Texila International Journal of Academic Research
ISSN: 2520-3088
DOI: 10.21522/TIJAR.2014.11.01.Art001

Open Label, Single Centre Study of Babao Relief Capsule as an Adjuvant to HAART in Antiretroviral Naive HIV Patients

Brig Gen Lawson F. Simapuka
School of Public Health, Texila American University, Lusaka, Zambia

Abstract

HIV continues to be a major global public health issue, having claimed 36.3 million [27.2–47.8 million] lives so far (WHO, 2021). Sub-Sahara Africa remains the far worst affected region, with 20.6 million [16.8 million– 24.4 million] people living with HIV at the end of 2010, compared to 24.4 (22.5-27.3 million) in 2020. Complementary and alternative therapy (CAM) has been used to treat HIV patients by clinicians in conventional health services in combination with highly active antiretroviral therapy (HAART). To determine efficacy of Babao relief capsule when used as an adjuvant to standard HAART in antiretroviral naïve HIV patients. The product is a biological Chinese medicinal preparation, made of herbs. Ingredients include ginseng, beer antler, musk, bezoar, fleeceflower, Chinese angelica, lyceum, pericarpium citri reticulatae, safflower and ophiopogn japonicus. Open Label Phase 1 bridging Clinical trial to study the efficacy of Babao relief capsule when used in combination standard HAART in antiretroviral naïve HIV patients. A total of one hundred and ninety-six (196) adult patients attending the HIV clinic were randomly selected. The interventional group was on Babao relief capsule and HAART while the control group was on HAART only. The study shows general efficacy of the standard HAART drugs. However, the interventional arm showed a significant increase in the CD4 cell count, showing that BRC had booster effects in the efficacy of HAART.

Keywords: *HIV, Complementary and alternative therapy, Babao relief capsule, standard highly active antiretroviral therapy.*

Introduction

HIV continues to be a major global public health issue, having claimed 36.3 million [27.2–47.8 million] lives so far [1]. According to the WHO report of 2021 there were an estimated 37.7 million [30.2–45.1 million] people living with HIV at the end of 2020, over two thirds of whom (25.4 million) are in the African Region. Sub-Sahara Africa remains the far worst affected region, with 20.6 million [16.8 million–24.4 million] people living with HIV at the end of 2010, compared to 24.4 (22.5-27.3 million) in 2020.

Sub-Sahara constitutes 10% of the world population yet just under two thirds (6%) of all the people living with HIV are in this region, as are more than three quarters (76%) of allwomen living with HIV. In Zambia, 1 in every 3 adults carries HIV or has AIDS, while Eswatini**,** Lesotho, and Botswana have the highest HIV prevalence. In 2020, Eswatini had the highest prevalence of HIV with a rate of almost 27 percent. Zambia has declared HIV/AIDS a national emergency in a bid to start manufacturing generic AIDS drugs underWorld Trade Organization (WTO) [2]. Patent western antiretroviral drugs cost between $300and $1000 for a month's dosage in this southern African country of 18 million people, the majority of which live below the World Bank poverty threshold of $2.15 per day [3]. While theface of the epidemic has changed in Western Europe and America with the coming of Highly Active Antiretroviral Therapy (HAART), the situation

Received: 07.02.2023 ***Accepted: 20.11.2023*** ***Published on: 31.01.2024***
****Corresponding Author: mutumba1965@gmail.com***

in Africa has been different, as most of the affected have limited access to antiretroviral drugs (ARVS) and reasonable nutrition; this picture has been changing as more people in developing countries are accessing HAART.

Complementary and alternative therapy (CAM) refers to the use of treatment not provided by clinicians in conventional health services, though both serve the same goal of pursuinggood health [4]. Traditional Chinese Medicine (TCM) constitutesone form of CAM which is widely used in Chinese communities around the world. Data from Asia in a Thailand study in 2003, 95% of the HIV patients reported the use of some forms of CAM, and 78% having visited a CAM provider [5]. A significant proportion of these studies were conducted before the introduction of highly active antiretroviral therapy (HAART), the latter becoming a gold standard in clinical HIV management [6].

With the widespread use of HAART in not just developed but developing countries, there is the new concern about interaction between CAM and HAART, which may potentially affect the outcome of treatment [7].

On average, published research indicates that 60% of HIV+ individuals use CAM to treatHIV-related health concerns [8]. In the context of conventional HIV care, where survival depends on proper use of and adherence to highly active antiretroviral treatment [9], the potential for CAM use to interfere with the success of HAART is a pressing concern as alluded to above. With little evidence supporting the safety and efficacy of CAM for HIV [10], research that identifies factors associated with CAMuse and the implications of CAM use for HIV care is of considerable importance.

The objective of the clinical trial is to determine efficacy of Babao relief capsule when used as an adjuvant to standard highly active antiretroviral therapy (HAART) in antiretroviral naïve HIV patients. If found efficacious it will go a long way in lowering the cost of treating HIV patients, joining the other Complimentary Alternative Medicines on the market. The disease has now become a controllable disease with people infected with HIV living almost normal life spans.

Literature Review

From the literature search three analytical studies have been conducted [11] with only one controlled trial which was identifiedconducted using Chinese traditional medicines for HIV-related peripheral neuropathy. Shlay et al recruited 250 patients for a double-blind, placebo-controlled, multicenter study of acupuncture and amitriptyline [12]. The design allowed comparisons to be made between any of the four groups: real acupuncture, sham acupuncture, amitriptyline, placebo medication. Patients in the acupuncture groups received 20 treatments, either: a. SP9, 7 and 6 as standard plus K13, 2 or Ba Feng points as indicated by symptoms or b. Superficial needles at three non-acupuncture points in the calves. Pain was assessed at 6 and 14 weeks (the end of the trial) using an appropriate rating scale (the Gracely scale). There were no significant changes in pain score to indicate that either acupuncture or amitriptyline were more effective than placebo.

This trial was large and well designed, and hence not subject to many of the usual criticisms of clinical trials of complementary therapies. However, the points chosen for the real acupuncture treatment have been criticized as being inappropriateand hence more suitable as a placebo [13]. The points had been chosen by consensus amongeight acupuncturists. This kind of debate will inevitably become more prominent if traditional Chinese protocols are used more frequently in research trials.

A review by Ozsoy and Ernst aimed to evaluate all randomized controlled trails of complementary therapies for HIV [14]. As well as the one acupuncture study, they also locatedtrials using herbs, supplements, stress management techniques and massage. After emphasizing the paucity of good evidence, they suggest that these therapies may best be employed in a “caring” rather than “curing” mode, looking to increase

quality of life.

Ten papers describe outcome trials, which, having no control groups, may therefore be influenced by the placebo response, the self-limiting nature of some conditions and by intervention from other forms of medical treatment.

There are three outcome audits analyzing treatment given in a Western setting [15]. Smith (1988) describes his experience at the Lincoln Hospital, New York, and two other metropolitan centers in the USA, in treating over 350 patients with AIDS over a 5-year period using acupuncture and Chinese herbal medicine. He offers an evaluation of the response of these patients to this treatment through looking at changes to symptoms and survival times as measures of benefit.

The exact methodology used is not described (what form of questionnaire was used etc.), nor are there details of the statistical analysis, but the conclusion to the study was that:

1. There was substantial reduction in symptoms such as fatigue, night sweats and diarrhea.
2. 30 – 40% of a small sample of 14 AIDS patients seen between 1982 – 83 had a five-year survival rate after receiving acupuncture frequently over a 2 – 6 months period of time.
3. Herbal interventions have proved results and have significantly reduced thedropout rate in the programs.
4. Two cases of early-stage Kaposi Sarcoma showed apparent remission.
5. There was a general report of fewer symptoms of infection and reduction in side effects from Western drugs.

This paper is not really a study but more a series of observations and a collection of case histories. It does not describe the methodology used, has no form of control, and reportson a very small sample of patients who regularly attended treatment. Whilst it is of somehistorical interest its clinical relevance is diminished by the fact that it precedes both viralload testing and other blood tests that could objectively correlate symptomatic changes, and predates combination therapy, which would now almost certainly be prescribed to most of the cases described.

A study [10] describe the underlying theory and practical structure of the HIV treatment program at the American college of TCM in San Francisco. 67 patient outcomes were evaluated over a three-month period using a symptom checklist and a quality-of-life survey administered monthly, with "significant improvements" noted for fatigue, loss of appetite, lymphadenopathy, and neuropathy. In general, not only did the total number of symptoms diminish but also the severity. The shortcomings are like those for Smith's work, with no control, a small sample group reporting on a wide range of 28 possible symptoms and no objective measurement to correlate to this reported improvement.

Flower uses the Measure Your Own Medical Outcome Profile (MYMOP) questionnaire as part of an outcomes audit of 18 patients seen over a six-month period at London Lighthouse. 15 out of 18 patients reported relief in their presenting symptoms and improvement in well-being. The shortcomings are the same as those mentioned above.

A Study [14] refer to the experience of a team ofsenior Chinese doctors invited to research the effect of Chinese herbal medicine on patients with AIDS in Tanzania [15]. Differentiation was made according to traditional Chinesecategories as well as a review of symptomatic changes and basic blood test results [14]. The conclusion of Xue and Su is that Chinese herbal medicine did bring some symptomatic relief for AIDS patients.

A study summarizes the pharmacological rationale and the clinical experiences of the Chinese team in Tanzania after having treated a total of 158 individuals over a three-yearperiod. The Karnofsky score – a measure of the degree of disability caused by an illness.

– showed improvement in 82 patients, and symptomatic improvements were noted in

lymphadenectasis, diarrhoea, anorexia, fever, weight loss, skin rashes and coughs. The methodology used to assess these changes is not given in the paper. The study also measured changes in T4 cells over time and T4/T8 ratios (3) and noted that 31% of patients showed at least temporary improvements in the former but the latter showed less response. Once again, the details of these measurements have been omitted from the article and the amount or the duration of the T4 cell is not clear.

A study report on eight cases of individuals converting from HIV + to HIV – after taking Chinese herbal medicine, which at the time of writing had never been reported in the medical literature and, if substantiated by future research under well-controlled conditions, is a potentially radical breakthrough. The subsequent absence of suchresearch suggests these results have proved difficult to replicate and may have been dueto an incorrect initial diagnosis of HIV status.

A study used traditional Chinese medicine for treating AIDS-related respiratory tract infection in a group of 58 patients, finding a clinical cure in 31% and therapeutic effectiveness in a further 12%. A contemporary group of 22 patients treated by combined Chinese and Western medicine had a less positive response but had started with more severe symptoms [15, 16].

The Products

Babao Relief Capsule

The product is a biological Chinese medicinal preparation, made of herbs. Ingredients include ginseng, beer antler, musk, bezoar, fleeceflower, Chinese angelica, lyceum, pericarpium citri reticulatae, safflower and ophiopogn japonicus.

Only one phase 1 clinical trial was conducted in Malaysia, 31 patients took part in the clinical trial. Since these patients were not on HAART, no study has been done to checkinteractions and side effects when Babao Relief capsule and HAART are used in combination. The objective of this clinical trial therefore is to assess the efficacy of BabaoRelief capsule when used as an adjuvant to HAART in antiretroviral naive HIV patients.

Each capsule of Babao is 0.5g and the dosage was 3g per day, one third of the current dosage. The viral load was substantially lowered by 60%. The CD4 count rose. Taking Babao Relief Capsule for 1-2 months showed a reduction in opportunistic infections and HIV/AIDS complications. Within 2-3 months, CD4 and CD4/CD8 rose considerably. The HIV viral load was reduced to undetectable level in 3 months. Bloating was the only reportedside effect from the clinical trial conducted in Malaysia.

Function: The product has anti-pyretic, analgesic; immune enhancer, anti-viral, anti-tumor, bactericidal and anti-inflammatory properties.

Application: Suitable for people infected with HIV and AIDS, anorexia, short of breath, emaciation, rash, diarrhea, night sweats, sore in the tongue and dry pharynx.

Dosage: The product is to be taken half an hour before meals or an hour after meals with lukewarm water.

Adults: 3g three times daily.

Children: 13-16 years, 2g three times daily. 7-12 years, 1.5g three times daily. 4-6 years, 1g three times daily. The course is for three months.

Tenofovir

VIREAD is the brand name for tenofovir disoproxil fumarate (a prodrug of tenofovir) which is a fumaric acid salt of bis-isopropoxycarbonyloxymethyl ester derivative of tenofovir. *In vivo* tenofovir disoproxil fumarate is converted to tenofovir, an acyclic nucleoside phosphonate (nucleotide) analog of adenosine 5'-monophosphate. Tenofovir exhibits activity against HIV-1 reverse transcriptase.

The chemical name of tenofovir disoproxil fumarate is 9-[(*R*)-2 [bis [(isopropoxycarbonyl)oxy] methoxy phosphinyl methoxy propyl] adenine fumarate (1:1). It has a molecular formula of $C_{19}H_{30}N_5O_{10}P$ $C_4H_4O_4$ and a molecular weight of 635.52. VIREAD (tenofovir disoproxil fumarate) tablets

are for oral administration. Eachtablet contains 300 mg of tenofovir disoproxil fumarate, which is equivalent to 245 mg oftenofovir disoproxil, and the following inactive ingredients: croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and pregelatinized starch. The tablet is taken once daily in combination with other antiretroviral drugs. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD (tenofovir disoproxilfumarate), in combination with other antiretrovirals. Many of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Caution should be exercised when administering nucleoside analogs to any patient with known riskfactors for liver disease; however, cases have also been reported in patients with no known risk factors. Discontinuation of anti-HBV therapy, including VIREAD (tenofovir disoproxil fumarate), may be associated with severe acute exacerbations of hepatitis.Patients infected with HBV who discontinue VIREAD (tenofovir disoproxil fumarate)should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapymay be warranted. Tenofovir is principally eliminated by the kidney. Renal impairment,including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of VIREAD. It isrecommended that creatinine clearance be calculated in all patients prior to initiating therapy and as clinically appropriate during therapy with VIREAD (tenofovir disoproxilfumarate)

Emtricitabine

EMTRIVA is the brand name of emtricitabine, a synthetic nucleoside analog with activity against HIV type 1 (HIV-1) reverse transcriptase. The chemical name of emtricitabine is 5-fluoro-1-(2*R*,5*S*)-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl] cytosine. Emtricitabine is the (-) enantiomer of a thio analog of cytidine, which differs from other cytidine analogs in that it has a fluorine in the 5-position. It has a molecular formula of $C_8H_{10}FN_3O_3S$ and a molecular weight of 247.24. EMTRIVA (emtricitabine) capsules are for oral administration. Each capsule contains 200 mg of emtricitabine and the inactive ingredients, crospovidone, magnesium stearate, microcrystalline cellulose, and povidone.

EMTRIVA (emtricitabine) is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

The most common adverse reactions include headache, diarrhoea and nausea, fatigue, dizziness, depression, insomnia, abnormal dreams, rash, abdominal pain, asthenia, increased cough, and rhinitis.

Efavirenz

SUSTIVA® (efavirenz) is an HIV-1 specific, non-nucleoside, reverse transcriptase inhibitor (NNRTI). Efavirenz is chemically described as (S)-6-chloro-4- (cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2H-3,1 benzoxazin-2-one. Its empirical formula is $C_{14}H_9ClF_3NO_2$. Efavirenz is a white to slightly pink crystalline powder with a molecular mass of 315.68. It is available as film-coated tablets for oral administration containing 600 mg of efavirenz and the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and sodium lauryl sulphate. in combination with other antiretroviral agents is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection. The most common side effects are rash, dizziness, nausea, headache, fatigue, insomnia, and vomiting.

Nevirapine

VIRAMUNE is the brand name for nevirapine, a non-nucleoside reverse

transcriptase inhibitor (NNRTI) with activity against Human Immunodeficiency Virus Type 1 (HIV-1). Nevirapine is structurally a member of the dipyridodiazepinone chemical class of compounds. The chemical name of nevirapine is 11-cyclopropyl-5, 11-dihydro-4-methyl- 6H-dipyrido [3,2-b:2',3'-e] [l,4] diazepin-6-one. Nevirapine is a white to off-white crystalline powder with the molecular weight of 266.30 and the molecular formula $C_{15}H_{14}N_4O$. IRAMUNE (nevirapine) Tablets are for oral administration. Each tablet contains 200 mg of nevirapine and the inactive ingredients microcrystalline cellulose, lactose monohydrate, povidone, sodium starch glycolate, colloidal silicon dioxide and magnesiumstearate.

VIRAMUNE (nevirapine) is indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection. The recommended dose for VIRAMUNE (nevirapine) is one 200 mg tablet daily for the first 14 days, followed by one 200 mg tablet twice daily, in combination with other antiretroviral agents. The lead-in period hasbeen observed to decrease the incidence of rash. The most serious adverse reactions associated with VIRAMUNE (nevirapine) are hepatitis, hepatic failure, Stevens-Johnson syndrome, toxic epidermal necrolysis, and hypersensitivity reactions. Hepatitis/hepatic failure may be isolated or associated with signs of hypersensitivity which may include severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, granulocytopenia, lymphadenopathy, or renal dysfunction.

Dolutegravir

The Dolutegravir Sodium is the sodium salt form of dolutegravir, an orally bioavailable integrase strand-transfer inhibitor (INSTI), with activity against human immunodeficiencyvirus type 1 (HIV-1) infection. Dolutegravir is chemically described as (3S,7R)-N-[(2,4-difluorophenyl) methyl]-11-hydroxy-7-methyl-9,12-dioxo-4-oxa-1,8- diazatricyclo [{8.4.0.03,8}] tetradeca-10,13-diene-13-carboxamide [17, 18]. Upon oral administration, dolutegravir binds to the active site of integrase, an HIV enzyme that catalyses the transfer of viral genetic material into human chromosomes. This prevents integrase from binding to retroviral deoxyribonucleic acid (DNA), and blocks the strand transfer step, which is essential for the HIV replication cycle [19]. This prevents HIV-1 replication.

The adult dose of dolutegravir is one 50mg tablet once a day. If a patient is taking medications that may lower the serum concentration, it may be prescribed in dose of one 50mg tablet twice a day [20]. [20] Common side effects include trouble insomnia, fatigue, diarrhea, hyperglycemia, and headache. Severe side effects may include allergicreactions and liver problems. There are tentative concerns that use during pregnancy canresult in harm to the baby. It is unclear if use during breastfeeding is safe. Dolutegravir is an HIV integrase strand transfer inhibitor which blocks the functioning of HIV integrase which is needed for viral replication. It is on the World Health Organization's List of Essential Medicines. As of 2019, the World Health Organization (WHO) recommends DTG as the first- and second-line treatment for all persons with HIV [21].

Justification

There is increased use of CAM by the people living with HIV and AIDS hence there is need to assess the efficacy and safety of use of these remedies. In in the BRC study in Malaysia viral load was substantially lowered by 60%. The CD4 count rose. Taking BabaoRelief Capsule for 1-2 months showed a reduction in opportunistic infections and HIV/AIDS complications. Within 2-3 months, CD4 and CD4/CD8 rose considerably. The HIV viral load was reduced to undetectable level in 3 months.

Bloating was the only reported side effect from the clinical trial. No studies have been conducted to determine interaction effects of the

Babao Relief Capsule withantiretroviral therapy. The product is currently available on the Zambian market as a Chinese herbal remedy and is being used by HIV infected patients.

Research Question (RQ). Does Babao relief capsule increase the efficacy of standard antiretroviral therapy when used as an adjuvant in antiretroviral naive HIV patients?

Hypotheses

Null Hypothesis

1. There is difference in efficacy when Babao relief capsule is used with standard antiretroviral therapy and an adjuvant in antiretroviral naive HIV patients.

Alternative Hypothesis

1. Babao relief capsule increases the efficacy of standard antiretroviral therapy whenused as an adjuvant in antiretroviral naive HIV patients.

Objectives

General Objective

To determine efficacy of Babao relief capsule when used as an adjuvant to standard highly active antiretroviral therapy (HAART) in antiretroviral naïve HIV patients.

Specific Objective

1. To determine the clinical improvement of antiretroviral naïve HIV patients on Babao relief capsule over a period of three months used in combination with HAART.
2. To determine the effects of Babao relief capsule on the hematological, biochemical, and immunological indices in antiretroviral naïve HIV patients at three months in combination with HAART.
3. To determine the safety and tolerance of Babao relief capsule in antiretroviral naïve HIV patients used in combination with HAART.

Methods and Materials

Study Design

An open Label Phase 1 bridging Clinical trial to study the efficacy of Babao relief capsulewhen used in combination standard highly active antiretroviral therapy (HAART) in antiretroviral naïve HIV patients. The HAART combination was the preferred first line therapy of a backbone of Tenofovir, Emtricitabine with Dolutegravir or Efavirenz. A total of one hundred and ninety-six (196) adult patients attending the HIV clinic were randomlyselected. There were one hundred and four participants in the interventional and 92 in thecontrol groups.

The interventional group was on Babao relief capsule and HAART while the control groupwas on HAART only.

Male and female volunteers between the ages of 18 and 55 years old with proven HIV 1 infection were recruited. During the study if it may become necessary to take other medications, the participants would inform study personnel. The participants did not take chemotherapeutic drugs, interferons or steroids while participating in the study. Pregnant women and HAART experienced patients were excluded from the clinical trial.

Blood samples were drawn at the beginning of therapy for immunological, hematological, and biochemical indices. Hematological and Biochemical indices were measured on monthly basis while immunological indices were done at the beginning of the clinical trialand three (03) months.

Study Setting

The study was conducted in Zambia at Maina Soko Military Hospital (MSMH). Maina Soko Military Hospital is situated in Woodlands in the city of Lusaka. The hospital is about 10 Km from the city center. The clients that attend the hospital are both military and civilians. The hospital accommodates the Family Support Unit (FSU), an HIV services center of excellence, which will be the study site.

Sample and Sample Size

There were close to 2,500 clients under care, and this formed the sampling framework from which the study sample was derived; the simple random sampling method was used to select the study participants. The participants did not depend on any of the investigators either as students, as employees or in any other ways. The target populationconsisted of male and female HIV positive clients aged between 18 and 55 years.

Sample size was calculated using the formulae below:

$$Sample\ Size = \frac{Z^2 P(100 - P)}{d^2}$$

Where: P = Proportion of estimated participation with HIV Infectiond = Sampling Error.

The power of power of the study will be expected to be 80 % or more.

The proportion of the clients taking part in clinical trials was estimated at 15 %, Z = 1.96 and the sampling error 5 %.

Therefore:

$$Sample\ Size = \frac{(1.96)^2 \times 15 \times (100 - 15)}{5^2}$$

$$= \frac{3.84 \times 15 \times 85}{25} = 196$$

Data Collection

The study was conducted from 8 – 12 hours in the morning and 14 – 16 hours in the afternoon on all working days starting from Monday to Friday. A coded questionnaire was prepared covering demographic information, socio-economic, haematological, biochemical, and immunological indicators of the participants.

Assessment

Efficacy

Primary

Improvement in immune response was measured by increase in CD4 Cell count and CD4/ CD8 ratio.

Secondary

Clinical benefit was assessed by changes in total body weight, karnofsky performance score, and amelioration of signs and symptoms of disease present at baseline including the remission or occurrence of opportunistic infections.

Safety

Vital signs, laboratory tests, clinical adverse events (AEs).

Procedures (Summary)

Complete pretreatment medical history, general physical and laboratory examinations prior to Babao relief capsule administration, then every four (04) weeks up to end of study. Symptom directed physical and vital signs will be conducted during four (04) weeks of follow up after therapy.

Data Processing and Analysis

The Epi-Info version 4.1 and SPSS software was used.

1. Design a questionnaire for data entry.
2. Enter data using Epi-Info.
3. For data Analysis, Chi-square and the student t-test were used in the analysis of the results.

Ethical Consideration

Approval was obtained from the ethics committee of the Zambia Defense Force Medical Services (ZDFMS) and University of Zambia (UNZA). Informed consent was obtained, and anonymity was maintained as regards the names of the subjects to preserve theirconfidentiality. Clearance was obtained from the Ministry of Defence to conduct the study.

Pilot Study

A Pilot Study was conducted using 10 participants at Maina Soko Military Hospital. This was used for redesigning and eliminating certain variables.

Prior to the pilot study the questionnaire was evaluated for face validity to assess whetherthe

questionnaire “looks valid” to the interviewees who took it and the administrator of thetool, and other technically untrained observers.

Research Outcomes

1. Improvement in immune response measured by increase in CD4 Cell count and CD4/CD8 ratio.
2. Clinical benefit assessed by improvement in the general physical wellbeing of the participants.
3. Improvement in immune function by reduction of viral load counts, leading to improvedquality of life of the patients.
4. Once the efficacy and safety of Babao Relief Capsule has been established, it shall be made available for use by our clients beyond the trial period.

Results

The study included males 118, (60%) and females 78 (40%) of the age groups rangingfrom 25-29 to those over 50 years. The 196 participants were included in the analysis with 104 participants being on the intervention arm and representing 53.1% of the trial population. In terms of the quality of life for the participants at baseline, 57% of the participants were in good health with a karnofsky score of 100%. This was one of the indicators in the exclusion criteria, those who were too sick were not included in the study. In line with the quality-of-life score, 62% of the participants were in World Health Organisation (WHO) HIV disease staging stage one (WHO Stage 1). In the summary statistics the median was used as the data was skewed.

The improvement of the immune system was measured by the CD4 increase. In the clinical trial, regardless of the arm where the patient was, the CD4 showed a steady increase over time. This started with a median of 267 at baseline (day 0) and rose to494 by the twelfth month (day 360). This is demonstrated in figure one and table one below.

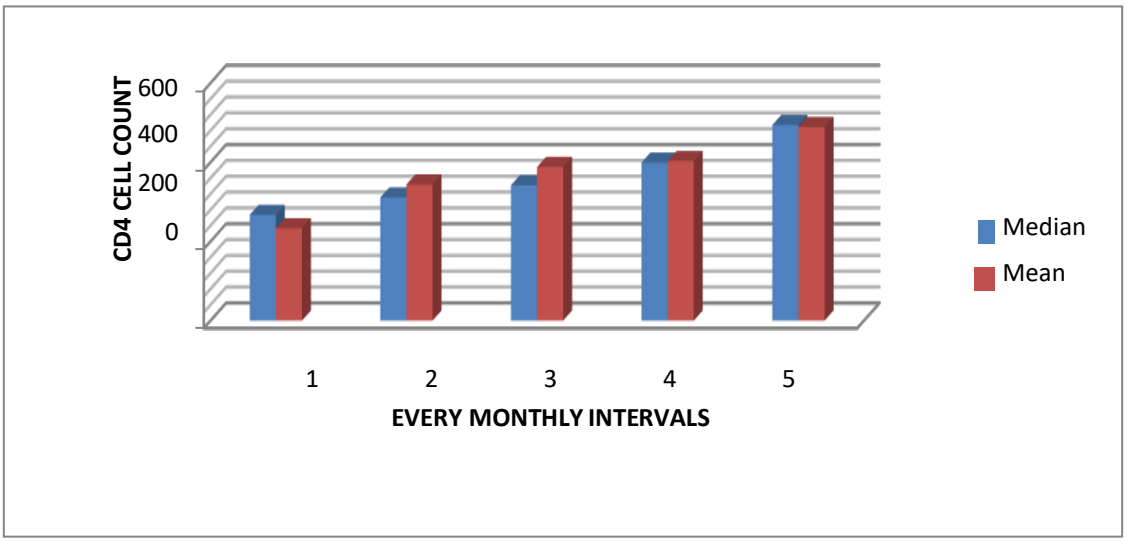

Figure 1. CD4 Increase Over Time in All Study Participants

Table 1. CD4 Trends Over Time in the Entire Trial Population

CD4	Min	Max	Median	Mean	STD Dev
1=CD4D0	19	452	267	233	126
2=CD4D90	63	765	311	344	191
3=CD4D180	183	667	432	388	161
4=CD4D270	150	621	399	403	144
5=CD4D360	282	766	494	489	160

The other indicator of immune system improvement was the viral load, demonstrated by the drop in the viral load over time. The median viral load was 72846 at baseline (day 0) and fell to 40 by the twelfth month (day 360). This is demonstrated in figure one and table two below.

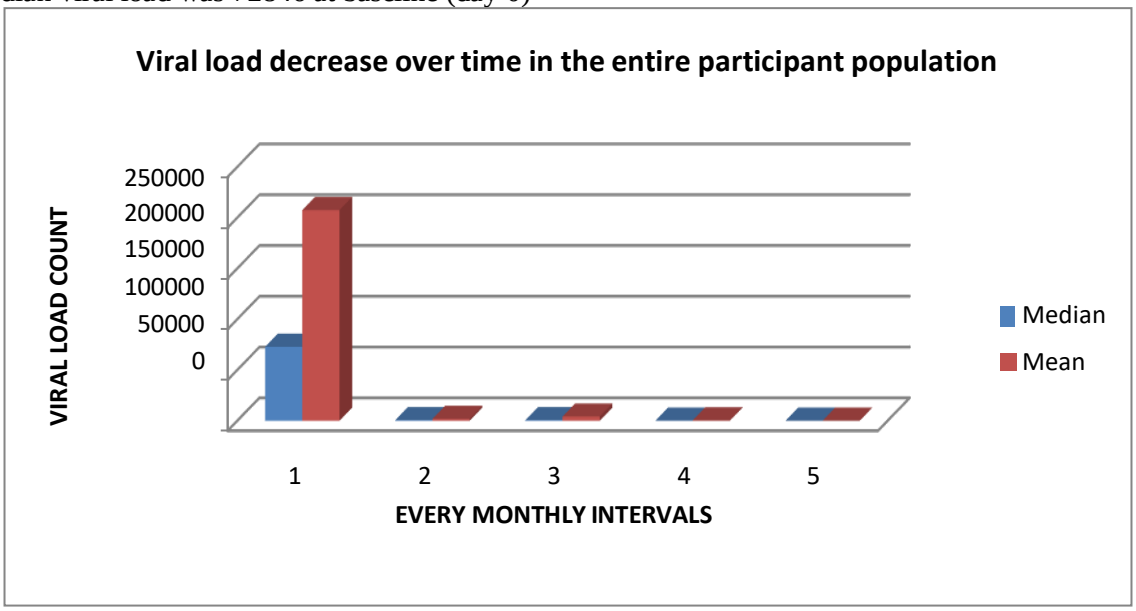

Figure 2. Viral Load Over Time for the Entire Trial Population

Table 2. Viral Load Over Time for the Entire Trial Population

Viral load	min	max	median	mean	Std dev
1 = Vl0	40	2,083500	72846	207485	407428
2 = Vl90	40	11808	606	1817	3018
3 = Vl180	40	41370	597	4181	11050
4 = Vl270	40	2885	143	421	832
5 = Vl360	40	323	40	92	113

In general, the indication was that all the patients in the clinical trial showed improvement in the immunity as shown by both the CD4 cell count increase over time and viral load drop over time. However, the picture was different when it came to weight, this variable was not very consistent and did not demonstrate any improvement.

In finding the difference between the interventional arm and control arm, the efficacy of BRC when used in combination with HAART compared with HAART when used alone. At baseline the median CD4 cells count was 213 in the control arm and 279 in the treatment arm. On day 360 the CD4 cell count in the treatment arm was 545 while the CD4 cell count in the control arm was 433. The CD4 cell count showed gradual improvement in both arms, however, the BRC with HAART combination demonstrated a consistent rise in CD4 as shown in figure four. The difference was significant with a p- value of 0.004, as shown in Table 5 below.

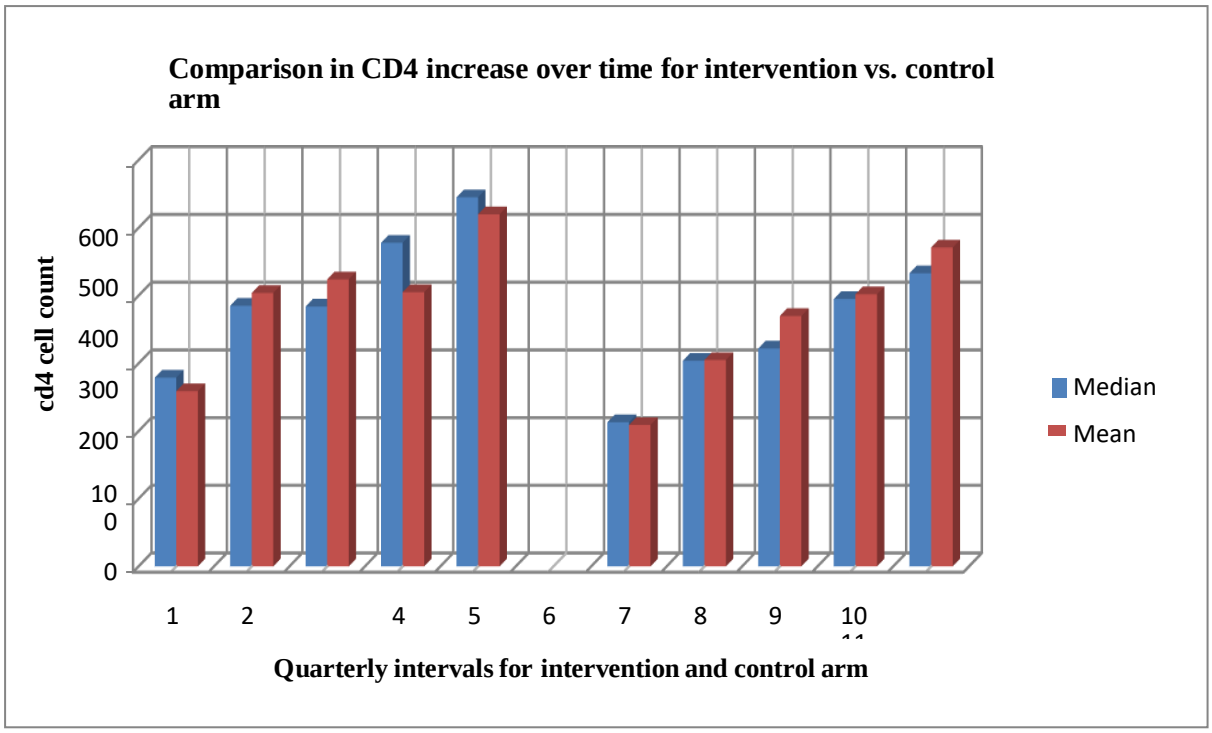

Figure 3. Comparison in CD4 Increase Over Time for Intervention vs. Control Arm

Table 3. Comparison in CD4 Increase Over Time for Intervention vs. Control Arm

Variable	Intervention Arm	Control Arm
CD4	Median	Median
D0	279	213
D90	385	304
D180	384	322
D270	478	395
D360	545	433

Table 4. Comparison CD4 Increase in the Intervention Arm Vs. Control Arm

Variable	Arm	N	Mean	SE Mean	StDev	Q1	Median	Q3	p-value
CD4	I	104	520	6.723	25.119	525.250	545	575.750	0.004
	C	92	471	5.258	20.394	410.500	433	450.000	

The viral load at beginning of the clinical trial was 302525 copies in the interventional arm and 88685 copies in the control arm. Both arms demonstrated a drop, but this was slightly more in the intervention arm, there was a significant drop in the viral load by the third month in both arms, 25207 copies and 912 copies respectively. Though in the controls, a blip was observed in viral load after twelfth month, there was a rise in viral load from 912.7 copies to 11072 copies after what looked like suppression, this was again followed by a fall in viral load to 597.6 copies. At the end of the clinical trial the viral load was 49 copies in the intervention arm compared to 134 in the control arm. The difference between the interventional arm and control arm was significant with a p-value of 0.013.

Table 5. Viral Load Over Time in the Intervention Arm Vs. Control Arm

Viral load	**Control Arm**	**Intervention Arm**
	Median	**Median**
D0	88685	302525
D90	912.7	2520.7
D180	11072	351
D270	597.6	113.5
D360	134	49

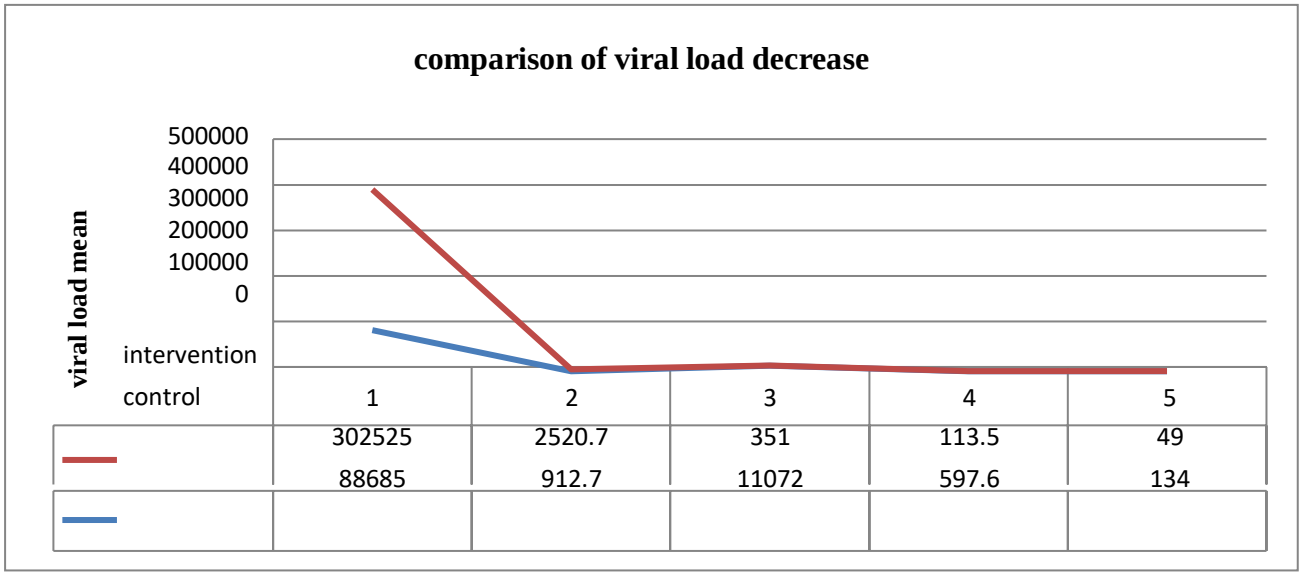

Figure 5. Viral Load Over Time in the Intervention vs. Control Arm

Table 6. Viral Load Over Time in Intervention Arm vs. Control Arm

Variable	**Arm**	**N**	**Mean**	**SE Mean**	**StDev**	**Q1**	**Median**	**Q3**	**p-value**
Viral load	I	104	60	1.723	5.119	25.250	49	75.750	0.013
	C	92	148	2.258	10.394	110.500	134	150.000	

There were no adverse events in the clinical trial, the surrogate markers for liver function test, renal function test and glucose remained within the normal range range withno red flags. See table 7 below.

Table 7. Hematologic and Chemistry Indices in Intervention Arm vs. Control Arm

Variable	**Intervention Arm**	**Control Arm**
HB (g/dL)	Median	Median
D0	13.9	13.5
D90	14.1	13.7
D180	14.0	13.6
D270	14.2	13.8
D360	545	433
Urea (mmol/l)		
D0	3.9	4.1
D90	4.1	4.3

D180	4.0	3.9
D270	4.2	3.8
D360	41.3	4.5
AST (U/L)		
D0	29.8	25.6
D90	32.1	26.5
D180	30.1	28.6
D270	29.5	27.5
D360	28.1	26.8
Glucose (g/dL)		
D0	4.5	4.8
D90	4.6	5.3
D180	5.2	4.9
D270	5.1	5.2
D360	5.6	4.9

In terms of clinical benefit assessed by improvement in the general physical wellbeing of the participants, the analysis focused on weight. The median weight at the beginning of the clinical trial was 59 kg and 63 kg at the of the twelfth's month, it did not show any significant fluctuation over the period of follow-up, as seen in table 8 below.

Table 8. Weight of All the Participants Over Time

Weight	Min	Max	Median	Mean	STD Dev
D0	44	89	59	62	11.4
D90	46	84	61.5	62.5	11.3
D180	53	80	60	63.8	9.6
D270	45	85	62	64.2	10.7
D360	43	76	63	62	10.6

Discussion

World over, HIV/AIDS service organisations have recognised that people affected or infected by HIV are increasingly choosing to use complementary and alternative medicine to cope with the disease. With the advent of HAART people infected with HIVcan now live normal lives as it has now become a controllable disease with lifelong implications for management of people living with HIV and AIDS. Insufficient evidenceexists to support the use of a particular complementary and alternate therapy to enhance the management of HIV disease. Safety risks and potential drug interactions are frequently ignored as people who use highly active antiretroviral therapy prefer to focus on the physical and mental benefits of using selected complementary and alternate therapies to promote their quality of life.

The clinical trial participants who were on Babao Relief Capsule and Highly Active Anti-Retroviral Therapy (HAART) showed a steady increase in the CD4 count. The difference in the intervention arm and control was significant with a p-value of 0.004, this indicates that the addition of Complimentary and Alternatives Medicine (CAM) to HAART increases the potency of HAART. This is supported by the fall in the viral load in the intervention arm as compared to the control arm, in this case the fall in the intervention arm was significant as

compared to the control arm, the p-value was 0.013.

The hematologic, liver function and renal function indices remained within the normal range, no red flags were observed throughout the period of follow up, this indicates that the combination of CAM and HAART did not have adverse effects on the target organs in the participants.

Clinical benefit assessed by improvement in the general physical wellbeing of the participants, the analysis focused on weight. The weight, however, did not give the bestparameter in terms of predicting improvement on therapy. This could be that the patients were already in good health as the clinical trial was only recruiting stable participants.

This clinical trial is a bridging study of the phase 1 clinical trial which was conducted in Malaysia, 31 patients took part in the clinical trial. In the Malaysian clinical trial BRC showed efficacy in the participants although HAART was not administered. The viral load was substantially lowered by 60%. There was a steady increase in the CD4 count. TakingBabao Relief Capsule for 1-2 months showed a reduction in opportunistic infections and HIV/AIDS complications. Within 2-3 months, CD4 and CD4/CD8 rose considerably. The HIV viral load was reduced to undetectable level in 3 months. This is consistent with the findings that in BRC and HAART clinical trial, showing evidence that BRC has boosting effects on HAART.

Conclusion

There was general improvement in the immune response for the overall population regardless of what arm of the study they were randomized to. This shows the general efficacy of the HAART drugs. However, the interventional arm showed a significant increase in the CD4 cell count, showing that BRC had booster effects in the efficacy ofHAART. This is supported by the decrease in the viral load which was significant in the interventional arm. The viral load decrease was sharper in the intervention arm and more towards clearing or towards zero.

The general wellbeing as measured by the weight of the patients was not very informative. The weight did not give the best parameter in terms of predicting improvement on therapy. This could be that the patients were already in stable health as the study was only recruiting stable patients in WHO Stage one.

The combination of BRC and HAART did not produce any adverse effects, therefore it issafe to conclude that it is safe to use BRC as an Adjuvant in the treatment of HIV patients.

It may be premature to conclude on the efficacy of BRC however the complimentary medicine may have potential booster effect that seems to impart the steady CD4 increase, and predictable viral load decrease compared to HAART alone. A larger studywould be ideal to confirm the findings in this clinical trial.

Recommendation

1. There seems to be boosting effects of the highly active antiretroviral therapy when used with Babao relief Capsule, but use should be guarded.
2. There will be a need for phase three clinical trials so that the findings can be extrapolated to the rest of the population.

Conflict of Interest Statement

The authors declare no conflicts of interest.

About the Author

Brig Gen Dr. Lawson F. Simapuka is an experienced medical director with a demonstrated history of working in the hospital, health care industry, academics, and forensics. Skilled Infectious diseases, forensic medical sciences, epidemiology, program evaluation and organizational leadership. Has made pivotal contributions to tropical medicine and clinical research. Now serving as ExecutiveDirector of the National Forensic Authority in Zambia.

References

[1] World Health Organization, UNAIDS (2021). Retried from http://www.unaids.org.

[2] Ministry of Health (1999), "HIV/AIDS in Zambia: Background, Projections, Impact, Interventions.

[3] Poverty Analysis Zambia (2018). Retrieved from https://cdn.sida.se/app/uploads/2021/08/24151354/Multidimensional-Poverty-Analysis-Zambia-2018.pdf.

[4] Ni, H., Simile, C., & Hardy, A. M. (2002). Utilization of complementary and alternative medicine by United States adults: results from the 1999 national health interview survey. Medical Care, 40, 353-358.

[5] Wiwanitkit, V. (2003). The use of CAM by HIV-positive patients in Thailand.Complementary Therapies in Medicine, 11, 39-41.

[6] Liu JP, Manheimer E, Yang M. (2005). Herb-al medicines for treating HIV infection and AIDS. Cochrane Database of Systematic Reviews;(3): Art. No.: CD003937. DOI: 10.1002/14651858.CD003937.pub2.

[7] Muller A, Kanfer I. (2011) Potential pharmacokinetic interactions between antiretrovirals and medicinal plants used as complementary and African traditional medicines. Biopharmaceutics and Drug Disposition;32(8):458-70.

[8] Mills, E., Montori, V., Perri, D., Phillips, E., & Koren, G. (2005). Natural health product-HIV drug interactions: a systematic review. *International Journal of STD & AIDS*, 16, 181-186.

[9] Felise B. Milan, Julia H. Arnsten, Robert S. Klein, Ellie E. Schoenbaum, Galina Moskaleva, Donna Buono, and Mayris P. Webber. (2010). Use of Complementary and Alternative Medicine in Inner-City Persons with or at Risk for HIV Infection. Retrieved from https://doi.org/10.1089/apc.2007.0159.

[10] Moffett H, Sanders P, and Sinclair T, Ergil K (1994): Using acupuncture and herbs for the treatment of HIV infection. *AIDS Patient care*; 8(4): 194-9.

[11] Ozsoy M, Ernst E (1990): How effective are complimentary therapies for HIV and AIDS? A systematic review. *Int J STD AIDS*; 10(10): 629-35.

[12] Shlay J., Chaloner. K, Mitchell. B. (1998). Acupuncture and Amitriptyline for Pain Due to HIV-Related Peripheral Neuropathy. A Randomized Controlled Trial. Retrieved from https://jamanetwork.com/journals/jama/article-abstract/188146.

[13] Smith M O (1988): AIDS: results of Chinese treatment show frequent symptom relief and some apparent long-term remissions. *AM J Acupunct;* 16(2): 20

[14] Su C (1991) (AIDS Trial Treatment Group, China Academy of TCM): Trial treatment of AIDS by TCM – A clinical report of 30 cases. *J Chin Med* (37): 17-20.

[15] Wiwanitkt, V. (2003). The use of CAM by HIV-Positive patients in Thailand. Complementary therapies in Medicine, 11, 39-41.

[16] Lohse. H Hansen. A, Pedersen. G, Kronborg. G, Gerstoft. J, Sørensen. T, Vaeth. M, Obel. N. (2007). Survival of persons with and without HIV infection in Denmark, 1995-2005. DOI: 10.7326/0003-4819-146-2-200701160-00003.

[17] WHO (2019). Dolutegravir (DTG) and the fixed dose combination of tenofovir/lamivudine/dolutegravir (TLD). Briefing Note.

[18] Min S, Song I, Borland J, Chen S, Lou Y, Fujiwara T, Piscitelli SC (2009): Pharmacokinetics and safety of S/GSK1349572, a next-generation HIV integrase inhibitor, in healthy volunteers. Antimicrob Agents Chemother. Jan;54(1):254-8. doi: 10.1128/AAC.00842-09.

[19] Katlama C, Murphy R (2012): Dolutegravir for the treatment of HIV. Expert Opin Investig Drugs. 2012 Apr;21(4):523-30. doi: 10.1517/13543784.2012.661713.

[20] Hare S, Smith SJ, Metifiot M, Jaxa-Chamiec A, Pommier Y, Hughes SH, Cherepanov P (2011): Structural and functional analyses of the second-generation integrase strand transfer inhibitor dolutegravir (S/GSK1349572). Mol Pharmacol. 2011 Oct;80(4):565-72. doi: 10.1124/mol.111.073189.

[21] World Health Organization (2019). World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization. hdl:10665/325771. WHO/MVP/EMP/IAU/2019.06. License: CC BY-NC-SA 3.0 IGO World Health Organization.