	2566(62.65)	
Condom use in last anal sex			0.1283
Yes	1550(76.39)	3056(74.61)	
No	479(23.61)	1040(23.39)	
Frequency of condom use during anal sex[ab]			0.6946
Consistent use	785(38.69)	1606(39.21)	
Inconsistent use	1244(61.31)	2490(60.79)	
Number of Sexual partners[b]			0.4535
<10	1709(84.23)	3480(84.96)	
More than 10	320(15.77)	616(15.04)	
STI[b]			0.7909
Yes	68(3.35)	132(3.22)	
No	1961(96.65)	3963(96.78)	
Inject drugs[b]			0.7625
Yes	22(1.08)	41(1.00)	
No	2007(98.92)	4053(99.00)	
Accept health service[c]			0.0001
Yes	938(46.23)	1681(41.04)	
No	1091(53.77)	2415(58.96)	
MSW[db]			0.0369
Yes	102(5.03)	159(3.88)	
No	1927(94.97)	3936(96.12)	

Abbreviations: STI, sexually transmitted infections; MSW, male sex workers.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

sTable2. Univariate and multivariate cox proportional hazard model with time-varying covariates for HIV infection risk

Variables	Univariate cox regression analysis			Multivariate cox regression analysis[e]		
	HR	95%CI	*P* value	HR	95%CI	*P* value
Age						
<45	REF					
45-60	1.14	0.78-1.69	0.4819			
>60	0.94	0.38-2.32	0.8956			
Marital status						
Married	REF			REF		
Unmarried	4.73	2.90-7.71	0.0001	4.72	2.86-7.78	0.0001
Education						
Below high school	REF			REF		
High school	0.51	0.24-1.06	0.0719	0.93	0.43-2.01	0.7619
College or more	0.29	0.13-0.63	0.0018	0.47	0.20-1.07	0.0574
Residence time in Tianjin						
<3 months	REF			REF		
3-7 months	0.52	0.12-2.19	0.3804	0.66	0.16-2.83	0.5718
7-12 months	1.71	0.72-4.05	0.2195	1.14	0.48-2.78	0.7572
1-2 years	0.27	0.06-1.14	0.0770	0.27	0.06-1.13	0.0727
>2 years	0.50	0.34-0.74	0.0005	0.68	0.46-1.07	0.0748
Condom use in last anal sex						
Yes	REF			REF		
No	12.39	8.53-17.99	0.0001	5.10	3.19-8.13	0.0001
Frequency of condom use during anal sex[ab]						
Consistent use	REF			REF		
Inconsistent use	10.13	6.14-16.69	0.0001	3.66	1.97-6.82	0.0001
Number of Sexual partners[b]						
<10	REF			REF		
More than 10	1.33	0.93-1.92	0.1173	1.53	1.05-2.24	0.0266
STI[b]						
Yes	REF					
No	0.88	0.36-2.15	0.7831			
Inject drugs[b]						
Yes	REF					
No	1.81	0.25-13.01	0.5512			
Accept health service[c]						
Yes	REF			REF		
No	1.55	0.96-2.49	0.0687	1.20	0.74-1.94	0.4501
MSW[db]						
Yes	REF			REF		
No	0.66	0.34-1.27	0.2183	1.39	0.71-2.72	0.3340

Abbreviation: STI, sexually transmitted infections; MSW, male sex workers; HR, hazard ratio; CI: confidence interval; REF, reference level.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

[e] Multivariate cox regression analysis included marital status, education, residence time in Tianjin, condom use during last sex, condom use during

anal sex, number of sexual partners, health service utilization, MSW.

sTable3. Definition of sexual behavior indicator levels

Variables	Ideal level	Risky level
Condom use in last anal sex	Yes	No
Frequency of condom use during anal sex	Consistent use	Inconsistent use
Number of sexual partners	<10	More than 10

sTable4. Total number of follow-up times among MSM in Tianjin from 2011-2019

Number of Follow-Up Times[a]	**Number of MSM** (%)	**Cumulative Percentage** (%)
2	832 (41.01)	41.01
3	378 (18.63)	59.64
4	240 (11.83)	71.46
5	142 (7.00)	78.46
6	111 (5.47)	83.93
7	67 (3.30)	87.24
8	56 (2.76)	90.00
9	25 (1.23)	91.23
10	33 (1.63)	92.85
>10	145 (7.15)	100.00
Total	2029 (100.00)	

[a] Represented the total number of follow-ups for each participant within the period from first enrollment to the last follow-up. Mean: 4.39 times; Standard Deviation: 3.96; Median: 3 times; P_{25}: 2 times; P_{75}: 5 times.

sTable5. HIV Incidence rates by year

Year	Number of MSM	HIV seroconversion	Incidence Rate (95%CI)[a]
2012[b]	454	8	2.86 (1.59-5.14)
2013	589	20	4.57 (3.31-6.31)
2014	702	18	3.43 (2.35-4.98)
2015	794	27	4.65 (3.53-6.12)
2016	860	16	2.50 (1.63-3.83)
2017	823	12	2.13 (1.29-3.53)
2018	776	10	2.27 (1.32-3.93)
2019	518	16	5.51 (3.97-7.66)

[a] When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participant in this year.

[b] The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

sTable6. HIV incidence rate among age subgroups

Age subgroup	Number of MSM	HIV seroconversion	Incidence Rate (95%CI)
<45	1504	85	3.83 (3.24-4.52)
45-60	464	37	2.81 (2.14-3.69)
>60	61	5	2.08 (0.95-4.55)

sTable7. Incidence rates for HIV infection among MSM with different follow-up times

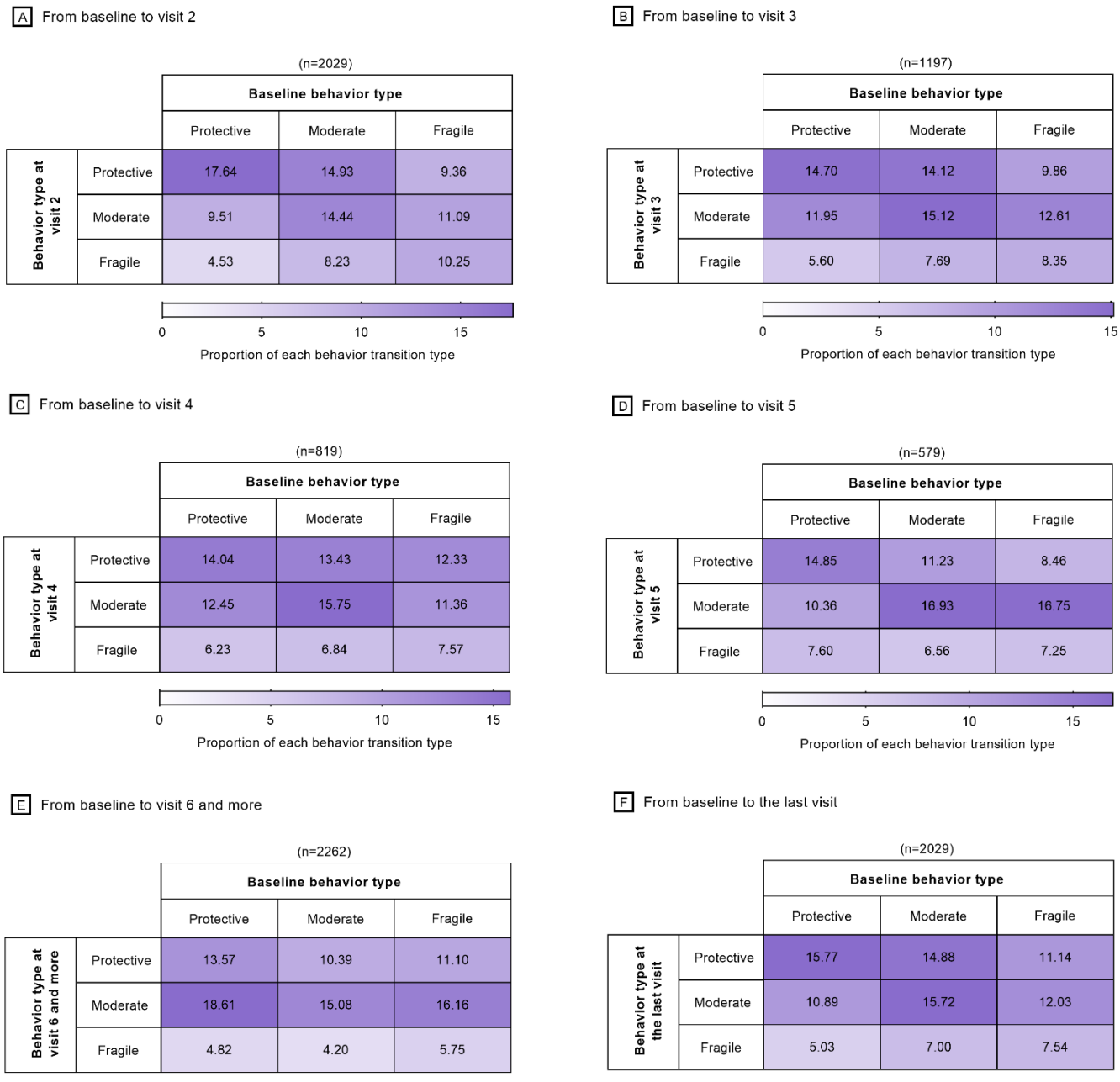
Behavior transition type		Incidence Rate Per 100 Person-Years (95%CI)			Total
		Baseline			
		Protective	Moderate	Fragile	
2 Times[a]	Protective	1.73 (0.44-6.83)	0 (0.00-0.00)	5.6 (2.39-13.12)	4.88 (3.65-6.53)
	Moderate	1.05 (0.15-7.38)	1.51 (0.38-5.97)	0.8 (0.11-5.63)	
	Fragile	10.27 (4.06-25.99)	14.07 (7.92-24.99)	16.97 (11.14-25.85)	
3 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	4.49 (3.06-6.59)
	Moderate	3.18 (0.81-12.44)	0 (0.00-0.00)	5.04 (1.67-15.18)	
	Fragile	13.83 (6.58-29.07)	21.07 (10.91-40.69)	14.73 (7.43-29.19)	
4 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	2.89 (1.72-4.84)
	Moderate	1.52 (0.22-10.63)	1.16 (0.17-8.14)	0 (0.00-0.00)	
	Fragile	15.24 (5.38-43.19)	19.03 (9.77-37.06)	9.45 (2.53-35.33)	
5 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	3.21 (1.74-5.91)
	Moderate	7.24 (1.91-27.51)	0 (0.00-0.00)	4.97 (1.29-19.19)	
	Fragile	7.86 (2.08-29.73)	22.69 (8.39-61.37)	6.92 (1.04-45.85)	
6 times And more	Protective	0 (0.00-0.00)	0.52 (0.07-3.67)	0.85 (0.21-3.38)	2.27 (1.64-3.15)
	Moderate	2.15 (0.90-5.12)	0.44 (0.06-3.11)	0.41 (0.06-2.9)	
	Fragile	16.08 (9.11-28.37)	9.92 (4.64-21.2)	13.68 (7.46-25.1)	
Overall	Protective	0.37 (0.09-1.48)	0.19 (0.03-1.35)	1.37 (0.66-2.86)	3.36 (2.83-3.99)
	Moderate	2.27 (1.27-4.07)	0.69 (0.26-1.83)	1.39 (0.67-2.9)	
	Fragile	13.18 (9.15-18.99)	15.37 (11.23-21.04)	14.51 (10.77-19.55)	
Total		3.14 (2.30-4.29)	2.92 (2.13-3.99)	4.02 (3.07-5.26)	

[a] 2 times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup.

sTable8. Behavior transition type from baseline to each visit

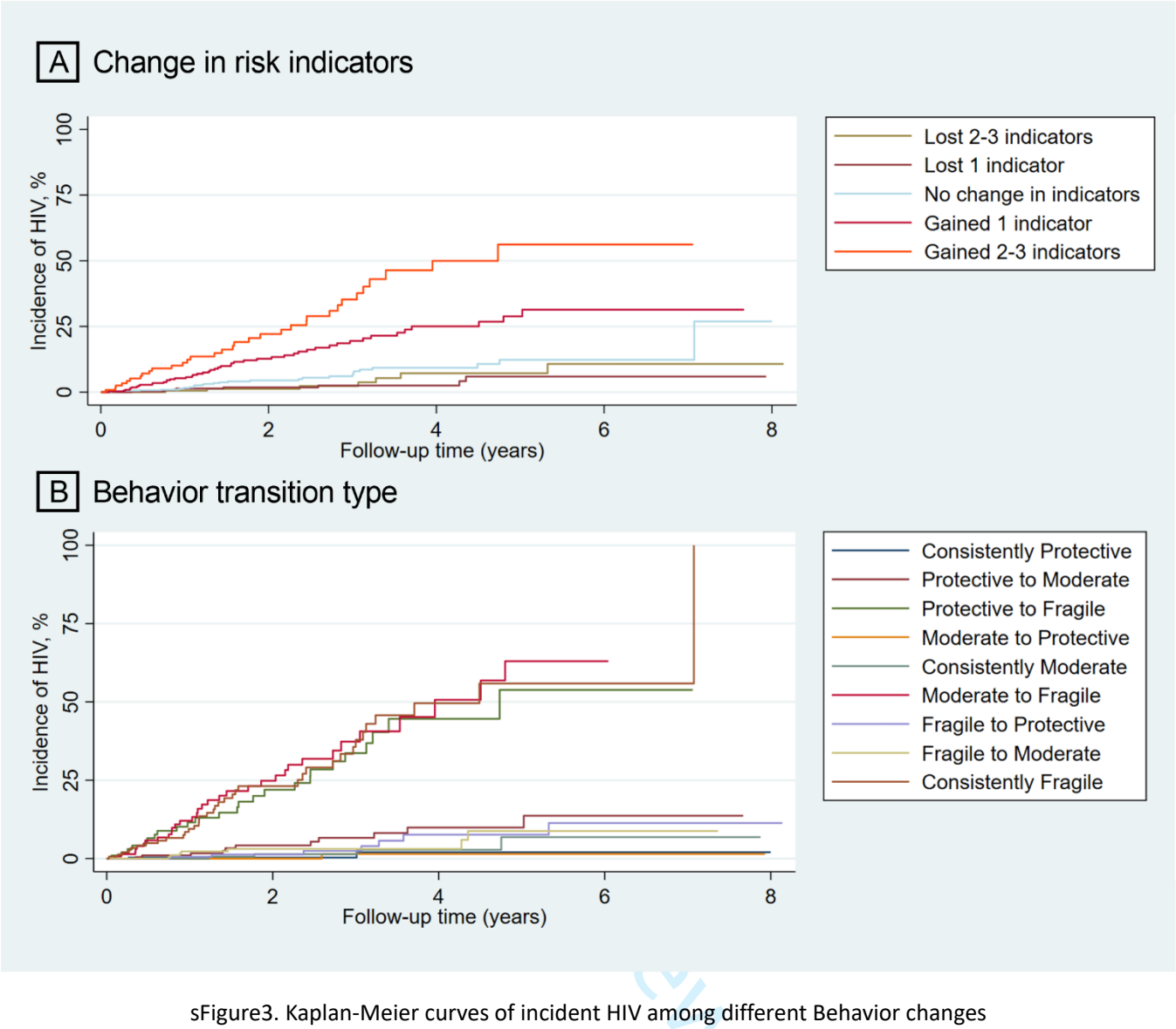
Behavior transition type in each visit[a] N (%)		Baseline			Total
		Protective	Moderate	Fragile	
2nd	Protective	358 (17.64)	303 (14.93)	190 (9.36)	851 (41.94)
	Moderate	193 (9.51)	293 (14.44)	225 (11.09)	711 (35.04)
	Fragile	92 (4.53)	167 (8.23)	208 (10.25)	467 (23.02)
3rd	Protective	176 (14.70)	169 (14.12)	118 (9.86)	463 (38.68)
	Moderate	143 (11.95)	181 (15.12)	151 (12.61)	475 (39.68)
	Fragile	67 (5.60)	92 (7.69)	100 (8.35)	259 (21.64)
4th	Protective	115 (14.04)	110 (13.43)	101 (12.33)	326 (39.80)
	Moderate	102 (12.45)	129 (15.75)	93 (11.36)	324 (39.56)
	Fragile	51 (6.23)	56 (6.84)	62 (7.57)	169 (20.63)
5th	Protective	86 (14.85)	65 (11.23)	49 (8.46)	200 (34.54)
	Moderate	60 (10.36)	98 (16.93)	97 (16.75)	255 (44.04)
	Fragile	44 (7.60)	38 (6.56)	42 (7.25)	124 (21.42)
6th And More	Protective	307 (13.57)	235 (10.39)	251 (11.10)	793 (35.06)
	Moderate	421 (18.61)	341 (15.08)	373 (16.16)	1135 (50.18)
	Fragile	109 (4.82)	92 (4.20)	130 (5.75)	334 (14.77)
Total		643 (31.69)	763 (37.60)	623 (30.70)	8915 (100.00)

[a] listed the number (proportion) of each behavior type in each visit.



sFigure2. Heatmap of percentage of each behavior transition type in each visit

Figure legends 1: Values and colors indicated the percentage of each behavior transition type in each visit (for example, in Figure 1A, 17.64 represented the percentage of “protective” to “protective” was 17.64% from baseline to visit2). A lighter color indicates that the percentage was lower for MSM in that subgroup, whereas a darker color indicated a higher percentage in that subgroup.



sFigure3. Kaplan-Meier curves of incident HIV among different Behavior changes

sTable9. OR and 95% CI for behavior transition-type of "fragile" or "moderate" in the last follow-up stratified by the behavior type categories at baseline

Behavior changes	"Fragile" or "Moderate" at the last follow-up as the dependent variable, OR (95% CI)[a]		
	Protective at baseline	Moderate at baseline	Fragile at baseline
Per 1-time increase in the total follow-up times	1.02 (0.98-1.06)	0.99 (0.95-1.03)	0.95 (0.91-0.99)
Age			
<45	REF	REF	REF
45-60	0.57 (0.37-0.87)	0.45 (0.29-0.68)	0.52 (0.35-0.78)
>60	0.48 (0.16-1.39)	0.23 (0.10-0.54)	0.71 (0.25-2.05)
Residence time in Tianjin			
<3 months	REF	REF	REF
3-7 months	0.51 (0.11-2.32)	1.31 (0.40-4.30)	3.54 (0.75-16.63)
7-12 months	1.06 (0.36-3.12)	1.53 (0.30-7.78)	1.76 (0.53-5.86)
1-2 years	1.93 (0.75-4.97)	0.89 (0.40-1.96)	1.88 (0.72-4.85)
>2 years	0.92 (0.59-1.43)	0.65 (0.45-0.99)	1.10 (0.73-1.66)

Abbreviation: OR, odds ratio; CI: confidence interval; REF, reference level.

[a] Multivariate logistic regression analysis included total follow-up times, age, marital status, education, residence time in Tianjin, health service utilization

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8, 9
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N/A
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	N/A

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sexual behavior changes and HIV infection among men who have sex with men: evidence from an open cohort in China

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Abstract

Background- The HIV epidemic in key population such as MSM is a public health issue of worldwide concern. China has seen an increasing in newly diagnosed HIV infections through male-male sexual contact in the past decade. In a long-term cohort, how the complex behavior pattern of MSM changed and the association with the HIV risk are unclear at present.

Methods- This study was conducted from October 2011 to December 2019 in Tianjin. MSM were recruited by snowball sampling through online and offline ways. Demographic and sexual behavioral data were collected for analysis. Using three indicators (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) to define the behavior change. Participants with 0, 1, and 2 or 3 risk indicators were categorized as behavior type of “protective”, “moderate”, and “fragile”. Change in behavior type between baseline and each visit was considered. Time-varying Cox models were performed to evaluate HIV infection risk.

Results- Of 2029 MSM include in the study, 127 were new HIV diagnoses. The overall incidence rate was 3.36 per 100 person-years. The percentage of “protective” and “moderate” behavior type had a conspicuous growth trend as the follow-up. Furthermore, the HIV incidence rate in each visit among different behavior transition types showed a general downward trend as the number of total follow-up times increased. Individual who remained in “fragile” (aHR, 25.86 [95%CI, 6.92-96.57]) or changed from “protective” to “moderate”, (aHR, 4.79 [95%CI, 1.18-19.47]) “protective”

to “fragile” (aHR, 23.03 [95%CI, 6.02-88.13]), “moderate” to “fragile” (aHR, 25.48 [95%CI, 6.79-95.40]) between baseline and the last follow-up had a higher HIV risk. Gained risk indicators were associated with the increase of HIV risk (gained 1 indicator, aHR: 2.67,95%CI: 1.68-4.24; gained 2 or 3 indicators, aHR, 4.99, [95%CI, 3.00-8.31]) while lost just one risk indicator could halve the risk (aHR, 0.43, [95%CI, 0.21-0.90]).

Conclusions- Among MSM in Tianjin, it is necessary to get timely behavior change for those with high-incidence behavior patterns while sustaining for those with low-incidence patterns.

Keyword: Men who have sex with men; HIV; Behavior change; Cohort study

Article summary

Strengths and limitations of this study

- This study was based on an open MSM cohort in China with long time span (2011-2019).
- Three indicators related to participants' sexual behaviors (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) were used to define the behavior change jointly.
- Associations between behavior change and risk of HIV infection were estimated through Cox models.
- Sexual behaviors were self-reported and measured retrospectively, and may have been misremembered or otherwise misreported.

Introduction

The epidemic of the human immunodeficiency virus (HIV) is a significant public health issue of worldwide concern(1-4). The prevalence of HIV have been low among the general population over the past three decades. However, the burden of HIV is disproportionately concentrated among men who have sex with men (MSM)(5-7). China's HIV epidemic began in the early 1990s among injecting drug users(8, 9). The main route of transmission was needle-sharing(10, 11). Due to China's effective legal control and intensive regulations on drugs(12, 13), the main spread route of HIV inevitably turned into sexual contact since the 21st century, especially male-to-male sexual contact(7, 14, 15). Corresponding studies aimed to ascertain the pattern of sexual behaviors among MSM had important practical significance though sexual behaviors between men were taboo both politically and by cultural tradition in China(16, 17).

Effective intervention and behavior change had been responsible for the HIV prevention successes to date(18, 19). HIV interventions typically concentrate on unprotected anal intercourse (UAI)(20), multiple sex partners(21), alcohol and drug use(13, 22), pre-exposure prophylaxis (PrEP)(23, 24) or post-exposure prophylaxis (PEP)(25, 26) utilization and adherence to antiretroviral therapy (ART)(27). It was well established from a variety of studies that timely behavior change and biomedical intervention can reduce HIV transmission(28-30). However, most studies used a single measurement to describe behavior change. In a long-term cohort, how the complex behavior pattern changed and the association with the HIV risk was largely unknown

at present.

This study was based on an open cohort among MSM in Tianjin, China, 2011-2019. The study collected each MSM's sexual behavior and HIV infection status at each visit. The aims of the present study were the following: (1) to describe the HIV incidence rate over the cohort; (2) to quantify the behavior changes over the follow-up and to address the association between behavior change and the risk of HIV infection; and (3) to explore influencing factors for progression to behavior change.

Methods

Study Design

The men who have sex with men health encouragement longitudinal project (MSMHELP) was a longitudinal cohort study among MSM launched in Tianjin, China. The main objectives of the project include: (1) establish community-based HIV prevention service stations aimed at the key population, (2) improve the accessibility and utilization of HIV testing and prevention services, (3) provide ART support services for people living with HIV. The organizations involved in the project included US Centers for Disease Control and Prevention (CDC); National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and prevention (NCAIDS/STD); Tianjin City CDC and Tianjin Shenlan Community-Based Organization (CBO). This study was registered with the Chinese Clinical Trials Registry (Identifier: ChiCTR2000039500).

Data Collection and Participants

Tianjin Shenlan CBO was a formally community-based organization that provided

community-based HIV voluntary counseling & testing (VCT) support services (including HIV testing, counseling, and psychological support) for MSM. Participants were mobilized to get tested for HIV in Shenlan's public health advisory service center. When participants came to the center for testing or counseling, experienced MSM investigators would conduct a face-to-face interview with participants in a private room. During this period, a structured questionnaire (included demographics and sexual behaviors information) was completed by the participants under the guidance of the investigators. The investigators of the organization mostly were also MSM. All investigators had undergone training before entering work, which would be a benefit for smooth unhindered communication with participants and could ensure the reliability of the results. After the interview, every participant would get several condoms and lubricant for free. Information collection adopted a real-name registration system (ID card number, mobile phone number and fingerprint information were collected). Prior to the interviews, all participants signed a written informed consent, including the objective, procedures, confidentiality and participants' rights. Enrolled participants were encouraged to routine HIV test every three months (90 days). The entire research process was supervised and coordinated by Tianjin City CDC.

The snowball sampling method was used to recruit participants. Participants were recruited from gay bars, gay bathhouses, social network sites (WeChat, QQ, gay chat website), gay apps and peer referrals. The initial enrollment took place on October 1, 2011, and follow-up ended up on December 31, 2019. Inclusion criteria were: (1) had

at least two visits during the cohort period and HIV serological test was negative when they first registered, (2) ≥ 16 years old, (3) biologically male, (4) reported anal intercourse with another man in the past six months. The participants of the cohort change dynamically, the original participants could drop out continuously, and the new participants could join at any time. Of 6565 MSM captured in this study, 4096 were excluded for having only one visit, 432 for having HIV seropositive result at baseline, and 8 for lack of behavioral information. 2029 MSM met the eligibility criteria and were included in the study eventually. The flow diagram of the study was listed in sFigure 1 in the Supplement. The comparison of baseline characteristics between included and excluded MSM were listed in sTable 1 in the Supplement.

Definitions of Behavior Changes

In this study, behavior changes include the change in the number of risk indicators and change in sexual behavior type. Sexual behavior type was used to represent different patterns of sexual behavior characteristics. It was collectively defined by three indicators related to participants' sexual behavior in the past six months. The three indicators included variables of condom use in last anal sex(31), frequency of condom use during anal sex(21), and the number of sexual partners(32). These three variables were related to the HIV infection (sTable 2 in the Supplement). Participants had the information of the three variables in each follow-up. Each indicator was divided into two levels: "ideal level" and "risk level" (sTable 3 in the Supplement). Among the three variables mentioned above, if one participant had one variable of "risk level" then meant the participant had one risk indicator, and so on. The number

of risk indicators was in the range of zero to three.

Behavior type was defined based on the risk indicators. Behavior type was categorized as “protective” if the participant had no risk indicator; as “moderate” if the participant had one risk indicator; as “fragile” if the participant had more than two risk indicators (two or three risk indicators). The behavior type and the number of risk indicators could change as time varying (during the follow-up period).

Change in the number of risk indicators was defined as the difference of risk indicators between any two follow-ups. Behavior transition type was defined as the change of behavior type between any two visits. Then the behavior transition type yielded nine possible combinations of behavior types: consistently protective, protective to moderate, protective to fragile, moderate to protective, consistently moderate, moderate to fragile, fragile to protective, fragile to moderate, consistently fragile.

HIV Laboratory Test

Before testing, MSM would choose to collect blood or saliva. Patrons’ oral mucosal exudate test (Mano Bio-Pharmaceutical Co., Ltd, Beijing, China) was used for the former and a blood rapid detection reagent (Wan Fu Biotechnology Co., Ltd, Guangzhou, China) for the latter. In addition, 5ml of blood sample was collected from those who get any positive tests above. Then, the blood sample was sent to Tianjin CDC to perform enzyme-linked immunosorbent (ELISA; Wan Tai Biological Pharmaceutical Co., Ltd, Beijing, China). HIV infection was by confirmed Western blot (WB) assay (MP Biomedical Asia Pacific Pte Ltd, Singapore). As the exact infection time

was hard to affirm, for the chronic infections (infection time over 6 months), the infection time was defined as the mid-point between last negative test date and first positive test time while the acute and early infection (<6 months) was the time diagnosed as HIV infection(33).

Statistical Methods

Category variables were described by frequencies and percentages. For the general demographic characteristics, differences were calculated using Pearson's chi-squared test or Fisher's exact test.

HIV incidence rates were estimated within each year and among subgroups of different behavior transition types in each visit, with person-year (PY) over the follow-up time as the denominator.

Change in behavior type was calculated in each visit (according to baseline behavior type). Considering that the total number of each participant was unequal, the proportion of each behavior type at each visit and the proportion of behavior transition type from baseline to each visit were calculated.

Univariate and multivariable time-varying Cox models were performed to evaluate (1) risk of HIV infection among different behavior type subgroups over each follow-up (all records of the participants were included in the model in counting process format) (2) behavior changes and association with the risk of HIV infection (two time points were opted to define the behavior change, baseline, and the last follow-up). Hazard ratios (HR), adjusted hazard ratios (aHR) and 95% confidence interval (95%CI) of the variables were estimated. The logistic regression model was applied to investigate the

influencing factors for progression to behavior type of “fragile” or “moderate” in the last follow-up among baseline behavior type subgroups. Odds ratios (OR), adjusted odds ratios (aOR) and 95% confidence interval (95%CI) were estimated. In addition, all models were adjusted for baseline covariates. All the data analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC).

Patient and public involvement

This study was mainly completed by Tianjin CDC, with Tianjin Shenlan CBO as the specific implementor of the study. Patients or the public were not directly involved in the design and implementation of the study. But the findings could influence the design of other subsequent studies, such as specific studies targeting drug users or male sex workers in the MSM population.

Results

Characteristics of the Participants

A total of 2029 MSM met the eligibility criteria and were included in the study eventually. The total follow-up person time was 3772.03 PY. The median total follow-up time was 1.28 years (interquartile range [IQR], 0.57 to 2.72; range, 8 days to 8.13 years) starting from baseline. Confirmed by the laboratory test, 127 participants were new HIV diagnoses. 63 were classified as acute and early HIV infected and 64 were chronic infected.

The characteristics of the participants when they first registered (baseline) were shown in Table 1. Among all the participants, the median age was 34 years old (P_{25},25; P_{75},45); 53.33% were unmarried; 57.76% had a high school degree; 39.48% had a

college degree or above; 71.87% had been lived in Tianjin for more than 2 years while 19.96% had been lived in Tianjin for less than 3 months; 76.39% used condom in last anal sex; 38.69% had a condom consistent use during anal sex over past six months; 84.23% had less than 10 sexual partners over past six months; 3.35% had STI over past six months; 46.23% had received HIV health service over past one year; 5.03% had been worked as MSW.

The total number of follow-up times of each participant were listed in sTable 4 in the Supplement. The median follow-up times were 3 times (range from 2 to 34, P_{25},2; P_{75},5). 41.01% of participants had 2 follow-up times; 78.46% had follow-up times no more than 5 times. Participants with a total number of follow-up times more than 10 times was 7.15%.

HIV Incidence Rate

Among the whole study population, the overall HIV incidence rate was 3.36 per 100 PY (95%CI, 2.83-3.99).

Figure 1 and sTable 5 in the Supplement showed the HIV incidence rates by years. The rates were relative higher in 2013 (4.57 per 100 PY [95%CI, 3.31-6.31]), 2015 (4.65 per 100 PY [95%CI, 3.53-6.12]) and 2019 (5.51 per 100 PY [95%CI, 3.97-7.66]), though the rates did not show a liner trend significance over 2011-2019. Among age subgroups, incidence rates were <45, 3.83 per 100 PY (95%CI, 3.24-4.52); 45-60, 2.81 per 100 PY (95%CI, 2.14-3.69); >60, 2.08 per 100 PY (95%CI, 0.95-4.55) (sTable 6 in the Supplement).

To compare the HIV incidence rate among different behavior transition types, participants were divided into subgroups according to their number of total follow-up times. The calculation of the HIV incidence rate was done within each subgroup. Stratified by the behavior type categories at baseline, the overall HIV incidence rates were: “protective”, 3.14 per 100 PY (95%CI, 2.30-4.29); “moderate”, 2.92 per 100 PY (95%CI, 2.13-3.99); “fragile”, 4.02 per 100 PY (95%CI, 3.07-5.26) (sTable 7 in the Supplement). On the whole, HIV incidence rate shown a general downward trend as the number of total follow-up times increased (2 times: 4.88 [95%CI, 3.65-6.53]; 3 times: 4.49 [95%CI, 3.06-6.59]; 4 times: 2.89 [95%CI, 1.72-4.84]; 5 times: 3.21 [95%CI, 1.74-5.91]; 6 times and more: 2.27 [95%CI, 1.64-3.15]). MSM who had more visits showed a low risk of infection in comparison with those who had fewer visits. Within each subgroup, the HIV incidence rate tended to concentrate towards the lower right corner of the heatmap (i.e., concentrate towards behavior type of “fragile”) (Figure 2).

Time-varying behavior type and risk of HIV infection

The risk of HIV infection was evaluated through Cox models with time-varying behavior types. Compared with “protective” behavior type, “moderate” behavior type (aHR, 2.22 [95%CI, 1.05-4.71]) and “fragile” behavior type (aHR, 16.53 [95%CI, 8.57-31.88]) were associated with a greater risk of HIV infection. Likewise, there was a significant and linear increase in the risk of HIV infection for each additional time-varying risk indicator (aHR, 3.37 [95%CI, 2.76-4.11]) (Table 2).

Behavior Types in Each Visit

The percentage of each behavior type ("protective", "moderate", and "fragile") at baseline were: 31.69% (643/2029), 37.60% (763/2029), and 30.70% (623/2029), respectively. As the number of follow-up visits increased, the percentage of "protective" and "moderate" had a growth trend (35.06% and 50.18% at 6th and more, respectively) while the percentage of "fragile" was declined (14.77% at 6th and more) (Figure 3).

Behavior Changes and Association with the Risk of HIV Infection from Baseline to the Last Follow-Up

The behavior types of baseline and the last follow-up was selected to evaluate the behavior changes (change in risk indicators: difference in risk indicators between baseline and the last follow-up; change in behavior type: "behavior types at baseline" to "behavior types in the last follow-up") and the association with the risk of HIV infection. The choice of two time points was based on a main argument: the pattern of behavior changes from baseline to each follow-up was relatively stable (details in sTable 8 and sFigure 2 in the Supplement). The first and the last visit were good proxy for behavior changes during follow-up.

In multivariable analysis, "no change in indicators" as the reference level, lost one risk indicator could decline the risk at 0.43 (95%CI: 0.21-0.90). While gained indicators were related to the increasing risk of HIV infection (gained one risk indicator: aHR, 2.67 [95%CI, 1.68-4.24]; gained two or three risk indicators: aHR, 4.99 [95%CI, 3.00-8.31]).

As for the different behavior transition types, the risk of HIV infection was not

statistically different from that of the consistently protective group (reference level) in the moderate to protective group (aHR, 0.65 [95%CI, 0.08-5.16]), the consistently moderate group (aHR, 1.52 [95%CI, 0.31-7.41]), the fragile to protective group (aHR, 2.87 [95%CI, 0.66-12.46]), and the fragile to moderate group (aHR, 2.66 [95%CI, 0.61-11.53]). Instead, the risk of HIV infection was distinctly greater in the protective to moderate group (aHR, 4.79 [95%CI, 1.18-19.47]), the protective to fragile group (aHR, 23.03 [95%CI, 6.02-88.13]), the moderate to fragile group (aHR, 25.48 [95%CI, 6.79-95.40]), and the consistently fragile group (aHR, 25.86 [95%CI, 6.92-96.57]) (Table 3 and sFigure3 in the Supplement).

Influencing Factors for Progression to Behavior Type of "fragile" or "moderate" in the Last Follow-Up

We also investigated which influencing factors were related to the progression of behavior transition type of "fragile" or "moderate" by the end of follow-up among baseline behavior type subgroups.

Within age subgroups, the younger participants had a higher likelihood of progression to behavior type of "fragile" or "moderate" by the end of follow-up.

Notably, the likelihood of progression to behavior type of "fragile" or "moderate" was weakened as the number of total follow-up times increasing (per 1-time increase in the total follow-up times, aOR, 0.95 [95CI%, 0.91-0.99]) among participants "fragile" at baseline.

Compared with participants who lived in Tianjin less than three months, participants who lived in Tianjin for more than two years had a lower likelihood of

progression to behavior type of “fragile” or “moderate” by the end of follow-up (aOR, 0.65 [95CI%, 0.37-0.87]) (sTable 9).

Discussion

The characteristics of MSM are mainly high mobility and concealment. It was a challenge to ensure long-term cohort retention and sustain routine HIV test programs among this population. Therefore, we conducted an open cohort study among MSM in Tianjin, China. 2029 MSM were included in the study eventually from 2011-2019. Among the whole study population, the overall HIV incidence rate was 3.36 per 100 PY (95%CI, 2.83-3.99). The incidence rate was at a lower level. Previous studies conducted in other cities in China had shown a pretty high HIV incidence among MSM, 6.6 per 100 PY in Hangzhou(34), 6.78 per 100 PY in Yangzhou, 5.77 per 100 PY in Guangzhou(35), 5.3 per 100 PY in Shenyang(36), 5.12 per 100 PY in Nanjing(37), 3.5 per 100 PY in Yunnan(38) and 7.1 per 100 PY in Beijing(39). The incidence is also at a low level compared with related studies in other regions (sub-Saharan Africa(40), Latin American(41), and United States(42-44)). In this study, the percentage of “protective” and “moderate” behavior types had a conspicuous growth trend as the follow-up. Furthermore, the HIV incidence rate in each visit among different behavior transition types showed a general downward trend as the number of total follow-up times increased. The evidence mentioned above indicated the effectiveness of the community-based VCT project in reducing HIV incidence. However, challenges still existed and need to be addressed. The incidence rate in 2019 was much higher than in other years (5.51 per 100 PY [95%CI, 3.97-7.66]). We speculated that the reason might be the publicity and promotion of PrEP/PEP started in 2018 among the MSM population in Tianjin. PrEP/PEP were effective biomedical strategies to prevent the

further transmission of HIV(23, 24). Although the utilization of PrEP/PEP was not widespread among MSM in Tianjin, this might promote the cognitive concepts of "treatment optimism" about HIV(45). MSM might rationalize their risk behavior before (or after) engaging in sexual behaviors(46), which promoted the generate of risk behaviors(47, 48).

Previous studies concentrate on using one stand-alone indicator to describe the behavior change. For example, one study in China(49) used the percentage of unprotected anal intercourse (UAI) occurrence to describe the behavior change. However, this study evaluated behavior change with greater precision (behavior changes were collectively defined by three indicators and divided into two patterns: change in the number of risk indicators and behavior transition type) among a great sample size (N=2029) in a long-term follow-up (2011-2019). What's more, this study quantified the behavior changes and association with the risk of HIV infection from baseline to the last follow-up. The results of this study showed, individual who remained "fragile" or changed from "protective" to "moderate", "protective" to "fragile", "moderate" to "fragile" between baseline and the last follow-up had a higher HIV risk as compared with individuals with persistently "protective". When this analysis was conducted in risk indicators, similar results were found. Gained risk indicators were associated with the increase of HIV risk while lost just one risk indicator could halve the risk (aHR:0.43). This study demonstrated the importance of maintaining protective sexual practices and timely behavior changes in high-incidence population could help reduce the risk of HIV infection.

The cohort had a high rate of loss to follow-up (for 4096 MSM only one visit record), which may have biased the results. Indeed, the complexity of the MSM population made maintaining a long-term follow-up cohort difficult. This study was based on an open cohort whose main purpose was to cover as many MSM as possible. Whether or not a participant will proceed to the next visit is entirely driven by their personal endogenous motivation, although messages were sent to MSM 90 days after their testing to remind them to perform another HIV testing. In the future, plans of following research including recruit more staff are under consideration. Special staff will conduct regular return visits and urge MSM to carry out routine HIV testing.

Limitations

This research has several limitations. First, in our study, the snowball sampling method was used to recruit participants, which may have selection bias. However, we recruited participants in a variety of ways (gay bars, gay bathhouses, social network sites, gay apps and peer referrals) to increase the representativeness. Second, our data lacked information on the use of alcohol, recreational drugs and PrEP usage. The presence of these substances might affect the sexual behavior of participants, which should be addressed in future research. Further, our data collection adopted a real-name registration system (ID card number, mobile phone number and fingerprint information were involved). Due to the privacy of some questions (such as whether you had ever had STI), the participants might have concealed the actual situation which may result in social expectation bias. We conducted an interview-style questionnaire collection to avoid this. Besides, all MSM investigators had received

professional training to ensure the authenticity of the data.

Conclusion

In this study, sexual behavior changes are collectively defined by three indicators (condom use in last anal sex, frequency of condom use during anal sex, and the number of sexual partners) related to participants' sexual behavior in the past six months. Behavior changes from 2011-2019 and ensuing HIV infection risk are calculated. Long-term sexual behavior patterns of MSM keep changing and gradually have a tendency to be less risky during the study period. The proportion of high-risk behavior pattern is 30.70% at baseline. This number decline to 14.77% at visit 6 and more. This result may provide clues for the effectiveness of community-based HIV/AIDS interventions.

Transition from low-incidence population to high- incidence is associated with a similar risk of HIV infection than continuing high- incidence. Further strategies are needed to promote the low-incidence change.

MSM should sustain low-incidence behavior patterns otherwise would undergo higher HIV infection risk. Future HIV interventions should prioritize not only to those MSM who were high-incidence population, but also to those MSM who have temporarily low-incidence but are at risk of switching to high-incidence population.

Contributorship

Zeyang Yu (ZY), Changping Li (CL), Zhuang Cui (ZC), Yuanyuan Liu (YL), and Jun Ma (JM) contributed to the conception of the study. Huijie Huang (HH), Tiantian Zhang (TZ) and Desheng Song (DS) contributed to the framework of the study. Maohe Yu (MY) and Jie Yang (JY) collected the data. Qinxue Chang (QC) and Xiaomeng Wang (XW) cleared the raw data. HH and Honglu Zhang (HZ) helped perform the analysis with constructive discussions. TZ and ZY analyzed the data and wrote the manuscript. ZC revised the manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethics approval

This study was reviewed and approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, China CDC [IRB approve number: X130205267].

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Data sharing

No additional data available

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Table1. Characteristics and sexual behaviors at baseline for MSM with HIV infection or negative HIV test

Variables at Baseline	Total N (%)	HIV Infection N (%)	HIV Negative N (%)
Age			
<45	1504 (74.13)	96 (75.59)	1408 (74.03)
45-60	464 (22.87)	27 (21.16)	437 (22.98)
>60	61 (3.01)	4 (3.15)	57 (3.00)
Marital status			
Married	947 (46.67)	70 (55.12)	877 (46.11)
Unmarried	1082 (53.33)	57 (44.88)	1025 (53.89)
Education			
Below high school	56 (2.76)	5 (3.94)	51 (2.68)
High school	1172 (57.76)	90 (70.87)	1082 (56.89)
College or more	801 (39.48)	32 (25.20)	769 (40.43)
Residence time in Tianjin			
<3 months	405 (19.96)	41 (32.28)	364 (19.14)
3-7 months	39 (1.92)	2 (1.57)	37 (1.74)
7-12 months	41 (2.02)	5 (3.94)	36 (1.89)
1-2 years	86 (4.24)	2 (1.57)	84 (72.61)
>2 years	1458 (71.86)	77 (60.63)	1381 (72.61)
Condom use in last anal sex			
Yes	1550 (76.39)	78 (61.42)	1472 (77.39)
No	479 (23.61)	49 (38.58)	430 (22.61)
Frequency of condom use during anal sex[ab]			
Consistent use	785 (38.69)	43 (33.86)	742 (39.01)
Inconsistent use	1244 (61.31)	84 (66.14)	1160 (60.99)
Number of Sexual partners[b]			
<10	1709 (84.23)	116 (91.34)	1593 (83.75)
More than 10	320 (15.77)	11 (8.66)	309 (16.25)
STI[b]			
Yes	68 (3.35)	2 (1.57)	66 (3.47)
No	1961 (96.65)	125 (98.43)	1836 (96.53)
Inject drugs[b]			
Yes	22 (1.08)	2 (1.57)	20 (1.05)
No	2007 (98.92)	125 (98.43)	1882 (98.94)
Accept health service[c]			
Yes	938 (46.23)	53 (41.73)	885 (46.50)
No	1091 (53.77)	74 (58.27)	1017 (53.50)
MSW[db]			
Yes	102 (5.03)	5 (3.94)	97 (5.10)
No	1927 (94.97)	122 (96.06)	1805 (94.90)

Abbreviations: STI, sexually transmitted infections; MSW, male sex workers.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

Table2. Univariate and multivariable Cox proportional hazard model with time-varying covariates for HIV infection

HIV infection risk models[a]	Per 1-risk indicator increase[b]	Categories of sexual behavior type		
		Protective	Moderate	Fragile
HR (95%CI)	3.68 (3.03-4.46)	REF	2.38 (1.12-5.02)	19.74 (10.28-37.91)
adjusted HR (95%CI)[c]	3.37 (2.76-4.11)	REF	2.22 (1.05-4.71)	16.53 (8.57-31.88)

Abbreviations: HR, hazard ratio; 95%CI, 95% confidence interval; REF, reference level.

[a] All follow-up records of each participants were included into the model in counting process format.

[b] The number of risk indicators were in range of 0 to 3. Per 1-risk indicator increase meant the number of indicators were included into the model as a continuous variable.

[c] Multivariable Cox regression analysis was adjusted for age, education, marital status, residence time in Tianjin, MSW.

Table3. Behavior changes and association with the risk of HIV infection between baseline and the last follow-up

Behavior changes[a]	HIV infection status (N, %)		Univariate Cox regression analysis			Multivariable Cox regression analysis[b]		
	Negative	HIV	HR	95%CI	*P* value	aHR	95%CI	*P* value
Change in risk indicators								
Lost 2-3 indicators	236 (12.4)	7 (5.5)	0.56	0.25-1.27	0.1680	0.57	0.25-1.29	0.1822
Lost 1 indicator	525 (27.6)	9 (7.1)	0.41	0.19-0.86	0.0182	0.43	0.21-0.90	0.0251
No change in indicators	725 (38.1)	30 (23.6)	REF			REF		
Gained 1 indicator	325 (17.1)	48 (37.8)	2.82	1.78-4.46	0.0001	2.67	1.68-4.24	0.0001
Gained 2-3 indicators	91 (4.8)	33 (26.0)	6.13	3.73-10.08	0.0001	4.99	3.00-8.31	0.0001
Behavior transition type								
Consistently Protective	318 (16.7)	2 (1.6)	REF			REF		
Protective to Moderate	210 (11.0)	11 (8.7)	4.78	1.18-19.26	0.0275	4.79	1.18-19.47	0.0283
Protective to Fragile	77 (4.0)	25 (19.7)	28.76	7.66-108.05	0.0001	23.03	6.02-88.13	0.0001
Moderate to Protective	301 (16.0)	1 (0.8)	0.64	0.08-5.03	0.6703	0.65	0.08-5.16	0.6912
Consistently Moderate	315 (16.6)	4 (3.1)	1.62	0.33-7.84	0.5449	1.52	0.31-7.41	0.6019
Moderate to Fragile	109 (5.7)	33 (26.0)	34.32	9.27-127.06	0.0001	25.48	6.79-95.40	0.0001
Fragile to Protective	219 (11.5)	7 (5.5)	2.95	0.68-12.67	0.1457	2.87	0.66-12.46	0.1590
Fragile to Moderate	237 (12.5)	7 (5.5)	3.06	0.71-13.17	0.1316	2.66	0.61-11.53	0.1906
Consistently Fragile	116 (6.1)	37 (29.1)	31.43	8.53-115.75	0.0001	25.86	6.92-96.57	0.0001
Total	1902	127						

Abbreviation: HR, hazard ratio; CI: confidence interval; REF, reference level.

[a] Two time points (baseline and the last follow-up) were opted to evaluate behavior changes.

[b] Multivariable Cox regression analysis was adjusted for age, education, marital status, residence time in Tianjin, MSW.

Figure legends:

Figure1. HIV Incidence rates by year

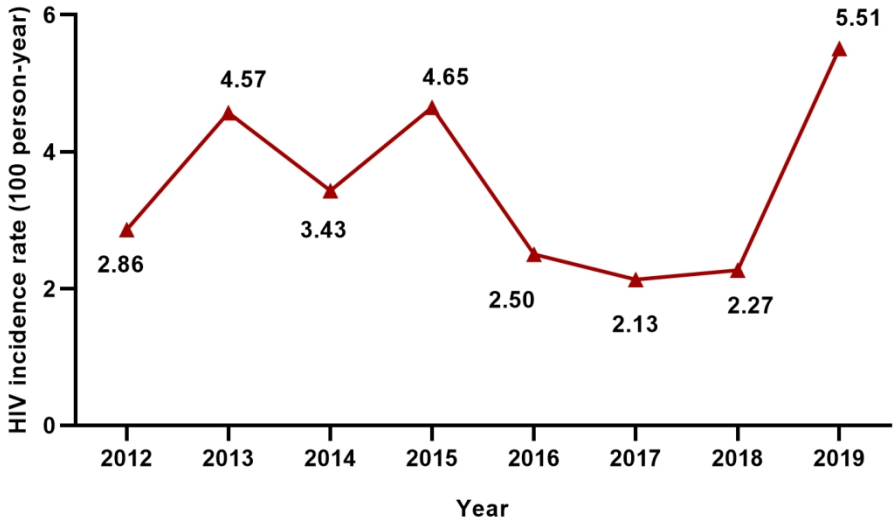
Figure legend 1: When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participant in this year. The first people newly diagnosed with HIV occurred in 2012, though the study started in 2011.

Figure2. Heatmap of HIV incidence rates among MSM with different follow-up times

Figure legend 2: MSM with 2 follow-up times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup. Values and colors indicated HIV incidence rate per 100 PY (for example, in Figure 2A, 0.37 represented the HIV incidence rate in "protective" to "protective" group was 0.37 per 100 PY). A lighter color indicates that the HIV incidence rate was lower for MSM in that subgroup, whereas a darker color indicated a higher incidence rate in that subgroup.

Figure3. Percentage of behavior type in each visit

Figure legend 3: Values and area of the rectangles indicated percentage of behavior type in each visit (for example, in Figure 3, 31.69 represented the percentage of "protective" behavior type was 31.69% at baseline).



When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participants in this year. The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

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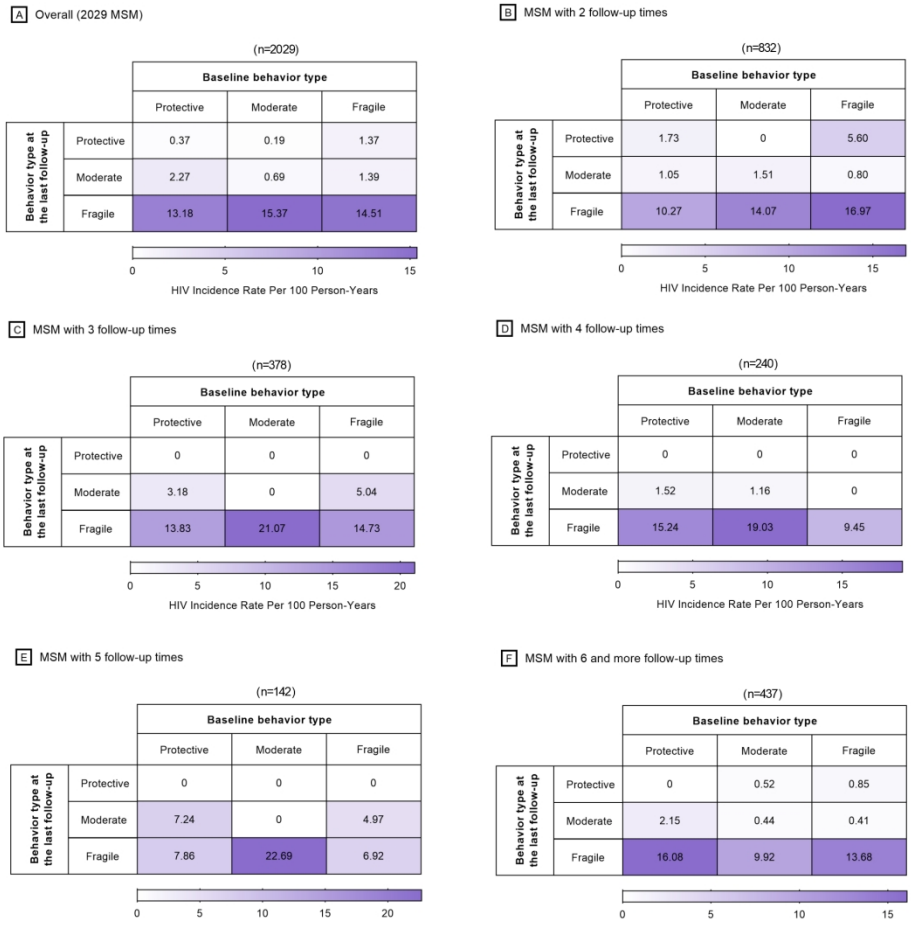

MSM with 2 follow-up times times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup. Values and colors indicated HIV incidence rate per 100 PY (for example, in Figure 2A, 0.37 represented the HIV incidence rate in "protective" to "protective" group was 0.37 per 100 PY). A lighter color indicates that the HIV incidence rate was lower for MSM in that subgroup, whereas a darker color indicated a higher incidence rate in that subgroup.

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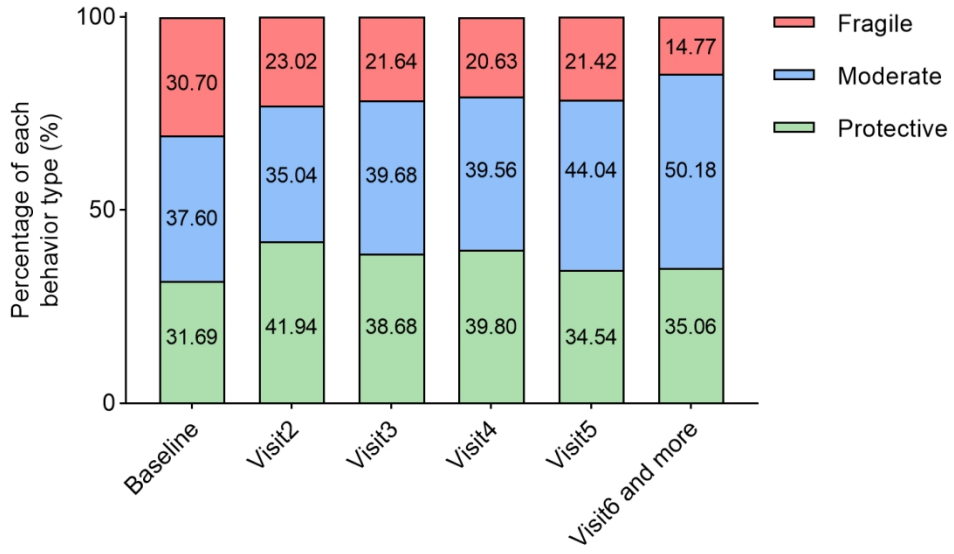
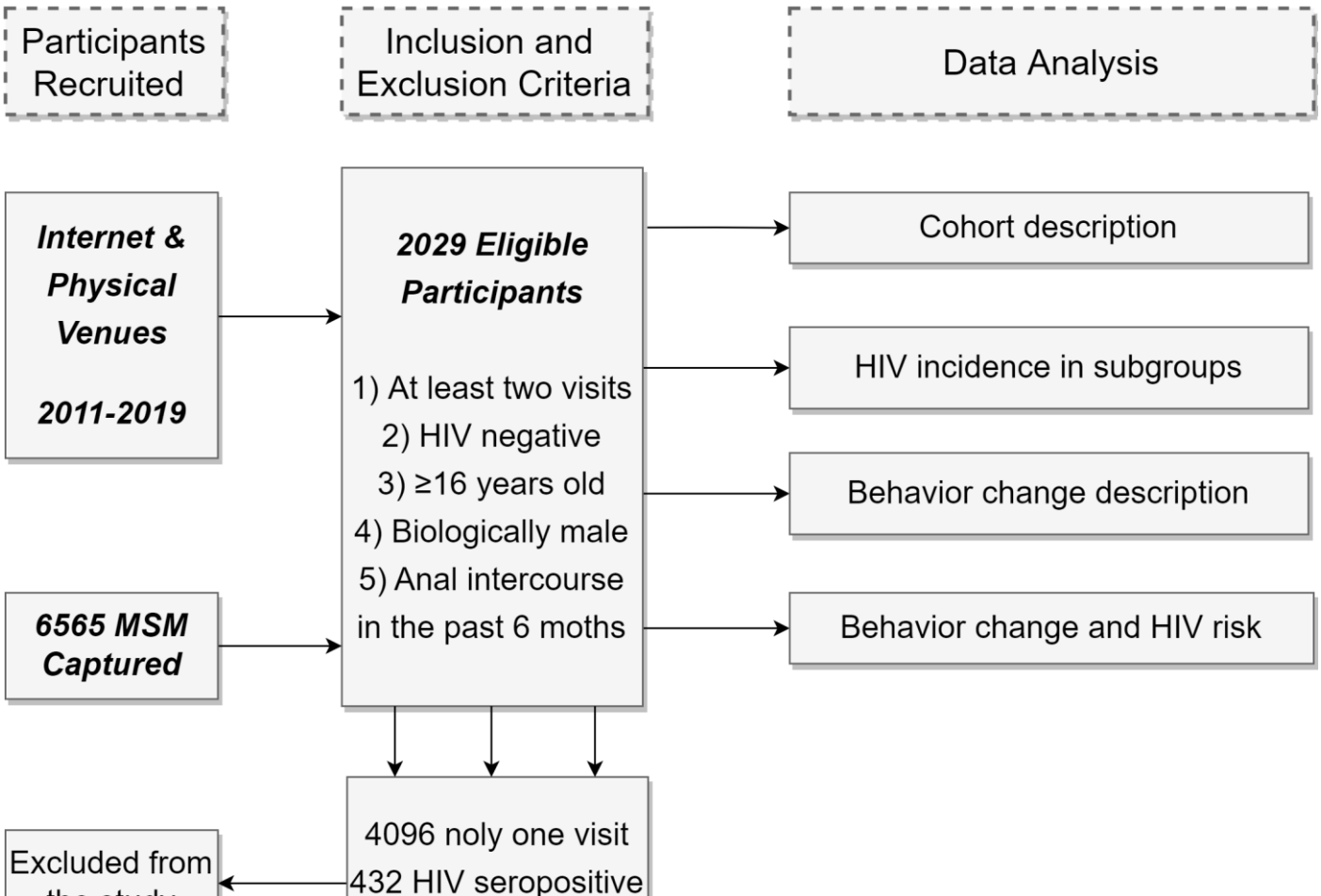


Values and area of the rectangles indicated percentage of behavior type in each visit (for example, in Figure 3, 31.69 represented the percentage of "protective" behavior type was 31.69% at baseline).

130x80mm (300 x 300 DPI)

Contents



sFigure1. Flow diagram of the study

sTable1. Characteristics of excluded and included study participants at baseline

Variables at Baseline	Included (N=2029) N (%)	Excluded (N=4096) N (%)	*P*
Age			0.1555
<45	1504(74.13)	3098(75.63)	
45-60	464(22.87)	856(20.90)	
>60	61(3.01)	142(3.47)	
Marital status			0.0198
Married	947(46.67)	1783(43.53)	
Unmarried	1082(53.33)	2313(56.47)	
Education			0.6467
Below high school	56(2.76)	125(3.05)	
High school	1172(57.76)	2322(56.69)	
College or more	801(39.48)	1649(40.26)	
Residence time in Tianjin			0.0001
<3 months	405(19.96)	1154(28.17)	
3-7 months	39(1.92)	125(3.05)	
7-12 months	41(2.02)	85(2.08)	
1-2 years	86(4.24)	166(4.05)	
>2 years	1458(71.86)	2566(62.65)	
Condom use in last anal sex			0.1283
Yes	1550(76.39)	3056(74.61)	
No	479(23.61)	1040(23.39)	
Frequency of condom use during anal sex[ab]			0.6946
Consistent use	785(38.69)	1606(39.21)	
Inconsistent use	1244(61.31)	2490(60.79)	
Number of Sexual partners[b]			0.4535
<10	1709(84.23)	3480(84.96)	
More than 10	320(15.77)	616(15.04)	
STI[b]			0.7909
Yes	68(3.35)	132(3.22)	
No	1961(96.65)	3963(96.78)	
Inject drugs[b]			0.7625
Yes	22(1.08)	41(1.00)	
No	2007(98.92)	4053(99.00)	
Accept health service[c]			0.0001
Yes	938(46.23)	1681(41.04)	
No	1091(53.77)	2415(58.96)	
MSW[db]			0.0369
Yes	102(5.03)	159(3.88)	
No	1927(94.97)	3936(96.12)	

Abbreviations: STI, sexually transmitted infections; MSW, male sex workers.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

sTable2. Univariate and multivariate cox proportional hazard model with time-varying covariates for HIV infection risk

Variables	Univariate cox regression analysis			Multivariate cox regression analysis[e]		
	HR	95%CI	*P* value	HR	95%CI	*P* value
Age						
<45	REF					
45-60	1.14	0.78-1.69	0.4819			
>60	0.94	0.38-2.32	0.8956			
Marital status						
Married	REF			REF		
Unmarried	4.73	2.90-7.71	0.0001	4.72	2.86-7.78	0.0001
Education						
Below high school	REF			REF		
High school	0.51	0.24-1.06	0.0719	0.93	0.43-2.01	0.7619
College or more	0.29	0.13-0.63	0.0018	0.47	0.20-1.07	0.0574
Residence time in Tianjin						
<3 months	REF			REF		
3-7 months	0.52	0.12-2.19	0.3804	0.66	0.16-2.83	0.5718
7-12 months	1.71	0.72-4.05	0.2195	1.14	0.48-2.78	0.7572
1-2 years	0.27	0.06-1.14	0.0770	0.27	0.06-1.13	0.0727
>2 years	0.50	0.34-0.74	0.0005	0.68	0.46-1.07	0.0748
Condom use in last anal sex						
Yes	REF			REF		
No	12.39	8.53-17.99	0.0001	5.10	3.19-8.13	0.0001
Frequency of condom use during anal sex[ab]						
Consistent use	REF			REF		
Inconsistent use	10.13	6.14-16.69	0.0001	3.66	1.97-6.82	0.0001
Number of Sexual partners[b]						
<10	REF			REF		
More than 10	1.33	0.93-1.92	0.1173	1.53	1.05-2.24	0.0266
STI[b]						
Yes	REF					
No	0.88	0.36-2.15	0.7831			
Inject drugs[b]						
Yes	REF					
No	1.81	0.25-13.01	0.5512			
Accept health service[c]						
Yes	REF			REF		
No	1.55	0.96-2.49	0.0687	1.20	0.74-1.94	0.4501
MSW[db]						
Yes	REF			REF		
No	0.66	0.34-1.27	0.2183	1.39	0.71-2.72	0.3340

Abbreviation: STI, sexually transmitted infections; MSW, male sex workers; HR, hazard ratio; CI: confidence interval; REF, reference level.

[a] The frequency of condom use during anal sex in the past 6 months was divided into two categories, consistent use (When engaging in anal intercourse, condoms were used in more than 80% of cases and condoms were used throughout the sex) and inconsistent use (other cases).

[b] In the past 6 months.

[c] Health service represented whether participants had accepted any HIV related health service (HIV testing, condom distribution, HIV risk reducing consult, peer education or HIV infection risk assessment) in the past 12 months.

[d] MSW stands for male sex workers. It represented if the participants have been obtained money or goods through sexual activity.

[e] Multivariate cox regression analysis included marital status, education, residence time in Tianjin, condom use during last sex, condom use during

anal sex, number of sexual partners, health service utilization, MSW.

sTable3. Definition of sexual behavior indicator levels

Variables	Ideal level	Risky level
Condom use in last anal sex	Yes	No
Frequency of condom use during anal sex	Consistent use	Inconsistent use
Number of sexual partners	<10	More than 10

sTable4. Total number of follow-up times among MSM in Tianjin from 2011-2019

Number of Follow-Up Times[a]	**Number of MSM** (%)	**Cumulative Percentage** (%)
2	832 (41.01)	41.01
3	378 (18.63)	59.64
4	240 (11.83)	71.46
5	142 (7.00)	78.46
6	111 (5.47)	83.93
7	67 (3.30)	87.24
8	56 (2.76)	90.00
9	25 (1.23)	91.23
10	33 (1.63)	92.85
>10	145 (7.15)	100.00
Total	2029 (100.00)	

[a] Represented the total number of follow-ups for each participant within the period from first enrollment to the last follow-up. Mean: 4.39 times; Standard Deviation: 3.96; Median: 3 times; P_{25}: 2 times; P_{75}: 5 times.

sTable5. HIV Incidence rates by year

Year	Number of MSM	HIV seroconversion	Incidence Rate (95%CI)[a]
2012[b]	454	8	2.86 (1.59-5.14)
2013	589	20	4.57 (3.31-6.31)
2014	702	18	3.43 (2.35-4.98)
2015	794	27	4.65 (3.53-6.12)
2016	860	16	2.50 (1.63-3.83)
2017	823	12	2.13 (1.29-3.53)
2018	776	10	2.27 (1.32-3.93)
2019	518	16	5.51 (3.97-7.66)

[a] When calculating the incidence rate, numerator was the number of HIV infection in each year and denominator was the sum of total actual survival time of each participant in this year.

[b] The first case of HIV seroconversion occurred in 2012, though the study started in 2011.

sTable6. HIV incidence rate among age subgroups

Age subgroup	Number of MSM	HIV seroconversion	Incidence Rate (95%CI)
<45	1504	85	3.83 (3.24-4.52)
45-60	464	37	2.81 (2.14-3.69)
>60	61	5	2.08 (0.95-4.55)

sTable7. Incidence rates for HIV infection among MSM with different follow-up times

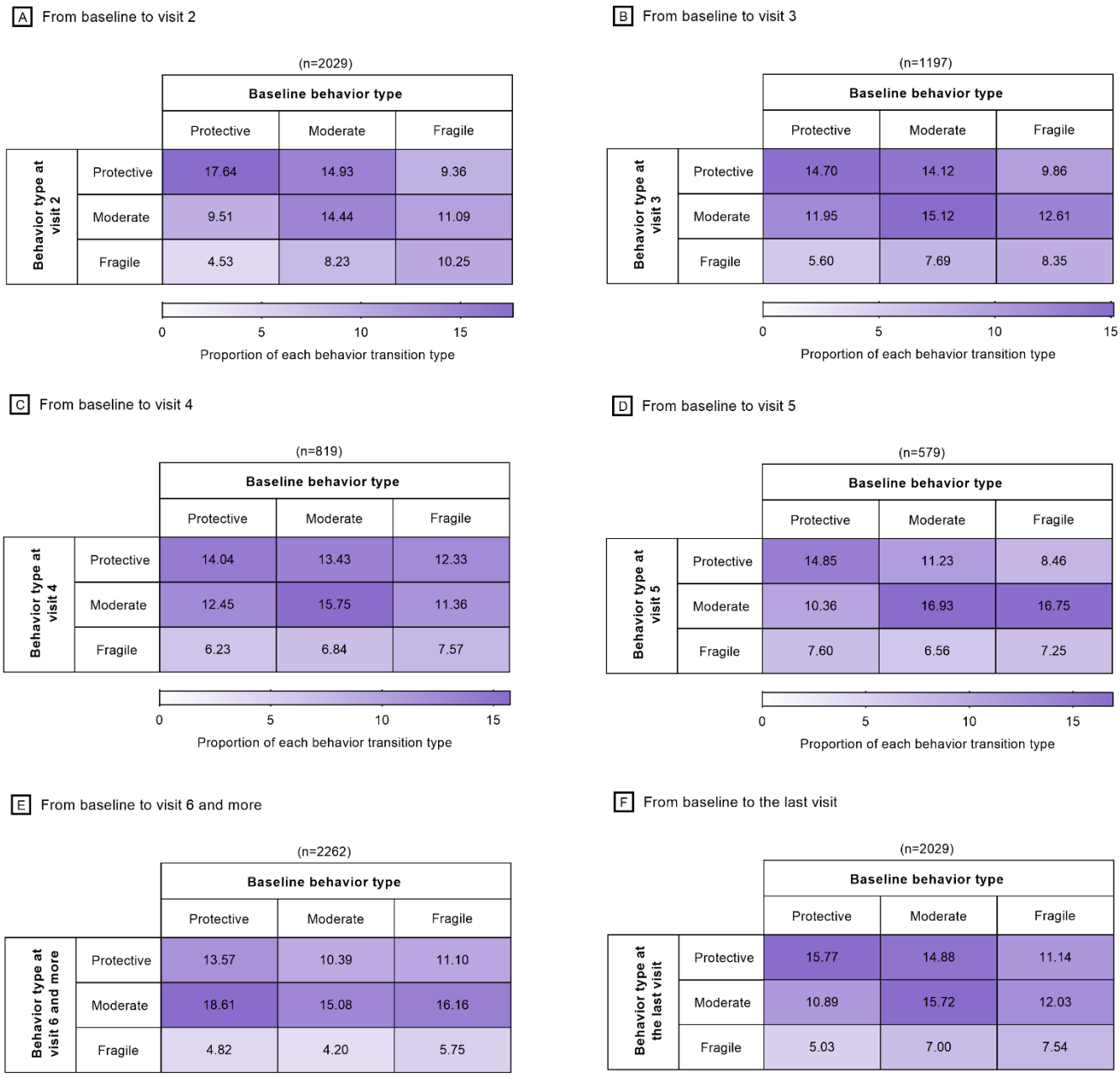
Behavior transition type		Incidence Rate Per 100 Person-Years (95%CI)			Total
		Baseline			
		Protective	Moderate	Fragile	
2 Times[a]	Protective	1.73 (0.44-6.83)	0 (0.00-0.00)	5.6 (2.39-13.12)	4.88 (3.65-6.53)
	Moderate	1.05 (0.15-7.38)	1.51 (0.38-5.97)	0.8 (0.11-5.63)	
	Fragile	10.27 (4.06-25.99)	14.07 (7.92-24.99)	16.97 (11.14-25.85)	
3 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	4.49 (3.06-6.59)
	Moderate	3.18 (0.81-12.44)	0 (0.00-0.00)	5.04 (1.67-15.18)	
	Fragile	13.83 (6.58-29.07)	21.07 (10.91-40.69)	14.73 (7.43-29.19)	
4 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	2.89 (1.72-4.84)
	Moderate	1.52 (0.22-10.63)	1.16 (0.17-8.14)	0 (0.00-0.00)	
	Fragile	15.24 (5.38-43.19)	19.03 (9.77-37.06)	9.45 (2.53-35.33)	
5 Times	Protective	0 (0.00-0.00)	0 (0.00-0.00)	0 (0.00-0.00)	3.21 (1.74-5.91)
	Moderate	7.24 (1.91-27.51)	0 (0.00-0.00)	4.97 (1.29-19.19)	
	Fragile	7.86 (2.08-29.73)	22.69 (8.39-61.37)	6.92 (1.04-45.85)	
6 times And more	Protective	0 (0.00-0.00)	0.52 (0.07-3.67)	0.85 (0.21-3.38)	2.27 (1.64-3.15)
	Moderate	2.15 (0.90-5.12)	0.44 (0.06-3.11)	0.41 (0.06-2.9)	
	Fragile	16.08 (9.11-28.37)	9.92 (4.64-21.2)	13.68 (7.46-25.1)	
Overall	Protective	0.37 (0.09-1.48)	0.19 (0.03-1.35)	1.37 (0.66-2.86)	3.36 (2.83-3.99)
	Moderate	2.27 (1.27-4.07)	0.69 (0.26-1.83)	1.39 (0.67-2.9)	
	Fragile	13.18 (9.15-18.99)	15.37 (11.23-21.04)	14.51 (10.77-19.55)	
Total		3.14 (2.30-4.29)	2.92 (2.13-3.99)	4.02 (3.07-5.26)	

[a] 2 times represented the participants whose number of total follow-up times was 2, and so on. Participants were divided into subgroups according to their number of total follow-up times. The calculation of HIV incidence rate was done within each subgroup.

sTable8. Behavior transition type from baseline to each visit

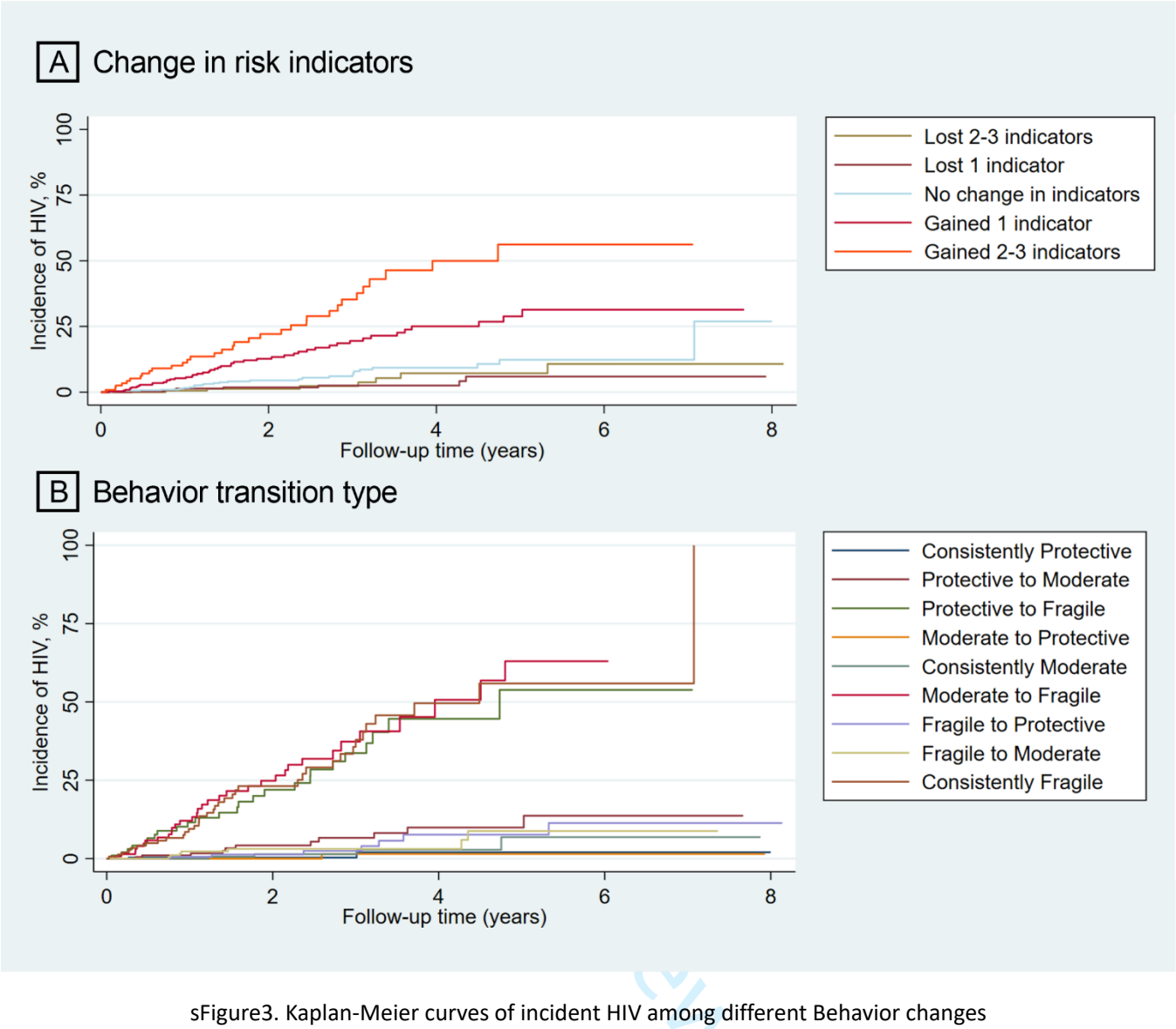
Behavior transition type in each visit[a] N (%)		Baseline			Total
		Protective	Moderate	Fragile	
2nd	Protective	358 (17.64)	303 (14.93)	190 (9.36)	851 (41.94)
	Moderate	193 (9.51)	293 (14.44)	225 (11.09)	711 (35.04)
	Fragile	92 (4.53)	167 (8.23)	208 (10.25)	467 (23.02)
3rd	Protective	176 (14.70)	169 (14.12)	118 (9.86)	463 (38.68)
	Moderate	143 (11.95)	181 (15.12)	151 (12.61)	475 (39.68)
	Fragile	67 (5.60)	92 (7.69)	100 (8.35)	259 (21.64)
4th	Protective	115 (14.04)	110 (13.43)	101 (12.33)	326 (39.80)
	Moderate	102 (12.45)	129 (15.75)	93 (11.36)	324 (39.56)
	Fragile	51 (6.23)	56 (6.84)	62 (7.57)	169 (20.63)
5th	Protective	86 (14.85)	65 (11.23)	49 (8.46)	200 (34.54)
	Moderate	60 (10.36)	98 (16.93)	97 (16.75)	255 (44.04)
	Fragile	44 (7.60)	38 (6.56)	42 (7.25)	124 (21.42)
6th And More	Protective	307 (13.57)	235 (10.39)	251 (11.10)	793 (35.06)
	Moderate	421 (18.61)	341 (15.08)	373 (16.16)	1135 (50.18)
	Fragile	109 (4.82)	92 (4.20)	130 (5.75)	334 (14.77)
Total		643 (31.69)	763 (37.60)	623 (30.70)	8915 (100.00)

[a] listed the number (proportion) of each behavior type in each visit.



sFigure2. Heatmap of percentage of each behavior transition type in each visit

Figure legends 1: Values and colors indicated the percentage of each behavior transition type in each visit (for example, in Figure 1A, 17.64 represented the percentage of “protective” to “protective” was 17.64% from baseline to visit2). A lighter color indicates that the percentage was lower for MSM in that subgroup, whereas a darker color indicated a higher percentage in that subgroup.



sFigure3. Kaplan-Meier curves of incident HIV among different Behavior changes

sTable9. OR and 95% CI for behavior transition-type of "fragile" or "moderate" in the last follow-up stratified by the behavior type categories at baseline

Behavior changes	"Fragile" or "Moderate" at the last follow-up as the dependent variable, OR (95% CI)[a]		
	Protective at baseline	Moderate at baseline	Fragile at baseline
Per 1-time increase in the total follow-up times	1.02 (0.98-1.06)	0.99 (0.95-1.03)	0.95 (0.91-0.99)
Age			
<45	REF	REF	REF
45-60	0.57 (0.37-0.87)	0.45 (0.29-0.68)	0.52 (0.35-0.78)
>60	0.48 (0.16-1.39)	0.23 (0.10-0.54)	0.71 (0.25-2.05)
Residence time in Tianjin			
<3 months	REF	REF	REF
3-7 months	0.51 (0.11-2.32)	1.31 (0.40-4.30)	3.54 (0.75-16.63)
7-12 months	1.06 (0.36-3.12)	1.53 (0.30-7.78)	1.76 (0.53-5.86)
1-2 years	1.93 (0.75-4.97)	0.89 (0.40-1.96)	1.88 (0.72-4.85)
>2 years	0.92 (0.59-1.43)	0.65 (0.45-0.99)	1.10 (0.73-1.66)

Abbreviation: OR, odds ratio; CI: confidence interval; REF, reference level.

[a] Multivariate logistic regression analysis included total follow-up times, age, marital status, education, residence time in Tianjin, health service utilization

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8, 9
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N/A
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	N/A

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.