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Impact of Mail Order Pharmacy Use and Travel Time to Pharmacy on Viral Suppression among People Living with HIV

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Abstract

This study aimed to evaluate the impact of mail order pharmacy services and travel time to pharmacy on HIV viral suppression rates among people living with HIV. For adult patients receiving HIV care from 2010–2015 at an urban HIV care clinic, we collected demographics, pharmacy type, viral load, and patient home and pharmacy address. We geocoded addresses and measured travel time to pharmacy by car and public transportation. No difference was observed in recent viral suppression rates based on pharmacy type ($p=0.41$), distance to pharmacy ($p=0.16$), or travel time to pharmacy by car ($p=0.20$) or public transportation ($p=0.15$). The only factors significantly associated with sustained viral suppression were number of doses per day of antiretroviral therapy, with patients prescribed twice daily regimens less likely to be virally suppressed than those prescribed once daily regimens (aOR 0.4, 95% CI, [0.1, 0.6]) and average household income in patients' zip code, with patients living in zip codes with average household income <\$40,000 per year less likely to be virally suppressed than those living in zip codes with average income >\$55,000 per year (aOR 0.2, 95% CI, [0.1, 0.7]).

Keywords

HIV; Adherence; Pharmacy; Antiretroviral therapy

Introduction

Among people living with HIV, adherence to antiretroviral therapy (ART) is crucial to prevent drug resistance, improve health outcomes, and increase survival (Pinoges et al., 2015; van Sighem et al., 2003). ART adherence also decreases the risk of transmission of HIV to others. HIV-positive individuals who are adherent to antiretroviral therapy and achieve an undetectable viral load have essentially no risk of transmitting HIV to others (Cohen, 2011; The Lancet, 2017). However, according to the Centers for Disease Control

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and Prevention, only 51% of people living with HIV in the United States were virally suppressed in 2015 (“Centers for Disease Control and Prevention. Continuum of Care. Updated July 23, 2018. Accessed January 21, 2019. <https://www.cdc.gov/hiv/policies/continuum.html>,”).

Various barriers to ART adherence exist. These may include lack of healthcare access, stigma, and comorbid mental illness or substance use (Kalichman, Kalichman, & Cherry, 2017; Shubber et al., 2016). Studies have shown that inaccessibility of a pharmacy also may pose a barrier to adherence (Castelino, Miah, Auyeung, & Vogt, 2015; Kalichman, et al., 2017). One way to overcome that barrier is through the use of mail order pharmacies. Mail order pharmacy use has been associated with higher medication adherence and improvement in the management of chronic diseases such as diabetes and cardiovascular diseases (Schmittdiel, Karter, Dyer, Chan, & Duru, 2013). However, studies regarding the impact of mail order pharmacy use for ART among people living with HIV have produced conflicting results. Castelino et al. examined the relationship between pharmacy delivery services and HIV viral load and found that the delivery mode did not have a significant impact on HIV viral load or ART adherence (Castelino, et al., 2015). In contrast, Pham et al. found that in a low income population, mail order delivery was associated with increased rates of viral suppression but proximity to pharmacy was not (Pham, Lewis, & Avery, 2018). It is unclear if these results apply to people living with HIV who do not live in poverty. To further elucidate the relationship between pharmacy characteristics and HIV viral suppression, we aimed to 1) determine if there is a difference in viral suppression rates among people living with HIV who utilize mail order versus in-person pharmacies, and 2) determine if distance or travel time to pharmacy is associated with viral suppression among patients utilizing in-person pharmacies.

Methods

Study Population and Setting

This was a single center, retrospective study of HIV-positive patients who were 18 years of age and older receiving HIV primary care at an urban academic institution. Study participants included all patients who received HIV care at least once between January 1, 2010-December 31, 2015 with a documented HIV viral load, home address, pharmacy address (if using in-person pharmacy), and electronic ART prescription. Patients recently diagnosed with HIV (i.e., first positive HIV antibody test less than 1 year prior to date of most recent viral load test) were excluded because their viral load may not reflect ART adherence.

Mail order pharmacy was defined as a pharmacy that either delivered or mailed medications directly to the patient’s home. In-person pharmacy was defined as a pharmacy where patients picked up their prescription in person. Recent viral suppression was defined as having an HIV viral load measurement ≤ 40 copies/mL in the last recorded viral load in the study period. Sustained viral suppression was defined as two HIV viral load measurements ≤ 40 copies/mL at least 90 days apart but no more than 365 days apart

For each patient, we collected the following data from the electronic medical record: age, sex, race, HIV viral load values, ART regimen, HIV transmission category, insurance information, pharmacy type, pharmacy address, home address, and nadir CD4 count. We also collected the average income for the zip code of the patient's home using US Census Bureau data ("U.S. Census Bureau (2016). Community Facts. Retrieved from https://factfinder.census.gov/faces/nav/jsf/pages/community_facts.xhtml?src=bkmk,").

For patients utilizing in-person pharmacies, home addresses and pharmacy location were geocoded using ESRI's StreetMap Premium geocoding service. Using the patient's home address as the origin and the pharmacy as the destination, three separate network calculations were performed in a manner previously described (Ridgway, Almirol, Schmitt, Schuble, & Schneider, 2018). The first calculation determined a patient's travel distance to the pharmacy along a street network in a private vehicle. The second calculation determined a patient's travel time to the pharmacy along a street network in a private vehicle. The third calculation determined a patient's travel time to pharmacy using only walking and public transportation as modes of transportation.

Statistical Analysis

Data were analyzed using SAS 9.4 (Cary, North Carolina) statistical software. All categorical data were analyzed with the Chi squared test or Fischer's exact test. Logistic regression analysis was used to test associations between variables and viral suppression, with 95% confidence intervals and adjusted (aOR) or unadjusted (OR) odds ratios.

Results

381 patients were included in the analysis of recent viral suppression (Figure I). The majority of patients (64%) had their last viral load during 2015, and 85% of patients had their last viral load in the last two years of the study. Baseline characteristics for the mail order and in-person pharmacy groups were similar with no significant differences between groups (Table I). The majority of patients included (86.9%, 331/381) were African American. Of the included patients, 79% (301/381) were recently virally suppressed with no significant difference between those utilizing mail order vs. in-person pharmacies (81% (157/194) vs. 78% (145/187), $p=0.41$). In hypothesis testing, most factors were not significantly associated with recent viral suppression. The only factor that was significantly associated with recent viral suppression was number of doses of ART medication per day ($p<0.0001$, Table II). Similarly, in unadjusted models, doses per day of ART was associated with recent viral suppression, where patients prescribed two doses ART per day were less likely to be recently virally suppressed than those prescribed one dose of ART per day (OR 0.4, 95% CI (0.2, 0.6)) (Table III). In the multivariable logistic regression model, doses per day remained significantly associated with recent viral suppression (aOR 0.4, 95% CI [0.2, 0.6]) (Table III).

218 patients were included in the analysis of sustained viral suppression (Figure I). For the sustained viral suppression analysis, demographic characteristics for the mail order and in-person pharmacy groups were similar with no significant differences between groups (data not shown). Of the included patients, 77% (167/218) were sustainably virally suppressed

with no significant difference between those utilizing mail order vs. in-person pharmacies (Table II). Similar to what was seen for the outcome of recent viral suppression, patients prescribed two doses of ART were less likely to be sustainably virally suppressed than those prescribed one dose (OR 0.4, 95% CI [0.2, 0.6], aOR 0.2, 95% CI [0.1, 0.6]). In addition, patients with incomes below \$40,000/year were less likely to be sustainably virally suppressed (OR 0.2, 95% CI [0.1, 0.7], aOR 0.2, 95% CI [0.1, 0.7]) than those with incomes above \$55,000/year (Table III).

For patients utilizing in-person pharmacies, 79% (147/187) of patients lived within 5 miles from their pharmacy. 58% (109/187) had less than 10 minutes travel time to pharmacy by car, and 65% (121/187) had less than 30 minutes travel time to pharmacy by public transit. There were no significant differences in the outcomes of recent viral suppression or sustained viral suppression based on distance to pharmacy ($p=0.16$, $p=0.41$, respectively), travel time to pharmacy by car ($p=0.20$, $p=0.41$, respectively) or travel time to pharmacy by public transportation ($p=.15$, $p=0.24$, respectively). In order to prevent collinearity, three separate adjusted models were run containing all factors examined in Table III. The adjusted models did not show a significant association between travel distance or travel time to pharmacy and recent or sustained viral suppression (data not shown).

Discussion

In this study, HIV viral suppression was not associated with in-person vs. mail order pharmacy services. The distance to pharmacy from a patient's home and travel time to pharmacy also did not have a significant impact on viral suppression. The only factor associated with recent viral suppression in a multivariable model was lower number of daily doses of ART. When sustained viral suppression was considered, both higher number of daily doses of ART and living in a zip code with average income of less than \$40,000 per year were associated with being less likely to achieve sustained viral suppression.

Prior studies regarding the impact of pharmacy delivery services on HIV viral suppression have produced conflicting results. One study by Pham and colleagues reviewed this topic but looked specifically at patients with incomes less than \$30,000 per year (Pham, et al., 2018). Their study examined the relationship between pharmacy delivery and sustained viral suppression. Multivariate analyses showed patients who used mail-order pharmacies had increased odds of viral suppression (aOR = 3.430, 95% CI 1.935–6.080) (Pham, et al., 2018). These results differed from our study, which did not show a difference in sustained viral suppression when using mail order pharmacy services. It is possible that mail order pharmacy is more effective for enhancing medication adherence among low income patients but not among the general population. Our patients tended to live in areas with higher average incomes, but we were unable to assess individual income and socioeconomic status. One study set in the United Kingdom (UK) found that there was no significant difference in viral suppression in patients who received home delivery of ART medications compared to those who received ART as part of clinic attendance (OR = 0.894, 95% CI 0.359–2.228, $p>0.05$) (Castelino, et al., 2015). In the UK, the standard of care involved patients receiving their ART medications as part of their clinic visit, thereby eliminating the need to pick medications up separately at a pharmacy (Castelino, et al., 2015). We similarly found no

significant difference in viral suppression among those receiving home delivery of ART vs. in-person pick up.

There are few published studies evaluating impact of travel time to pharmacy on viral suppression rates. Pham et al. found that travel time to pharmacy was not associated with viral suppression (Pham, et al., 2018), similar to our findings. Eberhart and colleagues examined the association between travel distance to pharmacy and residence in an area with low viral suppression. They found that average travel distance to the five closest pharmacies was inversely associated with residence in low viral suppression “hotspots” (Eberhart et al., 2015). Our study did not find an association with distance to pharmacy and viral suppression; however, we examined the travel time to patients’ personal pharmacies and not just the closest ones. Additionally, the majority of our patients lived within 5 miles (travel time 10–30 minutes) of in-person pharmacies, which may have influenced the observed lack of impact on recent viral suppression or sustained viral suppression.

We found that higher number of doses of ART per day was associated with decreased likelihood of viral suppression. This is similar to what was seen by Pham et al, where in bivariate analyses fewer doses of ART per day was associated with increased likelihood of suppression, an association that did not remain significant in the adjusted model. In our study this association remained significant in both bivariate and multivariate models. There are several possible explanations for this finding. It may be that individuals with resistant HIV were prescribed twice daily dosing of ART because HIV viral resistance mutations prevented them from taking once-daily ART regimens. If this is the case, then more frequent dosing of ART may reflect a patient’s past nonadherence to ART because inconsistent adherence can lead to resistance. Conversely, more frequent ART dosing can itself lead to decreased adherence as patients may forget to take their medication multiple times a day. Prior studies have found that once daily ART regimens are associated with better adherence than twice daily regimens (Gallant et al., 2006; Molina et al., 2007; Parienti, Bangsberg, Verdon, & Gardner, 2009).

We also found that residence in a low-income zip code was associated with decreased likelihood of sustained viral suppression. Goswami et al. similarly found that zip codes with higher levels of poverty had lower rates of community HIV viral suppression (Goswami et al., 2016). Other studies have identified additional risk factors associated with high HIV viral load, including race, lack of health insurance, and younger age (Jefferson et al., 2017; Nance et al., 2018; Yehia, Fleishman, Metlay, Moore, & Gebo, 2012). None of these factors were significantly associated with viral load in our study.

Our study has several limitations. This was a single center, retrospective study in an urban clinic with relatively high rates of viral suppression, which may limit the generalizability to other healthcare settings. Our patient population reflects the HIV epidemic in our location, with a largely African American patient population, and higher levels of heterosexual HIV transmission than may be seen elsewhere. Medication adherence was not evaluated in our study. We were unable to examine changes in pharmacy use over time, as our electronic medical record system only maintains the latest pharmacy information. Therefore, we were unable to assess the impact of pharmacy changes on viral suppression. The travel time to

pharmacy and travel distance were calculated assuming that the patient would be traveling to the pharmacy from their home and not from work or elsewhere. We excluded patients for whom there was no home address or pharmacy address recorded in the EMR, many of whom likely utilize in-person pharmacies. It is possible that these individuals were less likely to be virally suppressed than individuals with address information present in the EMR and by excluding them, we may have over-estimated the rate of viral suppression in the in-person pharmacy group. Our results showing no significant differences in viral suppression for mail order compared to in-person pharmacies may be due to the already well controlled patient population included in this study.

In conclusion, in a population of predominantly African American people living with HIV in an urban environment, mail order pharmacy and travel time to pharmacy were not associated with HIV viral suppression.

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Figure I.
Included & Excluded patients

Table I.

Baseline Characteristics for the exposure of mail order or retail pharmacy

		Retail (N=187)	Mail order (N=194)	Pearson χ Squared or Fishers exact test* P value
Age				
	30	20 (10.7%)	21 (10.8%)	0.53
	31–45	59 (31.6%)	54 (27.8%)	
	46–60	74 (39.6%)	72 (37.1%)	
	>60	34 (18.2%)	47 (24.2%)	
Sex				
	Female	80 (42.8%)	85 (43.8%)	0.84
	Male	107 (57.2%)	109 (56.2%)	
Race				
	Black/ African American	167 (89.3%)	164 (84.5%)	0.39
	White	14 (7.5)	21(10.8%)	
	Other	6 (3.2%)	9 (4.6%)	
Insurance				
	Medicaid	81 (43.3%)	82 (42.3%)	0.34
	Medicare	41 (21.9%)	39 (20.1%)	
	Self	18 (9.6%)	14 (7.2%)	
	Private	46 (24.6%)	53 (27.3%)	
	Other	1 (0.5%)	6 (3.1%)	
Average income of zip code				
	Low (<40,000)	19 (10.2%)	25 (12.9%)	0.50
	Medium (40,000–55,000)	126 (67.4%)	120 (61.9%)	
	High (>55,000)	42 (25.2%)	49 (25.3%)	
HIV risk factor				
	MSM	66 (35.3%)	54 (27.8%)	0.13
	Injection drug use	4 (2.1%)	12 (6.2%)	
	Heterosexual	96 (51.3%)	104 (53.6%)	
	Other	21 (11.2%)	24 (12.4%)	
Nadir CD4				
	Low (<200)	45 (24.1%)	42 (21.7%)	0.77
	Medium low (200–350)	24 (12.8%)	32 (16.5%)	
	Medium high (351–500)	33 (17.7%)	34 (17.5%)	
	High (>500)	85 (45.5%)	86 (44.3%)	
Doses per day				
	One	92 (49.2%)	109 (56.2%)	0.17
	Two	95 (50.8%)	85 (43.8%)	
Number of pills				
	One	49 (26.2%)	67 (34.5%)	
	Two	49 (26.2%)	48 (24.7%)	
	Three	53 (28.3%)	37 (19.1%)	

	Retail (N=187)	Mail order (N=194)	Pearson χ^2 Squared or Fishers exact test* P value
Four or more	36 (19.3%)	42 (21.7%)	0.11

*
fishers exact test used

Table II.

Baseline Characteristics for the outcome of viral suppression

	Recent viral suppression (n=302)	Recent non-viral suppression (n=79)	Pearson χ^2 Squared or Fishers exact test* P value	Sustained viral suppression (n=167)	Non-sustained viral suppression (n=51)	Pearson χ^2 Squared or Fishers exact test* P value
Age						
30	34 (11.3%)	7 (8.9%)		20 (9.2%)	4 (7.8%)	
31–45	91 (30.1%)	22 (27.9%)		46 (27.5%)	16 (31.4%)	
46–60	112 (37.1%)	34 (43.0%)		62 (37.1%)	21 (41.2%)	
>60	65 (21.5%)	16 (20.3%)	0.78	39 (21.5%)	10 (19.6%)	0.74
Sex						
Female	137 (45.4%)	28 (35.4%)		80 (47.9%)	18 (35.3%)	
Male	165 (54.6%)	51 (64.6%)	0.13	87 (52.1%)	33 (64.7%)	0.11
Race						
Black/ African American	265 (87.7%)	66 (83.5%)		149 (89.2%)	46 (90.2%)	
White	25 (8.3%)	10 (12.7%)		13 (8.3%)	3 (5.9%)	
Other	12 (4.0%)	3 (3.8%)	0.51 *	12 (4.0%)	2 (3.9%)	0.84 *
Insurance						
Medicaid	132 (43.7%)	31 (39.2%)		77 (46.1%)	25 (49.0%)	
Medicare	58 (15.2%)	22 (27.9%)		29 (17.4%)	13 (23.5%)	
Self	26 (8.6%)	6 (7.6%)		16 (9.6%)	3 (5.9%)	
Private	81 (26.8%)	18 (22.8%)		42 (25.2%)	10 (19.6%)	
Other	5 (1.6%)	2 (2.5%)	0.48 *	3 (1.8%)	1 (2.0%)	0.73 *
Pharmacy type						
In-Person	145 (48.0%)	42 (53.2%)		78 (46.7%)	28 (54.9%)	
Mail order	157 (52.0%)	37 (46.8%)	0.41	89 (53.3%)	23 (45.1%)	0.31
Average income of zip code						
<\$40,000	30 (9.9%)	14 (17.7%)		16 (9.6%)	11 (21.6%)	
\$40–55,000	196 (64.9%)	50 (63.3%)		108 (64.7%)	33 (64.7%)	
>\$55,000	76 (25.2%)	15 (19.0%)	0.12	43 (25.8%)	7 (13.7%)	0.03
HIV risk factor						
MSM	90 (29.8%)	30 (38.0%)		90 (29.8%)	22 (43.1%)	
Injection drug use	13 (4.3%)	3 (3.8%)		8 (4.8%)	1 (2.0%)	
Heterosexual	161 (53.3%)	39 (49.4%)		89 (53.3%)	22 (43.1%)	
Other	38 (12.6%)	7 (8.9%)	0.51	23 (13.8%)	6 (11.8%)	0.22
Nadir CD4						
<200	72 (23.8%)	15 (19.0%)		40 (24.0%)	10 (19.6%)	
200–350	42 (13.9%)	14 (17.7%)		20 (12.0%)	11 (21.6%)	
351–500	54 (17.9%)	13 (16.5%)		27 (16.2%)	11 (21.6%)	
>500	134 (44.4%)	37 (46.8%)	0.70	80 (47.9%)	19 (37.3%)	0.70

	Recent viral suppression (n=302)	Recent non-viral suppression (n=79)	Pearson χ^2 Squared or Fishers exact test* P value	Sustained viral suppression (n=167)	Non-sustained viral suppression (n=51)	Pearson χ^2 Squared or Fishers exact test* P value
Doses per day						
One	175 (58.0%)	26 (32.9%)		100 (60.0%)	15 (29.4%)	
Two	127 (42.1%)	53 (67.1%)	<0.0001	67 (40.1%)	36 (70.6%)	0.0001
Number of pills						
One	98 (32.5%)	18 (22.8%)		52 (31.1%)	11 (21.6%)	
Two	80 (26.5%)	17 (21.5%)		51 (30.5%)	16 (31.4%)	
Three	67 (22.2%)	23 (29.1%)		35 (21.0%)	17 (33.3%)	
Four or more	57 (18.9%)	21 (26.6%)	0.13	29 (17.4%)	7 (13.7%)	0.25

* fishers exact test used

Table III.

Factors associated with Viral Suppression in logistic regression

		Recent Viral Suppression Odds ratio (95% CI)	Recent Viral Suppression Adjusted Odds ratio (95% CI)	Sustained Viral Suppression Odds ratio (95% CI)	Sustained Viral Suppression Adjusted Odds ratio (95% CI)
Age					
	30	1.2 (0.5, 3.0)	0.9 (0.3, 2.6)	1.7 (0.5, 5.9)	2.1 (0.5, 8.8)
	31–45	Reference	Reference	Reference	Reference
	46–60	0.8 (0.4, 1.5)	1.0 (0.5, 1.9)	1.0 (0.5, 1.5)	1.3 (0.6, 3.2)
	>60	1.0 (0.5, 2.0)	1.1 (0.5, 2.4)	1.4 (0.6, 3.3)	1.3 (0.4, 4.0)
Sex					
	Female	Reference	Reference	Reference	Reference
	Male	0.7 (0.4, 1.1)	0.6 (0.3, 1.2)	0.6 (0.3, 1.1)	0.5 (0.2, 1.6)
Race					
	Black/ African American	1.6 (0.7, 3.5)	1.8 (0.7, 4.6)	0.8 (0.2, 2.7)	0.8 (0.2, 3.6)
	White	Reference	Reference	Reference	Reference
	Other/ Unknown	1.6 (0.4, 6.9)	1.8 (0.4, 9.3)	0.6 (0.1, 4.6)	0.8 (0.1, 9.7)
Insurance					
	Medicaid	1.0 (0.5, 1.8)	0.6 (0.3, 1.3)	0.7 (0.3, 1.7)	0.4 (0.1, 1.1)
	Medicare	0.6 (0.3, 1.2)	0.5 (0.2, 1.1)	0.6 (0.2, 1.5)	0.6 (0.2, 1.8)
	Self-pay	1.0 (0.3, 2.7)	0.7 (0.2, 2.1)	1.3 (0.3, 5.2)	1.0 (0.2, 5.4)
	Private	Reference	Reference	Reference	Reference
	Other	0.6 (0.1, 3.1)	0.3 (0.05, 2.2)	0.7 (0.1, 7.6)	0.4 (0.02, 7.5)
Pharmacy type					
	Mail order	0.8 (0.5, 1.3)	1.8 (0.7, 2.2)	0.7 (0.4, 1.4)	1.3 (0.6, 2.6)
	In-Person	Reference	Reference	Reference	Reference
Average income of zip code					
	<\$40,000	0.4 (0.2, 1.0)	0.4 (0.2, 1.0)	0.2 (0.1, 0.7)	0.2 (0.1, 0.7)
	\$40– 55,000	0.8 (0.4, 1.5)	0.7 (0.4, 1.4)	0.5 (0.2, 1.3)	0.7 (0.2, 1.6)
	>\$55,000	Reference	Reference	Reference	Reference
HIV risk factor					
	MSM	0.7 (0.4, 1.3)	1.0 (0.5, 2.1)	0.5 (0.3, 1.1)	0.6 (0.2, 1.7)
	Injection drug use	1.1 (0.3, 3.9)	1.5 (0.4, 6.1)	2.0 (0.2, 16.6)	4.0 (0.4, 42.4)
	Heterosexual	Reference	Reference	Reference	Reference
	Other	1.3 (0.6, 3.17)	1.8 (0.6, 5.0)	1.0 (0.3, 2.6)	1.3 (0.3, 4.9)
Nadir CD4					
	<200	1.3 (0.7, 2.6)	1.3 (0.6, 2.6)	1.0 (0.4, 2.2)	1.5 (0.6, 4.2)
	200–350	0.8 (0.4, 1.7)	0.9 (0.4, 1.9)	0.4 (0.2, 1.1)	0.6 (0.2, 1.7)
	351–500	1.1 (0.6, 2.3)	1.3 (0.6, 2.8)	0.6 (0.3, 1.4)	0.7 (0.3, 1.9)
	>500	Reference	Reference	Reference	Reference
Doses per day					
	One	Reference	Reference	Reference	Reference

		Recent Viral Suppression Odds ratio (95% CI)	Recent Viral Suppression Adjusted Odds ratio (95% CI)	Sustained Viral Suppression Odds ratio (95% CI)	Sustained Viral Suppression Adjusted Odds ratio (95% CI)
Number of pills	Two	0.4 (0.2, 0.6)	0.4 (0.2, 0.7)	0.4 (0.2, 0.6)	0.2 (0.1, 0.6)
	One	Reference	Reference	Reference	Reference
	Two	0.9 (0.4, 1.8)	1.2 (0.5, 2.9)	0.7 (0.3, 1.6)	0.9 (0.3, 2.9)
	Three	0.5 (0.3, 1.1)	0.9 (0.4, 2.2)	0.5 (0.2, 1.04)	1.1 (0.3, 4.1)
	Four or more	0.5 (0.3, 1.0)	0.9 (0.4, 2.4)	0.9 (0.3, 2.5)	2.3 (0.5, 9.9)