Acceptability and Consumer Willingness to pay for a hypothetical HIV vaccine in Northern Brazil: a cross-sectional study and the implications

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Abstract

The Human Immunodeficiency Virus (HIV) is considered one of the greatest public health challenges given its impact on morbidity and mortality and, there is currently no vaccine available. The costs for any vaccine have to be weighed against current preventative measures as well as its impact in reducing future infections. This was the rationale behind conducting a willingness to pay (WTP) study to guide future funding decisions. A cross-sectional study was conducted involving residents of Northern Brazil

regarding their WTP for a hypothetical vaccine against HIV with 70% effectiveness. 634 individuals were interviewed and 94% accepted to use this hypothetical vaccine. The WTP was US$ 47.54 (200.00BRL). We believe these findings can contribute to decision-making about pricing once a HIV vaccine becomes available in Brazil and in discussions with its acceptability.

Keywords: HIV, willingness to pay, vaccine, Brazil, contingent valuation.

Introduction

The Human Immunodeficiency Virus (HIV) was discovered in the early 1980s and, since then, HIV has become a global epidemic with a significant contributor to morbidity and health-related costs worldwide (Quiros-Roldan et al, 2016; Melo, 2018). There are two main types of virus, HIV-1, which is the most pathogenic and prevalent, and HIV-2, which is endemic in West Africa and present in other regions including Asia (Sharp & Hahn, 2011). HIV belongs to the *Lentivirus* genus and *Retroviridae* family and can lead to immunological depression by attacking and infecting all membrane glycoprotein cells (CD4 +), as well as macrophages and auxiliary T lymphocytes (Melo, 2018; Silva, 2018; WHO, 2020; Fernandes et al., 2020). HIV can be transmitted by unprotected sex, blood transfusions, blood products in contact with contaminated sharps and vertical transmission (Shaw & Hunter, 2012, German Advisory Committee Blood, 2016; Melo, 2018).

The Acquired Immunodeficiency Syndrome (AIDS) is the most advanced stage of HIV infection (Melo, 2018; Santos et al., 2020). Between 1980 and June 2019, there have been approximately 74.9 million patients worldwide identified with having AIDS. In 2019, there were 690,000 deaths associated with AIDS worldwide (UNAIDS, 2019; UNAIDS, 2020). Africa is the most severely affected region, accounting for approximately two thirds of global HIV infections (Roser & Ritchi, 2019; UNAIDS, 2020; OPAS, 2017). In 2016, the United Nations General Assembly (UN) sought to establish the end of the AIDS epidemic by 2030,

which demanded an accelerated expansion of services against HIV (UNAIDS, 2020). However, despite this goal, approximately 1.7 million people (62% adults) were infected with HIV worldwide in 2019, which represents more than three times the goal established to 2020 (UNAIDS, 2019; UNAIDS, 2020).

Overall, in Brazil, just under 1 million AIDS cases were identified between 1980 and June 2019 and in 2018, 43,941 new HIV infections and 37,161 AIDS cases were reported in the Information System for Notifiable Diseases (SINAN) (Brasil, 2018; Brasil, 2019a). Encouragingly, from 2012 to 2018, the number of patients with AIDS in Brazil decreased 16.8% from 21.4/100,000 inhabitants in 2012 to 17.8/100,000 inhabitants in 2018. This decrease may be related to the "treatment for all" program, implemented by the Ministry of Health in December of 2013, where antiretroviral treatment is recommended for all People Living With HIV/AIDS or People Living Positively (PLHIV) regardless of their CD4+ lymphocyte count (Brasil, 2019b), with pertinent medicines available free-of-charge in the Brazilian public health system (SUS) (Brasil, 1990; Brasil, 2018; Brasil, 2019a). Medicines also now include pre-exposure prophylaxis (PrEP), which is given to HIV-uninfected individuals to block HIV acquisition, with PrEP seen as one of the most effective prevention strategies. However, it is highly dependent on an individual's adherence and may cause adverse effects (Fonner et al., 2016). Annually, approximately thirty-nine thousand new cases are currently registered in Brazil. In the Northern region of Brazil, 63,527 HIV cases were notified in 2019, with the state of Pará having the third highest number of patients with AIDS at 28,655 cases as well as deaths due to AIDs in 2019 (Brasil, 2019a).

According to the United Nations Program, the total spending on HIV/AIDS services in low- and middle-income countries (LMICs) was approximately US$19 billion by the end of 2018 (UNAIDS, 2019). In Brazil in 2019, 338,966 cases of hospitalizations associated with HIV were reported costing R$ 451,391,793.16 (BRL) (US$ 107,310,715), of which 45.8% was

associated with patients admitted to the public health system. The average stay of hospitalizations in the public and private sectors in 2019 was 19.1 and 11.9 days, respectively (Santos et al., 2020). Overall, the Brazilian government spent R$ 5.3 billion (BRL) on treatment for individuals with HIV/AIDS between 2016 to 2019 (Brasil, 2019a; Brasil, 2019b), This was seen as a good use of resources with the survival of PLHIV in Brazil increasing by 12 years with treatment (Quiros-Roldan et al., 2016).

Currently, there is no cure for HIV/AIDS. However, combined antiretroviral therapy (cART) is highly effective, extending survival and decreasing HIV transmission by more than 95% (Antiretroviral Therapy Cohort Collaboration, 2017; Supervie et al., 2014). However, there are concerns with adherence to HIV treatments. This includes tenofovir, lamivudine, emtricitabine and efavirenz, that is recommended, regardless of the patient's CD4 count (WHO, 2016; Vagiri et al., 2018).

Despite the advances and achievements in cART, treatment is likely to be life-long, potentially leading to long-term side effects and HIV-1 resistance, besides contributing to health-related costs (Montessori et al., 2004; Paredes & Clotet, 2010; Long et al., 2016; Adebimpe et al., 2020). In study conducted in Guyana, the mean annual cost per of maintaining established adult and pediatric patients on ART were US$ 428 and US$ 410, respectively (Suraratdecha et al., 2020).

The National Immunization Program (PNI) in Brazil, founded in 1973, is a global reference in the fight against infections and was developed with the objective of coordinating immunizations, promoting the reduction of infectious diseases, assigning functions to supervise the use of immunobiological medicines including vaccines, and monitoring their performance (Brasil, 2018). Within PNI, 19 vaccines are offered according to the national vaccination calendar for more than 20 diseases (Brasil, 2021a) covering the elderly population, adults, in-

digenous peoples, pregnant women and children (Brasil, 2021a; Brasil, 2021b). On an emergency basis, three vaccines were approved for the prevention of COVID 19 from the Butantan Institute, Astrazenica/the Oswaldo Cruz Foundation (Fiocruz) and Janssen Ensemble (Brasil, 2021a; Brasil, 2021c).

There have been considerable efforts in recent years towards the development of an effective and safe vaccine against HIV, which will be an important strategy to assist in future control and prevention (Esparza, 2013; Barros & Vieira, 2017; Muniz Junior et al., 2019). Despite the different strategies that have been tested in more than 200 clinical trials, there is still no vaccine candidate that has proven successful (Chen et al., 2020). Current vaccine candidates include the ALVAC-HIV and AIDSVAX B/E (Rerks-Ngaorm et al., 2009), RV144 (Espaza, 2013), HVTN 505 (Robinson, 2018), HVTN 706 (Barouch et al., 2015), HVTN 702 and HVTN 705 (Koup et al., 2010; Robinson, 2018; Cruz, 2019). The candidates HVTN 705 and HVTN 706, respectively named Imbokodo and Mosaico, are currently in late-stage, multinational vaccine clinical trials and showing the most promise (GIV, 2019; Highleyman, 2019).

In Brazil, following compliance with all protocols and criteria determined by the Brazilian Health Regulatory Agency (ANVISA), a new product can be registered for potential commercialization. Any vaccine for HIV prevention will be classified as Category I in Brazil, in other words, a new product capable of bringing clinical benefits with proven efficacy (Brasil, 2008). Following registration by ANVISA, companies must first apply to CMED for pricing considerations. The Medicines Market Regulation Chamber (CMED) is the Brazilian authority responsible for evaluating and establishing prices and determines the limit for pricing in the country's medicine market (Godói et al., 2017; Muniz Junior et al., 2018; Brasil, 2020a; Brasil, 2020b). To establish potential prices of future medicines in Brazil, CMED evaluates current prices in several countries including Australia, Canada, Spain, United States of America France, Greece, Italy, New Zealand and Portugal (Brasil, 2020a; Muniz Junior et al., 2018;

Sarmento et al., 2019). The price companies apply to CMED for cannot be higher than the lowest value established for the same medicine in these countries and in the country of origin of the medicine itself. Only after approval from ANVISA and pricing considerations from CMED, can pharmaceutical laboratories request the incorporation of a new technology into SUS. The National Commission on Technology Incorporation of the National Health System (CONITEC) is responsible for organizing and conducting all assessments applied to this process (Brasil, 2008; Godói et al., 2017; Sarmento et al., 2019). This can include willingness to pay (WTP) studies especially for new technologies such as new vaccines that are currently not available in the basket of comparative countries for pricing considerations (Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021).

In the scenario of limited healthcare resources and growing demands in Brazil, it is important to emphasize the importance of undertaking studies in an economic context to support the process of rational decision-making (Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021). Accordingly, studies that seek to identify the value of technologies of clinical interest for a given country, such as a vaccine for the HIV prevention disease in Brazil, may contribute to future decision-making regarding their pricing.

WTP is a methodology that seeks to estimate the maximum individual value to be allocated to a specific program, clinical intervention, services or treatment to identify its monetary value (Haab & Mcconnell, 2002; Palanca-Tan, 2008). This approach enables decision makers to assess a point value, ranges of values, or the positive or negative response to a presented value, contributing to a better perception of an individual's preferences in health decision-making processes (Haab & Mcconnell, 2002; Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021). In general, ascertaining WTP is based on the application of a questionnaire, with prior presentation of the characteristics of the evaluated intervention to the interviewee, including the conditions and aspects relevant to the clinical context (Haab & Mcconnell, 2002).

Due to the lack of economic evaluation studies in the field of WTP for hypothetical vaccines for HIV infection in Brazil, as well as considerable prevalence of HIV not only in the North, but throughout the country, undertaking this type of study would seem to be helpful in framing future pricing considerations for possible vaccines. As stated, a vaccine to prevent HIV should significantly reduce current morbidity and mortality rates in Brazil with the potential to re-direct public funds to other high priority disease areas. In view of this, we undertook a WTP study in this area to assist in discussions on potential pricing, including decision making by CMED, and reimbursement strategies regarding any possible future HIV vaccine (Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021).

We believed a WTP would help understanding of the potential value of any hypothetical vaccine for HIV from the perspective of Brazilian consumers. As mentioned, this is seen as an increasingly important consideration to guide future pricing considerations in Brazil (Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021). Consequently, we undertook research into this area. We believe this is the first study undertaken in Brazil applying the WTP technique in the context of an infection of high relevance in Brazil to help guide future pricing considerations. We believe our findings will also be relevant to other countries especially sub-Saharan African countries building on other published studies (Bishai et al., 2004; Ngambi et., 2017; Usman & Usman, 2019).

Materials and Methods

We used the contingent valuation analysis methodology to estimate the WTP of Brazilian consumers from the northern region of Brazil regarding a hypothetical vaccine for the prevention of HIV infections. As mentioned, WTP is a method used to estimate the maximum amount an individual is willing to pay for health services and technologies in order to quantify

the real monetary value of the intervention (Haab & Mcconnell, 2002; Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019). This type of approach allows the verification of the market's price for future interventions, which can contribute to health decision making including potential prices within public healthcare systems (Haab & Mcconnell, 2002; Godói et al., 2017; Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021).

The WTP technique consists of applying a questionnaire to selected participants, with a prior presentation of the disease and the technology related to the decision scenario (Haab & Mcconnell, 2002; Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019; Godói et al., 2021).A questionnaire with open and closed questions was developed based on previous publications using the same methodological approach (Haab & Mcconnell, 2002; Godói et al., 2017; Muniz junior et al., 2018; Godói et al., 2021).

Design and study location

The study was conducted in ten municipalities in the state of Pará, including the metropolitan region (Belém, Marabá, Parauapebas, Abaetetuba, Jacunda, Itupiranga, Rondón do Pará, São Domingos do Araguaia, São João do Araguaia and Baião). Pará is the ninth most populous state in Brazil with, approximately, 8.6 million inhabitants, of which just over 2 million are registered in the metropolitan region of Belém, Pará's capital (IBGE, 2021). The mean Human Development Index is similar between Belém (0.746) and Brazil in general (0.737) (Atlas de desenvolvimento humano no Brasil, 2013; IBGE, 2020a; IBGE, 2021). In 2019, the mean gross monthly income *per capita* was R$1,439 BRL for Brazil and R$ 807 BRL for the Northern Region (IBGE, 2021).

The research was undertaken in the second semester of 2019 and interviews were conducted in November and December by undergraduate healthcare students, mainly from the Public Health School at the Federal University of the South and Southeast of Pará (Unifesspa).

Before applying the questionnaire, all interviewers were trained by the researchers responsible for this study following recommendations adopted in previously published studies (Godói et al., 2017; Muniz junior et al., 2018; Sarmento et al., 2019; Godói et al., 2021).

Data collection instrument

The methodological approach adopted to measure the WTP of a hypothetical vaccine for HIV infection consisted of the application of a questionnaire along with prior presentation to the respondent of all the features of the infection as well the hypothetical technology applied (including its effectiveness and adverse effects, epidemiological data and inclusion criteria for vaccination); with both seen as important for decision making. All respondents received the same information (Haab & Mcconnell, 2002; Godói et al., 2017; Muniz junior et al., 2018; Sarmento et al., 2019; Godói et al., 2021).

The questionnaire was divided into five sections: (1) Questions to understand what the participants knew about the HIV virus; (2) Information about the disease, intervention and alternatives for disease prevention; (3) Questions to evaluate the understanding of the information provided; (4) Discrete Choice, Bidding game and Open-Ended questions (Haab & Mcconnell, 2002). The discrete choice aimed to identify whether individuals would pay US$ 35.65 (150.00BRL) for a single dose of the hypothetical HIV vaccine. The bidding game included a range of values that respondents would pay for a potential new vaccine, and the open-ended question assessed the maximum value associated with their WTP. Finally, in section five, we collected socioeconomic information.

The base value of US$ 35.65 (150.00BRL) for the vaccine was defined based on values established by the Medicines Market Regulation Chamber (CMED) through the factory price (PF) applied to vaccines available to purchase in the private market in Brazil, involving several types of products and infections, e.g. yellow fever and influenza (Anvisa, 2021). The protection

efficacy of the hypothetical vaccine was 70% and there could be possible local and systemic adverse effects included swelling and pain at the application site.

All questions related to the research context or difficulties in completing the questionnaire were explained by the interviewers. In addition, a figure was used to illustrate and facilitate the understanding of the percentage of protection of the hypothetical vaccine against the HIV virus.

Sampling and selection criteria

The selection of respondents was performed in a convenient sampling. Individuals passing by areas of great circulation such as squares, parks, markets and fairs in the cities involved in the study were invited to participate. Those who agreed to participate answered the questionnaire at the same location. The sample size calculation considered a scenario of greater uncertainty, where 50% of respondents would agree to pay the amount of US$ 35.65 (150.00BRL). Considering a confidence level of 95% and margin of error of 4%, we estimated that a minimum of 600 respondents would be necessary. The value of US$ 35.65 (150 BRL) was utilized considering, as mentioned, the prices of vaccines approved in Brazil. The number of individuals to be interviewed in each of the ten cities was defined according to the relative population size of each the municipalities.

Respondents could not have symptoms or a diagnosis of the disease at the time of the interview (Haab & Mcconnell, 2002; Godói et al., 2017; Sarmento et al., 2019), consequently, only individuals without a diagnosis of HIV at the moment of the interview were included. In addition, individuals were required to be at least 18 years old and to declare their family income (those without a monthly income were excluded). Individuals who would not use the vaccine even if it was free-of-charge, and those who declared a WTP more than twice the amount of their declared monthly family income, were excluded from the analysis in line with previous

studies (Lee et al., 2015; Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019; Godói et al., 2021).

Data analysis

The WTP for the HIV vaccine was estimated from the median value declared by individuals who were willing to pay any value greater than or equal to zero. The median value is often used in WTP analysis to minimize the influence of minimum and maximum outliers obtained during data collection (Lee et al., 2015; Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021).

The median WTP value was compared among participant characteristics using the Mann-Whitney test (two groups) or the Kruskal-Wallis test (three or more groups). The level of significance was 5%. We also evaluated the correlations between socioeconomic characteristics and the maximum WTP value for the hypothetical HIV vaccine. The individuals were organized into groups and stratified by *per capita* wage income (number of minimum wages) into '0–0.25,' '0.25–0.50,' '0.50–1.00' and '1.00–20' groups, which were defined based on quartiles and median (with each category containing 25% of the sample), similar to the method applied in a previous study (Athie et al., 2021). These income strata ("0 - 0.25 ", "0.25 - 0.50 ", "0.50 - 1.00 ", and "1.00 - 20") represents family income values between US$ 0 and US$ 59.43 (250.00 BRL), US$ 59.44 (BRL 250.01) and US$ 118.86 (BRL 500.00), US$ 118.87 (BRL 500.01) and US$ 237.73 (BRL 1000.00) and US$ 237.74 (BRL 1000.01) to a maximum of US$ 4754.65 (BRL 20,000.00), respectively.

Regarding education, respondents were stratified into "never studied or did not complete primary education", "complete primary education", "complete high school" and "complete college or more" in line with previous studies (Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021). We also classified participants in terms of any health insurance, i.e. if they have a private health insurance or not. This is because participants who have private insurance

in Brazil may well be willing to pay more for a new effective vaccine (Gustafsson-Wright et al., 2009).

WTP means (on the natural logarithm scale) were compared between groups using the ANOVA test. Subsequently, an initial multivariate linear regression model was adjusted with the significant variables ($p < 0.20$) in the univariate analysis. Variables with $p < 0.05$ were maintained in the final model. Regression analysis was undertaken to investigate whether the maximum amount the respondent is willing to pay for the vaccine (dependent variable) is affected or correlated with characteristics such as gender, age and income (independent variables). In addition, all linear regression model assumptions have been examined. The analyzes were performed as recommended in the literature (Weisberg, 2005).

For comparative purposes, we adopted the conversion value provided by the Brazilian Central Bank (2020: 1 US$ = 4.2064 BRL) (Brasil, 2020b). All analyses were conducted using Microsoft Excel 2010 and R.

Ethics statement

All interviews were conducted after reading and signing the Term of Free and Clarified Consent and participation of the respondents was voluntary. All researchers of the project signed a confidentiality agreement prior to the interviews. This study was approved by the Ethics Committee of the Federal University of Pará (COEP) under the CAAE 12943619.5.0000.8607.

Results

Population characteristics

We conducted a total of 634 interviews with individuals between 18 and 84 years old. Table 1 shows the characteristics of the participants. The mean age of the interviewees was 36.4 years (Standard Derivation (SD) =13.3), 46% were male, 86% were employed at the time

of the interviews and 18.6% had higher education or more. Only 1.7% respondents reported living with at least one HIV-positive individual in the same house. 92% of the participants declared having a family income below five times the minimum. In addition, the acceptability for this hypothetical vaccine was 94%.

Table 1: Characteristics of respondents (n=634)

Variable	**n**	**(%)***
Age in years [mean (SD)]	36	13.3
Man	292	46.6%
Have children	394	62.1%
Education level		
Never attended school	68	10.7%
Completed elementary school	72	11.3%
Completed high school	376	59.3%
Completed college or more	118	18.6%
Employment status		

Currently working	542	86.2%
Have private health insurance	194	30.6%
Other people in the household with HIV infection	11	1.7%
Family income (number of times the minimum wage) **		
<1		24.2%
1-2		35.0%
2-3		18.7%
3-5		14.1%
5-10		6.0%
10-20		1.7%
>20		0.0%

Notes: * The difference to reach 100% for all questions is due to answers such as “I don`t know” and “I don`t want to answer”. **3.2% of the respondents refused to respond to questions regarding family income; Brazilian minimum wage in 2019 was 998.00 BRL (US$ 237.25) per month.

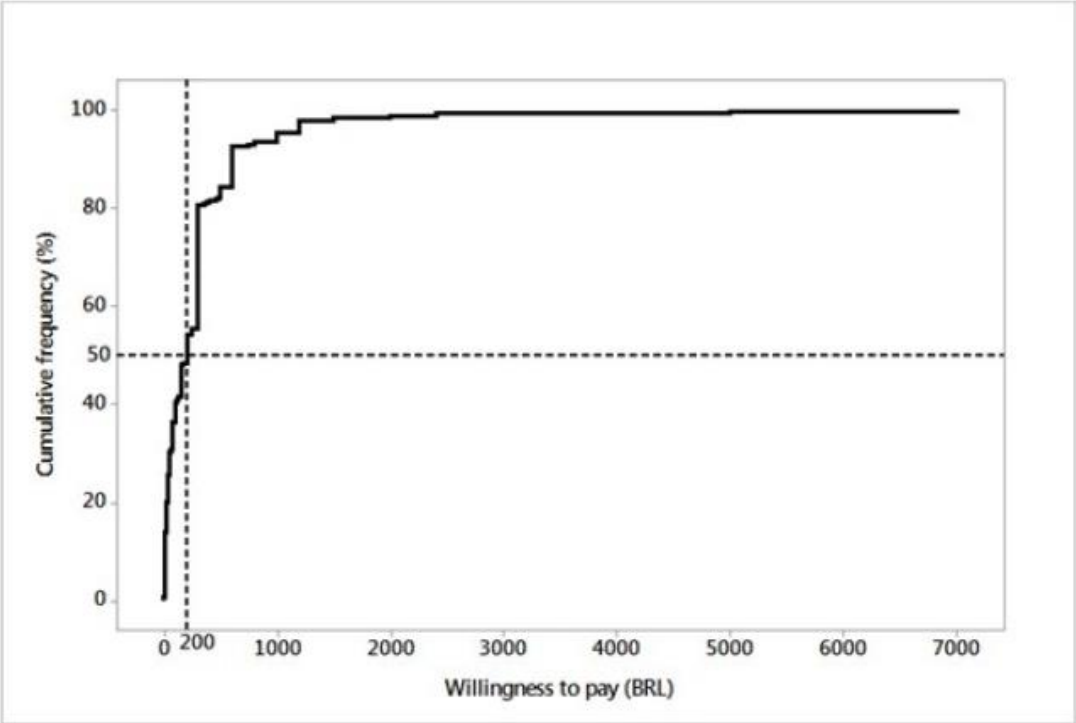
WTP for a hypothetical HIV vaccine

Of the 634 individuals interviewed, seven individuals were not eligible for the WTP analysis since their reported maximum amount of WTP was twice the value of their monthly family income. Consequently, 627 interviewees were finally included in the WTP analysis.

From the discrete choice technique, 72% were WTP US$ 35.65 (150.00BRL) for a single dose of this hypothetical vaccine. In addition, 40.8% of the respondents declared a WTP to this vaccine between US$ 17.82 (75.00 BRL) to US$ 71.31 (300.00 BRL) and the mean value obtained was US$ 71.05 (298.90 BRL). The minimum and maximum values reported were US$ 0.00 and US$ 1,664.1 (BRL 7,000.00), respectively.

The median of the maximum WTP value for a single dose of the hypothetical HIV vaccine was US$ 47.54 (200.00BRL). In other words, approximately 50% of the participants mentioned maximum WTP values equal or less than US$ 47.54 (200.00BRL) (Fig.1).

Figure 1. Cumulative percentage of the willingness to pay for a hypothetical HIV vaccine according to the reported maximum values.



Note: BRL: Brazillian real.

The median WTP was higher among men than among women (US$ 65.37/275.00BRL versus US$ 35.65/150.00BRL; p-value = 0.007). In addition, only three variables demonstrated statistical significance (p-value ≤ 0.05) (Table 2).

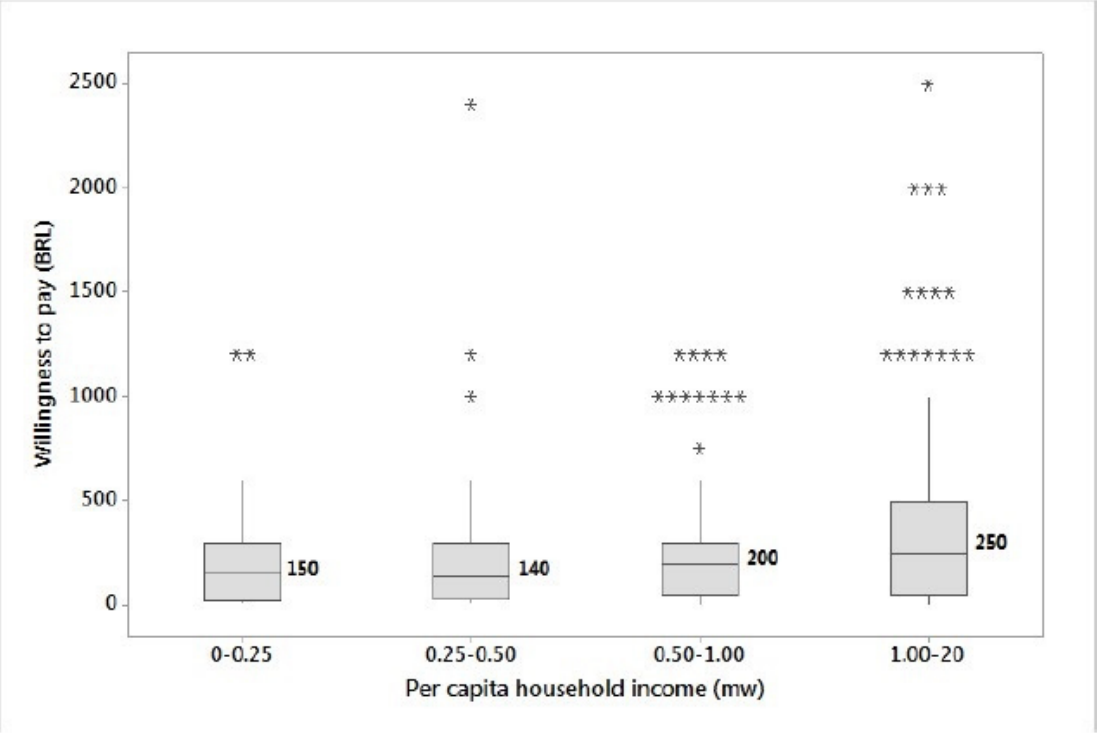
Table 2: Univariate analysis of WTP associated for each variable

Variable	WTP (BRL)			p-value*
	Median	Q1	Q3	
Per capita household income (mw/BRL)				0.011
0 – 250	150.00	18.80	300.00	
250.01 – 500	140.00	30.00	300.00	
500.01 – 1,000	200.00	50.00	300.00	
1,000.01 – 20,000	250.00	50.00	500.00	
Education level				0.004
Never attended school	150.00	22.50	300.00	
Completed elementary school	200.00	30.00	300.00	
Completed high school	200.00	37.50	300.00	
Completed college or more	300.00	75.00	600.00	
Gender				0.007
Men	275.00	52.5	300.00	
Women	150.00	30.0	300.00	
Insurance health				0.071
No	150.0	35.0	300.0	
Yes	200.0	71.3	300.0	
Working at the moment				0.119
No	150.0	9.5	287.5	
Yes	200.0	37.5	300.0	
Had children				0.474
No	175.0	38.1	300.0	
Yes	200.0	37.5	300.0	

*Mann-Whitney/Kruskal-Wallis test; BRL: Brazillian Real; mw: minimal wage; Q1: first quartile; Q3: third quartile.

The income strata ("< 0 - 0.25 ", "0.25 - 0.50 ", "0.50 - 1.00 ", and "1.00 - 20") represents family income values below US$ 59.43 (250.00 BRL), between US$ 59.43 (250.00 BRL), US$ 118.86 (BRL 500.00) and US$ 237.73 (BRL 1000.00) and a maximum of US$ 4754.65 (BRL 20,000.00), respectively. The median value of WTP for the hypothetical vaccine among the respective income groups were US$ 35.65, US$ 33.28, US$ 47.54 and US$ 59.43 (p-value = 0.011) (Fig.2). In the final multivariate linear regression model for WTP, there was no statistically significant difference whether individuals had private insurance or not (p-value = 0.071). The final regression model and analysis are displayed in Table 3.

Figure 2: Box plots indicating willingness to pay for a hypothetical vaccine against HIV according to *per capita* household income range.



Note: BRL: Brazillian real; mw: Minimum wage.

Table 3: Regression Model and analysis

Variable	Unstandartized Coefficients				Estimated WTP (BRL)	
	Beta	**SE**	**95% CI**	**p value**	**Mean**	**95% CI**
Intercept	4.720	0.108	(4.508; 4.931)	0.001	-	-
*Per capita household income (BRL)**	0.00018	0.00005	(0.00008; 0.0003)	0.001	-	-
Gender	-	-	-	0.034		
Female (*reference category*)	-	-	-	-	265	(218 ; 311)
Male	0.274	0.129	-	-	339	(271; 408)
Model Fit Statistics						
Mean squared error (MSE)	2.452					
Geneal F value (p value)	8.98 (<0.001)					
Lack-of-fit F value (p value)	0.94 (0.622)					
R^2	2.9%					
Skapiro-Wilk test p-value	0.005					

BRL: Brazillian Real, CI: Confidence Interval, SE: Standart Error.
*Continuous variable

Discussion

We believe this is the first study evaluating the WTP of Brazilians for a hypothetical vaccine with 70% efficacy against HIV, which demonstrated a WTP of US$ 47.50 (200.00BRL). Our sample's profile is similar to some characteristics of the Brazilian population, that is a higher percentage of females (54%) and individuals who have completed high school (59%) (IBGE, 2020b).

Of the 100 Brazilian municipalities with the highest number of records linked to HIV infection, ten are from the state of Pará (IBGE, 2021) and four (Belém, Marabá, Parauapebas and Abaetetuba) were included in this study to help give guidance on the potential WTP for a new vaccine from pertinent locations. Pará is the fourth state with the highest rate of AIDS cases in the country and the first considering the Northern region. In addition, the metropolitan region Belém has among the three highest detection rates for HIV in Brazil (Brasil, 2018; G1, 2018).

Encouragingly, 94% of our interviewees accepted to be vaccinated with a hypothetical HIV vaccine in Brazil. This high acceptability has also been observed in other studies. This includes 94% acceptability in Uganda (Bishai et al., 2004) and 90% to 95% acceptability in United States of América (Lally et al., 2006; Wang et al., 2017). These studies demonstrated the WTP of hypothetical vaccines against HIV using, in general, the mean value or specific methods. However, several studies have used the median maximum value to estimate the WTP for hypothetical vaccines (Lee et al., 2015; Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019; Athie et al., 2021; Godói et al., 2021). The considerable acceptability for a hypothetical HIV vaccine across countries and regions reinforces the need for investment to develop vaccines against HIV.

This study demonstrates that the willingness to pay Brazilian consumers for a hypothetical vaccine for HIV infection is US$ 47.50 (200.00BRL). However, considerably less than a study conducted in Thailand where respondents would pay US$ 383 for a hypothetical 99% effective vaccine (Cameron et al., 2013). Higher figures was seen in another study in Thailand where the WTP for two hypothetical vaccines, one with 50% and the other 95% of efficacy, was US$ 610 and US$ 671, respectively (Whittington et al., 2008). Overall, it appears that the WTP for a hypothetical vaccine tends to be higher the greater the efficacy (Whittington et al., 2002). In addition, several studies have reported the acceptability to pay for a vaccine

in the United States with 72.2%/ WTP: US$ 250.00 (Lee et al., 2008), 93%/WTP: US$ 100.00 (Young et al., 2014) and 90%/WTP: US$ 40.00 (Nunn et al.; 2017) and in Australia with acceptability of 86.9% and WTP of US$ 394 (Wang et al., 2017).

According to our findings, individuals with higher levels of income (p-value = 0.011) declared a higher value of WTP for a vaccine, in accordance to other studies (Keyserlingk & Rhodes, 2007; Wright et al., 2009; Ahmed et al., 2016; Godói et al., 2017; Javan-Noughabi et al., 2017; Mbachu et al., 2018; Muniz Júnior et al., 2018; Sarmento et al., 2019).

Whilst the number of respondents with private health insurance was 31% in our study, higher that for Brazil as a whole (24.1%) and the state of Pará (9.8%) (Brasil, 2014), there appeared to be no correlation between WTP values and participants who had health insurance or not (p-value = 0.071). In other words, individuals who had private insurance did not have higher values of WTP compared to those individuals who only use SUS, which is similar to the findings with dengue vaccine in Brazil using the same methodology (Godói et al., 2017). It is noteworthy that despite having a public health system (Brasil, 1990; Tenório et al., 2019), many Brazilians still have private health plans for greater convenience and better access to services such as medical specialists. However, this did not appear to make a difference in this study.

It is important to emphasize that a future vaccine will not replace current strategies to prevent HIV transmission, particularly condom use and pre-exposure prophylaxis. Condom use reduces the probability of HIV transmission by as much as 95% (Foss et al., 2004) and PrEP may also have a 70% reduction in HIV infection if medication adherence is high (Fonner et al., 2016). Consequently, a vaccine of at least 70% efficacy would be a promising additional technology to prevent HIV; however, only if combined with other different methods of prevention. Interventions associated with the prevention of HIV will still be necessary to help further reduce the morbidity and mortality associated with HIV as well as the financial

implications with treated infected patients. Carvalho and collaborators (2011) showed an increase in the number of outpatient treatments for HIV, and already in 2009, the average outpatient cost was 9,268.58 BRL (US$ 2,203.45; 2020: 1 US$ = 4.2064 BRL) and, approximately, 52.41% was associated to the medicines. In addition, Luz and collaborators (2018) demonstrated that, in the Brazilian context, the PrEP increased the per-person life expectancy from 36.8 years to 41.0 years and associated costs from US$ 4100 to US$ 8420, considering data of the Ministry of Health published in 2017.

The development of an effective and safe vaccine against HIV that could be available to all people around the world is an essential strategy for reducing the cases and mortality associated with this infection, mitigating a long-standing global health challenge. Considering the clinical, epidemiological and social relevance of HIV, the possibility of marketing an anti-HIV vaccine may be of interest to different populations, not just individuals at risk.

We are aware of a number of limitations with our study. Firstly, our study only involved the evaluation of WTP for a hypothetical vaccine with 70% efficacy. Secondly, there could be selection bias associated with the recruitment process and inclusion criteria. However, to minimize this, individuals from different municipalities and different scenarios from large groups of individuals who were in major circulation places of each city of this study were invited to participate, thus representing the different social, economic and educational levels in the state of Pará and wider. Furthermore, all the conditions in our study were similar to previous published studies published in this area (Godói et al., 2017; Muniz Junior et al., 2018; Sarmento et al., 2019; Athie et al., 2021).

Conclusion

This study demonstrated that 94% of participants from Northern Brazil would consider using a hypothetical HIV vaccine with 70% efficacy with a WTP for this vaccine of US$ 47.50

(BRL 200.00). Economic studies such as this can contribute to the discussions regarding the pricing of new vaccines to prevent HIV infections alongside existing preventive measures when they become available.

HIV will continue to pose an important challenge to health systems since it represents a severe public health problem with a high number of cases and deaths not only in Brazil but worldwide. In this scenario, the search for a safe, effective and cost-effective HIV vaccine continues to represent an important strategy to control this infection. It is anticipated that during the coming years, more advances will be made with vaccine development building, involving especially the candidates HVTN 705 (Imbokodo) and HVTN 706 (Mosaico), which are currently in late-stage development. Consequently, it is essential to investigate possible prices based on the profile of possible patients and consumers when searching for a new vaccine. In this context, researchers from the most affected countries continue to support efforts and government investment to encourage the development of medicines and vaccines targetted against HIV infection. This is the first study to assess the WTP for a hypothetical HIV vaccine in Northern Brazil, an important clinical and epidemiological region for this infection. As a result, can contribute to decision-making regarding potential prices for a future vaccine once it becomes available in Brazil, as well as contribute to discussions in other endemic countries.

Conflicts of Interest

The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Author Contributions

GCN, MJLC, TSA, IPDG, and JSS devised the study and the instruments as well as wrote the first draft building on input from CCAB and BG with earlier studies of this nature; GCN, MJLC, TSA, IPDG and EAR undertook the study and the analysis. All authors subsequently revised the draft and produced the final manuscript. All authors approved the final manuscript.

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Author Disclosure Statement

No competing financial interests exist.

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