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COLLEGE OF HEALTH SCIENCES

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Christopher Tex

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2012

Abstract

The CDC Western Blot Standard for HIV Confirmatory Testing and Clinical

Laboratory Administrator Demographic Characteristics

by

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M.P.H., Medical College of Ohio, The University of Toledo,

Bowling Green State University, 2003

B.S., University of Findlay, 2001

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

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Abstract

Although HIV Western blot (WB) antibody tests are used to screen and diagnose HIV infection, the manufacturers of the test kits disclaim their use for such practices. Currently, there is no globally accepted standard for what constitutes a positive result on a WB test, as there are 11 standards across the world. Consequently, a person could conceivably test positive at one laboratory and test negative at another. The Centers for Disease Control and Prevention Western blot standard (CDC WBS) is one standard used at a majority of the United States clinical laboratories. The purpose of this quantitative correlational study was to determine if there is a relationship between the demographic characteristics (geographic location, education major, years of experience) of clinical laboratory administrators and the likelihood that they would use the CDC WBS to evaluate Western Blot results. The social ecological model was the conceptual framework model for this study. A telephone survey was completed by 163 clinical laboratory administrators who conducted WB tests in their facilities and participated in a 2008 CDC survey. Clinical laboratory administrators who held their highest degrees in the biological or health sciences were 5 times more likely to use the CDC WBS. The positive social change implications of this study include evidence for the need to educate certain clinical laboratory administrators in using a standard test, namely the CDC WBS, to eliminate inconsistencies in HIV test results nationally.

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Dedication

This dissertation is dedicated to my loving family. Without their love and support,

this dissertation would not have come to fruition.

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I would like to thank my committee members, Dr. Ferraro and Dr. Rea, whose continual support and guidance have allowed me to become a scholar practitioner. I would also like to acknowledge my editor, Ardella Crawford, whom has also been instrumental in ensuring that my work reflects excellence. Bob Leppo is another source of support, as he saw the importance of my research and how it would have positive societal implications.

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Chapter 1: Introduction to the Study

Introduction and Background

HIV is said to be the etiological cause of AIDS (Gallo et al., 1984; Rajadurai, Arthy, Muthulakshmi, & Rajan, 2010). For accurate identification of HIV infection in clinical and public health surveillance initiatives, antibody testing is essential. The detection of HIV antibodies occurs when the immune system responds to viral antigens contained in the reagents. HIV is composed of envelope, core, and polymerase antigens. All antigens are located within the virion in precise locations, depending on chemical composition and molecular weight. The accuracy of the diagnostic tests depends on the identification of the specific HIV antigen. In fact, from a screening and confirmatory perspective, the configuration and quantity of the antigens contained in the reagents are important if the test is to be advocated for identifying all individuals who are infected (Cohen, Hellman, Levy, DeCock, & Lange, 2008).

Antibody testing remains a cost effective tool for detecting HIV antibodies. Tests such as these were initially employed to screen the blood, ensuring that the blood supply was safe. From a diagnostic perspective, antibody tests are also used to verify infection in individuals and to assess exposure to HIV in relatively healthy populations. The enzyme-linked immunosorbant assay (ELISA) and Western blot (WB) tests are two common antibody tests that screen and confirm HIV infection, respectively (Constantine & Zink, 2005). The former test is to identify infection in all persons, while the latter was constructed to separate falsely reactive (false positive) ELISA results from those whose results are genuine (Syed et al., 2005).

Errors and variations exist for all methods of analytic techniques, such as antibody testing. Uncertainty with achieving accurate results can affect the quality of the laboratory result. For this reason, laboratory personnel must be cognizant of such issues in order to employ foundational principles to identify the performance and limitations of the test. Criteria have been established to verify the efficacy or effectiveness of any given test, supposing that an evaluation of the test has been conducted appropriately by trained personnel. The manufacturer guidelines should also serve to assist in correctly performing the test (Omersel, Zager, Kveder, & Bozic, 2010; Peeling, Smith, & Bossuyt, 2008).

Despite over 2 decades of HIV/AIDS research, clinicians and public health professionals remain able only to prevent and reduce the number of HIV infections in the population. A cure for AIDS has not been found (Barouch, 2008; Cohen, 2007; Flynn et al., 2005). Furthermore, although a variety of antibody tests exists on the market, an examination of what these tests purport has not been readily evidenced in the literature. The HIV antibody tests currently used to screen for and diagnose HIV have certain limitations. As will be shown in Chapter 2, many cases have been documented in the literature pertaining to the nonspecificity of the antibodies used in HIV antibody test-kits (Johnson, 1996). This study helps elucidate whether the demographic characteristics of clinical laboratory administrators are correlated with use of the WB standard and provides a contextual framework for WB testing standards.

The results of this study help explain user influences in false positive reactions. It may also provide evidence for why the CDC standard for the WB test is employed. This

information, in turn, can ameliorate the burden of effort required by laboratory practitioners in the diagnosis of true HIV cases and reduce the number of false positives. A comprehensive assessment of HIV antibody testing, associated epidemiological concepts, and references are presented in Chapter 2.

Problem Statement

Currently, no standard is globally accepted for what constitutes a positive result on a WB test, though it is widely presumed to be a confirmatory test because 11 standards currently exist. The licensing limitations for use by the Food and Drug Administration (FDA) include all HIV antibody tests, such as ELISA, WB, and Viral Load. These tests should be limited to confirmation of seropositivity and not used for screening or diagnostic purposes (Abbott Laboratories, 2002; Bio Rad Laboratories, 2007; Roche Diagnostic Systems, Inc., 2007). In fact, these tests have been shown to have a very low positive predictive value of only 2% (Steckelberg & Cockerill, 1988). Over 66 health conditions can cause cross-reactions. The standards vary, depending on the number of proteins the agency designates as being specific to HIV. For this reason, the choice of which standard to use is left to the administrators of the clinical laboratories. Consequently, a patient could conceivably test positive at one laboratory and negative at another laboratory that uses a different WB test standard. In fact, it was found that in one laboratory, two separate standards were used (Leung, 2009). While WB standards vary globally, this study will focus on the CDC WBS.

Purpose of the Study

The purpose of this quantitative correlational study was to determine whether there is a relationship between the demographic characteristics of the clinical laboratory administrator and the odds that he or she uses the CDC standard to evaluate WB results. This study examined the demographic characteristics of geographic location, education major, and years of experience as they relate to use of one standard, the CDC WBS. This standard was chosen because 88.5% of the participating clinical laboratories stated on the CDC survey that they use this standard (CDC, 2008). The data for this study were obtained via an electronic survey of clinical laboratory administrators that are representative of the United States clinical laboratories.

Nature of the Study

Twenty-six years ago, Dr. Robert Gallo held a joint press conference with the United States Department of Health and Human Services (HHS) to announce that he had discovered the probable cause of AIDS: HIV (Leung, 2009). Although Gallo, the presumed codiscoverer of HIV, issued no empirical evidence, the HHS concluded that the discovery of this accepted virus was a foundational piece for the success of science in combating the disease. Once Gallo had published his research regarding the development of his HIV antibody test, he discovered that he was unable actually to find the virus in 64% of the patients he studied who were classified as having AIDS (Gallo et al., 1984). Furthermore, Luc Montagnier, Nobel Laureate in Medicine for his discovery of HIV, acknowledged that not only did he not purify this virus, but that individuals could be exposed many times and be clear of the virus within a matter of weeks (Leung, 2009;

Tahi, 1988). Therefore, ambiguity still exists both in the use of HIV antibody testing and in HIV diagnosis.

Since the discovery of HIV in 1984, clinicians and public health professionals have advocated widespread use of antibody tests so that individuals can know their HIV status. ELISA, WB, and Viral Load tests have been approved by the FDA with test package inserts that disclaim the use of their products for uses other than their intended purposes (Abbott Laboratories, 2002; Bio Rad Laboratories, 2007; Roche Diagnostic Systems, Inc., 2007). In fact, different interpretations for what constitutes a positive result on a WB test comprise varying standards on a global scale. Furthermore, six standards are evident in the United States. However, the use of these standards has not been well studied. Although there are various standards across the globe, this research study examines only the CDC WBS.

The CDC standard classified a WB as being positive if the sample included two particular proteins, p24 and p41 (Wilber, 1991). The American Red Cross has designated a positive reaction if antibodies are present in the group-associated (gag), polymerase (pol), and envelope (env) regions of the protein, regardless of the band (Healey et al., 1992; Lundberg, 1988). A positive reaction, according to the Association of State and Territorial Public Health Laboratory Directors, is designated as a sample that reacts to two protein combinations—namely, p120/p160, p41, and p24 (Mylonakis et al., 2000). Similarly, the Consortium for Retrovirus Serology Standardization (CRSS) characterizes a sample as positive if p120/p160 or p41 is present. The sample must also be reactive to p32 or p24. Interestingly, MP Diagnostics (2005) asserts that the interpretation of WB

results should be at the discretion of local agencies who have "accepted" policies. A negative result on a WB occurs when the sample does not react to any of the bands, in addition to those proteins that are nonHIV proteins. A laboratory may designate a sample as WB indeterminate if it does not fulfill the criteria used by the laboratory (Lundberg, 1988). Therefore, in order to expand our knowledge of improving HIV prevention and control within the United States, it is essential to research how various laboratories across the nation determine a positive reaction on a WB antibody test.

This research used a quantitative correlational design to assess whether demographical characteristics, namely, geographical location, educational major, and years of experience, of the clinical laboratory administrator influenced their decision to use the CDC WBS for confirming HIV infection. The sample population consisted of 163 clinical laboratory administrators, obtained from the CDC. Upon obtaining this list, I developed a telephonic survey to capture demographical data.

Research Questions and Hypotheses

The overarching research question was this: How do demographic characteristics of the clinical laboratory administrator predict use of the CDC standard to evaluate WB results? This study aimed to answer four specific questions:

1. Does the administrator's geographic location (GL) predict the use of the CDC WBS to evaluate WB results?

$H_0 1$: The administrator's GL does not predict the use of the CDC WBS to evaluate WB results.

H_a1: The administrator's GL predicts the use of the CDC WBS to evaluate WB results.

2.   Does the administrator's education major (EM) predict the use of the CDC WBS to evaluate WB results?

H_02: The administrator's EM does not predict the use of the CDC WBS to evaluate WB results.

H_a2: The administrator's EM predicts the use of the CDC WBS to evaluate WB results.

3.   Do the administrator's years of experience (YE) predict the use of the CDC WBS to evaluate WB results?

H_03: The administrator's YE do not predict the use of the CDC WBS to evaluate WB results.

H_a3: The administrator's YE predict the use of the CDC WBS to evaluate WB results.

4.   Do the administrator's GL, EM, YE predict the use of the CDC WBS to evaluate WB results?

H_04: The administrator's GL, EM, and YE do not predict the use of the CDC WBS to evaluate WB results.

H_a4: The administrator's GL, EM, and YE predict the use of the CDC WBS to evaluate WB results.

Chapter 3 will discuss the data analysis procedures and ways to control for potential confounding variables.

Conceptual Framework

In order to explain the phenomenon of HIV and the various U.S. testing standards, the social ecological model (SEM) was employed. Successful HIV-prevention interventions require unambiguous results following antibody tests. Various standards exist for interpreting HIV test results. Thus, a positive HIV test may not arise from the existence of antibodies for the disease but could rather be due to other extrinsic factors. The basis of the SEM is to recognize that a person's ecosystem is influential in his or her daily activities (Institute of Medicine, 2003). Furthermore, this influence of the ecosystem can occur at many levels. Therefore, a person and his or her characteristics fit in such a way that each level incorporates a progression in indirect environmental influences (Bronfenbrenner, 1977). From a hierarchical perspective, influence is exerted on consecutive layers of proximal and distal entities (Kaplan, Everson, & Lynch, 2000). According to Fisher et al. (2005) and Glass (2000), the levels are typically identified from the individual, organization, community, and policy. By applying this theoretical framework to HIV and antibody testing, clinical laboratory professionals can recognize how environmental factors, such as standards for confirmatory testing, may influence identification of the disease, which in turn, affects disease transmission and prevention. The SEM will be further discussed in Chapter 2.

Four parameters can be used to determine how useful a test is—namely, sensitivity, specificity, efficiency, and predictive values. Furthermore, the concepts of reproducibility and precision are tacit for assessing the accuracy of the test (Gatsonis & Paliwal, 2006; Leeflang, Deeks, Gatsonis, & Bossuyt, 2008). Screening tests are thought

to be highly sensitive intrinsically. Therefore, an antibody test that possesses such a characteristic should yield a low number of false-negative reactions. A confirmatory test, such as the WB test, is highly specific in that it yields low numbers of false-positive reactions. From a laboratory perspective, a diagnosis of HIV is asserted when a specific set of antibodies reacts with the antibody test kit. However, for an accurate diagnosis, the antibody test should identify only antibodies that are specific to HIV, rather than other antibodies that may cross-react because of similarities to the HIV antigens (Guan, 2007).

Sloland, Pitt, Chiarello, and Nemo (1991) assert that the testing technology available can accurately diagnose HIV infection in both the general and high-risk populations. Furthermore, the World Health Organization (WHO) and Joint United Nations Programme on HIV/AIDS (2001) state that HIV antibody tests are highly sensitive and specific—namely, having over a 98% specificity. Interestingly, from a predictive value perspective, if two persons out of 100 are actually infected, and if, within a population of 100 negative individuals, there are two false positive reactions, then the specificity would be 98% because there are four positive reactions whereby two are actually identified accurately. Such a phenomenon would yield a 50% probability of identifying an individual who is actually infected. However, several researchers assert that the progression of new testing methodologies has allowed validation of antibody tests (Busch et al., 1991; Jackson et al., 1990; Nkengasong et al., 1999; Samdal et al., 1996; Silvester, Healey, Cunningham, & Dax, 1995; Urassa et al., 1999). For this reason, it is important to recognize that the specificity of presumed HIV proteins can create ambiguity in test results (Bess, Gorelick, Bosche, Henderson, & Arthur, 1997; Corbett,

2009; Erickson, McNiff, & Klausner, 2006; Garcia, Tormo, Gimeno, de Lomas, & Navaro, 2009; Gluschankof, Mondor, Gelderblom, & Sattentau, 1997; Strandstrom, Higgins, Mossie, & Theilen, 1990). Therefore, a gap in the literature exists, which will be discussed further in Chapter 2.

Definitions of Key Variables

Antibody: A protein that recognizes foreign material and neutralizes the material to prevent re-infection (United States Department of Health Services, 2008).

Antiretroviral: A medication that disrupts the replication of HIV (United States Department of Health Services, 2008).

Education major: Refers to the clinical laboratory manager's education that may influence the manager in making decisions about which WB standard to use.

Enzyme-linked immunosorbant assay: An antibody test that determines whether HIV is present in blood or saliva. A positive result is interpreted to mean that the individual is infected with the virus (United States Department of Health Services, 2008).

False positive: A test that is interpreted as positive when the condition is not actually present (United States Department of Health Services, 2008).

Geographical location: Refers to the location of the clinical laboratory manager.

Highly active antiretroviral therapy: A pharmacotherapy regiment, generally a combination of other HIV antiretroviral therapies from various drug classes, which stops the replication of HIV in an aggressive fashion (United States Department of Health Services, 2008).

Western blot: An antibody test that detects specific proteins (United States

Department of Health Services, 2008).

Assumptions

Participation in this survey was voluntary, and the data provided was anonymous

and confidential. Responses for the questions were designated as closed-ended format. As

a result, it was assumed that participants responded honestly. It was also assumed that

there was no difference between responding and nonresponding clinical laboratory

directors. A third assumption was that the survey was completed only by persons meeting

the inclusion criteria.

Scope, Limitations, and Delimitations

This quantitative correlational study employed a telephone survey to describe the

association between the use of the CDC WBS for HIV confirmatory testing and

characteristics of the clinical laboratory administrator in charge of making the decision

about which standard to use. Such a study will quantify whether this relationship varies

according to GL, EM, and YE. While anonymity and confidentiality were assured, self-

reporting of data presupposes a level of imprecision. Such data may infer participant

recall bias. A second limitation pertains to the study design. This study was correlational

in nature; therefore, any relationships between variables do not necessarily mean that

there are causal inferences (Aczel & Sounderpandian, 2006; Singleton & Straits, 2005).

The analysis of this survey was delimited to a quantitative, correlational methodology.

Variables within this study included geographical location, education major, and years of

experience. Because these variables were found to be correlated with use of the CDC

standard, investigation of potential confounders is warranted, and the discussion chapter includes recommendations for such an investigation.

Significance of the Study

In 2008, it was estimated that 33.4 million people worldwide were living with HIV. New infections were projected to be at 2.7 million in the same year. Two million deaths were calculated to be attributable to AIDS in 2008 (WHO/UNAIDS, 2009, November). This study provides the public health and clinical communities with an improved understanding of how standards used by a laboratory can influence whether individuals receive a positive or negative HIV test result.

While over 66 conditions from antibodies' cross-reacting to the HIV proteins found in the antibody test kits have been studied, the promotion of HIV testing continues to be a priority for public health and medical entities in preventing and reducing the epidemic. When a person receives a diagnosis of AIDS because of testing positive, clinicians advocate for pharmacotherapy to reduce or eliminate the virus from the body. In order for antiretroviral therapy to be successful, the results from the antibody tests should be unambiguous so that persons do not receive unnecessary medications because of a misdiagnosis.

Implications for Social Change

The social change aspect of my research is significant, not only to persons diagnosed as having HIV, but also to the global population. The reason this research affects everyone is that the CDC strongly recommends that all persons in the United States receive an HIV antibody test (Bransom et al., 2006). Presently, HIV has not been

subjected to viral isolation. This may be why the test kit manufacturers disclaim their use for screening or confirmatory purposes. We must recognize that cross-reactions are common and that a misdiagnosis can have a profound effect on the person on a variety of levels—namely, physical, psychological, mental, emotional, spiritual, and financial. As a result, it is important to have a decisive criterion that constitutes a positive HIV result, regardless of GL. Recognizing that several standards can be used, the choice to use the CDC WBS may be subjective according to the GL, the EM, and the YE. The results of this study will allow recommendations to be made to the CDC regarding educational opportunities for clinical laboratory managers that are using WB standards other than the CDC criteria.

Stigma associated with an HIV diagnosis is one potential concern for people who test positive on the WB test. This phenomenon implies that the individual possesses a condition that other people regard as negative, with the result that the individual is ostracized (Tardy, Dindia, & Hargie, 2006). While actual stigmatization is unsettling, perceived stigmatization can play a major factor as well (Brown, Macintyre, & Trujillo, 2003). Stigma associated with AIDS can increase when individuals perceive that they were to blame for becoming infected with HIV (Crowley & Guni, 2004).

Self-esteem and depression are two themes that have been researched extensively (Burkholder, Harlow, & Washkiwich, 1999; Preston, D'Augelli, Kassab, & Starks, 2007). Perceived stigma from HIV/AIDS has been described by Herek, Capitanio, and Widaman (2003). Approximately 75% of the participants stated that they stigmatized people who were living with AIDS (Herek et al., 2003). A year earlier, the authors studied the

perceptions of mandatory testing and reporting. Nearly 30% of the participants suggested that individuals having AIDS be quarantined. Furthermore, public disclosure of HIV test results was encouraged (Herek et al., 2003). A longitudinal study compared sero-discordant women who were African American concerning their experiences with perceived stigmatization over the course of 6 years. Clark, Lindner, Armistead, and Austin (2003) found that such stigmatization did not fluctuate over the period.

Although stigmatization, whether perceived or actual, is significant for persons misdiagnosed as having AIDS, economical considerations also arise. The federal budget for 2010 in HIV/AIDS treatment was nearly $26 billion. Domestically and internationally, the federal government has allocated close to $19.5 billion and $6.5 billion, respectively. Of the domestic allocation, about $13.2 billion is used for the treatment and care of individuals with this syndrome. According to Roberts et al. (2006), the annual average cost per patient with HIV/AIDS is between $20,114 and $20,387. A misdiagnosis, thus, potentially creates a financial burden.

Financial issues can also arise in litigation from an HIV misdiagnosis. For instance, a woman received $2.5 million after taking HIV medications over a 9-year period after being diagnosed with AIDS; yet she was later found to be HIV-negative (CDC National Prevention Information Network, 2007). In January of 2010, a woman filed a five-count lawsuit against her doctor for emotional distress, as he had misdiagnosed her as having HIV (Holleran, 2010). According to Klopott (2009), medical malpractice suits could become a reality in the future because of such issues.

In the absence of a universally accepted standard for what constitutes a positive antibody result on a WB test, vulnerable populations, such as pregnant women and children, may inadvertently be diagnosed positively for AIDS when they may not have said infection (Bayer & Fairchild, 2006; Beckwith et al., 2005; Simpson & Forsyth, 2007). Therefore, physicians are encouraged to be more aware of misdiagnosis and unnecessary treatment (Deng, Ma, Li, & Qui, 2010). A misdiagnosis can have further implications, particularly on the psychological state of the individual. Such an issue becomes amplified in countries that do not have the resources to diagnose HIV infection accurately (Bhattacharya, Barton, & Catalan, 2008). Prior to 2009, 35% of 186 countries had travel restrictions for those who were HIV positive (Wiessner & Lemmen, 2008). In fact, 30 countries had policies in place to deport infected individuals. One of these countries was the United States, in which the ban was lifted in January 2010 (James, 2010).

Adopting a universal WB standard is important for several reasons, given that this antibody test is the industry standard for confirmation. Foremost, clinical and public health officials have accountability in upholding ethical standards when diagnosing, reducing, and preventing HIV infection. Therefore, informed consent is important when advocating for HIV antibody testing (Van Norman, 2008). The implementation of state-mandated HIV testing will be successful if the antibody tests are deemed accurate via viral isolation. The adoption of a universally accepted standard may also alleviate legal cases whereby individuals are considered criminals and placed in prisons or even on death row for their presumed infection (American Civil Liberties Union, 2008; Boren,

2009; D C Thomson and Company Ltd., 2010; Webster, 2009; Willyard, 2007). Furthermore, adoption of a universal standard would prevent the administration of toxic medications based on an invalidated antibody test because the WB would have a set of criteria for what constitutes a positive result (Bruzzone et al., 2008). If we acknowledge that diverging standards exist because of stringency, a universal standard may be evident once the isolation of the virus occurs.

Summary

Antibody tests have been promoted by public health and medical professionals in identifying and diagnosing HIV and AIDS. Yet, such technologies are not currently marketed for such purposes. Recognizing that there are various criteria for what constitutes a positive result on a WB, which is a confirmatory test, it is inherent for both constituents to be accountable for establishing the presence of a true HIV infection. The study described herein quantifies the number of clinical laboratories in the United States that adopt the CDC WBS for HIV confirmatory testing. This study used a researcher-developed demographic questionnaire. The questionnaire measured factual information and did not measure any psychometric constructs. Therefore, the validity and reliability were self-evident. By identifying such data, a universally accepted standard may become evident so that HIV/AIDS statistics can be compared accurately. Chapter 1 draws upon the SEM as the conceptual framework to drive the current research with regard to the testing parameters for antibody testing technologies. Chapter 2 describes in detail the SEM, history of HIV/AIDS, antibody tests, and recommendations for screening practices and differing methodologies of prior research. A description of the methodological

considerations, along with the study design and the justification for such, is found in Chapter 3. The sample size, instrumentation, and materials, data collection and analyses will also be discussed in Chapter 3. Results, discussion, and recommendations for social change and action will be discussed in Chapter 4 and Chapter 5.

Chapter 2: Literature Review

Introduction

Chapter 2 presents a literature review of peer-reviewed sources regarding HIV/AIDS and antibody testing, as well as the conceptual framework and methodology used in this study. The SEM serves to explain how the environment plays a major part in how an individual operates in socioecological settings. A discussion on the history of HIV/AIDS will follow. Evidence of the value of HIV antibody testing in screening and diagnosing HIV infection will also be examined. The antibody WB testing standards that clinical laboratories in the United States use will be critically reviewed. Contemporary recommendations for HIV antibody testing practices will end the chapter.

Several key words and phrases were used to conduct the literature review, employing the following online search engines: The Health Sciences database, Health and Medical Complete database, MEDLINE, and CINAHL Plus. A few of the key words used for the literature review included, but were not restricted to, *HIV antibody standards, HIV testing standards, HIV, AIDS, ELISA, WB,* and *false positive*. Using *HIV testing standards* yielded 11,308 results. This search was then narrowed further by using subsequent searches on the key words *HIV antibody testing standards*.

This chapter employs a critical review of the SEM in order to reveal how basic concepts should drive the process of advocating for antibody testing in the identification of HIV in biological samples, because the environment influences such behavior. A review of the literature serves as a foundation for understanding the historical context of the HIV/AIDS epidemic. A general overview of antibody testing, as it relates to

HIV/AIDS, will facilitate a discussion on the importance of its applicability in screening and/or diagnosing HIV infection. A discussion of standard laboratory practices will serve as a transition into a final discussion of recommendations pertaining to clinical and public health practice.

Social Ecological Model as the Conceptual Framework of the Study

The SEM provides a clear understanding of how the environment in which individuals live can influence their actions. This theoretical perspective is not new to public health matters (Gregson et al., 2001; Newes-Adeyi, Helitzer, Caulfield, & Bronner, 2000; Stokols, 1996), including HIV (Davis et al., 2011; Larios et al., 2009; MacPhail, Pettifor, Coates, & Rees, 2008). Indeed, the United States, United Kingdom, and countries in Scandinavia have adopted the SEM to frame efforts in public health (Institute of Medicine, 2003). Furthermore, the SEM has been used by the CDC to address HIV prevention programs (Fraze et al., 2009).

Bronfenbrenner's (1977) SEM is separated into four distinct hierarchical systems: macro, exo, meso, and micro. Each level is influential and includes cultures, communities, organizations, and individuals. While several theorists focus on differing perspectives, such as micro and macrosystems, it should be noted that none of the systems is independent of any of the others. In fact, variables are present between all hierarchical systems. These factors influence these systems (Bronfenbrenner, 1979). By thinking of the SEM as a concentric circle, one would be able to recognize that each echelon would be operational as it is nested within the circle that is larger than the prior circle. Such factors would range from the individual to the culture. In effect, the SEM is a

systems theory in which variables interact continuously (Klein, Tosi, & Cannella, 1999; Rousseau & House, 1994).

Some nuances should be noted for these systems. Social identity encompasses the interpersonal factors that influence the microsystem. For example, the components of a family unit play clearly defined roles. Such interpersonal elements influence how individuals see themselves operationally in the family unit (Gregson, 2001). Although learning these qualities is possible, some factors, such as race and gender, can also influence the role with which a person identifies. Factors such as personality, beliefs, and knowledge can make up individuals' psychological and cognitive functions. As a result, individuals are influenced by the environment every time they interact with others in that environment. Therefore, the microsystem serves to identify how children are shaped as they develop and relate to people inside and outside the family circle (Gregson, 2001).

Organizationally, the mesosystem serves as the conduit through which interpersonal relationships occur. Factors such as policies and procedures can influence the individual in this environment. Examples of the mesosystem include sports teams, companies, schools, and churches. Essentially, the individual is influenced to act a certain way in the organization (Gregson, 2001). The extent to which communication is valued within the mesosystem, the more influential the mesosystem is (Bronfenbrenner, 1979).

Although the micro and mesosystems are important as influential entities, exosystems are also influential, albeit on a community level. Social networks and established standards are influenced by what takes place in this environment.

Interpersonal relationships with several organizations are commonplace (Gregson,

2001). Such a network of organizations will establish community relationships. From a

size perspective, the community encompasses a larger area than the mesosystem.

However, this community is substantially smaller in relation to the culture or nature it

comprises (Gregson, 2001). For example, a community may be thought of

geographically, for example, when an individual states that he or she is a New

Englander; yet, if one were to go to the next echelon, that community would be

referred to as American (Gregson, 2001). In contrast to the mesosystem, the individual

does not have to participate actively in the exosystem (Bronfenbrenner, 1979).

The relationship to all the systems continues throughout the macrosystem.

Within this system, cultural perspectives are identified from an emotional and

ideological perspective. Influential factors are easier to recognize in this system than in

the others because the effects have a visible impact on the culture. For example,

religious and political ideologies affect the sustainability of the culture. The magnitude

of this influence can be heightened with the use of media because media allows

information to be disseminated to the people living in the community. As a result,

expectations are established within the community (Bronfenbrenner, 1979).

Social Ecological Model Implications

The SEM relates to this proposed study for a variety of reasons. Recognizing that

the SEM involves environmental influences upon individuals as they move from one

echelon to the next, a clinical laboratory administrator may have personal reasons for

using a particular standard, as evidenced in Figure 1. Furthermore, if various standards

are used to interpret a WB test, it may be challenging to decipher individuals who are accurately infected with HIV. For this reason, the results of this study may yield important findings for the designation of a universally accepted standard.
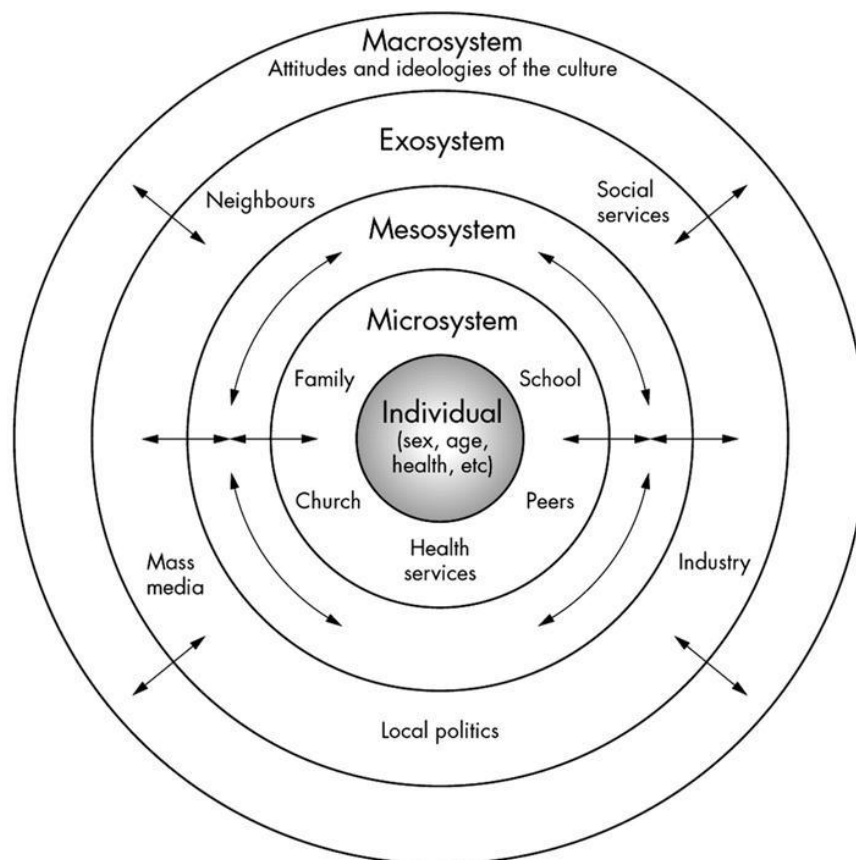
Figure 1: Graphical representation of the SEM (McLaren &Hawe, 2005)

From a microlevel perspective, the characteristics of clinical laboratory administrators may influence which type of WBS is used for interpretation within the laboratory. As a result, this decision can affect the results of the HIV test because of inconsistent results between laboratories. Furthermore, the decisions that laboratory administrators communicate to the rest of their staff, which are indicated at the meso level, determine which standard will be used at that particular laboratory (McLaren et al.,

2005). It may be that an individual clinician believes that the CDC WBS is better, but he or she will not be able to use this standard if the laboratory administrator dictates that only one particular standard can be used. Finally, if the CDC were to mandate their WBS nationally (macro level), then a universal standard might be used. The result would be that the reliability and comparability of HIV test results could be improved (McLaren et al., 2005).

Historical Overview of HIV/AIDS

The first five patients diagnosed with *Pneumocystis carinii* pneumonia (PCP) represented the first cases of what would eventually be defined as AIDS (CDC, 1981). Despite the fact that HIV does not fulfill Koch's postulates as the etiologic agent of AIDS, HIV is assumed to be the cause (Gallo et al., 1984). Presently, the CDC case definition of AIDS includes 30 indicator diseases. Although cervical cancer and dementia are not thought to be immunosuppressive, they are in the case definition (CDC, 1992). Notwithstanding, transmission of HIV is primarily postulated to occur through sexual intercourse, intravenous drug use (IDU), perinatal routes, and contaminated blood products (Aberg et al., 2009). In fact, the various modes of transmission have played a significant role in the shifting epidemiology of this epidemic. Each year in the early 1980s, it was estimated that 150,000 people were infected with HIV. Between the early 1990s and the present, this annual rate has decreased to nearly 56,300 infections (CDC, 3 September 2008). According to the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the WHO (2009), the HIV/AIDS epidemic has been declining since 1996.

In fact, the WHO Director of the HIV/AIDS section acknowledged that there was never a heterosexual epidemic outside the African continent (Laurance, 2008).

Sexual transmission of HIV/AIDS accounts for nearly 80% of the cases. In 1981, men having sex with men (MSM) were diagnosed with PCP and/or Kaposi sarcoma (KS). People who were injecting drugs, receiving blood transfusions, or were hemophiliacs were also presenting similar trends in disease status (Hariri & McKenna, 2007; Nelson & Williams, 2007). Interestingly, the mortality rates in hemophiliacs who were also HIV positive did not rise until 1987 (Darby et al., 1995). This was also the same year that Zidovudine (AZT), a DNA chain terminator, was marketed as an anti-HIV medication. In fact, in a cohort of hemophiliacs who took this medication, the risk of AIDS and death was 4.46 and 2.37 times greater, correspondingly (Goedert et al., 1994).

During the 1980s, most of the infections were occurring in New York and Los Angeles. Currently, HIV/AIDS cases occur throughout the nation, commonly in urban areas (Nelson et al., 2007). In 2007, California had the highest number of AIDS cases, nearly 4,955 (Centers for Disease Control and Prevention, 2009). NonHispanic Whites made up nearly 50% of the HIV cases between 1981 and 1995. Conversely, nonHispanic Blacks made up the same percentage between 2001 and 2004. Heterosexual transmission of HIV/AIDS accounted for 10% of the cases between 1981 and 1995. The same population saw an increase to 30% between 2001 and 2004. In 2002, 44% of HIV/AIDS cases occurred in MSM (CDC, 2006).

Although HIV/AIDS occurs predominantly in persons who engage in sexual intercourse, IDU and perinatal transmission are two other widely known methods for

spreading this illness (Nelson & Williams, 2007). Between 25% and 40% of HIV/AIDS cases attributed to IDU occur in the northeastern states, such as New York, Connecticut, New Jersey, Pennsylvania, and Maryland. IDU cases associated with AIDS between 1981 and 1995 were nearly 27%. Between 1996 and 2000, this rate increased almost 1%. The rate of HIV/AIDS in this group decreased to 17.3% between 2001 and 2004. There were 147,724 AIDS cases attributable to IDU between 1981 and 1995 (CDC, 2006). Perinatal transmission accounted for nearly 200 cases in 1985. Seven years later, there were 855 reported cases. From 1992 to 2005, there were 57 cases, which illustrated a 93% decline in perinatal transmission (CDC, 2007). In 2007, Florida, New York, and California had 13, 12, and 11 cases of AIDS in children under the age of 13, respectively (CDC, 2009). Despite the dramatic changes in numbers of AIDS cases and new infections, the total number of people estimated to be HIV-infected in America has stayed at approximately one million for the entire time (CDC, 2008; Curran et al., 1985).

Comparatively, Statistics South Africa (2007) indicated that out of 1000 positive test results, one death is attributed to the virus on an annual basis. Between 1980 and 2008, the population in South Africa rose from 29 million at a rate of 2.4 million annually in the 1980s to 49 million at a rate of 1.1 million after 1990 (Statistics South Africa, 2000, 2007b; United States Census Bureau, 2008). Most interesting is that the generated statistics for HIV prevalence come from women in prenatal clinics (Statistics South Africa, 2007a). In fact, the United Nations (2007) publicly acknowledged that they had overestimated the 2007 incidence rate for HIV by 15%. The reason for the differences in HIV rates is that the United Nations bases its HIV surveillance data on pregnant women

who are in prenatal clinics (WHO/UNAIDS, 2003). Recognizing that pregnancy is one of over 66 conditions that can cause a false-positive result on an HIV antibody test, the overestimation of HIV cases is not surprising (Cordes & Ryan, 1995). For this reason, clinicians and public health professionals should be cognizant of false positive reactions that occur so that they can accurately account for HIV/AIDS cases.

Common Antibody Tests

The development of HIV antibody tests began in the early 1980s. The goal of developing these tests was to identify persons infected with the virus. This technology predates the advent of pharmacotherapy. However, HIV antibody tests were promoted as great public health interventions for combating the virus (Maman & King, 2008). Education and counseling were encouraged for supplementing such interventions because testing was seen as dangerous and dispensable, according to Bayer and Edington (2009).

Two common antibody tests conducted *in vivo* that identify HIV are the ELISA and the WB (Constantine, Saville, & Dax, 2005). The former test contains a mixture of the presumed HIV proteins. Indirect ELISAs are the primary method for identifying the antibodies of HIV in serum or plasma (Constantine et al., 2005). This particular method employs antigens to confine HIV antibodies in a biological sample, whereby antibodies that are detected by enzymes will change a substrate to yield a change in the color of the sample that will be measured (Constantine et al., 2005).

From a procedural perspective, the biological sample is placed on a microtiter plate that incorporates antigens, which are then placed in an incubator at a designated temperature for a specified time (Constantine et al., 2005). Diluents are also added in

order to reduce the probability that nonspecific reactions will occur. An antigen/antibody complex will be evident on the microtiter plate if anti-HIV is seen in this sample. The enzymes are then added and incubated after the sample is washed to eliminate materials that do not bind to the microtiter plate (Constantine et al., 2005). An antigen/anti-HIV antibody/conjugate complex will occur when the conjugate affixes to the antigen/antibody complex. A second washing of the sample will remove a surplus of the enzymes. The addition of a substrate will then be incubated (Lequin, 2005). While this process occurs, the conjugate in this immobilized complex will cleave to the substrate so that a colorimetric reaction is visualized. Although the ELISA is said to be a common format for detecting HIV due to its high sensitivity and specificity, an accurate result is dependent on the antigens that are incorporated into the test kit (Lequin, 2005).

While ELISAs are employed for screening purposes, the WB is used for confirmatory purposes. The WB was originally developed by W. Neal Burnette (Burnette, 1981). Criteria for interpreting WB results began in the early 1980s (Wilber, 1991). However, subsequent definitions of WB criteria were developed for 1987-1993 and post-1993 (Leung, 2009). The WB tests were determined to be the best standard for confirming HIV because they were thought to indicate antibodies that were specific to HIV. In fact, such tests were considered to have a high specificity, rather than sensitivity, as seen with ELISA tests (Constantine et al., 2005).

The specificity of the WB relies on the separation and concentration of the component. Following the application of the HIV lysate to a polyacrylamide nitrocellulose strip that is electrically charged, bands of the viral proteins are separated by

molecular weight and designated with a lowercase p and number, indicating the molecular weight of the protein. The HIV lysate is what biochemists call the solution prepared after the cell membrane of HIV is degraded by the use of strong biochemicals, such as interleukin 2 or phytohemagglutinin (Ratner et al., 1985).

The entire WB procedure occurs in three sections. First, sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis (PAGE) separates the HIV antigen lysates by their molecular weight (Read & the Committee on Pediatric AIDS, 2007). Second, the antigens are transferred to a nitrocellulose strip. Third, the enzyme-substrate reaction is employed to test the sample on this nitrocellulose strip. Although the WB procedure is simple to perform, the laboratory personnel completing this technique must be able to interpret the results properly (Read & the Committee on Pediatric AIDS, 2007).

Both the ELISA and the WB antibody tests require a serum specimen to interact with the prepared antigens (Constantine et al., 2005). The WB antibody test is considered to be sensitive and specific to HIV (Uneke, Alo, Ogbu, & Ngwu, 2007). Therefore, this test is commonly employed for confirming HIV infection (Kiptoo et al., 2009). Recognizing that a positive result on an HIV antibody test can have profound implications, the verity and reading of the test results should be free of ambiguity. The interpretation of the tests results should be uniform so that a person in one geographic location would be tested the same as another person in another geographical location, such as another country. Ambiguity in test results occurs because one laboratory may consider a result positive, while another laboratory considers a result negative (Corbett, 2009).

Proteins Regarded as Antigens to HIV

The proteins reported as belonging to HIV are acquired from patients with AIDS who have had their cells cultured with cell lines from leukemic patients. In order for the cells to become cocultured, mitogenic stimulation is required. In fact, coculturing techniques require strong chemicals, such as interleukin 2 or phytohemagluttinin, to stimulate the cells potentially to make ribonucleic acid (Ratner et al., 1985). Reverse transcriptase within the culture is detected, whereby the supernatant and lysate is eventually centrifuged into density gradients. Pure HIV is then deemed evident when the material bands at 1.16 gm/ml (Ratner et al., 1985). The proteins at this molecular weight are said to consist of group-associated antigens (gag), polymerase antigens (pol), and envelope antigens (env; Watts et al., 2009). The former antigen initially codes p53/p55. A cleavage occurs to p24/p25 and p17/p18. The pol antigen codes p31/p32. Finally, the env antigen codes the initial p160 protein. A cleavage occurs to p120 and p41/p45 (Ratner et al., 1985).

It is a commonly held view that p160 is a cleavage product of p120 and p41 (Hausman, Gelderblom, Clapham, Pauli, & Weiss, 1987). This protein is present in cells that are infected rather than within the virus. The surface spikes of HIV particles contain only p120 (Hausmann et al., 1987). However, these spikes occur only in budding particles instead of in mature particles. Interestingly, the budding particles are infrequent (Hausmann et al., 1987). Nevertheless, when the sera from AIDS patients react with what is considered to be pure HIV, p120 and p160 reactions occur (Pinter et al., 1989). However, p80 and the constituencies depicted between the 120 and 160 kilodalton region

were found not to represent p120 or the precursor to p120. Instead, these proteins were p41 oligomers (Pinter et al., 1989).

Both Gallo and Montagnier detected p41 in the initial isolates of HIV. Yet later Barre-Sinoussi et al. 1983) found that this protein was present in both infected and noninfected sera. The authors concluded that cellular debris—namely, actin—was contaminating the cell cultures (Baree-Sinoussi et al., 1983). Gallo and colleagues were unable to find this protein in uninfected cells. Though the authors found p80, they considered the reaction as nonspecific (Schepbach et al., 1984).

Actin is ubiquitous in nature. It is found in all cells and in bacteria and viruses. Actin has been theorized to play a major role in the assembly and budding of retroviruses—for example, the Rous sarcoma virus and mouse mammary tumor virus (Damsky, Sheffield, Tuszynski, & Warren, 1977; Stanislawsky, Mongiat, & Neto, 1984). Persons diagnosed with AIDS have been found with polymerized actin as a result of cellular sulphydryl groups being oxidized. The interaction in the cellular actin is a determinant of how physiologically stable the cells are. Hence, actin serves as a biological marker when lymphocytes are stimulated mitogenically (Bach et al., 1986; Finzi, Orthwein, Mercier, & Cohen, 2007).

Isolation techniques were employed by Henderson et al. (1987) to describe proteins 30 through 32 and proteins 34 through 36 in the double banding of purified HIV at density gradients of sucrose. The authors drew a comparison of the protein amino-acid sequences with the DR proteins that formed a Class II histocompatability complex. The DR proteins are a surface cell receptor heterodimer that are peptide antigens. The alpha

DR chains were indistinguishable from proteins 34 through 36. Furthermore, the beta DR proteins were similar to proteins 30 through 32 (Henderson et al., 1987).

The presence of protein 24 is presently thought to be equivalent to the isolation of HIV. Despite a single publication coauthored by Gallo and Montagnier (2008) asserting that p24 is unique to HIV, Wong and Gallo (1985) have continually theorized that an immunological cross reaction takes place between this protein in HTLV-I and HIV. An example of such a disconnection was found in a study by Genesca et al. (1989). Following an analysis of 100 negative ELISA samples from healthy persons donating blood, 20 samples were shown to react with bands that did not conform to the criteria established in 1989 for confirming a WB positive result. Of the indeterminate results, 70% were due to p24. Furthermore, the rate of false-positive reactions would be dependent upon the absence of the virus in the sample. Thirty-six percent of the persons who received a blood transfusion with this indeterminate blood were still indeterminate a half year later. Similarly, 42% of persons receiving blood from donors who were HIV negative by the WB continued to stay at this same status. As a result, Genesca et al. (1989) postulated that the indeterminate WB tests were so frequent in a randomized sample of donors and recipients that there was no correlation between the presence and transmission of HIV. The blood samples from blood donors in Hungary have reacted with p24, but they were not infected with HIV (Barabas & Brozik, 2007).

The blood of one out of every 150 healthy persons has been found to react to p24. In a randomized sample of persons who have generalized warts, yet who are otherwise healthy, 13% have p24. Patients who have prodome and T-cell lymphoma have p24, 24%

of the time. Forty-one percent of multiple sclerosis patients also have p24 (Ranki, Johansson, & Krohn, 1988).

The antigen p24 is absent from some persons who are HIV positive or who have AIDS. Delord et al. (1991) found that only 24% of HIV-positive patients had p24. Recognizing that medications can influence the levels of the p24 antigen, Todak et al. (1991) described a situation in which the patient initially reacted to p24, but p24 was not detected later. Thus, the authors cautioned against the use of p24 as an indicator for infection because "the test is clinically erratic" (Todak et al., 1991, p. 326). Infants born to HIV positive mothers have been shown to have false-positive results (Jayasuriya & Allan, 2007; Nastouli et al., 2007). Therefore, it is interesting that Keele et al. (2006) acknowledge that between 10% and 15% of the serum from noninfected persons is considered to elicit false-positive reactions on the WB test.

Although healthy blood donors can react to p24, the second frequent band that is identified on this particular antibody test is p17/p18 (Courouce, Muller, & Richard, 1986). In fact, p120, p24, and p17 have been found in the placentas of 25 women who had normal term pregnancies (Faulk & Labarrere, 1991). Blood serum from patients with AIDS typically attaches to p18 after the T-cells infected with HIV have been stimulated mitogenically. In fact, p18 does not bind with the serum of persons who are neither infected nor have unstimulated lymphocytes. The mitogenic stimulation of noninfected lymphocytes of AIDS patients allows the binding of p18 to these lymphocytes (Stricker et al., 1987). The p18 protein also reacts to monoclonal antibodies found within the dendrite cells of lymphatic tissues. This reaction occurs in many persons who do not have

AIDS-defining illnesses (Chassagne et al., 1986). Moreover, similar reactions have been evident in comparing the normal tissues found in persons who are HIV-negative to the tissues found in persons who are HIV-positive (Parravicini, Klatzmann, Jaffray, Costanzi, & Gluckman, 1988).

Each of the aforementioned proteins that are presumed to be specific for HIV has been documented as cross-reacting with numerous antibodies from a variety of health conditions. To date, over 66 conditions have been noted that can cause a sample to cross-react with these proteins (Johnson, 1996). There are many noninfectious examples. For instance, pregnancy has been shown as a risk factor for false positive results on an HIV test (Cremonezi, Mesquita, Romano, & Prestes-Carneiro, 2005; Garcia et al., 2009; Ng, 1991; Profitt & Yen-Lieberman, 1993; Steckelberg & Cockerill, 1988; Voevidin, 1992). Antibodies that occur naturally in humans can also cross-react with HIV proteins (Baracid, Bolgnesi, & Aaronson, 1980; Healey & Bolton, 1993). Renal failure has also been shown to cause false-positive reactions (Chou, Sun, & Wu, 2007). Cordes and Ryan (1995) found that blood samples exposed to the filter paper of the HIV test kit could cause a false positive result. Specimens that are heat-treated can also yield the same result (Jungkind, DiRenzo, & Young, 1986; Smith, Dewhurst, Shepherd, Volsky, & Goldsmith, 1987). Lupus, an autoimmune disease, has been found to cross-react with the HIV antibodies p120 and p41 (Obermoser et al., 2006). The HIV protein p120 has been found to cross-react with the serum of persons with ovarian cancer and breast cancer (Rakowicz-Szulczynska, Jackson, Szulczynska, & Smith, 1998; Rakowicz-Szulczynska, McIntosh, & Smith, 1999).

Antibodies found in individuals who have a variety of infectious diseases cross-react with the HIV proteins as well. For instance, Kashala et al. (1994) described the cross-reaction between the HIV proteins and tuberculosis, an illness that occurs frequently in Africa. The HIV protein p120 cross-reacted with the serum of tuberculosis patients (Swaminathan et al., 2008). Stephan et al. (2008) found that the purified proteins in tuberculosis can cause cross-reactions. The antibodies against malaria are also found to cross-react with HIV proteins p32, p120, and p18 (Biggar et al., 1985; Biswas et al., 2007; Gasasira et al., 2006; Okitsu et al., 2007). The blood of persons with leprosy was found by Hussain et al. (2007) to react with p41, p55, and p18. Leishmaniasis has also been found to make the serum of a patient cross-react with the HIV proteins (Salinas, Gorgolas, & Fernandez-Guerrero, 2007).

Blood drawn from persons having upper respiratory infections, such as a cold or the influenza, has been found to cross-react with the HIV proteins (Challakere & Rapaport, 1993). Therefore, it is not surprising that vaccination for flu allows the same cross-reaction to occur (Erickson et al., 2006; Hsia, 1993; Mackenzie et al., 1992). Persons with SARS have been found to have cross-reactions to the HIV proteins (Tsao et al., 2005). Furthermore, persons who have had measles have also had cross-reactions to p18, p24, p41, and p55 (Baskar et al., 1998).

While false positive reactions in humans have been documented, some researchers have found that the blood of nonhuman animals can also react with the HIV proteins. Strandstrom et al. (1990) found that 50% of the canines they tested for HIV using the WB reacted to such proteins. Kion and Hoffmann (1991) found that

alloimmune mice were making antibodies against HIV, although they had not been exposed to the virus. Alloimmunity means that the mice were gaining immunity from one another against foreign cells, as they were bred for that purpose. It is worthwhile to note that further studies to ascertain why there are cross-reactivity issues regarding the WB tests have not been conducted. Such cross-reactions are important to acknowledge when analyzing the significance of what a positive test result means.

Development of Standards for HIV Antibody Tests

Accuracy signifies the capacity of an analytical technique to produce the correct or true result. A primary oversight in laboratory evaluations of new analytical methods is the absence of samples that are well characterized in regard to what they are measuring. It is important that an analytic method, such as a WB assay, be evaluated with samples that are unequivocally from individuals who are either infected or not infected. Equally important, an accurate test would have sole biological markers, such as specific antigens that would react with specific antibodies. Therefore, there should be no ambiguity as to the sample's category (Bossuyt, 2008).

Achieving accuracy involves the sensitivity and specificity of the test. The former parameter quantifies the ability for the test to correctly classify a population as being infected, while the latter quantifies the level of correctness in identifying individuals who are not infected. Both parameters can be 100%, implying perfect accuracy, depending on whether the sample status is known.

Sensitivity is used analytically and epidemiologically (Bossuyt, Irwig, Craig, & Glasziou, 2006). Analytical sensitivity quantifies the degree to which the test identifies

minute amounts of the antigen or antibody. Although a test may have excellent analytical sensitivity, some individuals who are infected may not be classified as such because the antigens may be nonspecific or in low concentrations (Lord, Irwig, & Simes, 2006). Epidemiologic sensitivity, on the other hand, quantifies the ability of the test to correctly identify individuals who are infected. Therefore, the higher the epidemiologic sensitivity, the less likely it is to have false-negative results. In order to calculate sensitivity, one would divide all the true positives—i.e., persons who have been identified from the test to be infected—by all the true positives and multiply by 100. In contrast, one would calculate the specificity by dividing the true negatives by all the true negatives and multiplying by 100 (Bossuyt et al., 2006; Lord et al., 2006).

Sensitivity and specificity together yield the test efficiency. This third parameter measures how effective the test is at identifying samples that are positive as positive and those that are negative as negative. If a test is said to be 100% efficient, this means that no false-positive or false-negative results will occur. Therefore, the test efficiency is a direct measure of the accuracy of the test. In order to calculate test efficiency, one would divide all the true positive and true negative results by the total of these results, in addition to the false positive and false negative results. This equation would then be multiplied by 100 (Pepe, 2007).

Although sensitivity and specificity together yield the test efficiency—a parameter that is synonymous with the degree of accuracy—the parameters of reproducibility, precision, and predictive value yield important information regarding the utilization of the test and the probability that the test will achieve accurate results.

Reproducibility is a test's ability to obtain the same result, regardless of external conditions. Conditions that may influence the reproducibility of the test include differences in laboratory personnel practices, instruments, instrument storage practices, and laboratory environmental conditions (Omersel et al., 2010). In order to calculate reproducibility, one would divide the number of the test results from a range of days by the total number of tests completed on these same samples over a period of days, thereafter multiplying the equation by 100. Precision, on the other hand, is the ability for the test to produce similar results when multiple runs of the sample have been conducted in a simultaneous fashion (Banoo et al., 2006).

Positive predictive value (PPV) refers to the likelihood that a test with a known sensitivity and specificity will perform in a population where the prevalence of a condition is also known. In order to calculate a PPV, one would divide the true positives from the test by the number of true positives and false positives from the test; this ratio would then be multiplied by 100. For this reason, the test value is not so much dependent on the sensitivity or specificity, as it is on the predictive value of a testing population. Interestingly, the PPV is the probability that the positive result will actually come from an individual who is infected (Puhan, Steurer, Bachmann, & ter Riet, 2005; Wald, 2008).

Meaningful interpretation of an antibody test occurs when standardization practices are employed universally (Peeling et al., 2008). A positive result should be interpreted the same in every patient, laboratory, and country. Early researchers Montagnier and Gallo found that the serum from persons with AIDS did not react to all the HIV proteins. In contrast, the sera could also cross-react with proteins of other

conditions not considered specific to HIV. This gulf occurred with the same sera at various times of testing (Genesca et al., 1989; Popovic et al., 1984). Therefore, a requirement for standardization was to develop a set of criteria for the interpretation of a positive WB result.

Originally, a WB positive result was indicated by p24 and p41, according to Montagnier and Gallo, respectively. Most laboratories adhered to the CDC guideline, which considered a reaction to p24 or p41 as being positive. As mentioned in a previous section of the literature review, both proteins were found to be nonspecific. Up until 1987, the number of laboratories doing WB equaled the number of WB assays. As a result, the criteria vary for what constitutes a positive result on a WB test, as there is no recognized standard in the United States (Wilber, 1991).

In 1987, the DuPont WB kit, licensed by the FDA, was used. However, a minimal number of laboratories used this antibody test. A possible reason is that the criteria are very stringent: p24 and p31/p32 are required. A reaction to p41, p120, or p160 is also necessary (Wilber, 1991). Kleinman et al. (1998) have asserted that individuals have been misclassified as HIV-positive on the WB tests. However, the frequency of such occurrences is unknown. For this reason, the authors conducted a retrospective cohort study in five United States blood banks to ascertain the false positive rate of WB tests. The polymerase chain reaction (PCR) and HIV culture were used to confirm the false positive results. Five million blood donors were reviewed in the blood bank database. In order to reduce the number of indeterminate HIV tests, the FDA reduced the criteria for what constitutes a positive test result by eliminating p31 as an indicator in 1993. Using

this criterion, the authors found that 421 individuals would be classified as being HIV positive. Out of this group, 39 did not have the p31 band on the WB test. PCR analysis of this data found that 20 did not have HIV. As a result, nearly 5% of this cohort was misdiagnosed as being HIV positive (Kleinman et al., 1998).

Healey et al. (1992) and Lundberg (1988) explained the American Red Cross criteria by stating that regardless of the band, a positive result is one in which the antibody presence is found in each of the genes, gag, pol, and env. A positive reaction, according to the Association of State and Territorial Public Health Laboratory Directors, is one designated as a sample that reacts to two protein combinations, namely, p120/p160, p41, and p24 (Mylonakis et al., 2000). The Consortium for Retrovirus Serology Standardization (CRSS) characterizes a sample as positive if p120/p160 or p41 is present. The sample must also be reactive to p32 or p24. A negative result on a WB occurs when the sample does not react to any or all of the bands, in addition to those proteins that are nonHIV proteins. A laboratory may designate a sample as WB indeterminate if it does not fulfill the criteria used by the laboratory (Lundberg, 1988).

While some standardization issues have yet to be resolved, the interpretations of each of criteria also have limitations. Using the interpretation of the FDA, only 50% of persons with AIDS would be positive on the WB. The implication then is that these AIDS patients do not have HIV. The use of the CRSS criteria increases the number of AIDS patients to 79%. More notably, when the FDA criteria are used, 10% of healthy blood donors will be told they are positive on the WB (Lundberg, 1988). Although not showing a complete list of every interpretive criterion, Figure 1 lists regulatory bodies that have

various HIV WB standards. Keep in mind that this study focuses only on the CDC WBS.
MP Diagnostics (2005) states that local "accepted" policies should be followed in order
to interpret WB antibody tests.

REGULATORY BODY	INTERPRETATION ON CRITERIA
Centers for Disease Control (CDC) and ASTPHLD	At least one ENV (gp41 and gp120/160) and p24
American Food and Drug Administration (FDA)	p24 and p31 and gp41 or gp120/gp160
Center Nationale Transfusion Sanguine	Two ENV bands with GAG or POL
World Health Organization (WHO)	Two ENV bands with or without GAG or POL
Consortium for Retrovirus Serology Standardization	One band of p24 or p31 and ENV band
American Red Cross (ARC)	One band each of GAG, POL and ENV
German Association for Control of Viral Diseases (DVV)	One ENV and at least one GAG or POL band, see also DIN 58 969, part 41

Figure 2. Interpretive Criteria for WB Positive Results. From MP Diagnostics
(2005).

Insight into antibody testing criteria becomes more complex considering that the
definition of AIDS in Africa is based upon clinical symptoms (WHO, 1990). Recognizing
that the WHO standard for a positive HIV test result consists of two positive ELISA tests
in the absence of a confirmatory test, it is interesting to note that p41 was found by
Klarkowski et al. (2009) to account for 50% of the false positive reactions in a large
cohort of persons living in the eastern Democratic Republic of the Congo. The CDC
began recommending that the ELISA be used to assist in defining AIDS. The specificity
of this antibody test is limited. For example, in 1990 this test was used in Russia.
Following the screening of 20,000 positive samples, the WB, presumed to be the gold

standard, confirmed 112. A year later, 66 samples were confirmed out of 30,000 positive samples in the same manner (Voevidin, 1992).

The criteria used by laboratories can come from the manufacturer of the test kit. However, the FDA has never approved an antibody test kit for the purpose of screening or diagnosing HIV infection. In fact, package inserts illustrate such disclaimers. For instance, Abbott Laboratories (2002, p. 6) stated, "At present there is no recognized standard for establishing the presence or absence of antibodies to HIV-1 and HIV-2 in human blood." Similarly, Bio Rad Laboratories (2007, p. 2) markets a more confirmatory test, the WB, with the disclaimer that "[a] person who has antibodies to HIV-1 is presumed to be infected with the virus." Moreover, a viral load test manufactured by Roche Diagnostic Systems, Inc. (2007, p. 1) mentions within its test package insert that it "is not intended to be used as a screening test for HIV or as a diagnostic test to confirm the presence of HIV infection." The varying sets of criteria for determining if a person is infected with a lethal virus can inhibit the progression of HIV research if there is no way to diagnose cases effectively and efficiently on the basis of these test kits.

Reproducibility

If one recognizes that test kit manufacturers disclaim the use of their products for diagnosing HIV and that there are no currently accepted criteria for asserting that a person is HIV-positive on a WB, the issue of reproducibility becomes inherently important. To illustrate the challenges of reproducibility, a single blood sample was sent to 19 clinical laboratories in a blind fashion. The clinical laboratories that participated in this study were part of the CRSS Conference, which met to discuss issues with the

present WB standards. While each laboratory found the blood specimen to be positive, every laboratory had varying band patterns they designated as positive (Lundberg, 1988).

A second example of how difficult it is to adhere to a single standard for what constitutes a positive result on a HIV test was found in a study by Edwards and Mosley (1991). Nearly 100 blood specimens from patients were sent to three reference laboratories on a weekly basis from the Transfusion Safety Study (TSS) Group. Four quality control samples sent along blind with the samples included two samples that were positive and two specimens that were negative. The first positive specimen from the quality control protocol was sent to laboratory A, laboratory B, and laboratory C—40, 5, and 45 times, respectively. The second positive specimen from the quality control protocol was sent to the three laboratories 89 times. Both quality control negative specimens were also sent to each of the laboratories. Out of the 101 specimens sent, p24 and "other" bands were found 18 and 13 times, correspondingly (Edwards et al., 1991).

The results of the Edwards et al. (1991) study indicate that there is variation between the laboratories in how they interpret banding patterns on the WB test. Laboratory C was the only one with consistent results. The first positive quality control sample was deemed positive with banding patterns from p41, p55, and p65. An indeterminate result was found with a single band to p41. An indeterminate result from a negative quality control specimen was found due to a single band to p41 (Edwwards et al., 1991). Such variance is significant because these laboratories were all considered reference laboratories, which are premier laboratories that represent a small number of those that perform confirmatory testing with WB across the nation (Edwards et al., 1991).

Furthermore, the use of unlicensed WB antibody tests continues as a result of cost effectiveness and the strict standards for interpreting tests that are licensed (Centers for Disease Control and Prevention, 1989). The significance of reproducibility is that an accurate diagnosis of HIV infection requires the same interpretation of the banding patterns from laboratory to laboratory.

<div align="center">**Universal Testing**</div>

AIDS policy with regard to HIV testing was revised on September 22, 2006. Previously, the CDC had recommended that persons who were in high-risk populations or in medical facilities where HIV was prevalent receive HIV testing (Bransom et al., 2006). Such a recommendation involved expensive and time-consuming counseling interventions and written informed consent. The reason clinicians did not test all populations was that it was costly or impractical from a risk assessment and administrative perspective (Gostin, 2006).

The present CDC guidelines are advocated for all public and private healthcare facilities. This institution now advises screening for HIV in all persons between the ages of 13 and 64 as part of routine medical screenings, even though some populations may not have high-risk factors for HIV infection (Bransom et al., 2006; Millen, Arbelaez, & Walensky, 2008). The guideline includes a clause known as "opt out," meaning that the clinician will test individuals' blood with an HIV test unless they decline this service. While the guidelines do not define how the patients would receive information regarding HIV testing, it is no longer necessary to have written informed consent; rather, routine consent for medical services would suffice. Furthermore, counseling is required neither

for HIV testing nor for screening interventions (Chua, 2009; Gostin, 2006; Holtgrave, 2007).

As mentioned previously, pregnancy is a risk factor for false-positive reactions. The employment of universal testing for HIV in this subpopulation is significant to address because highly active antiretroviral therapy (HAART) has been recommended to pregnant women to reduce perinatal transmission (Peckham & Gibb, 1995). The level of toxicities from these medications raises questions as to the safety of such pharmacotherapy. In fact, children had a standardized morbidity ratio of 2.79 for a major birth defect because their mothers took Zidovudine (AZT) compared to a placebo cohort in one study (Newschaffer, Cocroft, Anderson, Hauck, & Turner, 2001). Each class of antiretrovirals (ARVs) and every FDA-approved ARV have been associated with near fatal and fatal events (Reisler, Han, Burman, Tedaldi, & Neaton, 2003). Moreover, the largest, randomized, double-blind, and placebo controlled AZT study was conducted to find out whether it was effective in reducing HIV. Unfortunately, the death rate was 1.26 times higher in the AZT cohort than in the placebo (Concorde Coordinating Committee, 1994). Comparatively, 77% of a large cohort of close to 20,400 adults, 50 years or older, was estimated as having died within five years of taking HAART. In fact, 79% of this cohort developed one AIDS event within this period (May et al., 2007).

While the aforementioned studies provide a historical context for medicating pregnant women and children following an HIV positive result, some contemporary research emphasizes the importance of the informed consent process. Studies have shown that medications used to treat infection actually increase the rate of acquiring the disease

(De Souza et al., 2000). Bong et al. (2007) found that nearly 90% of infants that received HAART died within 6 months. Additionally, mitochondrial dysfunction was increased by a magnitude of 10 when HAART was given (Brogly et al., 2007). Therefore, it is not surprising that Bisson et al. (2008) found that 60% of their cohort died after being treated with HAART. Furthermore, Lawn and Wood (2007) found that 90% of individuals who received treatment died within 16 weeks. Interestingly, GlaxoSmithKline (2009, November), manufacturer of AZT, acknowledged that fatal cases have been associated with the use of AZT in mono- or poly-therapy with other antiretroviral medications. Moreover, differentiating between the effects of HIV/AIDS and the medications used to treat HIV/AIDS is difficult (WHO, 2006).

Although the aforementioned studies have emphasized the civil liberties of informed consent, the State of New York mandated that all newborns be screened for HIV. In 1999, the Institute of Medicine recommended that all pregnant women undergo universal screening as part of their routine medical services. While Gostin (2006) examined the new guidelines for universal HIV screening, the author did not discuss the possibility for false positive results as a result of reversing the guideline to include low-risk populations. From an epidemiological perspective, the prevalence of the disease is equally as important as the sensitivity and specificity of the medical test being performed to assess predictive value.

The CDC (2007) state that if a population were tested where the prevalence of the disease is 0.2% and 0.1%, 50% and 67% of the testing results would be false positives, respectively, when the test is 99.9% sensitive and 99.8% specific. Interestingly, many of

the rapid HIV test kits have such criteria. Therefore, if a population of 1 million persons were tested where the prevalence of HIV were 0.1%, 2,000 individuals would be misdiagnosed as having HIV so that additional testing might be required. If one were to increase the population to 100 million, the false-positive number would increase to 200,000 (CDC, 2007). Comparatively, in the months following the approval of HIV antibody tests for the detection of the virus in blood donors, 44% of the samples had positive reactions to the test kit, yet the virus could not be found by a culture. Equally important, 40% of homosexual males had positive reactions as well. However, the result was the same. Therefore, a cohort of low-risk and high-risk populations were given a diagnosis of HIV positive, yet they lacked HIV (Centers for Disease Control and Prevention, 1985). For this reason, clinicians and public health professionals should address the significance of a false positive result, given that universal HIV testing invariably increases the number of false positive results on an HIV test.

Methodologies Used in the Literature

Various studies have elucidated the variance of WB protein bands with regard to the interpretations from different organizations. Some studies have employed biological samples in order to analyze the protein bands (Jamjoom et al., 1997; Sivakuman et al., 2008; Soriano et al., 1993; Tebouriski, Slim, & Elgaaied, 2004). Retrospective studies have also been conducted (Sudha, Lakshmi, & Teja, 2006; Syed et al., 2005). Collectively, these studies are significant in assessing how varying WB standards are used for confirming HIV infection.

Although the current study focuses on the CDC WBS, research has been conducted on the various standards being used around the globe. Sivakuman et al. (2008) employed the WB test to identify banding patterns of proteins, as a result of HIV progression of disease, in 40 sero-positive individuals in Namakkal, South India. The WHO interpretive criteria were used to determine which bands were present throughout the four stages of HIV infection. Regardless of the clinical stage of HIV, the main proteins found in this sample cohort were gp160, gp120, and gp41. The authors concluded their study by claiming that p17 could serve as a biological marker for the progression of HIV infection because this protein was detected in stage 1 and stage 4 64% and 33% of the time, respectively (Sivakuman et al., 2008).

Although the WHO criteria for confirming HIV infection was discussed in the aforementioned paragraph, Tebourski, Slim, and Elgaaied (2004) compared this standard to the CDC criteria. This study had two particular aims—namely, elucidation of discordant results between both standards and establishment of an algorithm to reduce indeterminate results by employing the PCR. Nearly 470 blood samples were subjected to the WB test. Interestingly, the CDC standard yielded more positive results than did the WHO criteria. Therefore, all indeterminate results were higher when analyzing the samples using the WHO criteria. The main proteins that were found in indeterminate samples were p24, p55, and gp160. Celum et al. (2004) acknowledged that such a phenomenon may have been due to a variety of factors, including autoimmune disease and causes that have yet to be explained.

Jamjoom et al. (1997) and Soriano et al. (1993) provided a historical survey of discordant results pertaining to HIV WB tests. The authors asserted that indeterminate results have been found to be nearly 50% in some instances. The WHO criteria again were employed to assess 214 biological samples that were found to be indeterminate. Not surprisingly, p24 was observed frequently in such results. It is of interest that one sample could have been designated as either positive or negative, depending on which standard was used. The later author used a variety of standards across the globe to determine the discordance between criteria. In fact, Soriano et al. (1993) called into question the reliability of such standards because there is no globally accepted standard for what constitutes a positive result on a WB test. Therefore, the sensitivity and specificity of five standards was analyzed. Following WB analysis of 1,261 biological samples, it was determined that approximately 98% of the samples were positive by the CRSS standard. The WHO, CDC, American Red Cross, and FDA had sensitivities of 96.6%, 95.9%, 95.6%, and 99.8%, correspondingly. While the highest sensitivity was the CRSS standard, the highest specificity, 99.8%, was from the WHO and FDA. The glycoprotein gp160 was found in 99% of HIV sero-positive individuals. The proteins p24 and p17 were two common proteins found in noninfected individuals. Soriano et al. (1993) concluded their study by stating that discordant results remain because the WB test is not standardized and that interpretation of the banding patterns is subjective in nature.

Two retrospective studies were completed in order to describe the protein banding patterns of the WB tests. Sudha et al. (2006) analyzed biological samples from approximately 1470 sero-positive individuals. The intent was to establish which proteins

were indicative of a particular stage of HIV infection. The National AIDS Control Organization standards, which mirror the WHO criteria, were used to interpret the results. All protein bands were reactive with the exception of p31, which had discordance in 7% of the samples. The glycoprotein gp160 was found in each of the reactive specimens. Sudha et al. (2006) asserted that the use of WB patterns and clinical characteristics may assist clinicians in predicting at which stage an individual is with regard to HIV infection.

A second retrospective study by Syed et al. (2005) set out to describe whether the interpretation criteria differed between three WB manufacturer test kits. Between 2000 and 2004, nearly 560 biological specimens were collected. Each specimen was interpreted with six organization criteria standards. Interestingly, the LAVBLOT I test kit yielded significant differences concerning varying results. In fact, the WHO criteria were used for interpretation. A more liberal approach for HIV confirmation was seen with the CDC standard. The authors concluded their study by asserting that the criteria for what constitutes a positive result on a WB test is important. However, the manufacturer of the WB test kit may have more practicality (Syed et al., 2005).

A Case for Research

Confirmation of HIV consists of subjecting a biological sample to the WB antibody test. However, manufacturers of such tests disclaim their use for confirming infection with HIV. Furthermore, no globally accepted criteria exist for what constitutes a positive result on a WB test. Therefore, the decision to use a particular WB interpretive standard is at the discretion of the clinical laboratory administrator. No quantitative research has been conducted to describe whether an association exists between the use of

the CDC WB standard and the demographical characteristics of the clinical laboratory administrator. If demographical characteristics are associated with a particular standard, an individual could conceivably be given a diagnosis based upon such characteristics. A correlational study will be conducted to fill a literature gap in assessing whether the demographic characteristics of a clinical laboratory administrator are associated with the CDC WB standard for confirming HIV infection. This standard is used is because a majority of clinical laboratories in the United States use this standard (CDC, 2008).

Conclusion

This chapter outlined important concepts, such as the SEM, in order to describe how the etiology of diseases is classified and how the agent, host, and environment are vital to understanding the issue of HIV antibody testing standards. The epidemiology of HIV/AIDS was also examined. In order to tie both the aforementioned concepts together, it was important to describe the fundamental constructs of HIV antibody tests. The history of the various HIV WB standards was also evaluated. In Chapter 3, the methodology to address the research hypotheses will be discussed, and the null and alternative hypotheses will be listed. Issues such as the design of the study, participant selection, research questions, and protection of participants' rights will be incorporated into Chapter 3. Additionally, a discussion of the collection and analysis of data will end the chapter.

Chapter 3: Research Method

Introduction

Chapter 3 discusses the methodology of my quantitative correlational study pertaining to HIV WBS. The sample population of clinical laboratory administrators will also be examined in depth, for example, in terms of eligibility criteria and sample size. The telephonic survey will be explained, as will variable descriptions. Procedures for extracting and analyzing the data will follow, including a discussion of how the clinical laboratory administrators were protected throughout the study.

Research Design

The overarching research question was as follows: Is there a relationship between the demographic characteristics of the clinical laboratory administrator and use of the CDC standard to evaluate WB results? The CDC WBS is one of 11 standards used around the world, particularly in the United States. Recognizing that this study captures data from just one point in time, a quantitative research design is appropriate (Creswell, 2005). Such a research design can show whether a correlation exists between the demographic characteristics of the clinical laboratory administrator and the CDC WBS for confirming HIV. Logistic regression was used to analyze whether an association exists regarding the data.

This quantitative correlational study fills a knowledge gap in the literature pertaining to the demographic characteristics—namely, the GL, EM, and YE—of clinical laboratory administrators and their decision to employ the CDC WBS for confirming HIV infection. Currently, it is unknown whether there is a correlation between these

demographic characteristics and the CDC WBS for HIV confirmatory testing. Stakeholders, such as department of public health policy makers, may not have all the information they need to ensure that WB standards for HIV confirmatory testing are used consistently among clinical laboratories throughout the United States. As a result, it is important to see whether this relationship exists. Therefore, regression analysis was included in this quantitative correlational study.

Sample

Sampling Frame

Several organizations were considered for recruiting the sample population. First, a list of labs licensed by the Clinical Laboratory Improvement Amendments (CLIA) is obtainable on the CDC website. Lab types include community clinics (6,958), hospitals (8,858), physicians' offices (112,027), public health laboratories (485), and independent laboratories (5,253). The numbers in parentheses indicate the number of cases, based on a query for all the lab types. The advantage of using the CDC data is the large source of potential participants. However, limited time and financial resources made it difficult to mail out invitation-to-participate letters to each of the constituents listed above. In addition, although this CDC information was helpful, it did not appear that these constituents conduct HIV WB testing at their facilities, with the exception of independent laboratories. Rather, they send the samples out to be tested at a clinical laboratory (e.g., Lab Corp, Sonora Quest). Moreover, there may be an inadvertent bias toward using the CDC standard because the CDC supplies the demographic data for these facilities.

A second potential source for recruiting participants was the American Public Health Laboratories Association (APHLA). However, this organization has information only on public health laboratories, not national clinical laboratories. The American Clinical Laboratory Association (ACLA) was a third potential source for obtaining a sample cohort. Following correspondence with this association, it was determined that the researcher would have to mail invitation letters to participate to each clinical laboratory.

The Clinical Laboratory Management Association (CLMA), a fourth potential sampling frame, was initially thought of as an ideal population. Based upon the CLMA ThinkLab 2009 Annual Meeting demographics, obtained from a CLMA spokesperson, approximately 27% of the members are directors of clinical labs. Because the CLMA membership is over 3000, it was estimated that the minimum sample population needed was 120 participants. An electronic email blast was purchased so that all members of the CLMA were equally able to participate in the electronic survey, so long as they fulfilled the inclusion criteria. The invitation to participate, including the electronic survey link, was sent to the CLMA so that a representative could post this as an email blast. After 2 weeks, it was found that the response rate was less than 1%; only two participants completed the electronic survey. Following this response rate, it was determined that the CLMA website had a database of CLMA members. As a result, personalized emails similar to the email blast were sent to 600 CLMA members. However, no electronic surveys had been completed after a 2-week period.

A fifth sampling frame came from the CDC. Following correspondence with personnel from this organization, the researcher was able to obtain a list of 163 clinical laboratories where WB HIV tests are interpreted. This list was used in a CDC survey pertaining to HIV diagnostic testing (CDC, 2008). In order to inquire about the WB standard clinical laboratory administrators in the United States use, a telephone survey was employed (see Appendix A).

Sample Size

The sample size is a function of the target population size, the percentage of the target population that meets eligibility requirements (e.g., lab directors), and the percentage of the eligible target population that agrees to participate. According to the CDC list of clinical laboratories where WB HIV tests were conducted, 163 clinical laboratories participated in a 2008 CDC survey. For purposes of this power analysis, it was assumed that directors are the ones most likely to meet eligibility requirements for the study, although in reality not everyone would respond. Based upon studies by Dillman et al. (2009) and Bech and Kristensen (2009), response rates to email solicitations to participate in online surveys tend to be somewhat lower than typical survey response rates. Dillman et al. (2009) and Bech and Kristensen (2009) found that online survey response rates were 13% and 17%, correspondingly. The former authors studied a population of people who made decisions pertaining to long-distance telephone service. Bech and Kristensen (2009) studied the demographic characteristics of potential residents' attitudes toward future nursing home construction issues. Based on these studies, a response rate of approximately 15% was anticipated for this study. Therefore, a

sample size of nearly 120 was expected. Power calculations were performed using professional power analysis software (PASS 2008) to determine the effect size that can be detected with an alpha level of 0.05 and power of 80% (Hintze, 2008).

Sampling Justification

Fundamentally, the procedure for a power analysis is to determine the expected effect size based upon a literature review and then determine the necessary sample size to have a given level of power (typically 80%) at a given alpha level (.05 by convention) to detect that effect size (Cohen, 1998; Cohen, 1992). However, there is no precedence in the literature for a study like this one, so there was no evidence of what effect size to expect. A convenience sample was chosen due to the nature of the sampling frame and because this type of sample is sufficient for correlational studies like this one. The sample size was limited by the fact that convenience sampling was necessary, a fixed population size was available for the study, and participation was voluntary; based upon a literature review, the expected response rate was 15%. Therefore the power calculations are based upon the expect sample size of 120.

Hypotheses 1 through 4 were tested using logistic regression analysis. A logistic regression analysis of a binary dependent variable (CDC WBS) on a binary independent variable (e.g. EM) with a sample size of 120 achieves 80% power at a 0.05 significance level to detect an odds ratio of 2.93. A literature review did not reveal any publications reporting on the percentage of administrators with an education in the biological or health services or the percentage that uses the CDC standards. Therefore, for the purpose of this power analysis, it was assumed that 50% of administrators without an education major in

the biological or health sciences use the CDC standard, and that 50% of administrators

have an education major in the biological or health sciences. For example, if the

probability of using the CDC standard is 50% among administrators without an education

major in the biological or health sciences and the probability of using the CDC standard

is 75% among administrators with an education major in the biological or health sciences,

this would correspond to an odds ratio of 2.93. This study would have an 80% chance of

detecting this difference at the 0.05 level of significance. Because it was not known how

many study participants would be in each education major (EM) group, Table 1 shows

how the detectable effect size changes under different assumptions about the distribution

of education major.

Table 1

Detectable Odds Ratios Under Different Group Size Assumptions

Number of Study Participants		Odds Ratio
Education Major in Biological or Health Sciences	Education Major not in Biological or Health Sciences	
60	60	2.93
80	40	3.11
100	20	4.12

Note. Based on binary logistic regression analysis with a sample size of 120, an alpha level of 0.05 and 80% power.

Instrumentation and Materials

A telephone survey was employed to collect the demographic characteristics of

the clinical laboratory administrator and to ascertain the WB standard the laboratory uses

to confirm HIV infection. Following approval by the Walden University Institution Review Board (IRB Approval #01-10-11-0373310xxx), the researcher invited all 163 clinical laboratory managers who conduct WB testing at their facilities and who were participants in a 2008 CDC survey to participate in the telephone survey if they met the inclusion criteria of being a clinical administrator or someone in charge of making decisions pertaining to the use of WB standards. No information pertaining to the identity of the participants was collected, so anonymity and confidentiality were assured.

Five of the survey questions (see Appendix B) pertained to demographic data, the WB test kit used by the clinical laboratory, and the standard the clinical laboratory uses to interpret HIV WB results. The questions that incorporate the last two variables came from a national survey by the CDC (2008). In fact, the questionnaire measured factual information and did not measure any psychometric constructs.

The dependent variable was the CDC Western blot standard (CDC WBS). This variable was measured on a categorical scale with two categories. The type of WBS currently in use by the clinical laboratory administrator was measured as 1 = CDC or 0 = Other.

There were three independent variables—namely, the GL, EM, and YE. The GL was measured on a categorical scale with four categories. The clinical laboratory administrator's location was recorded as follows: 1 = Northeast, 2 = Midwest, 3 = South, or 4 = West. Nine states were included in the Northeast region, 12 in the Midwest, 17 in the South (in addition to Washington, DC), and 13 in the West—so that all 50 states were represented, including the District of Columbia (Energy Information Administration,

2000). The EM was measured on a categorical scale with two categories. The clinical

laboratory administrator's college education major was recorded as either 1 = biological

or health sciences (i.e., Biology, Medicine, Public Health), or 0 = Other. The YE were

measured on a continuous measurement scale. The range was not known but was

expected to be approximately 1 to 30 years. The clinical laboratory administrators' years

of experience working in the clinical laboratory setting was measured. For descriptive

purposes, the name of the WB test kit that the clinical laboratory administrator used was

also collected.

Data Collection and Analysis

In order to collect survey data, potential participants were contacted by phone. I

used a verbal script to describe the consent form to potential participants, including the

purpose, procedures, voluntary nature of the survey, and contact information for the

researcher, the faculty advisor, and the Director of the Research Center at Walden

University. The advantage of this method was that it was cost-effective and time

efficient. In fact, such a method allowed me to contact the maximum number of clinical

laboratory administrators in a short amount of time, while keeping a representative

sample population.

All statistical analyses were performed using PASW (formerly SPSS) for

Windows (PASW 18.0, SPSS Inc., Chicago, IL). All of the analyses were two-sided with

a 5% alpha level. Demographic variables were summarized using the mean standard

deviation, a range for continuous scaled variables, and frequency and percent for

categorical scaled variables. Table 2 lists the hypotheses, variables, and statistical tests used.

Table 2

Summary of Research Hypotheses

Hypothesis Number	Independent Variable	Dependent Variable	Statistical Test
Hypothesis 1	GL	CDC WBS	Simple Logistic Regression
Hypothesis 2	EM	CDC WBS	Simple Logistic Regression
Hypothesis 3	YE	CDC WBS	Simple Logistic Regression
Hypothesis 4	GL, EM, YE	CDC WBS	Multiple Logistic Regression

The overarching research question was this: How do the demographic characteristics of the clinical laboratory administrator predict use of the CDC standard to evaluate WB results? There were four specific questions the study was intended to answer.

Research Question 1

1. Does the administrator's geographic location (GL) predict the use of the CDC WBS to evaluate WB results?

H_01: The administrator's GL does not predict the use of the CDC WBS to evaluate WB results.

H_a1: The administrator's GL predicts the use of the CDC WBS to evaluate WB results.

Hypothesis 1 was tested using simple logistic regression analysis. The dependent variable was the CDC WBS. The independent variable was the GL. When conducting a logistic regression analysis with a categorical independent variable that has more than two categories, such as GL, the categorical independent variable must first be recoded into dummy variables. Dummy variables are dichotomous variables that are coded as 0 or 1. A categorical variable with K categories requires K-1 dummy variables. For example, GL has four categories, 1 = Northeast; 2 = Midwest; 3 = South, or 4 = West. Thus, the analysis of hypothesis 1 required three dummy variables for geographic location. The Northeast location was treated as the referent group and did not have a dummy variable. This location was selected as the referent group as a matter of convenience; any other location could just as easily have been selected without causing any change to the statistical significance of the hypothesis test. The three dummy variables for GL were defined as follows: GL1 = 0 if the clinical laboratory administrator was not located in the Midwest, or 1 if the administrator was located in the Midwest; GL2 = 0 if the clinical laboratory administrator was not located in the South, or 1 if the administrator was located in the South; GL3 = 0 if the clinical laboratory administrator was not located in the West, or 1 if the administrator was located in the West. Residual plots were inspected to identify any outlying values. If extreme outliers had been detected, they would have been omitted from the analysis. The independent and dependent variables for any outlying values were inspected for patterns.

Geographic location was measured on a categorical nominal measurement scale. If the odds ratio for the Northeast versus the Midwest, for example, was less than 1, this

would simply mean that lab directors in the Northeast are "less likely" to use the CDC standard than lab directors in the Midwest. If the regression coefficient for GL1, GL2, or GL3 was statistically significant, then the null hypothesis would be rejected and it would be concluded that there is a relationship between GL and the odds of using the CDC WBS. If the null hypothesis was rejected, then the model would be reported and interpreted.

Research Question 2

2. Does the administrator's education major (EM) predict the use of the CDC WBS to evaluate WB results?

$H_0 2$: The administrator's EM does not predict the use of the CDC WBS to evaluate WB results.

$H_a 2$: The administrator's EM predicts the use of the CDC WBS to evaluate WB results.

Hypothesis 2 was tested using simple logistic regression analysis. The dependent variable was the CDC WBS, and the independent variable was the EM. Education was measured on a categorical measurement scale. If the odds ratio for lab directors who majored in the something other than the biological sciences or health sciences versus those who majored in those fields was less than one, this simply meant that lab directors who did not major in the biological sciences or health sciences are "less likely" to use the CDC standard compared to those lab directors who did. If the regression coefficient for EM was statistically significant, then the null hypothesis would be rejected and it would be concluded that there is a relationship between EM and the odds of using the CDC

WBS. If the null hypothesis was rejected, then the model would be reported and interpreted.

Research Question 3

3.   Do the administrator's years of experience (YE) predict the use of the CDC WBS to evaluate WB results?

$H_0 3$: The administrator's YE does not predict the use of the CDC WBS to evaluate WB results.

$H_a 3$: The administrator's YE predicts the use of the CDC WBS to evaluate WB results.

Hypothesis 3 was tested using simple logistic regression analysis. The dependent variable was the CDC WBS. The independent variable was the YE, which were measured on a continuous measurement scale. If the odds ratio for YE was less than one, this simply meant that more experienced lab directors are "less likely" to use the CDC standard. If the regression coefficient for YE was statistically significant, then the null hypothesis would be rejected, and it would be concluded that there is a relationship between YE and the odds of using the CDC WBS. If the null hypothesis was rejected, then the model would be reported and interpreted.

Research Question 4

4.   Do the administrator's GL, EM, YE predict the use of the CDC WBS will be used to evaluate WB results?

$H_0 4$: The administrator's GL, EM, and YE do not predict the use of the CDC WBS to evaluate WB results.

H_a4: The administrator's GL, EM, and YE predict the use of the CDC WBS to evaluate WB results.

Hypothesis 4 was tested using multiple logistic regression analysis. The dependent variable was the CDC WBS. The independent variables were the GL, EM, and YE. All three independent variables were entered into the model simultaneously. If the regression coefficients for all three independent variables were statistically significant, then the null hypothesis would be rejected, and it would be concluded that GL, EM, and YE add independent information in predicting WBS. If the null hypothesis was rejected, then the model would be reported and interpreted.

Logistic Regression Justification

Logistic regression was the best statistical method for testing the hypotheses. The odds ratio is an inherent part of a logistic regression analysis. Therefore, odds ratios are relevant to this study. There are four specific reasons that logistic regression analysis was appropriate for testing such hypotheses. First, I wanted to know to what extent the selected demographic variables are valid predictors of whether or not the CDC WBS is used. Second, because the dependent variable was dichotomous, logistic regression was a natural choice, given that I wanted to identify predictors of the dependent variable. However, logistic regression analysis can also be applied when many independent variables are present. Simple logistic regression analysis is appropriate when the goal is to predict a dichotomous dependent variable, based upon a single independent variable. Third, multiple logistic regression analysis was the best method for testing hypothesis 4

because the dependent variable was dichotomous and several independent variables were considered collectively. Fourth, hypothesis 4 built on hypotheses 1 through 3.

Alternative statistical tests could have been used to test hypotheses 1 through 3 (e.g., Chi-square test, along with various measures of effect size, such as Cramer's v, Phi or Eta). However, simple logistic regression is a bivariate analysis, just as a Chi-square test of independence is a bivariate analysis. In fact, simple logistic regression and a Chi-square test would both produce exactly the same p-value. Thus, both tests are equally valid for determining if individual predictors show a significant association with the dependent variable (Garson, 2008).

Central tendencies and transformations were not relevant to this study given that the dependent variable was dichotomous. It was possible that some of the odds ratios would be less than 1. This would mean simply that the odds of using the CDC standard were lower for one group than for another. While central tendencies are not relevant to logistic regression analysis, as described earlier in this chapter, demographic variables were summarized using the mean standard deviation, a range for continuous scaled variables, and frequency and percent for categorical scaled variables. Logistic regression analysis was suitable for both categorical and continuous independent variables. The logistic regression model predicts the log-odds of the dichotomous dependent variable.

Alternative tests, such as MANOVA, were not appropriate for this study because the dependent variable in this study was measured on a dichotomous categorical measurement scale. In fact, MANOVA requires more than one dependent variable, each of which is measured on a continuous measurement scale. Furthermore, when the

dependent variable is dichotomous, logistic regression analysis is preferable to discriminate analysis (Grimm & Yarnold, 1995; Tabachnick & Fidell, 1996). In addition, it has been shown that under most conditions, logistic regression and discriminate analysis produce virtually identical results (Antonogeorgos, Panagiotakos, Priftis, & Tzonou, 2009).

Protection Measures for Participants' Rights

Because this population-based survey was completed by telephone, participants did not incur any known risks by taking part in the survey. No participant names, email addresses, or any other person-identifiable information was collected. Responses were collected via telephone. Complete anonymity and confidentiality was assured. In order to initiate the survey, IRB approval was warranted. A change of procedures was also submitted and approved. Furthermore, the risks, benefits, freedom to withdraw, contact information, and other applicable information were explained before initiating the survey.

Summary

This chapter described the proposed study methodology and illustrated the research design. Following a discussion on the research design, the sample population was explained. For example, inclusion criteria for the sample population were mentioned, as was an appropriate sample size. The researcher-developed survey, along with variable descriptions, was clarified. Extraction and analysis procedures for data retrieval were elucidated, and procedures for how the participants were protected throughout the study were clarified. The following chapter describes the results of the telephone survey.

Chapter 4: Results

The purpose of this quantitative correlational study was to determine whether there was a relationship between the demographic characteristics of clinical laboratory administrators and the odds that they use the CDC standard to evaluate WB results. In this study, I examined the demographic characteristics of these administrators—geographic location (GL), education major (EM), and years of experience (YE)—as they related to the use of the CDC WBS standard. This standard was chosen because 88.5% of the participating clinical laboratories stated on the CDC survey that they use this standard (CDC, 2008). Procurement of potential relationships was obtained via an electronic survey of clinical laboratory administrators that are representative of the U. S. clinical laboratories.

Descriptive Statistics

Study participants were clinical laboratory administrators, and the sample size for this study was 163. A Microsoft spreadsheet that included all the participants in a 2008 CDC survey pertaining to clinical laboratories and that used the confirmatory WB test to identify persons with HIV was used to identify 163 clinical laboratories. Contact was made with 163 clinical laboratory administrators, all of whom responded. The average (and standard deviation) years of experience working in any clinical laboratory setting was 31.5 (6.6), and the range was 20 to 44. A total of 142 (87%) study participants had obtained their highest earned degrees in the biological and health sciences, and 21 (13%) had obtained their highest degree in business. A total of 30 (18%) study participants were located in the Northeast region of the United States, 33 (20%) in the Midwest, 74 (45%)

in the South, and 26 (16%) in the West. See Appendix D for detailed descriptive statistics and frequency tables for all of the survey questions.

Hypothesis Test Results

Hypothesis 1

H_01: The administrator's GL does not predict the use of the CDC WBS to evaluate WB results.

H_a1: The administrator's GL predicts the use of the CDC WBS to evaluate WB results.

A simple logistic regression analysis was performed in order to test the hypotheses. The dependent variable was CDC WBS status, which was coded as 0 = *No, I do not use the CDC WBS to evaluate WB results,* and 1 = *Yes, I use the CDC WBS to evaluate WB results*. The independent variable, GL, is a categorical variable with four categories, Northeast, Midwest, South, and West. Categorical independent variables in a logistic regression model must first be recoded into dummy variables. Dummy variables are dichotomous variables that are coded as 0 or 1. A categorical variable with K categories requires K-1 dummy variables. The Northeast location, which was treated as the referent group, did not have a dummy variable. The three dummy variables for GL were defined as follows: GL1 = 0 if GL is not the Midwest, 1 if Midwest; GL2 = 0 if GL is not the South, 1 if South; and GL3 = 0 if GL is not the West, 1 if West. Table 3 shows there was no statistically significant relationship between CDC WBS status and geographic location, $p = .99$. Therefore, the null hypothesis was not rejected, and it was

concluded that there is no relationship between CDC WBS status and geographic

location.

Table 3

Simple Logistic Regression Analysis to Test Hypothesis 1

	B	S.E.	Wald	Df	p-value	Odds Ratio	95% C.I. for Odds Ratio Lower	Upper
GL			.012	3	.999			
GL1	20.356	6996.698	.000	1	.998	<.001	<.001	.
GL2	-.051	.471	.012	1	.914	.950	.378	2.392
GL3	20.356	7882.490	.000	1	.998	<.001	.001	.
Constant	.847	.398	4.523	1	.033	2.333		

Note. Dependent variable = CDC WB Status: 0 = Did not use the standard, 1 = used the
standard. Independent variable = Geographic Location: GL1 = 0 if geographic location is
not Midwest, 1 if Midwest; GL2 = 0 if geographic location is not South, 1 if South, and;
GL3 = 0 if geographic location is not West, 1 if West.

Hypothesis 2

$H_0 2$: The administrator's EM does not predict the use of the CDC WBS to

evaluate WB results.

$H_a 2$: The administrator's EM predicts the use of the CDC WBS to evaluate WB

results.

A simple logistic regression analysis was performed in order to test the

hypotheses. The dependent variable was CDC WBS status, which was coded as 0 = *No, I*

do not use the CDC WBS to evaluate WB results, and as 1 = *Yes, I use the CDC WBS to*

evaluate WB results. The independent variable, EM, is a categorical variable with two

categories. Education major was coded as EM = 0 if highest degree earned was not in the

biological or health sciences, or 1 if highest degree earned was in the biological or health

sciences. Table 4 shows there was a statistically significant relationship between the CDC

WBS status and EM, p = .001. The odds ratio was 4.96, which means the odds that a

study participant used the CDS WBS to evaluate HIV-1 test results were nearly 5 times

greater for a person who earned his or her highest degree in biological or health sciences

compared to those who did not. Therefore, the null hypothesis was rejected, and it was

concluded that those who earned their highest degree in the biological or health sciences

are more likely to use the CDC WBS to evaluate HIV-1 test results than those whose

highest degree was not in biological or health sciences.

Table 4

Simple Logistic Regression Analysis to Test Hypothesis 2

	B	S.E.	Wald	Df	p-value	Odds Ratio	95% C.I. for Odds Ratio Lower	Upper
EM	1.601	.495	10.477	1	.001	4.959	1.881	3.075
Constant	.095	.437	.048	1	.827	1.100		

Note. Dependent variable = CDC WBS: 0 = did not use the standard, 1 = used the standard. Independent variable = Education Major: EM = 0 if highest degree earned was not in the biological or health Sciences, or 1 if highest degree earned was in the biological or health sciences.

Hypothesis 3

H$_0$3: The administrator's YE does not predict the use of the CDC WBS to

evaluate WB results.

H$_a$3: The administrator's YE predicts the use of the CDC WBS to evaluate WB

results.

A simple logistic regression analysis was performed in order to test the hypotheses. The dependent variable was the CDC WBS status, which was coded as 0 = *No, I do not use the CDC WBS to evaluate WB results,* and as 1 = *Yes, I use the CDC WBS to evaluate WB results*. The independent variable, YE in any clinical laboratory setting, was measured on a continuous measurement scale with a range of 20 to 44. Table 5 shows there was no statistically significant relationship between CDC WBS status and years YE, *p* = .20. Therefore, the null hypothesis was not rejected, and it was concluded that there is no relationship between CDC WBS status and years of experience working in any clinical laboratory setting.

Table 5

Simple Logistic Regression Analysis to Test Hypothesis 3

		B	S.E.	Wald	Df	p-value	Odds Ratio	95% C.I. for Odds Ratio Lower	Upper
Step 1	YE	.039	.031	1.642	1	.200	1.040	.979	1.105
	Constant	.190	.956	.040	1	.842	1.210		

Note. Dependent variable = CDC WBS: 0 = did not use the standard, 1 = used the standard. Independent variable = Years of experience working in any clinical laboratory setting (YE), which was measured on a continuous measurement scale with a range of 20 to 44.

Hypothesis 4

$H_0 4$: The administrator's GL, EM, and YE do not predict the use of the CDC WBS to evaluate WB results.

$H_a 4$: The administrator's GL, EM, and YE predict the use of the CDC WBS to evaluate WB results.

A multiple logistic regression analysis was performed in order to test the hypotheses. The dependent variable was CDC WBS status, which was coded as 0 = *No, I do not use the CDC WBS to evaluate WB results,* and as 1 = *Yes, I use the CDC WBS to evaluate WB results*. The independent variables were GE, EM, and YE. Table 6 shows that only EM was statistically significantly associated with CDC WBS status, *p* = .024. The interpretation of the model is that when controlling for GL and YE working in any clinical laboratory setting, the odds that a person uses the CDC WBS to evaluate HIV-1 test results are 3.39 times greater for those with their highest degree in the biological or health sciences compared to those whose highest degree was not in those fields. Therefore, the null hypothesis was not rejected, and it was concluded that GL, EM, and YE do not collectively better predict CDC WBS status than education major alone.

Table 6

Multiple Logistic Regression Analysis to Test Hypothesis 4

							95% C.I. for Odds Ratio	
	B	S.E.	Wald	Df	p-value	Odds Ratio	Lower	Upper
GL			.004	3	.999			
GL(1)	20.257	6937.671	.000	1	.998	6.274E8	.000	.
GL (2)	.031	.486	.004	1	.950	1.031	.397	2.675
GL (3)	20.332	7746.225	.000	1	.998	6.764E8	.000	.
EDU	1.221	.542	5.086	1	.024	3.391	1.173	9.803
YE	.038	.034	1.239	1	.266	1.039	.971	1.111
Constant	-1.376	1.187	1.344	1	.246	.253		

Note. Dependent variable = CDC WB Status: 0 = did not use the standard, 1 = used the standard. Independent variables: GL = Geographic Location where the referent group is Northeast; GL(1) = 0 if location is not Midwest, 1 if Midwest; GL(2) = 0 if location is not South, 1 if South; GL(3) = 0 if location is not West, 1 if West. EDU = education major for highest degree earned, 0 if not biological or health sciences, 1 if biological or health

sciences. YE = Years of experience working in any clinical laboratory setting (YE), which was measured on a continuous measurement scale with a range of 20 to 44.

Summary

The purpose of this quantitative correlational study was to determine whether there was a relationship between the demographic characteristics of the clinical laboratory administrator and the odds that the clinical laboratory administrator would use the CDC standard to evaluate WB results. This study provides strong evidence that those who earned their highest degrees in the biological or health sciences are more likely to use the CDC WBS to evaluate HIV-1 test results compared to those who did not. There was no evidence to suggest that CDC WBS status was associated with either geographic location or years of experience working in any clinical laboratory setting.

Chapter 5: Discussion, Conclusions, and Recommendations

Study Overview

This study used the SEM to assess how demographic factors influence the interpretation of the CDC WBS for diagnosing HIV within the United States. By focusing on demographic characteristics like geographic location, education major, and years of experience, this quantitative correlational study assessed possible associations between these variables and the CDC WBS for interpreting HIV results. In order to identify whether such variables were influential in the interpretation of the testing result, simple and multiple logistic regression analyses were performed. The results of the analyses indicate that persons earning their highest degree in the biological or health sciences are more likely to use the CDC WBS to evaluate HIV-1 test results compared to those who did not. Analysis results of the geographic location or years of experience working in any clinical laboratory setting did not indicate that these two independent variables influenced the clinical laboratory administrator to use the CDC WBS.

This chapter is divided into three parts. First, the interpretation of findings will include conclusions that address all of the research questions referencing the outcomes in Chapter 4. The implications for social change are clearly grounded in the significance section of Chapter 1 and the outcomes presented in Chapter 4. The implications are expressed in terms of tangible improvements to individuals, communities, organizations, institutions, cultures, or societies. As a result, positive social change can be promoted. The last part of Chapter 5 assesses practical recommendations for action and future research.

Interpretation of Findings

This study is the first known to use the demographic characteristics of clinical laboratory administrators to identify whether geographical location, educational major, and years of experience influence whether such administrators use the CDC WBS for interpreting HIV test results. The sample size for this research study comprised 163 clinical laboratory administrators. A list of clinical laboratories that processed WB HIV test results was obtained by the CDC.

Research Question 1

Does the administrator's geographic location (GL) predict the use of the CDC Western Blot standard (CDC WBS) to evaluate WB results?

$H_0 1$: The administrator's GL does not predict the use of the CDC WBS to evaluate WB results.

$H_a 1$: The administrator's GL predicts the use of the CDC WBS to evaluate WB results.

A simple logistic regression analysis indicated that there was no statistically significant relationship between CDC WBS and GL ($p = 0.99$), as identified in Table 3. Of the geographic locations listed for this research study, the percentages of states in the South, Midwest, Northeast, and West that used the CDC WBS were 45%, 20%, 18%, and 16%, respectively. However, there is no universally accepted standard. Because no globally recognized standard exists for what constitutes a positive WB HIV test, someone can be diagnosed by a mere interpretation of the WB test (Leung, 2009). For instance, the FDA WBS was used as a screening tool between 1987 and 1993 to

diagnose persons with HIV. The FDA criteria, albeit stringent, required the person to have p24 and p31/p32. A reaction to p41, p120, or p160 was also necessary (Wilber, 1991). However, Mortimer (1991) emphasized that the WB test, which began as a research tool, should have remained as such rather than being employed as a diagnostic tool. In fact, the WB test is not used for diagnostic purposes in England (Leung, 2009).

It is not known how many people were diagnosed using the FDA criteria before 1987. However, it is important to know whether in 1993, when the criteria changed for what constitutes a positive diagnosis, those previously diagnosed would still be considered as infected with HIV. Up until 1993, only 80% had a positive WB test. Therefore, 20% were not positive by the FDA criteria. After 1993, the FDA dropped the need to have p31/p32. More positive tests resulted. The FDA standard is the most specific. Nevertheless, the CDC WBS was the most used in the United States at this time (Leung, 2009).

In contrast to the FDA WBS, the CDC WBS requires one ENV protein, either gp41 or gp120/160, and p24 (MP Diagnostics, 2005). It is important to remember that each of these proteins is nonspecific. For instance, gp41 has been found in both infected and noninfected sera, as this glycoprotein was identified as cellular debris—i.e., actin (Barre-Sinoussi et al., 1983). Actin serves as a biological marker when lymphocytes are stimulated mitogenically (Bach et al., 1986; Finzi et al., 2007). Such stimulation was evident in developing the first ELISA antibody test. Furthermore, gp41 was responsible for 50% of false positive reactions in a study by Klarkowski (2009).

The second protein classified as a specific protein pertaining to HIV is

gp120/160. This protein has been found to cross-react with conditions such as lupus, ovarian cancer, and breast cancer (Obermoser et al., 2006; Rakowicz-Szulczynska et al., 1998; Rakowicz-Szulczynska et al., 1999). Persons with tuberculosis have gp120/160 (Swaminathan et al., 2008). Persons with malaria have the same glycoprotein (Biswas et al., 2007; Okitsu et al., 2007; Biggar et al., 1985).

A third protein, gp24, has been found in the blood of 1 out of 50 healthy persons (Ranki et al., 1988). A year later, Genesca (1989) found that 70% of indeterminate HIV results were due to gp24. The authors found that the indeterminate WB results were so frequent that no correlation between gp24 and HIV transmission could be determined (Genesca, 1989). Caution is warranted when using gp24 as an indicator for infection because "this test is clinically erratic" (Todak et al., 1991, p. 326).

Although false positive reactions in humans have been documented from these proteins, some researchers have found that the blood of nonhuman animals can also react with these HIV proteins. Strandstrom et al. (1990) found that 50% of the canines they tested for HIV using the WB reacted to such proteins. The most common proteins in the canines were p24, gp41, p31, and gp120. These proteins were present at percentages of 43%, 23%, 22%, and 21.5%, respectively (Strandstrom et al., 1990). Kion and Hoffmann (1991) found that alloimmune mice were making antibodies against HIV, although they had not been exposed to the virus. Alloimmunity means that the mice were gaining immunity from one another against foreign cells, as they were bred for that purpose. The proteins found in the blood of these alloimmune mice were gp120 and p24. It is worthwhile to note that further studies to ascertain why there are cross-reactivity issues

regarding the WB tests have not been conducted. Such cross-reactions are important to acknowledge when analyzing the significance of a positive test result.

From a geographical perspective, Kleinman et al. (1998) found that when the FDA criteria were used on blood donors living in California, Maryland, and Michigan, 9.3% were falsely positive, because the p31 band was not present. In the current study, none of the 163 clinical laboratory administrators used the FDA criteria to interpret HIV WB test results. Of the 32 clinical laboratory administrators who used the WHO standard to interpret WB HIV tests, nine were from states in the Northeast and 23 were from states in the South. The WHO standard requires two bands of ENV proteins in the presence or absence of GAG or POL (MP Diagnostics, 2005). Compared to the CDC WBS and the FDA WBS, the WHO WBS is less stringent (MP Diagnostics, 2005).

From the literature review, it was evident that geographic location may be an appropriate factor to look at in relation to the SEM. Recognizing that community is an important component in how a person develops, the SEM can be used to identify how the community of one geographical region may be different than another region. This exosystem, as Bronfenbrenner (1979) explained, does not require participation by the person. Therefore, a community of people in a particular region can be classified as Northeasterners, Midwesterners, Southerners, or Westerners. By ascending to the next level on the hierarchical chain, these people would be categorized as Americans (Gregson, 2001). The attitudes and behaviors of people, however, differ by region. Therefore, it is possible that clinical administrators' choice of WB test could differ by geography as well. However, this study did not support that theory.

Research Question 2

Does the administrator's education major (EM) predict the use of the CDC WBS to evaluate WB results?

$H_0 2$: The administrator's EM does not predict the use of the CDC WBS to evaluate WB results.

$H_a 2$: The administrator's EM predicts the use of the CDC WBS to evaluate WB results.

A simple logistic regression analysis indicated that there was a statistically significant relationship between use of the CDC WBS and EM ($p = 0.001$), as identified in Table 4. Clinical laboratory personnel who have degrees in clinical laboratory science, which fall into the biological or health sciences, are more likely to produce acceptable results regarding proficiency testing (Delost, Miller, Chang, Korzun, & Nadder, 2009). In this study, clinical laboratory administrators who obtained their highest degrees in the biological or health sciences were nearly 5 times more likely (*OR*= 4.96) to use the CDC WBS to interpret HIV test results. However, it should be noted that 21 clinical laboratory administrators held their highest degree in business. Persons holding such a degree could be found in all regions of the United States. Furthermore, nearly half of all persons with their highest degree in business chose not to use the CDC WBS. Rather, they used the WHO standard for interpreting WB test results. Of the 32 clinical laboratory administrators that used the WHO standard, 19 used Gen-Labs, 11 used Cambridge, and two used Bio-Rad WB test kits. Price quotes from each of the manufacturers who made the test kits demonstrated that there were no price discrepancies.

The SEM can be used for a better understanding of potential influences, such as EM, on using a particular WB standard to interpret HIV test results. Interpersonal relationships occur through the education process. The mesosystem within the SEM is where organizational factors shape the educational pursuits of the student. Therefore, persons obtaining a degree in a particular area will be educated in that specific ideology. Such ideologies are learned within such environments as schools (Gregson, 2001). The degree of influence depends on whether there is value in communication between persons in the mesosystem (Bronfenbrenner, 1979).

Clinical laboratory administrators influence the communication and standards that occur within their labs. A laboratory technologist might think the CDC standard is better, but he or she will follow the directive of the administrator. Therefore, the mesosystem includes the education of the administrator, who in turn, educates his or her employees. Based on the SEM, it appears that factors involved in the mesosystem have strong influences on the type of WB test used. Herein we see that programs and policies could be targeted to improve the quality of HIV testing standards (Bronfenbrenner, 1979).

Research Question 3

Do the administrator's years of experience (YE) predict the use of the CDC Western Blot standard (CDC WBS) to evaluate WB results?

$H_0 3$: The administrator's YE does not predict the use of the CDC WBS to evaluate WB results.

H_a3: The administrator's YE predicts the use of the CDC WBS to evaluate WB results.

A simple logistic regression analysis indicated that there was no statistically significant relationship between CDC WBS and YE working in any clinical laboratory setting ($p= 0.20$), as indicated by Table 5. Out of the 163 clinical laboratory administrators surveyed, none had fewer than 20 YE. Through YE, clinical laboratory personnel are able to obtain particular competencies in their field of study, such as clinical laboratory science (Constantine et al., 2005). The more YE a person has at doing clinical testing, the fewer mistakes are made (Delost et al., 2009).

Years of experience play a role in the microsystem of the SEM (Bronfenbrenner, 1979). Individual level characteristics appear not to influence the test choice. However, if all clinical laboratory administrators have over 20 YE, then the lack of significance for this statistical test may be due to low variability.

Research Question 4

Do the administrator's GL, EM, and YE predict the use of the CDC WBS to evaluate WB results?

$H_0 4$: The administrator's GL, EM, and YE do not predict the use of the CDC WBS to evaluate WB results.

$H_a 4$: The administrator's GL, EM, and YE predict the use of the CDC WBS to evaluate WB results.

A multiple logistic regression analysis was performed in order to test whether there was an association between the three independent variables—GL, EM, and YE—

and the dependent variable, use of the CDC WBS. From this multiple logistic regression analysis, EM was the only statistically significant variable associated with the use of the CDC WBS (p= 0.024), as indicated by Table 6. Such a result is consistent with the finding by Delost et al. (2009) that education plays an important role in correctly identifying diagnostic testing. Furthermore, clinical laboratory administrators were 3.39 times more likely to use the CDC WBS, after controlling for GL and YE, as indicated in Table 6.

Because errors do occur in the clinical laboratory, the variables were used to assess whether singularly or collectively they have influenced clinical laboratory administrators to interpret HIV WB test results using one of several HIV WB testing standards, the CDC WBS. Such quality indicators within the clinical laboratory setting include credentials and lab experience. The results of this study indicate that education plays a role in the type of HIV WB testing standard used within a laboratory, because clinical laboratory administrators with a degree in health sciences (as opposed to business) tend to prefer the CDC WBS. Currently, perfect laboratory quality indicators do not exist. However, proficiency testing can be used to assess the performance of the clinical personnel (Hoeltge, Phillips, Styer, & Mockridge, 2005; Jenny & Jackson, 1993; Peddecord, 1996; Shahangian & Snyder, 2009), despite the educational background. Therefore, in order to identify whether laboratory results are acceptable for clinical practice, proficiency testing serves as one quality control tool (Hoeltge & Duckworth, 1987; Hurst, Nickel, & Hilborne, 1998; Lunz, Castleberry, James, & Stahl, 1987; Miller, 2003).

Implications for Social Change

The epidemic of HIV/AIDS has been part of the global culture since the early 1980s. Yet, the HIV antibody or molecular tests approved by the Food and Drug Administration can only subjectively, not objectively or definitively, diagnose a person's HIV status, as the interpretation of such tests is made by clinical laboratory personnel, who rely on criteria established by organizations around the world (Abbott Laboratories, 2002; Bio Rad Laboratories, 2007; Roche Diagnostic Systems, Inc., 2007). In fact, the most common WB test kit clinical laboratory administrators use for diagnostic purposes, as found in the present study has the disclaimer, "[a] person who has antibodies to HIV-1 is presumed to be infected with the virus" (Bio Rad Laboratories, 2007, p. 2). This disclaimer is presumably based upon the common screening antibody test kit from Abbott Laboratories (2002, p. 1), which states, "At present there is no recognized standard for establishing the presence or absence of antibodies to HIV-1 and HIV-2 in human blood". As a result, it would be challenging to screen or diagnose a person as having HIV if the test kits have such disclaimers.

Although anecdotal evidence persists about persons' going to various clinical laboratories to know their status and receiving differing HIV test results, the purpose of this quantitative correlational study was to identify whether demographic characteristics, such as GL, EM, and YE, influenced the clinical laboratory administrator to use the CDC WBS, as this standard was in common use within the United States. From this current study, it was determined that clinical laboratory administrators who have their highest degree in the biological or health sciences are more likely to use the CDC WBS for

diagnosing HIV. Such results emphasize the need for education among clinical laboratory personnel who use a particular WB standard other than the CDC WBS. By educating clinical professionals who have their highest degree in a field of expertise other than the biological or health sciences, the scientific community may close the gulf between diverging HIV Western blot standards. Such interventions can bring about positive social change.

In order to advocate for HIV antibody testing in the community, it is imperative to understand the scientific underpinning of the antibody tests. In an exhaustive literature review, various discrepancies were found regarding such testing technologies. Some of these discrepancies include the nonspecificity and nonsensitivity of the test kits, antibodies presumed to be indicative of HIV, standards for interpreting HIV test results, and HIV pharmacotherapy. The study presented here has identified factors that may influence clinical laboratory administrators to decide on the use of the CDC WBS, even though various other standards are used across the world. The results of this study indicate that education is important so that public health and clinical personnel can design HIV testing interventions appropriately and effectively.

Recommendations for Action

This study identified the problem that there is no globally accepted standard for what constitutes a positive result on an HIV antibody test, as there are 11 standards that currently exist. This means that the choice of which standard to use is left to the administrator of the clinical laboratory. Consequently, a patient could conceivably test positive at one laboratory and negative at another laboratory that uses a different WB test

standard. In fact, in one case it was discovered that two separate standards were being used within the same laboratory (Leung, 2009). The results of this study indicate that there are areas of concern and educational strategies. Such findings justify particular recommendations to address the problem evident in the present study. The SEM used in this study is recommended as a theoretical model that can serve as a useful tool for understanding and predicting HIV testing decisions among clinical laboratory administrators. Educational status, a meso-level characteristic, proved to be a significant predictor for using the CDC WBS. Therefore, educational interventions for this population who do not have their highest degree in the biological or health sciences should aid in increasing the use of the CDC WBS within the United States. In particular, conferences may be an initial venue for disseminating information advocating for a universal standard, CDC WBS, pertaining to HIV diagnostic processes. Subsequent to such a process, federal policy may be instituted as an increasing number of clinical professionals see the value of using a single CDC WBS.

A second source for recommendation pertains to operator error. Even as we recognize that all methods of analytical techniques, including antibody testing, are prone to error and variation, it is important also to understand that such uncertainty can influence the quality of the laboratory testing results (Omersel, Zager, Kveder, & Bozic, 2010; Peeling, Smith, & Bossuyt, 2008). Although the manufacturer offers stated guidelines for how to perform the test, the foundation of the antibody test should be based on a gold standard, the isolation of HIV. To date, this has not been accomplished, as evidenced in the foregoing literature review. Based upon the results of this study, it is

recommended that proficiency testing be incorporated into clinical laboratory standards and procedure policies (Hoeltge et al., 2005; Hurst et al., 1998; Lunz et al., 1992; Lunz et al., 1987; Miller, 2003; Peddecord, 1996; Shahangian et al., 2009) to overcome the lack of a definitive antibody test.

Although operator error is a real problem that requires attention, the administration of HIV medication, based upon an HIV antibody test that has yet to be validated by HIV isolation, should also be addressed. Advocating for HIV medication to persons being diagnosed as having HIV should be based upon scientific studies that show their benefit. The WHO (2006) asserted that it is difficult to ascertain the differences between the effects of HIV/AIDS and the medications used to treat said condition. This may be why the manufacturer of one HIV medication, AZT, has documented fatal cases associated with this particular medication (GlaxoSmithKline, 2009).

Each class of antiretrovirals (ARVs) and every FDA-approved ARV have been associated with near fatal and fatal events (Reisle et al., 2003). The largest clinical trial to date, the Concorde Study, found that the death rate in an AZT clinical trial was 1.26 times higher in the AZT cohort than in the placebo group. Furthermore, it was estimated that 77% of a large cohort of close to 20,400 adults, 50 years or older, died within 5 years of receiving highly active antiretroviral therapy (Concorde Coordinating Committee, 1994). In fact, 79% of this cohort developed one AIDS event within this period (May et al., 2007). If such medications are being administered, subsequent to HIV antibody tests that have not been validated against viral isolation, it is recommended that such administration of these HIV medications be reduced.

Recommendations for Further Study

This study has a few limitations that should be addressed. First, the study was correlational in nature. For this reason, any relationships between variables did not necessarily mean that there were causal inferences (Aczel et al., 2006; Singleton et al., 2005). Furthermore, the sample population of clinical laboratory administrators may have been small. Therefore, expanding the sample population may provide more data on the WBS used in the United States and around the world. Second, as GL or YE were not statistically significant variables for influencing the clinical administrator to use the CDC WBS, other variables may have elucidated statistical significance. Third, operator error was not established in relation to the other variables. These three limitations can serve as areas for future research study to improve HIV testing research within and outside the United States, from a validity and generalizability perspective.

Operator error, as a viable variable, appears to be the impetus for future study on HIV antibody testing. In particular, research may be warranted on why no other antibody test requires serum to be at a dilution rate of 1:400. The thought is that if undiluted whole blood, which most diagnostic tests use for that purpose, were tested, each test result would be positive (Metlas, 1999). The test kit literature for the most common HIV WB antibody test used by clinical laboratory administrators in this research study states that the dilution factor is 1:101. Typical diagnostic tests used to identify rubella virus, hepatitis A and B virus, and syphilis, on the other hand, use undiluted serum. Such research could show that operator error may be associated with misdiagnosis of HIV.

Conclusion

Although there were limitations, this study was the first to identify the demographic characteristics of clinical laboratory administrators that may influence their decision to use the CDC WBS for interpreting positive test results. The study results suggested that clinical laboratory administrators who have their highest educational degree in the biological or health sciences were more likely to use the CDC WBS. Recommendations for action included educational opportunities and operator error analysis. Future studies with a larger sample population, controlling for other variables, and assessing operator error may aid in identifying an association between the CDC WBS and interpretation of HIV WB test results. As this study is the first known to use the demographic characteristics of the clinical laboratory administrator to identify whether these characteristics influence clinical laboratory administrators' choosing to use the CDC WBS for interpreting HIV test results, this study demonstrated that EM has a practical application to interpreting HIV WB test results. Recognizing that the WB test is used to confirm HIV infection in the United States, further research into educational opportunities for clinical laboratory administrators who are not using the CDC WBS should be explored in order to identify accurately the persons who have HIV antibodies. The results of this study provide a consistent way to identify people who have antibodies to HIV. This may improve confidence in HIV testing, identification of HIV/AIDS, and the management of treatment regimes, helping to lower the overall rates of this pervasive disease.

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Appendix A

TELEPHONE SURVEY SCRIPT

Hello,

My name is Christopher Tex. I'm a doctoral student at Walden University. I'm working on my dissertation in Public Health. I'm calling because I would like to conduct a 4-question survey with the person in charge of making the decision for which Western blot standard to use when interpreting HIV positive results. Would you please direct me to this person? The entire survey will take less than 3 minutes to complete. I assure you that this survey is confidential and anonymous; no names will be recorded. If you agree to take part in the survey, I can send you a copy of the consent form by fax or email so you have a copy for your records.

IF RESPONDENT IS CORRECT PERSON:

Is this a good time to go forward with the survey? As I said before, it will take less than 3 minutes to complete.

IF IT IS A GOOD TIME TO RESPOND:

Great, thanks so much for your cooperation. Before we begin, I would like to review the consent form with you. Also, I can send you a copy of the consent form. The consent form will further explain the purpose of the study, procedures, voluntary nature of the survey, and contact information for me, my faculty advisor, and the Director of the Research Center at Walden University.

You are invited to participate in a doctoral dissertation research study entitled: "A Correlational Study of the CDC Western Blot Standard for HIV Confirmatory Testing and Clinical Laboratory Administrator Demographic Characteristics." You were selected to participate in the study because you are a clinical laboratory professional. To be eligible, you must be fluent in English, work in the United States, and be in charge of making decisions pertaining to the use of Western blot (WB) standards. This form is part of a process called "informed consent" to allow you to understand this study before deciding whether to take part.

This study is being conducted by Christopher A. Tex, who is a doctoral student at Walden University. This study is being conducted as part of doctoral dissertation requirements.

Background Information:

The purpose of the study is to determine if there is an association between the use of the CDC WB standard for HIV confirmatory testing and the characteristics of the clinical laboratory administrator.

Procedures:

If you agree to be in this study, you will be asked to:

- Participate in a telephone survey that captures information about geographic location, education major, and years of experience. Completion time is estimated to be less than 3 minutes.

Voluntary Nature of the Study:

Your participation in this study is voluntary. This means that everyone will respect your decision about whether or not you want to be in the study. No one at your place of employment will treat you differently if you decide not to be in the study. If you would like, I can send you a copy of the consent form so you have it for your records.

If you feel stressed during the study, you may stop at any time. You may skip any questions that you feel are too personal.

Risks and Benefits of Being in the Study:

There are no risks of being in this study. The survey is anonymous and confidential. You may benefit from being in this study by adding your contribution as an administrator or individual in charge of making decisions regarding WB standards to stakeholders in clinical laboratory science. Furthermore, you may have the self-satisfaction of participating in research anticipated to benefit society through understanding why particular WB standards are used in clinical laboratories.

Compensation:

There is no compensation for being in the study.

Confidentiality:

This survey is completely anonymous and confidential. This means your name, laboratory name, or other identifying information will not be reported. I will maintain your contact information in a secure location during the duration of the study. All I need to know is information regarding the HIV Western blot standard you use, Western blot

test kit, years of experience, and geographical location. This information will be aggregated for reporting of final results.

Contacts and Questions:

The researcher's name is Christopher A. Tex. The researcher's faculty advisor is Aimee Ferraro, Ph.D. You may ask any questions you have now. Or if you have questions later, you may contact the researcher via 419-206-0108 and/or christopher.tex@waldenu.edu or the advisor at aimee.ferraro@waldenu.edu. If you want to talk privately about your rights as a participant, you can call Dr. Leilani Endicott. She is the Director of the Research Center at Walden University. Her phone number is 1-800-925-3368, extension 1210.

Statement of Consent:

In order to protect your privacy, signatures are not being collected. Therefore, completion of the survey will indicate your consent, if you so choose to participate.

IF RESPONDENT WOULD LIKE A COPY OF THE CONSENT FORM:

Would you like me to send this consent form to your fax or email? Keep in mind that I will not disclose this information to anyone. I understand that it is not acceptable to disclose confidential information even if the participant's name is not used.

IF RESPONDENT SAYS FAX OR EMAIL:

I will record the fax number or email in a Microsoft Excel spreadsheet so that I will be able to send the consent form via email or fax.

DO YOU HAVE ANY QUESTIONS BEFORE WE BEGIN THE SURVEY?
IF RESPONDENT WANTS TO KNOW THE PURPOSE OF THE SURVEY:

The purpose of the study is to see if using the CDC Western blot standard for confirming HIV is associated with the characteristics of the clinical laboratory administrator.

IF THE RESPONDENT WANTS TO KNOW HOW THE DATA WILL BE USED:

The survey results will be used to identify whether certain Western blot standards are used in the United States. The survey includes questions about Western blot test kit, years of experience, and geographical location.

IF THE RESPONDENT DOES NOT WANT TO ANSWER A QUESTION:

None of the questions in this 3-minute survey are personal or sensitive in nature, but you may feel free to skip any question you wish.

IF THE RESPONDENT WANTS TO KNOW WHETHER THIS IS A LEGITIMATE SURVEY:

This information is found on the consent form. My name is Christopher Tex. I am the doctoral student conducting this survey. My number is 419-206-0108. My email is **Christopher.tex@waldenu.edu**. My faculty advisor is Dr. Aimee Ferraro. Her email is **aimee.ferraro@waldenu.edu.** If you want to talk privately about your rights as a participant, you can call Dr. Leilani Endicott. She is the Director of the Research Center at Walden University. Her number is 1-800-925-3368, extension 1210.

IF THE RESPONDENT WANTS TO KNOW HOW HE OR SHE WAS CHOSEN FOR THE SURVEY:

In 2008, the CDC conducted a performance evaluation survey regarding HIV testing. After I talked with a CDC staff member who was affiliated with this survey, the CDC sent me a list of laboratories that had participated in the 2008 CDC survey and that conducted Western blot testing for HIV. Keep in mind that the only information that was on this list was the laboratory name, address, and phone number. No personally identifiable information was disclosed.

IF NO QUESTIONS, BEGIN SURVEY.

Now do you feel ready to begin? I will read each of the four questions, along with the answer choices, in the order presented, exactly as written. After reading the answer choices, I will record your answer.

AFTER COMPLETING SURVEY:

Thank you for your time and answers to these questions.

Goodbye.

IF RESPONDENT IS NOT THE RIGHT PERSON TO COMPLETE THE SURVEY:

Could you please refer me to the correct person?

IF ANSWERING MACHINE:

My name is Christopher Tex. I'm a doctoral student at Walden University. I'm working on my dissertation in Public Health. I am calling because I would like to conduct a 4-question survey with the person in charge of making the decision for which Western blot standard is used to interpret HIV positive results. The entire survey will take less than 3

minutes to complete. I assure you that this survey is confidential and anonymous; no names will be recorded. If you agree to take part in the survey, I can send you a copy of the consent form by fax or email so you have a copy for your records. I will call back again in a few days to see if you are available to complete the survey. Thank you.

IDENTIFYING AND ADDRESSING RESPONDENTS' RELUCTANCE TO PARTICIPATE

IF RESPONDENT SAYS HE OR SHE IS NOT INTERESTED IN PARTICIPATING:

Before you hang up, let me tell you a little bit more about this scientific survey. You, as a clinical laboratory administrator, represent an important group in diagnostic testing. This type of survey gives important information that can guide public policy including health and public safety. This survey is particularly important especially now because people are receiving differing diagnostic results from Western blot tests. One benefit to participating in this 4-question survey, which would take less than 3 minutes, is that you would be participating in research anticipated to benefit society through understanding why particular Western blot standards are used in clinical laboratories.

IF RESPONDENTS SAY THEY DO NOT KNOW MUCH ABOUT THE TOPIC:

The results of this survey are based upon the fact that your laboratory does HIV Western Blot testing. For that reason, you are considered an expert in the field of diagnostic testing. The four questions to the survey will take less than 3 minutes to complete. I would like to point out that there are no right or wrong answers.

IF RESPONDENTS SAY THEY ARE TOO BUSY OR DO NOT HAVE TIME TO PARTICIPATE:

I appreciate that you have a busy schedule. This survey consists of four simple questions, which will take less than 3 minutes to answer. In order to get a true representation of clinical laboratory administrators in the United States, it is important that I speak with busy people like you. I would be happy to call back at a more convenient time. Please tell me when would be a good time.

IF RESPONDENTS SAY THEY ARE CONCERNED ABOUT PRIVACY ISSUES:

This survey is completely anonymous and confidential. This means your name, laboratory name, or other identifying information will not be reported. I will maintain your contact information in a secure location during the duration of the study. All I need to know is information regarding the HIV Western blot standard you use, Western blot test kit, years of experience, and geographical location. This information will be aggregated for reporting of final results.

Appendix B

Administrator HIV WB Standard Survey

Thank you for taking the time to participate in this telephone survey. Your completion of this survey will help to gain an understanding of the decisions that persons in charge of making decisions about Western blot (WB) standards for HIV confirmatory testing use when selecting a standard.

This survey is directed at persons in charge of making decisions about WB standards within the clinical laboratory setting. This Administrator HIV WB Standard Survey will consist of five questions. The survey should take less than 3 minutes to complete.

I know your time is valuable, and I sincerely appreciate your participation in this electronic survey.

Administrator HIV WB Standard Survey Procedures
Participate in a telephonic survey that captures demographic data—namely, geographic location, education major, and years of experience. Information on the WB test kit and interpretive criteria for WB HIV test results are also collected. Completion time is estimated to be less than 3 minutes.

Administrator HIV WB Standard Survey Instructions

After reading each of the following questions verbatim with the possible answer choices, I will ask the participant to select an answer choice.

1. Please indicate which Western blot test kit(s) is/are used in the clinical laboratory.
   Check all that apply.
           Bio-Rad Genetic Systems HIV-1
           Bio-Rad New LAV Blot 1
           Cambridge Biotech HIV-1 Western Blot
           Genlabs Diagnostics HIV-1 Western Blot
           In House (prepared by own laboratory)
           Noncommercial (e.g., supplied by the state laboratory)
           Other (please specify):_____

2. Please indicate the organization whose criteria you currently use to interpret HIV-1
   Western blot results. Check all that apply.
       A.   Association of Public Health Laboratories/Centers for Disease Control
   and Prevention (APHL/CDC)
       B.   Consortium for Retrovirus Serology Standardization (CRSS)
   C. World Health Organization (WHO)

D.   OTHER (please specify): _____

3. How many total years of experience do you have working in any clinical laboratory setting?

_____

4. What is your education major for your highest degree earned?

Biological or Health Sciences (e.g., Biology, Medicine, Public Health)
Business (e.g., Administration, Management)
Social Sciences (e.g., Economics, Sociology, Political Science)
Education
Psychology
Other (please specify): _____

5. What is the geographic location of your clinical laboratory based on the U.S. Census?

Northeast (MN, NH, VA, MA, RI, CT, NY, NJ, PA)
Midwest (IL, IN, IA, KS, MI, MN, MO, NE, ND, SD, OH, WI)
South (DC, FL, GA, MD, NC, SC, VA, WV, DE, AL, KY, MI, TN, AR, LA, OK, TX)
West (AK, AZ, CA, CO, HI, ID, MT, NV, NM, OR, UT, WA, WY)

Appendix C

Descriptive Statistics for all Survey Questions

How many total years of experience do you have working in any clinical laboratory setting?

N					
Valid	Missing	Mean	Std. Deviation	Minimum	Maximum
163	0	31.51	6.645	20	44

What is your education major for your highest degree earned?

		Frequency	Percent
Valid	Biological or Health Sciences	142	87.1
	Business	21	12.9
	Total	163	100.0

If your education major for your highest degree earned was other, please specify.

		Frequency	Percent
Valid	No	163	100.0

What is the geographic location of your clinical laboratory based on the U.S. Census?

		Frequency	Percent
Valid	Northeast	30	18.4
	Midwest	33	20.2
	South	74	45.4
	West	26	16.0
	Total	163	100.0

Do you use the Bio-Rad Genetic Systems HIV-1 Western blot test kit?

		Frequency	Percent
Valid	No	34	20.9
	Yes	129	79.1
	Total	163	100.0

Do you use the Bio-Rad New LAV blot 1 Western blot test kit?

		Frequency	Percent
Valid	No	163	100.0

Do you use the Cambridge Biotech HIV-1 Western blot Western blot test kit?

		Frequency	Percent
Valid	No	149	91.4
	Yes	14	8.6
	Total	163	100.0

Do you use the Genlabs Diagnostics HIV-1 Western blot Western blot test kit?

		Frequency	Percent
Valid	No	144	88.3
	Yes	19	11.7
	Total	163	100.0

Do you use an In-House (prepared by own laboratory) Western blot test kit?

		Frequency	Percent
Valid	No	162	99.4
	Yes	1	.6
	Total	163	100.0

Do you use a Noncommercial (e.g., supplied by the state laboratory) Western blot test kit?

		Frequency	Percent
Valid	No	163	100.0

Do you use some other (please specify) Western blot test kit?

		Frequency	Percent
Valid	No	163	100.0

Do you use the Association of Public Health Laboratories/Centers for Disease Control and Prevention (APHL/CDC) criteria to interpret HIV-1 Western blot results?

		Frequency	Percent
Valid	No	32	19.6
	Yes	131	80.4
	Total	163	100.0

Do you use the Consortium for Retrovirus Serology Standardization (CRSS) criteria to interpret HIV-1 Western blot results?

		Frequency	Percent
Valid	No	163	100.0

Do you use the World Health Organization (WHO) criteria to interpret HIV-1 Western blot results?

		Frequency	Percent
Valid	No	131	80.4
	Yes	32	19.6
	Total	163	100.0

Do you use some other (please specify) criteria to interpret HIV-1 Western Blot results?

		Frequency	Percent
Valid	No	163	100.0

Curriculum Vitae

Christopher A Tex

Work Experience

09/11-Present　Carrington College　　　　　　　　Phoenix, AZ
Medical Laboratory Technology Program Director
- Monitor academic progress of MLT students
- Obtain clinical externship sites for MLT students
- Lecture Anatomy/Physiology, Basic Laboratory Techniques, Cell Biology, Serology, Immunology and related courses for the Medical Laboratory Technology program

04/11-Present　Carrington College　　　　　　　　Phoenix, AZ
Adjunct Professor
- Lecture Anatomy/Physiology, Basic Laboratory Techniques, Cell Biology, Serology, Immunology and related courses for the Medical Laboratory Technology program

02/11-Present　University of Phoenix　　　　　　　Phoenix, AZ
Adjunct Professor
- Lecture Health Administration and related courses for the College of Humanities and Natural Sciences and Nursing departments

06/09-09/11　　Arizona Department of Health Services　　Phoenix, AZ
Newborn Screening Epidemiologist
- Analyze statistical data on newborn screening for the state of Arizona
- Complete annual reports, including recommendations for increased quality measures regarding metabolic and hearing status
- Contact clinicians and families to ensure timely follow-up hearing services

07/07-Present　Carrington College　　　　　　　　Phoenix, AZ
Adjunct Professor
- Lecture Anatomy/Physiology and Microbiology classroom and laboratory courses for nursing students

01/07-06/09　Arizona Department of Health Services　　Phoenix, AZ
Birth Defects Epidemiologist
- Analyze statistical data on birth defects for the state of Arizona
- Conduct active surveillance for birth defects by reviewing medical charts
- Complete annual reports, including recommendations for prevention of birth defects

10/05-01/07　　Harris HealthTrends, Inc.　　　　　　Toledo, OH
Supervisor/Health Advisor
- Monitor the weekly progress of health advising team
- Serve as a motivational force in driving the health team to make constant improvements in both areas of quantity and quality
- Coached and motivated participants through a series of lifestyle modifications

- Worked together with participants to set and accomplish specific goals that will improve the participant's health and reduce his/her risk factors

4/05-9/05   Findlay City Health Department   Findlay, OH

Bioterrorism Emergency Response Coordinator/

Health Inspector

- Created a template for Mass Prophylaxis during a disaster incident
- Inspected food establishments to maintain sanitary conditions
- Conducted active West Nile Virus surveillance on mosquito and bird populations
- Conducted active Rabies surveillance on bats, dogs, and cats

9/04-3/05   Harris HealthTrends, Inc.   Toledo, OH

Health Advisor

- Coached and motivated participants through a series of lifestyle modifications
- Made goal setting agendas and achievement exercises
- Worked together with participants to set and accomplish specific goals that will improve the participant's health and reduce his/her risk factors

01/04-07/04   Medical College of Ohio   Toledo, OH

Research Technician

Performance of industrial hygiene duties for Tobacco research grant:

- Researched and created database of all potential sampling locations
- Assisted with recruiting potential sampling locations
- Collected personal, area, and biological samples for laboratory testing
- Collected and created database for tracking literature related to environmental tobacco smoke
- Assisted with writing sections of technical document

08/02-05/03   Medical College of Ohio   Toledo, OH

Graduate Assistant

- Compiled lecture notes for Occupational Health Seminar
- Assisted with creation of a template for post-event smallpox planning
- Teacher-Assistant for Epidemiology course
- Fungal and bacterial sampling and analysis for IAQ Assessment

09/02-11/02   Wood County Health Department   Bowling Green, OH

Intern

- Participated in various functions of the Health Department
- Assisted Registered Sanitarians on scheduled inspections
- Compiled files to be used as a tool for up-coming storm drain issues
- Data entry of parcel numbers for GIS mapping purposes

07/96-11/05   Animal Medical Center   Litchfield, IL

Veterinary Assistant

- Microbiological analysis on canine and feline biological samples
- Assisted in veterinary surgical procedures

Education

| 09/07-present | Walden University | Minneapolis, MN |

- Doctorate in Philosophy-Epidemiology
- Graduating summa cum laude

| 08/01-06/03 | Northwest Ohio Consortium for Public Health | Toledo, OH |

- Member Institutions: Bowling Green State University, Medical College of Ohio, University of Toledo
- Masters of Public Health-Environmental and Occupational Health degree obtained June 2003
- Accredited by CEPH
- Received a Graduate Assistantship for Fall, Spring and Summer 2002-2003

| 08/97-06/01 | University of Findlay | Findlay, OH |

- Bachelor of Science in Biology
- Took several classes in the pre-veterinary medicine major
- Honor Roll Recipient 1997-2001

| 08/93-06/97 | Sacred Heart Griffin High School | Springfield, IL |

- Diploma received June 1997

Membership Affiliations/ Community Service

- Member of the Data Committee for the National Birth Defects Prevention Network
- Member of the American Public Health Association
- Member of the Public Health Student Organization
- I've volunteered for the Flying Samaritans, a volunteer organization which operates free medical clinics in Baja California, Mexico

Skills/Abilities

- Exceptional organizational, oral, and written communication skills
- Knowledge of SAS, SPSS, EpiInfo, MS Word, Access, Excel and Power Point
- Strong background in Anatomy/Physiology, Microbiology, Epidemiology, and Biostatistics

Publications

- Milz, S., Akbar-Khanzadeh, F., Ames, A., Spino, S., Tex, C., & Lanza, K. (2007). Indoor air quality in restaurants with and without designated smoking rooms. *Journal of Occupational and Environmental Hygiene* 4(4), 246-52.

- Akbar-Khanzadeh, F., Milz, S., Ames, A., Spino, S., & Tex, C. (2004). Effectiveness of clean indoor air ordinances in controlling environmental tobacco smoke in restaurants. *Archives of Environmental Health* 59(12), 677-85.
- Emergency Preparedness and Planning for Natural and Manmade Disasters Brochure

References

- Enclosed upon request