

THE PENNSYLVANIA STATE UNIVERSITY  
SCHREYER HONORS COLLEGE

EBERLY COLLEGE OF SCIENCE

THE PROS AND CONS OF PERCEIVED HIV-RELATED STIGMA IN YOUNG AND  
OLDER ADOLESCENTS IN BOTSWANA

KARINA GRULLON PEREZ  
SPRING 2019

A thesis  
submitted in partial fulfillment  
of the requirements  
for a baccalaureate degree in Biology  
with honors in Science

Reviewed and approved\* by the following:

Joshua Rosenberger  
Assistant Professor of Biobehavioral Health  
Thesis Supervisor

Ronald Markle  
Director of Premedicine and General Science Majors  
Professor of Biology (Physiology)  
Honors Adviser

Kari Kugler  
Assistant Professor of Biobehavioral Health  
Affiliate, The Methodology Center  
Faculty Reader

\* Signatures are on file in the Schreyer Honors College.

## ABSTRACT

The HIV Stigma Framework suggests that HIV-related stigma impacts individuals living with HIV via a series of stigma mechanisms, which includes experienced stigma (i.e., be subject to discrimination), anticipated stigma (i.e., change thoughts or behaviors to avoid discrimination), and internalized stigma (i.e., think less of themselves because of their HIV serostatus). HIV-related stigma in adults living with HIV has been associated with increased risk-taking behavior, reduced uptake of HIV testing, and decreased adherence to antiretroviral therapy (ART). Children with perinatally acquired HIV, whose caregivers have experienced or anticipated stigma, have excellent adherence in an effort to prevent the unnecessary disclosure of the child's status; however, the effect of HIV-related stigma on adolescents with perinatally acquired HIV remains unknown. Using data from 289 adolescents living with HIV (ALWH) in Botswana, we tested the hypotheses that adolescents' self-reports of perceived stigma are associated with virologic failure (VF) and the association between perceived stigma and VF differs in younger and older adolescents. Results suggest that age is an effect modifier of the relationship between perceived stigma and VF. For older adolescents (>17 years of age), there was an increased risk of VF with increasing stigma, but for younger adolescents ( $\leq 17$  years of age) there was a decreased risk of VF with increasing stigma (interaction  $p < 0.001$ ). Further research is needed to understand the reason why younger adolescents are protected from stigma, but the results from this study reinforce that the transition to young adulthood increases the risk for stigma to influence HIV-related health outcomes.

**TABLE OF CONTENTS**

LIST OF FIGURES .....	iii
LIST OF TABLES .....	iv
ACKNOWLEDGEMENTS .....	v
Chapter 1 Introduction .....	1
Chapter 2 Methodology .....	9
Chapter 3 Results .....	13
Chapter 4 Discussion .....	18
Chapter 5 Limitations and Future Directions.....	21
Appendix A HIV Stigma Scale.....	22
BIBLIOGRAPHY .....	24

**LIST OF FIGURES**

Fig. 1 Hypothesized associations between HIV-perceived stigma domains and virologic failure  
among ALWH..... 8

Fig. 2 Association between Perceived Stigma and VF in Younger and Older Adolescents.... 16

Fig. 3 Association between Domain Specific Stigma and VF in Younger and Older Adolescents 17

**LIST OF TABLES**

Table 1. Subject Characteristics.....	14
Table 2. Univariable Analysis of Association between Stigma and Virologic Failure (VF)...	15

## ACKNOWLEDGEMENTS

I would like to thank from the bottom of my heart my research mentor, Dr. Elizabeth Lowenthal at the Children's Hospital of Philadelphia, for her guidance through this project and teaching me everything I needed to know about global health research and biostatistics. Dr. Lowenthal took me under her wing as a CRISSP intern in 2017 and helped me every step of the way. I would also like to thank Jennifer Chapman for her unwavering support and encouragement to get involved in the local community of Philadelphia. I would also like to thank the adolescent study participants and the staff at the Botswana-Baylor Children's Clinical Centre of Excellence. I would like to thank my thesis supervisor, Dr. Joshua Rosenberger, faculty reader, Dr. Kari Kugler, and honors advisor, Dr. Ronald Markle, for their guidance and support which helped me complete this project.

Finally, I would like to thank my family and friends for their continued encouragement and emotional support throughout the writing process. This project would have not been made possible without the help of every single person mentioned above. I'm forever grateful for each and every one of you.

# Chapter 1

## Introduction

Nearly three decades after the discovery of HIV/AIDS, it continues to be a serious health problem affecting 36.9 million people globally as of 2017.<sup>1</sup> Sub-Saharan Africa is one of the regions that has been most affected by the HIV/AIDS epidemic. It is home to approximately 66% of the world's HIV+ population.<sup>2</sup> An estimated 1.8 million children (<15 year old) worldwide were perinatally infected with HIV in 2017, approximately 90% of whom live in sub-Saharan Africa.<sup>3</sup> Botswana is one of the sub-Saharan African countries most affected by the disease, with an adult HIV/AIDS prevalence (ages 15-49) of 21.9%, making it the country with the third highest HIV prevalence in the world. In 2017, UNAIDS reported that 380,000 individuals were living with HIV in Botswana. Although Botswana has demonstrated a strong commitment towards addressing the HIV epidemic by becoming the first country to offer universal free antiretroviral treatment (ART) to people with HIV, treatment of children still lags behind that of adults with only 68% of children living with HIV on ART compared with 84% of adults.<sup>4</sup>

As the HIV epidemic matures and more children are accessing ART, the number of HIV-infected children aging into adolescence is increasing. Adolescents living with HIV (ALWH) must depend on maintaining their lifelong adherence to ART in order to limit their morbidity and mortality. Unfortunately, compared to both younger children and adults, adolescents have higher rates of poor treatment adherences and virologic treatment failure.<sup>5</sup> Some consequences of poor medication adherence include the more rapid clinical progression of HIV and development of resistant virus strains.<sup>6,7,8</sup> Improving treatment adherence among ALWH will allow this

population to age into adulthood and live a healthier lifestyle, while helping decrease the HIV transmission from individuals with excellent control of their infection.<sup>9</sup> Limiting the spread of resistant HIV virus and the success of HIV treatments depends on maintaining lifelong adherence to ART especially in aging children and adolescents.<sup>10</sup> In order to maximize ART adherence of adolescents, and their overall health and survival, it is vital that we understand the multi-level factors that affect pediatric adherence and treatment outcomes.

HIV/AIDS is a highly stigmatized disease and this stigma has been recognized as a major impediment to HIV prevention and treatment.<sup>11</sup> HIV-related stigma is a structural level phenomenon that maintains and reproduces social inequalities— specifically those associated with race, gender, and sexuality. HIV-related stigma can exist when HIV+ individuals are labeled, stereotyped, and/or discriminated against by a member of society from a perceived higher status.<sup>12</sup> Amongst the general population, HIV-perceived stigma has been associated with reduced voluntary counseling and testing, and increased sexual risk-taking behavior.<sup>11</sup> Individuals who endorse HIV-related stigma beliefs are less likely to get tested for HIV compared to individuals who do not endorse HIV-related stigma.<sup>13,14</sup> In adults living with HIV, HIV-related stigma can become a chronic stressor. Stress has been previously linked to the clinical progression of HIV via a decrease in CD4 T lymphocytes and contributing to the development of co-morbid chronic illnesses such as diabetes, heart disease, and cancer.<sup>12,15,16,17</sup> Studies of adults living with HIV in the U.S. have demonstrated a relationship between stigma and poor ART adherence, and increased HIV symptoms and depression.<sup>15,16,17</sup> Adults living with HIV face the burden of having acquired the virus through behavioral means, while children who were vertically infected typically the HIV-infected mother carries the burden of having infected her child.<sup>18</sup> Understanding the impact HIV-related stigma has on the health of ALWH



remains limited even though the epidemic continues to impact several countries worldwide, including Botswana.

Children's adherence to ART is particularly vulnerable because they must rely on caregivers for the administration of their medications, attending doctor visits, and obtaining medication refills at the pharmacy. A single study conducted previously at the clinic where we performed our study found that caregivers who anticipated or experienced stigma were more likely to have children with excellent adherence in order to avoid the disclosure of the child's status to family and community members.<sup>19</sup> The caregiver's understanding of the benefits ART provides, such as an adherent child is more likely to stay health and reduces the potential of revealing the child's status to stigmatizing family and community members. The identified relationship between adherence, disclosure, and stigma suggest that perceived stigma has a positive effect and it can be described as "protective stigma" in children living with HIV.<sup>19</sup> The children enrolled in this study were younger than 15 years old, which raises the question of how perceived stigma could impact the adherence of adolescents older than 15 years old. A study based in Côte d'Ivoire found that older children (13 years old or older) had decreased adherence most likely due to lack of supervision from caregivers. An important factor identified in this study was that non-adherence was associated with the child's age suggesting that special attention must be paid to the transitional period when taking and giving ART medication is shared between the child and caregiver. It's critical that older children and adolescents undergoing this transformation be monitored closely to ensure adherence is maintained.<sup>20</sup>

Adolescents are the only age group for whom AIDS-related deaths increased during 2005-2012, an estimated 50% increase in adolescent deaths compared to a 32% decrease in AIDS-related deaths among all other age groups.<sup>21</sup> A previous study sampled the most and least

adherent adolescents (ages 10-19) and concluded that non-adherent adolescents were older than the adherent adolescents (median age of 18 years old vs. 14 years old). The results of this study described changes in adherence across the adolescent age spectrum suggesting that adolescents between the ages of 16 and 17 are undergoing a transitional period where the responsibility of taking ART medication could be the adolescent's, and not of the caregiver.<sup>22</sup> Typically, the adherence of adolescents is affected by knowledge of their HIV serostatus, availability of parental care, caregivers' educational levels, and understanding of ART. However, these factors may not strongly influence late adolescents (ages 15-19) because compared to early adolescents (ages 10-14), they are more likely to know their HIV status, be independent from their caregivers, take responsibility for managing their medication, and have wider social interactions. Late adolescents may have challenges to adherence that they did not encounter earlier, such as psychosocial problems and engagement in sexual activity.<sup>23</sup> Studies assessing the treatment outcomes of adolescents must account for the adolescent age spectrum to understand the potential differences that could exist between early and late adolescents.

To further understand the effect of HIV-related stigma at an individual's level, it's proposed that ALWH can be exposed to experienced, anticipated, and internalized HIV-related stigma. The HIV stigma framework was developed by Earnshaw and Chaudoir to uncover the mechanisms and outcomes of HIV-related stigma for individuals living with HIV.<sup>24</sup> Experienced stigma involves the experience of discrimination, stereotypes, and/or prejudice from others in the past. HIV+ individuals may experience poor health care from healthcare providers, social rejection from friends or family, physical violence from others, and job loss from employers due to their HIV status.<sup>12</sup>

Anticipated stigma involves the perception of discrimination from others and potential change thoughts or behavior to avoid discrimination. Individuals living with HIV may avoid certain situations wherein they expect to be treated poorly due to their HIV status and these negative expectations may take a physical toll on them.<sup>12</sup> Anticipated stress can place a huge burden on the individuals to the point where it can become a chronic stressor and impact their health via the neuroendocrine and sympathetic nervous system pathways.<sup>15,25</sup> It has been suggested that experienced and anticipated stigma can affect the individual's physical health and well-being because they both can act as chronic stressors and affect physical health.<sup>12</sup> Anticipated stigma has been shown to be related to physical health in the form of more HIV symptoms among adults living with HIV in the U.S. and social support has been found to buffer this relationship.<sup>12,26</sup>

Internalized stigma involves the acceptance of these negative attitudes as true and internalization of these beliefs.<sup>11</sup> Internalized stigma encompasses the feelings of being “less than” others, dirty/not clean, and/or deserving of the negative symptoms associated with HIV.<sup>12</sup> Internalized stigma has been shown to be related to lower ART adherence among adults living with HIV in the U.S. and depression among men who have sex with men in China.<sup>27,28</sup> Additionally, internalized stigma has been found to be related to higher virus levels for adults living with HIV in Italy.<sup>29</sup> By making a distinction between these three domains that encompass HIV-related stigma, researchers are able to gain a more nuanced understanding of how HIV-related stigma impacts the health and well-being of individuals living with HIV.<sup>12</sup> Adolescents, with their growing autonomy, are at this interesting intersection where the role HIV-related stigma plays remains unknown.

In countries like Botswana where ART is widely available, its availability is thought to reduce HIV-related stigma amongst the general population since people who are living with HIV are less commonly sick and become increasingly known as productive members of society.<sup>11</sup> The ability of ART to allow people who would otherwise be target of stigma to more easily “pass” in society as “normal” should not be confused with the overall HIV-related stigma reduction from family and community members. It’s possible that stigmatization of individuals living with HIV will change from being visible stigma, such as significant loss of weight, to instead being provoked by frequent doctor follow-up visits, pharmacy visits, medication taking, and potential side effects of ART medication.<sup>19</sup> This concern may be outweighed by the positive health benefits of consistent medication taking adherence and reduction of HIV-related symptoms, which can to an extent reduce internalized stigma beliefs amongst individuals living with HIV. These interactions and reduction in internalized stigma may occur more frequently in countries with high HIV prevalence, such as Botswana, because the general population has more encounters with HIV+ individuals and opportunities to learn about the restorative effects of ART.<sup>11</sup>

The effect of ART-scale up on the different domains of HIV-related stigma, specifically anticipated stigma, and its impact on the adolescent population remains unclear. A previous cross-country analysis of 18 African countries revealed that there is an association between ART coverage and HIV-related stigma in the general population in countries with a high HIV prevalence.<sup>30</sup> This cross-country analysis used a composite measure of HIV-related stigma, which did not distinguish between experienced, anticipated, and internalized HIV stigma. There is a possibility that these HIV stigma domains diverge within African countries, but it remains unknown.<sup>11</sup>

## Specific Aims

Using quantitative methods, this study examined the relationship between HIV-related stigma and treatment outcomes among ALWH. Examining the extent to which experienced, anticipated, and internalized HIV stigma affect ALWH is important because the effect of HIV-related stigma on treatment outcomes in an African context has been examined at the adult and children level, but no studies have been published examining adolescents, who are in the middle of the intersection.

The specific aims of this study are as follows:

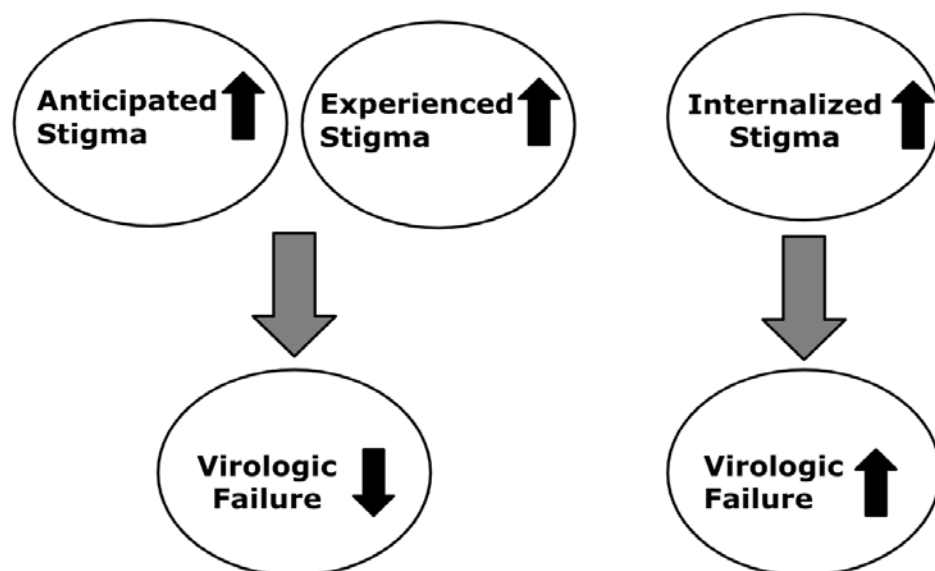
**Primary Aim:** To evaluate the association between perceived stigma and virologic failure (VF) in adolescents living with HIV.

**Primary hypotheses:** Adolescents with higher levels of anticipated and experienced stigma would be less likely to have virologic failure. Adolescents with higher levels of internalized stigma would be more likely to have virologic failure.

**Secondary Aim:** To evaluate age as an effect modifier of the association between perceived stigma and VF in adolescents living with HIV.

**Secondary Hypothesis:** The association between perceived stigma and VF is different in younger and older adolescents.

The purpose of this research study is to identify potential areas where interventions could be designed for ALWH who experience HIV-related stigma. Interventions could be appropriate at a number of different levels: the individual level, between the parents and child, within the family unit, at the clinical level, and at the community level.



**Fig. 1 Hypothesized associations between HIV-perceived stigma domains and virologic failure among ALWH**

## **Chapter 2**

### **Methodology**

#### **Participants**

A total of 300 ALWH (aged 10-20 years) were enrolled in a longitudinal observational adherence study at the Botswana-Baylor Children's Clinical Center of Excellence (COE) in Gaborone, Botswana. The 5-year observational study started in October 2012. The adolescents enrolled in the study received antiretroviral therapy through the Botswana National HIV Treatment Program at the Botswana-Baylor COE, which serves HIV+ children living in the capital and areas surrounding the capital, Gaborone. To ensure that "high-risk" and "low-risk" adolescents representative of the clinic population were enrolled in the study, participants with detectable and undetectable viral loads in proportions equal to those in the general clinic population were included in the study. Of the 300 adolescents enrolled in the study, 150 were on protease inhibitor (PI)-based antiretroviral therapy, and 150 were on non-nucleoside reverse transcriptase inhibitor (NNRTI)-based therapy.

The study participants received standard-of-care monitoring and treatment per the Botswana National HIV Treatment Guidelines, which include quarterly study visits and HIV viral load testing every 3 months. Study participants received medication refills based on the patients' need determined by the pharmacy staff and treatment team. At each medication refill, participants were given a 4- to 6-week supply. Virologic response is only a reliable measure of adherence to HIV treatment if the individual's virus is susceptible to the medication the person is taking (i.e. has not developed medication resistance). Because virologic suppression is our

endpoint in this analysis, adolescents were excluded from the study if baseline resistance test showed the virus was not susceptible to their prescribed regimen or if susceptibility was uncertain. The stigma measures were not introduced at the beginning of the longitudinal study because there was a concurrent process of culturally adapting and validating the measures, which took approximately two years. Once the validation studies were encouraging, the stigma measures were used in the larger cohort. Data from the first 12 months of follow-up after the stigma measure was introduced were included in the analysis.

## Measures

### HIV Viral Load

Each adolescent was classified as having a detectable HIV viral load if any plasma viral load measurement during the 12-month period following the baseline stigma measure was  $\geq 400$  copies per milliliter. Virologic failure was defined as having a single detectable HIV viral load ( $\geq 400$  copies/ml; coded as 1) in 12-month period following the baseline stigma measure.

### HIV-Perceived Stigma

HIV-perceived stigma was measured at baseline using *The Stigma Scale Revised*, which was developed from the HIV Stigma Scale and specifically used for ALWH.<sup>31</sup> The Stigma Scale Revised assessed personalized stigma, disclosure concerns, negative self-image, and concern with public attitudes toward people with HIV. HIV-perceived stigma was measured with an audio computer-assisted self-interview. The questions were scored using a 5-point Likert scale from “definitely false” (1 point) to “definitely true” (5 points).

The total stigma score was calculated as follows: (anticipated stigma Q1, Q3)/2 + (internalized stigma Q6) + (experienced stigma Q7, Q8)/2 (see Appendix A). These five



questions represented the individual domains of HIV-related stigma evaluated in this study. Total stigma and domain-specific stigma scores were analyzed as continuous and discrete variables. As discrete variables, the three-domain stigma scores were dichotomized as high or low ( $>3$  vs.  $\leq 3$ ). The above cutoff point of three was selected because it represented a neutral response in the 5-point Likert scale for each individual item. Participants who scored above three on an item were considered to be part of the high stigma group, but participants who scored less than or equal to three were considered to be part of the low stigma group. The total stigma score was dichotomized as high or not high ( $>9$  vs.  $\leq 9$ ). The above cutoff was selected for total stigma after the weighted average of each stigma domain was calculated and it was determined that the domain specific cutoff was three; therefore, the three domains combined had a cutoff of nine.

### **Age**

Study participants were categorized as older ( $>17$  years) or younger adolescents ( $\leq 17$  years). The above cutoff point of 17 years old was chosen because a previous study found differences in non-adherence between younger and older adolescents at this transitional age.<sup>22</sup> It's a critical age for many adolescents who are starting to exercise their autonomy over medication taking, engaging in sexual activity, expanding social network, and preparing to enter adulthood.<sup>23</sup>

## **Data Analysis**

Subject characteristics were compared using t-tests and Chi squared tests for categorical data. A Chi squared test assessed for difference in virologic failure rates between those with a high/not high total stigma score and the three domain specific scores. Logistic regression was used to evaluate the bivariate relationship between stigma scores and VF. Multivariable logistic

regression was used to assess effect modification, controlling for potential confounders. Potential confounding variables included demographic and clinical characteristics such as age, gender, years on ART, orphan status, and detectable VLs. The multivariable model evaluated for effect modification by age.

Data were collected and stored using REDCap Software, version 5.6.3.<sup>32</sup> STATA version 15 software was used for statistical analyses.<sup>33</sup>

## **Ethical Considerations**

The study was approved by the Botswana Health Research Development Committee and the institutional review boards at the University of Pennsylvania and Baylor College of Medicine. Written informed consent was obtained from a parents or guardian of each adolescent study participant under the age of 18 years old and assent was obtained for each adolescent participant. Written informed consent was obtained from each adolescent participant if over the age of 18 years old.

## Chapter 3

### Results

289 adolescents were included in the analyses. Eleven subjects were excluded for the following reasons: 3 subjects had high-grade resistance to antiretroviral regimen; 5 subjects had unknown suppression status; and 3 subjects had <12 months of follow-up time. Subject characteristics are summarized in Table 1. The participants were enrolled in the longitudinal study for approximately two years prior to the start of the sub-study. The age range at study entry was 10.1 to 19.9 years with age skewed toward younger adolescents. The age range at sub-study entry was 14.1 to 18.1 with age skewed toward younger adolescents. Of the sample, 124 adolescents were in the older adolescent group (>17 years), and 175 were in the younger adolescent group ( $\leq 17$  years). Time on ART at study entry ranged from 6 months to 11.5 years. Time on ART at sub-study entry ranged from 7.8 to 11.4 years. Of the sample, 105 adolescents (35%) met the pre-defined criteria for VF. A total of 121 adolescents were classified as having a high total stigma score (>9). A total of 168 adolescents were classified as having a low total stigma score ( $\leq 9$ ) (Table 1).

**Table 1. Subject Characteristics**

	All (n=289)	Total Stigma Score (>9) (n=121)	Total Stigma Score (≤9) (n=168)	P-value*
Female	159 (53.2%)	81 (65.3%)	78 (44.6%)	<0.01
Male	140 (46.8%)	43 (34.7%)	97 (55.4%)	<0.01
Age (median, IQR)	15.9 [14.1-18.1]	16.8 [14.9-19.1]	15.4 [14-17.2]	<0.01
Years on ART (median, IQR)	10 [7.8-11.4]	9.9 [7.3-11.2]	10.1 [7.9-11.6]	0.35
Orphan**	39 (13.0%)	18 (14.5%)	21 (12.0%)	0.52
Detectable VLs	105 (35.0%)	49 (40.5%)	56 (33.3%)	0.21
*p-value for comparison between those with Total Stigma (>9) or Total Stigma (≤9)				
**orphans defined by loss of both parents				

**Univariable Analysis of Stigma and Virologic Failure (VF)**

Out of the 105 (35.0%) adolescents who met the pre-defined criteria for VF, 49 (40.5%) were classified as having a high total stigma score, and 56 (33.3%) were classified as having a low total stigma score (p=0.21) (Table 1).

There was no significant association between dichotomized total stigma and VF (median total stigma score 9 (IQR 6.5-11), p=0.74). Considering total stigma score as a continuous variable resulted in an odds ratio of 1.0 (95% confidence interval (CI): 0.94-1.06). Neither dichotomized anticipated stigma (p=0.51), experienced stigma (p=0.66), or internalized stigma (p=0.64) were associated with VF (Table 2). Considering anticipated, experienced, and

internalized stigma as continuous variables resulted in odds ratio of 1.1 (95% CI: 0.89-1.26), 0.96 (95% CI: 0.80-1.15), and 1.0 (95% CI: 0.89-1.20), respectively.

**Table 2. Univariable Analysis of Association between Stigma and Virologic Failure (VF)**

	Median, IQR	Odds Ratio w/ 95% CI	P-value
Total Stigma	9 [6.5-11]	1.0 [0.94-1.06]	0.74
Anticipated Stigma	3 [2-4]	1.1 [0.89-1.26]	0.51
Experienced Stigma	3 [2-4]	0.96 [0.80-1.15]	0.66
Internalized Stigma	3 [1-4]	1.0 [0.89-1.20]	0.64

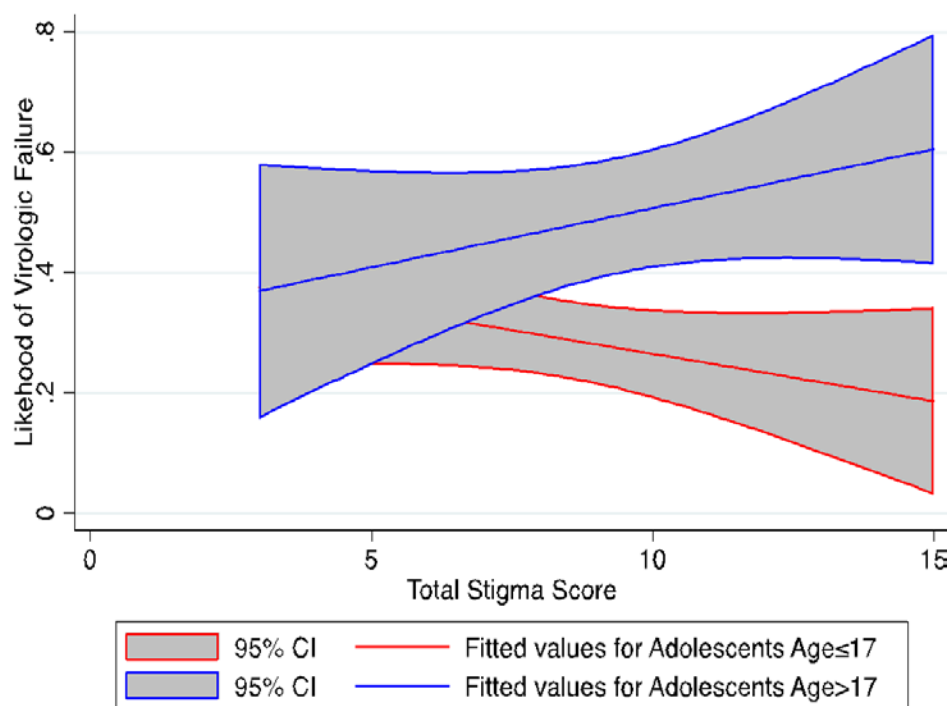
#### **Multivariable Analysis of Stigma and Virologic Failure (VF)**

Table 1 shows that there is a difference between participants in either the Total Stigma (>9) or Total Stigma (≤9) group depending on their age and gender. Older adolescents were more likely than younger adolescents to have a high total stigma score (median age 16.8 (IQR 14.9-19.1) versus 15.4 (IQR 14-17.2),  $p<0.01$ ). Female participants were more likely to have a high total stigma score than a low total stigma score (81 (65.4%) versus 78 (44.6%),  $p<0.01$ ). Male participants were more likely to have a low total stigma score than a high total stigma score (97 (55.4%) versus 43 (34.7%),  $p<0.01$ ) (Table1).

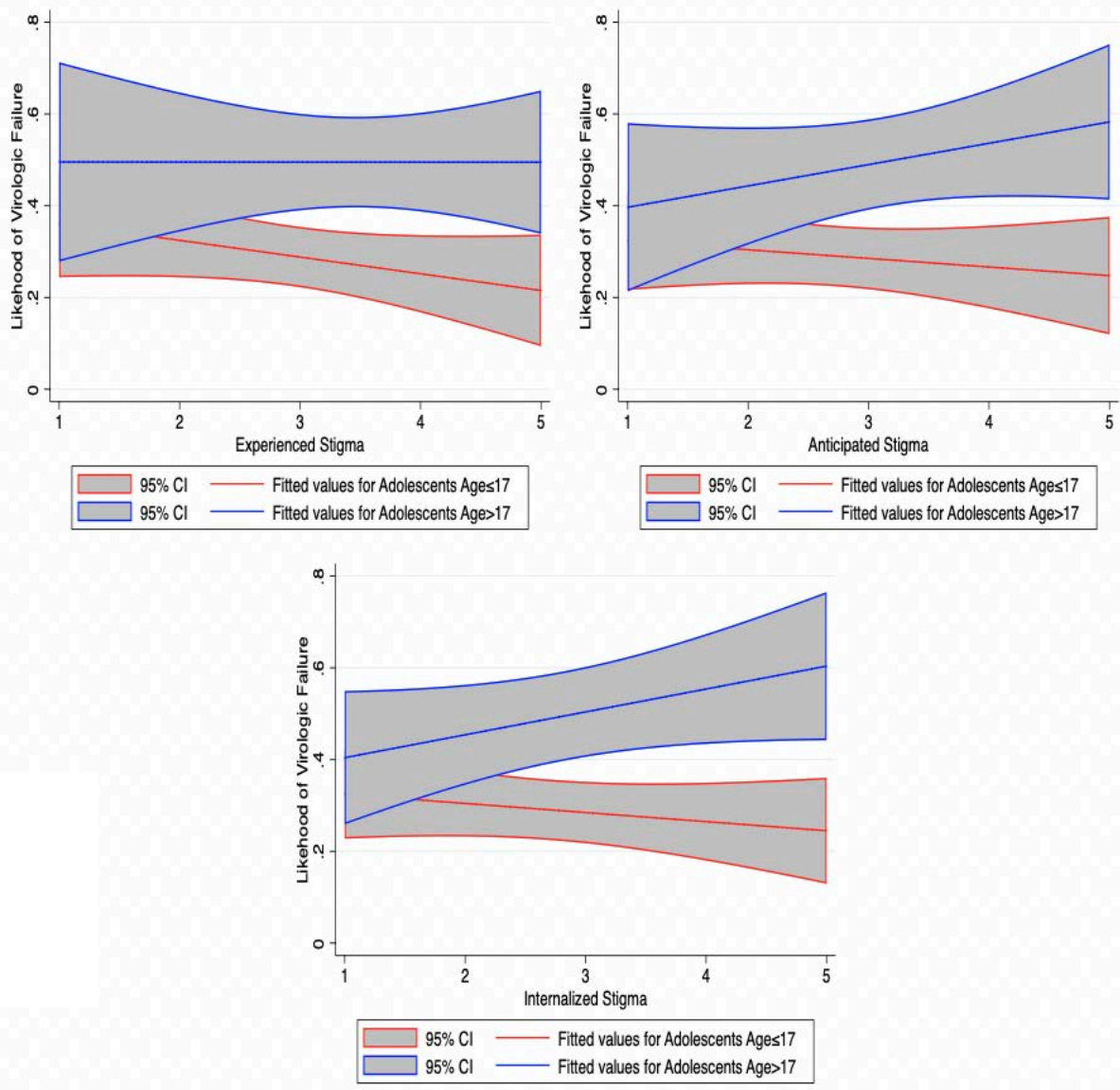
Controlling for age changed the odds ratio of VF with increasing stigma score from 1.01 (95% CI 0.94-1.06) to 1.23 (95% CI 1.10-1.36). There was confounding by age for each of the stigma domains when evaluated individually as the outcome of interest. There was no confounding by any of the other tested covariates which included gender, years on ART, orphan status, and detectable VLs.

## Perceived Stigma and VF in Younger and Older Adolescents

Age was an effect modifier of the association between Stigma and VF. For older adolescents (>17 years of age), the odds of VF increased with increasing stigma score. However, for younger adolescents ( $\leq 17$  years of age), the odds of VF decreased with increasing stigma score (interaction p-value < 0.001; Figure 2). For older adolescents, VF increased with increasing stigma score when each domain of stigma was evaluated separately (Figure 3). For younger adolescents, VF decreased with increasing stigma score when each domain of stigma was evaluated separately (Figure 3).



**Fig. 2 Association between Perceived Stigma and VF in Younger and Older Adolescents**



**Fig. 3 Association between Domain Specific Stigma and VF in Younger and Older Adolescents**

## Chapter 4

### Discussion

The clear evidence of effect modification by age in the relationship between perceived stigma and virologic outcomes is the most remarkable finding of this study. Prior studies of HIV-related stigma in adults suggest that stigma has a consistently negative effect on medication adherence and treatment outcomes.<sup>12,15,16,17</sup> A single study done previously at the clinic where we performed our study suggested that caregivers of young children living with HIV who experienced or anticipated high levels of stigma had increased motivation to support their children to maintain high levels of treatment adherence. Visible illness plays an intermediary role between adherence and perceived stigma for caregivers because caregivers understand that ART suppresses the physical manifestation of HIV, and in an effort to prevent the disclosure of the child's status, the children have excellent adherence. The caregiver's commitment to having a child with excellent adherence helps hide "the family secret" and prevents stigmatizing family or community members from finding out the child's status.<sup>19</sup>

For older adolescents (>17 years of age) the pattern of increased risk of VF with increasing stigma scores that has previously been reported in adults was seen. Previous studies of adults living with HIV have found that anticipated stigma remains a barrier to care because adults remain hesitant to seek care as long as they fear that doing so will lead to prejudice and discrimination. Anticipated stigma, as a result, is associated with a greater likelihood of chronic illness comorbidity because adults living with HIV spend so much time avoiding care that their disease progresses significantly.<sup>12,34</sup> Experienced stigma has been associated with a greater



likelihood of having a CD4 count lower than 200, which is a result of medication non-adherence. Internalized stigma in adults living with HIV has been associated with poor adherence due to lower acceptance of HIV status, lower perceived benefits of ART, greater helplessness, and greater number of days in medical care gap.<sup>12</sup> Overall, stigma is a known barrier to HIV testing and care, and causes adults living with HIV to have worse adherence. Older adolescents in our study could be affected by HIV-perceived stigma in a similar manner to adults living with HIV, which could put their overall health at a greater risk due to emergence of resistant virus strains, chronic illness comorbidity, and greater likelihood of infecting a potential partner.

Contrary to our hypothesis, the direction of risk associated with anticipated and experienced stigma was the same as that for internalized stigma. The variable of age as an effect modifier followed similar patterns for each domain of stigma (Figure 3). When adolescents experienced, anticipated, or internalized stigma, the risk of VF increased or decreased as a result of their individual age, and not of the specific stigma domain. Older adolescents are in the process of maturing into young adults and gaining more autonomy over their medication-taking; therefore, parental supervision may decrease, and perceived stigma may have a greater impact over their decision-making process. Compared to adults, adolescents tend not to consider future consequences when making the decision to not take their medications, it's typically more important for them to consider how not taking their medications makes them feel good at that moment and decreases the potential chance of someone finding out about their HIV status. In adults living with HIV, perceived stigma is associated with increased risk behavior and poor adherence, which suggest that stigma could aid in the raise of the HIV epidemic if interventions addressing these vulnerable groups are not implemented. In South Africa, adults living with HIV who experienced stigma were less likely to disclose their HIV status to their sexual partner,

which was associated with transmission risk behavior.<sup>35</sup> Additionally, a sample of over 2,000 sexually active adults living with HIV in France experiences of discrimination were associated with increased unsafe sex.<sup>36</sup> In a study in China of individuals who were HIV-negative or whose status was unknown, those holding greater stigmatizing attitudes were more likely to engage in high risk behaviors.<sup>37</sup> Perceived stigma in adults living with HIV results in increased risk behaviors as a result of anticipated or experienced stigma suggesting that although adults are more likely than adolescents to understand the potential future consequences associated with non-adherence behaviors, they are still likely to non-adherence to their medication. There is a need for cultural acceptance of individuals who are seropositive especially in countries with a high-prevalence of HIV, such as Botswana.

The observed differences in effects of perceived stigma in younger and older adolescents creates a paradox that is important for clinicians to recognize. In younger adolescents, perceived stigma can be described as a “protective stigma” similarly to how it’s described in children living with HIV whose caregivers have experienced or anticipated stigma. The opposite is observed in older adolescents whose perceived stigma increases their likelihood of VF similar to adults living with HIV. In busy clinics where children who have maintained virologic suppression may be perceived by clinicians to need less support, it’s critical for clinicians to consider screening those who are doing well when they are younger. Identifying younger adolescents with higher stigma would allow for stigma-reduction interventions to start earlier and may allow them to maintain better outcomes as they enter older adolescence and early adulthood.

## Chapter 5 Limitations and Future Directions

This study was performed in a pediatric and adolescent specialty center where >95% of patients are believed to have been perinatally infected with HIV, the generalizability of the findings to behaviorally-infected adolescents is uncertain. The generalizability of this study might also be limited by the fact that our patients, unlike most in resource-limited settings, received regular virologic testing through the universal ART coverage in Botswana and are offered regimen switch when they have persistent virologic failure. Additionally, the generalizability of this study might be limited by the unknown relationships between medication-taking autonomy, HIV status disclosure, and perceived stigma among younger and older adolescents. The level of medication-taking autonomy may differ between younger and older adolescents depending on the parental supervision, which as a result could impact the observed relationship between stigma and HIV treatment outcome.

Future studies should aim to evaluate these relationships to identify potential factors, which could mitigate the association between perceived stigma and treatment outcome. Qualitative analyses might also elucidate the reasons for our findings by providing study participants the opportunity to share instances when they experienced, anticipated, and/or internalized stigma. Nevertheless, this study has contributed to previous HIV-related stigma research by demonstrating that the association between HIV-related stigma and treatment outcomes in adolescents depends on age.

## Appendix A

### HIV Stigma Scale

1. I am afraid that people will find out that I have HIV.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
2. I am very careful who I tell that I have HIV	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
3. I worry that people who know that I have HIV will tell others.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
4. I feel that I am not as good a person as others because I have HIV.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
5. Having HIV makes me feel unclean.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
6. Having HIV makes me feel that I am a bad person.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
7. Most People think that a person with HIV is disgusting.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
8. Most people with HIV are rejected when others find out.	<input type="radio"/> Definitely False <input type="radio"/> Somewhat False <input type="radio"/> Not True or False <input type="radio"/> Somewhat True <input type="radio"/> Definitely True
9. Have you ever told anyone that you have HIV?	<input type="radio"/> Yes <input type="radio"/> No
10. I have been hurt by how people reacted to learning I have HIV.	<input type="radio"/> Yes <input type="radio"/> No

11. I have lost friend by telling them I have HIV.	<input type="radio"/> Yes <input type="radio"/> No
--	---

## BIBLIOGRAPHY

- 1 UNAIDS. Global HIV & AIDS statistics 2018. <http://www.unaids.org/en/resources/fact-sheet>.
- 2 Global HIV and AIDS statistics 2018. <https://www.avert.org/global-hiv-and-aids-statistics>.
- 3 Treatment of children living with HIV 2014.  
<https://www.who.int/hiv/topics/paediatric/hiv-paediatric-infopage/en/>.
- 4 HIV and AIDS in Botswana 2018.  
<https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/botswana>.
- 5 Khan, M., Song, X., Williams, K., Bright, K., Sill, A., Rakhmanina, N. Evaluating adherence to medication in children and adolescents with HIV. *Arch Dis Child*. 2009;94(12):970-973.
- 6 Deeks, S.G. Protease inhibitors as immunomodulatory drugs for HIV infection. *Clin Pharmacol Ther*. 2007;82(3):248-250.
- 7 Bangsberg, D.R., Moss, A.R., Deeks, S.G. Paradoxes of adherence and drug resistance to HIV antiretroviral therapy. *J Antimicrob Chemother*. 2004;53(5):696-699.
- 8 Pham, P.A. Antiretroviral adherence and pharmacokinetics: review of their roles in sustained virologic suppression. *AIDS Patient Care STDS*. 2009;23(10):803-807.
- 9 Ferrand, L.S., Whande, B., Munaiwa, L., Langhaug, L., Cowan, F., Mugurungi, O., Gibb, D., Munyati, S., Williams, B.G., Corbett, E.L. Survey of children accessing HIV services in a high prevalence setting: time for adolescents to count? *Bull World Health Organization*. 2010;88(6):428-434.
- 10 Attia, S., Egger, M., Muller, M., Zwahlen, M., Low, N. Sexual Transmission of HIV

- according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS*. 2009;23(11):1397-1404.
- 11 Chan, B.T., & Tsai, A.C. HIV stigma trends in the general population during antiretroviral treatment expansion: analysis of 31 countries in sub-Saharan Africa, 2003-2013. *Journal of acquired immune deficiency syndromes*. 2016;72(5), 558-564.
- 12 Earnshaw, V.A., Smith, L.R., Chaudoir, S.R., Amico, K.R., & Copenhaver, M.M. HIV stigma mechanisms and well-being among PLWH: a test of the HIV stigma framework. *AIDS and Behavior*. 2013;17(5), 1785-1795.
- 13 Pitpitan, E.V., Kalichman, S.C., Eaton, L.A., et al. AIDS-related stigma, HIV testing, and transmission risk among patrons of informal drinking places in Cape Town, South Africa. *Ann Behav Med*. 2012;43(3):362---371.
- 14 Delavande, A., Sampaio, M., Sood, N. HIV-related social intolerance and risky sexual behavior in a high HIV prevalence environment. *Soc Sci Med*. 2014;111:84-93
- 15 Leserman, J. HIV disease progression: depression, stress, and possible mechanisms. *Biol Psychiatry*. 2003;54(3):295-306.
- 16 Leserman, J. Role of depression, stress, and trauma in HIV disease progression. *Psychosom Med*. 2008;70(5):539-45.
- 17 Kiecolt-Glaser, J.K., McGuire, L., Robles, T.F., Glaser, R.E. Emotions, morbidity, and morality: new perspectives from psychoneuroimmunology. *Annu Rev Psychol*. 2002;53(1):83-107.
- 18 Fielden, S. J., Chapman, G. E., & Cadell, S. Managing stigma in adolescent HIV: silence, secrets and sanctioned spaces. *Culture, health & sexuality*. 2011;13(03), 267-281.
- 19 Tippett Barr, B. A. (2006). Pediatric antiretroviral adherence and child disclosure in

- botswana (Order No. 3259514). Available from ProQuest Central; ProQuest Dissertations & Theses A&I; ProQuest Dissertations & Theses Global. (304981566). Retrieved from <http://ezaccess.libraries.psu.edu/login?url=https://search.proquest.com/docview/304981566?accountid=13158>.
- 20 Arrive, E., Anaky, F., Wemin, M., Diabate, B., Rouet, F., Salamon, R., Msellati, P.  
Assessment of adherence to highly active antiretroviral therapy in a cohort of African HIV-infected children in Abidjan, Cote d'Ivoire. *Journal of Acquired Immune Deficiency Syndrome*. 2005;40(4), 498-500.
- 21 Idele, P., Gillespie, A., Porth, T., Suzuki, C., Mahy, M., Kasedde, S., & Luo, C.  
Epidemiology of HIV and AIDS among adolescents: Current status, inequities, and data gaps. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2014;66(Suppl 2), S144–S153.
- 22 Yang, E., Mphele, S., Moshashane, N., Bula, B., Chapman, J., Okatch, H., ... & Lowenthal, E.  
Distinctive barriers to antiretroviral therapy adherence among non-adherent adolescents living with HIV in Botswana. *AIDS care*. 2018;30(2), 224-231.
- 23 Okawa, S., Mwanza Kabaghe, S., Mwiya, M., Kikuchi, K., Jimba, M., Kankasa, C., & Ishikawa, N. Psychological well-being and adherence to antiretroviral therapy among adolescents living with HIV in Zambia. *AIDS care*. 2018;30(5), 634-642.
- 24 Earnshaw, V.A., Chaudoir, S.R. From conceptualizing to measuring HIV stigma: a review of HIV stigma mechanism measures. *AIDS Behav*. 2009;13(6):1160–77.
- 25 Link, B.G., Phelan, J.C., Stigma and its public health implications. *Lancet*. 2006;367:528-9
- 26 Earnshaw, V.A., Lang, S.M., Lippitt, M., Jin, H., Chaudoir, S.R. HIV stigma and physical health symptoms: do social support, adaptive coping, and/or identity centrality act as



- resilience resources? *AIDS Behav.* 2015;19(1):41–9.
- 27 Helms, C.B., Turan, J.M., Atkins, G., Kempf, M.C., Clay, O.J., Raper, J.L., et al. Interpersonal mechanisms contributing to the association between HIV-related internalized stigma and medication adherence. *AIDS Behav.* 2017;21(1):238–47. 19.
- 28 Li, J.H., Mo, P.K.H., Wu, A.M.S., Lau, J.T.F. Roles of self-stigma, social support, and positive and negative affects as determinants of depressive symptoms among HIV infected men who have sex with men in China. *AIDS Behav.* 2017;21(1):261–73.
- 29 Prati, G., Zani, B., Pietrantonio, L., et al. The role of knowing someone living with HIV/AIDS and HIV disclosure in the HIV stigma framework: a Bayesian mediation analysis. *Qual Quant.* 2016;50(2):637–51.
- 30 Chan, B.T., Tsai, A.C., Siedner, M.J. HIV treatment scale-up and HIV-related stigma in sub Saharan Africa: a longitudinal cross-country analysis. *Am J Public Health.* 2015;105:1581-1587.
- 31 Wright, K., Naar-King, S., Lam, P., Templin, T., Frey, M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health.* 2007;40(1):96-98.
- 32 Harris, P.A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., Conde, J.G. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42:377–381.
- 33 STATA Statistical Software: Release 15 [computer program]. College Station, TX: StataCorp LP; 2017.
- 34 Treves-Kagan, S., Steward, W. T., Ntswane, L., Haller, R., Gilvydis, J. M., Gulati, H., ... & Lippman, S. A. Why increasing availability of ART is not enough: a rapid, community

- based study on how HIV-related stigma impacts engagement to care in rural South Africa. *BMC public health*. 2015;16(1), 87.
- 35 Simbayi, L.C., Kalichman, S.C., Strebel, A., et al. Disclosure of HIV status to sex partners and sexual risk behaviours among HIV-positive men and women, Cape Town, South Africa. *Sex Transm Infect*. 2007;83:29–34.
- 36 Peretti-Watel, P., Spire, B., Obadia, Y., et al. Discrimination against HIV-infected people and the spread of HIV: some evidence from France. *PLoS One*. 2007;2:e411.
- 37 Liu, H., Hu, Z., Li, X., et al. Understanding the interrelationships among HIV-related stigma, concern about HIV infection, and intent to disclose HIV serostatus: a pretest-posttest study in a rural area of Eastern China. *AIDS Patient Care & STDs*. 2006;20:133–142.

## ACADEMIC VITA

Karina Grullon Perez

k.grullonperez@gmail.com

### EDUCATION

**Schreyer Honors College at the Pennsylvania State University**, University Park, PA

B.S. Biology – Vertebrate Physiology Option, Honors General Science, May 2019

Spanish and Psychology Minors

Thesis Title: **The Pros and Cons of Perceived HIV-Related Stigma in Young and Older Adolescents in Botswana**

Thesis Supervisor: **Dr. Joshua Rosenberger**

**Fudan University**, Shanghai, China, July 2016

### RESEARCH EXPERIENCE

**Icahn School of Medicine at Mount Sinai**, New York, New York

*June 2018 – August 2018*

**Summer Undergraduate Research Program**

**Research Intern**

- Investigated the role of NKX2-1 in Small Cell Lung Cancer under the mentorship of Ranran Kong, MD

**Children's Hospital of Philadelphia (CHOP)**, Philadelphia, PA

*August 2017 – May 2019*

**Research Intern**

- Investigated the effect of perceived stigma on treatment outcome of HIV+ adolescents in Botswana using STATA and Excel

**CHOP Research Institute Summer Scholars Program (CRISSP) Intern**

*June – August 2017*

- Competitive ten-week research internship and professional development experience

**Dr. Melissa Rolls Lab, Biochemistry and Molecular Biology**, University Park, PA

*August 2016 – May 2018*

**Research Assistant**

- Investigated the role of potential genes required for dendrite regeneration under mentorship of Richard Albertson, MD, PhD candidate

### LEADERSHIP EXPERIENCE

**Ritner Experience Program**, University Park, PA

*August 2016 – May 2019*

**Program Assistant**

- Devoted approximately 20 hours per week to conducting programs, peer-mentoring, and keeping office hours to help first-year students in Ritner Hall have a successful first-year at Penn State

**Student Minority Advisory and Recruitment Team, University Park, PA**

*September 2015 – May 2019*

**Overnight Co-Director**

- Worked alongside Penn State admissions to plan and host Spend a Fall Day, an overnight recruiting event for underrepresented students

**Treasurer**

- Organized fundraisers and managed account funds
- Served as a tour guide for the university and assisted with special recruitment activities such as Spend a Fall Day and Achievers

**Director of Hispanic/LatinX Recruitment Initiative**

- Collaborated with admissions and LatinX student organizations on campus to coordinate the first Hispanic Heritage Bus Trip

**National Organization for the Professional Advancement of Black Chemist and Chemical Engineers, University Park, PA**

*January 2018 – May 2019*

**Outreach Director**

- Planned and organized outreach programs to high schools in Philadelphia to provide mentorship and guidance to students interested in a career in STEM

**COMMUNITY INVOLVEMENT**

**Teaching Assistant, Biology Department, University Park, PA**

*January – May 2019*

- Held regularly scheduled office hours to provide Biology 411 – Medical Embryology students with help understanding the lecture material and practice questions

**Penn State Alternative Breaks, Philadelphia, PA, Detroit, MI, Niagara Falls, NY**

*November 2016, March 2018, November 2018*

- Traveled to various cities to volunteer in homeless shelters, soup kitchens, and non-profit organizations

**Mount Nittany Medical Center, State College, PA**

*September 2016 – May 2018*

- Volunteered in patient floors assisting nurses and physicians with daily tasks

**Assistant Teaching Assistant, Biology Department, University Park, PA**

*August – December 2017*

- Provided students in Biology 110 with additional assistance during regularly scheduled laboratories by answering questions and demonstrating proper laboratory techniques

**Learning Assistant, Chemistry Department, University Park, PA**

*January – May 2017*

- Attended Chemistry 112 – General Chemistry II lectures, helped facilitate student discussions during clicker questions, and led weekly homework sessions

## HONORS AND AWARDS

<b>Multicultural Resource Center (MRC)'s Inspiring Student Leader Award</b>	<i>Spring 2019</i>
<b>University Fellowships and Phi Kappa Phi Peter T. Luckie Award for Outstanding Juniors in Science and Engineering</b>	<i>Spring 2018</i>
<b>CHOP Research Institute Summer Scholars Program Outstanding Clinical Research Poster Award</b>	<i>Summer 2017</i>
<b>Gateway Scholar Schreyer Honors College</b>	<i>Spring 2017</i>
<b>Dean's List-every semester</b>	<i>Fall 2015 – Spring 2019</i>

## LANGUAGE PROFICIENCY

**English and Spanish**