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## Association between dog guardianship and HIV clinical outcomes

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### Abstract

Despite numerous potential health outcomes of dog guardianship, their value has not been examined in the HIV-positive population. The study objective was to examine the relationship between dog guardianship and HIV clinical outcomes (antiretroviral adherence [ 95% versus <95%], HIV viral load [ 48copies/mL versus <48copies/mL], and CD4+ cell count) among HIV-positive individuals. We conducted a secondary analysis of baseline data of 370 HIV-positive men on antiretrovirals enrolled in the Duo Project. Generalized estimating equations were used for inferential regression analyses, while controlling for the focal dog guardianship variable and non-focal covariates. Current dog guardianship was reported in 28.7% of participants. Dog guardianship may be associated with higher CD4+ (coefficient=60.6, p=0.052) and adherence 95% (OR=1.80, p=0.048); however, having a detectable viral load was not related to dog guardianship (OR=0.94, p=0.85). Further clinical research with detailed dog guardianship data is needed to further examine the association between dog guardianship and HIV clinical outcomes.

### Keywords

dog; canine; HIV/AIDS; adherence; antiretroviral therapy; CD4+ cell count

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## INTRODUCTION

Animal guardianship is an integral part of life in the United States with 39% of households claiming at least one dog, which is equivalent to approximately 78.2 million dogs<sup>1</sup>. Pet companionship, particularly dog guardianship, has been associated with numerous health behaviors and outcomes, including greater exercise duration and frequency<sup>2-7</sup>; higher capacity to carry out activities of daily living<sup>8</sup>; decreased blood pressure and heart rate<sup>9-11</sup>; lower triglycerides<sup>12,13</sup>; improved survival post-myocardial infarction<sup>14,15</sup>; and reduced anxiety, stress<sup>16-18</sup>, depressive symptoms<sup>19,20</sup>, and other symptoms associated with psychiatric disorders and diseases<sup>21-23</sup>. Additionally, there are data regarding the potential benefit of dogs in programs in incarcerated populations<sup>24</sup>, reduction of depression and increased arterial oxygen saturation in those undergoing chemotherapy<sup>25</sup>, and improved clinical outcomes and decreased hospital stay in patients with heart failure<sup>26,27</sup>

HIV-positive individuals have increased risk of hypertension, hyperlipidemia, and cardiovascular events<sup>28,29</sup>, which can lead to higher pill burden and increased likelihood of drug-drug interactions and adverse effects, which in turn may result in antiretroviral (ARV) non-adherence<sup>30,31</sup>. Additionally, depression and stress are independent barriers to ARV adherence<sup>32,33</sup>. Despite their potential benefits and ubiquitous nature, the value of dog guardianship has not been examined in the HIV-positive population. Therefore, the objective of this study was to examine the correlation between dog guardianship and HIV clinical outcomes, such as adherence to ARV therapy, HIV viral load, and CD4+ cell count, among HIV-positive individuals.

## METHODS

We conducted a secondary analysis of baseline data of HIV-positive men on ARV medications enrolled in the Duo Project, a longitudinal study of how relationship dynamics among men who have sex with men can influence ARV adherence<sup>34,35</sup>.

Participants included in this secondary data analysis were men who were 18 years of age, had been in a primary relationship with another man for 3 months, were HIV-positive, and had been taking ARVs for at least 30 days. Participants for the Duo Project were recruited from the San Francisco Bay Area using referrals from other participants and passive recruitment through advertisement. The University of California, San Francisco Committee on Human Research granted approval for this research and participants signed an informed consent form prior to study initiation.

Data were collected using Audio Computer Assisted Self Interviewing (ACASI). We inquired about the participant's dog guardianship ('yes' versus 'no'). ARV adherence was assessed by self-report using the visual analog scale which estimates 30-day adherence to ARVs on a scale of 0% to 100%<sup>36</sup>. Demographics (age, race/ethnicity, education, income, and employment), ever homeless, relationship length, depression (assessed using the Center for Epidemiologic Studies Depression (CES-D) scale), substance use (crack, cocaine, heroin, street methadone, and other stimulants) in the past three months, length of time since HIV diagnosis, ARV regimen, and HIV clinical parameters (CD4+ cell count and

HIV viral load) were also included. The viral load test was performed using the COBAS® AmpliPrep/COBAS® TaqMan® HIV test kit (Roche Molecular Systems, Inc.), which has a limit of quantification of 48 copies/mL.

We used descriptive statistics to generate frequencies, means, and standard deviations (SDs). Using bivariable regression, we examined the associations between three key HIV outcome variables (ARV adherence [dichotomized as ≥95% versus <95%], CD4+ cell count, and HIV viral load [dichotomized as ≥48 copies/mL versus <48 copies/mL]); focal covariate (dog guardianship); and hypothesized confounders (age, race/ethnicity, education, yearly income, employment status, ever homeless, substance use, relationship length, and depression).

To account for clustering of individuals within couples, generalized estimating equations (GEE) with an exchangeable correlation structure and robust standard errors were used for inferential regression analyses<sup>37</sup>. Multivariable regression models corresponding to the three HIV outcome variables were fitted including the focal dog guardianship independent variable and other non-focal covariates where the bivariable p-value was less than 0.25<sup>38</sup>. Non-focal covariates were removed using backward elimination, until all remaining non-focal covariates were significant at  $p < 0.05$ . All analyses were conducted using Stata, version 12.1 (StataCorp, College Station, TX).

## RESULTS

Data from 370 HIV-positive men on ARVs were analyzed; see Table for sample characteristics. Mean length of time since HIV diagnosis was 160.5 months (SD= 96.5). Approximately 73% of individuals reported adherence ≥95%, 76.5% had an undetectable viral load (N= 366), and mean CD4+ cell count was 564 cells/mm<sup>3</sup> (SD= 260.8; N= 366). Forty-six percent reported taking protease inhibitor (PI)-based ARV regimens, 41% reported taking non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens and 13% reported combined PI/NNRTI-based regimens or other. Current dog guardianship was reported in 28.7% of participants.

The Table includes the correlates of ARV adherence, viral load, and CD4+ cell count in bivariable analyses. Variables with a  $p$ -value  $< 0.25$  are bolded and were examined in multivariable regression models. In the final multivariable model with adherence as the outcome, reported dog guardianship (OR= 1.80; 95% CI= 1.00, 3.24;  $p = 0.048$ ) and substance use (OR= 0.46; 95% CI= 0.28, 0.76;  $p = 0.002$ ) were statistically significant. In the final CD4+ cell count multivariable model, dog guardianship was marginally significant (coefficient= 60.6; 95% CI= -0.62, 121.8;  $p = 0.052$ ) and race ( $p = 0.01$ ) and having ever been homeless (B= -66.9; 95% CI= -124.9, -8.9;  $p = 0.02$ ) were statistically significant. Dog guardianship was not associated with having a detectable viral load (OR= 0.94, 95% CI= 0.51–1.72,  $p = 0.85$ ). Race/ethnicity had a statistically significant association with having a detectable viral load ( $p = 0.0003$ ) with Black individuals having four times the odds of having a detectable viral load in comparison with White individuals (95% CI= 2.15, 7.68). Substance use was also associated with having a detectable viral load (OR= 2.0; 95% CI= 1.17, 3.47;  $p = 0.01$ ).

## DISCUSSION

Our findings supply preliminary evidence that dog guardianship may be associated with higher CD4+ cell count and higher ARV adherence. However having a detectable HIV viral load was not related to dog guardianship, which may have been due to the fact that most participants had an undetectable viral load. Alternatively, the finding could represent a true lack of association. Further research with primary collection of more extensive dog guardianship data is needed to cast further light on this and other relevant links between dog guardianship and HIV clinical outcomes.

In general, the mechanisms underlying the correlation between dog guardianship and improved physical and psychological health are not well-understood. There are potentially indirect relationships related to an increase in the number of and duration of recreational activities and walks<sup>3-7,39-41</sup>, as well as an enhanced social interaction and contact with other people<sup>42-45</sup> and alleviation of the feelings of loneliness<sup>46</sup>. The potential impact of pet guardianship on increased social support and decreased loneliness has been examined in two prior studies in HIV-positive individuals<sup>19,47</sup>. A theorized direct effect of contact with animals on improved well-being may result from the presence or the observation of animals reducing physiological and psychological response to stress and anxiety, which may yield decreased blood pressure and heart rate<sup>11,17,48</sup>. The role of neuropeptides in the mechanism underlying human-dog bonding have also been explored, with a significant increase in oxytocin, prolactin, phenylacetic acid, and dopamine levels in humans and dogs and a decrease in cortisol in humans being observed<sup>49-51</sup>.

While the role of neuropeptides or the stress- and anxiety-reducing effect of dog guardianship, leading to fewer comorbidities are possible explanations for the results of our study, we hypothesize several other possible mechanisms for these associations. The first potential mechanism is related to the role of organization and routinization. Individuals caring for a dog likely maintain organized schedules, which include daily recreational walks and feedings, based on the needs of the dog. The beneficial role of organization and ARV adherence has been examined in prior research<sup>52</sup>; routines associated with caring for a dog may similarly promote a higher level of adherence. Conversely, dog guardianship may be a proxy for other factors. For example, it is possible that individuals who are more organized, have more housing stability, have less psychosocial distress, and are overall more likely to have higher adherence, are also more likely to have the capability and inclination to care for a dog.

Another hypothesized mechanism involves a sense of responsibility. Caring for a dog means taking care of another dependent being; this may translate to better self-care in order to maintain a level of health that can enable a person to take care of that being. This responsibility may motivate an individual to have a high degree of medication adherence, start ARVs earlier, and participate in other activities that may result in a stronger immune system.

A limitation of our study includes the cross-sectional approach with which causal order cannot be established. Additionally, a drawback of self-reported medication adherence data

is that respondents tend to over-report this value. Therefore, despite the relative ease of collection, these data are less objective and may be less reliable than other methods, such as pharmacy refill records or electronic drug monitors. Lastly, the couples-focus and location of the parent study indicates that our results can only be generalized to gay male couples living in San Francisco; therefore, we view this study as exploratory and believe that future research should examine these results in a larger and more generalizable population, with more objective measures of adherence, and more extensive measures of dog guardianship and dog-related behaviors (e.g., mean time spent with the dog per day).

We believe that our results warrant a closer examination and larger studies that can discern the directionality of cause and effect need to be conducted. Future research that may support and further expand and justify our results may provide an incentive to promote dog adoption for appropriate individuals, support dog companionship programs, and promote evidence-based updates to regulations governing requirements for dog guardianship in housing units to render such regulations more pet-friendly while still satisfying regulatory goals.

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Table

Univariable analysis and bivariable regression models of hypothesized correlates of ARV adherence, CD4+ cell count, and HIV viral load

Independent Variables	Categories	Univariable analysis (N=370)	Adherence (95% vs. <95%) (N=370)	p-value	CD4+ cell count (N= 366)	p-value	HIV viral load (<48 vs. <48 copies/mL) (N= 366)	p-value
Age, mean years (SD)		46.1 (10.0)	1.01 (0.98, 1.03)	0.52	1.7 (-0.6, 3.9)	0.15	0.97 (0.95, 1.0)	0.04
Race/Ethnicity, n (%)			-	0.02 <sup>c</sup>	-	0.02 <sup>c</sup>	-	0.0002 <sup>c</sup>
	Black	59 (16.0)	-	Ref	-	Ref	-	Ref
	White	207 (56.0)	2.33 (1.25, 4.36)	0.008	72.5 (-7.9, 152.9)	0.08	0.25 (0.13, 0.47)	<0.001
	Latino	71 (19.2)	2.36 (1.09, 5.09)	0.03	-18.1 (-104.3, 68.1)	0.68	0.40 (0.19, 0.87)	0.02
	Other	33 (8.9)	1.05 (0.43, 2.61)	0.91	28.5 (-63.6, 120.7)	0.54	0.64 (0.28, 1.48)	0.30
Greater than high school education, n (%)		257 (69.5)	1.80 (1.10, 2.95)	0.02	63.0 (2.7, 123.3)	0.04	0.48 (0.29, 0.81)	0.005
Yearly income, n (%)			-	0.45 <sup>c</sup>	-	0.33 <sup>c</sup>	-	0.07 <sup>c</sup>
	< \$10,000	85 (23.0)	-	Ref	-	Ref	-	Ref
	\$10,000–\$19,999	108 (29.2)	0.71 (0.37, 1.37)	0.31	-11.4 (-87.0, 64.1)	0.77	0.86 (0.44, 1.67)	0.66
	\$20,000	177 (47.8)	0.96 (0.52, 1.78)	0.90	32.9 (-37.9, 103.7)	0.36	0.52 (0.27, 0.97)	0.04
Employed, n (%)		165 (44.6)	1.29 (0.80, 2.09)	0.29	4.0 (-50.0, 57.9)	0.89	0.75 (0.46, 1.23)	0.26
Ever homeless, n (%)		109 (29.5)	0.55 (0.33, 0.90)	0.02	-81.0 (-137.3, -24.6)	0.005	1.77 (1.07, 2.90)	0.03
Length of time together with partner, mean months (SD)		78.3 (79.6)	1.00 (0.99, 1.00)	0.79	0.2 (-0.2, 0.5)	0.36	1.0 (0.99, 1.0)	0.04
Depression score (based on CES-D), mean (SD) <sup>a</sup>		15.0 (10.5)	0.99 (0.97, 1.01)	0.36	-1.9 (-4.5, 0.7)	0.16	1.00 (0.98, 1.02)	0.99
Substance use, n (%) <sup>b</sup>		104 (28.1)	0.47 (0.28, 0.76)	0.002	-57.0 (-118.8, 4.8)	0.07	2.08 (1.24, 3.48)	0.005
Dog guardianship, n (%) <sup>c</sup>		106 (28.7)	1.87 (1.05, 3.32)	0.03	75.6 (14.9, 136.4)	0.02	0.74 (0.41, 1.33)	0.31

OR: odds ratio; CI: confidence interval; Ref: reference; B = unstandardized linear regression coefficient representing mean change in outcome per unit change in the independent variable.

<sup>a</sup>Depression score based on CES-D

<sup>b</sup>Substance use: street methadone, crack, cocaine, heroin, and stimulants

<sup>c</sup>Omnibus Wald test