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RESEARCH ARTICLE

A THREE SOURCE CAPTURE RECAPTURE ESTIMATE OF THE NUMBER OF HIV POSITIVE PREGNANT WOMEN IN GEMBU, TARABA STATE NIGERIA

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ABSTRACT

Capture recapture is a method that involves estimating the number of cases in a defined population by crosslinking registrations of individual records of names. This study seeks to present the capture recapture technique as a more appropriate approach to use in estimating the number of population that are difficult to count. To illustrate the method, secondary data were obtained from three health facilities: Gembu Centre for HIV/AIDS Advocacy in Nigeria (GECHAAN), Mambilla Baptist Hospital (MBH), and General Hospital Gembu (GH) all located in Gembu, Taraba state and was used to estimate the prevalence of HIV in pregnant women from 2013 -2015. Log linear model was used to analyse the capture recapture data. Results show that the estimated completeness of the three sources was 14 % with the total prevalence of HIV in pregnant women estimated at 4372(95% CI [2274 - 9767]), thus 3760were not registered by any of the three health facilities, since only 612 patients were identified by the centres. Validity of the results obtained was tested and was found to corroborate with the results obtained from existing alternative models. Result obtained shows that capture recapture technique has the ability to provide comprehensive data with a near accurate estimate.This method is useful for estimating elusive populationsas itis cost effective and an alternative to carrying out population based survey.

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INTRODUCTION

Knowing the number of infected, sick or dead individuals in a population is a vital step in investigating the health of a population (Stephen, 1996). It is also crucial for forecasting health needs and guiding regional and national health policy in resource allocation (Abeni *et al.,* 1993). According to an analysis of demographic and surveillance survey collected from 1989-2012, about one in four pregnancy related deaths in sub-Saharan Africa are attributable to HIV (Zaba *et al.,* 2013). Seventeen percent of women in the study areas were infected with HIV, and the mortality rate was substantially higher among these women, than among pregnant women without the virus. Overall about 88% of deaths among pregnant women with HIV were attributable to the virus. (International Perspectives on Sexual and Reproductive Health, 2013). Obtaining accurate estimates of these infected women has become crucial as the figure can be used to infer the status of the sexual partners and babies of these women, but the estimation of HIV prevalence of infected pregnant women has become complex due to multiple registrations of infected patients in different health facilities. This is because the desire of Government and privately funded non-governmental organisations (NGOs) in eradicating HIV/AIDS has resulted in the establishment of various HIV testing centres. This has complicated the estimation of the numbers of pregnant women infected with HIV as they could be tested at different centres. This therefore makes itdifficult to determine the accurate number of infected pregnant women as one woman can go to different facilities to be tested, thereby resulting in multiple counting of the same person in one or more facilities.. Furthermore, population based surveys may reflect the situation of a country but its methodology is expensive to researchers. Such surveys could still present bias to the results as participation is voluntary rather than obligatory. The desire to obtain accurate population estimatesof hard to count populations particularly those infected with HIV, has brought about the development and applications of various approaches, such as mathematical models, surveillance systems, surveys and screening program, however no single epidemiologic methodology yields completely reliable estimates (Abeni *et al.*, 1993). Capture recapture methods which is being used in estimating wildlife populations is seen as a near accurate method and has recently being applied to the estimation of the prevalence of infectious diseases. This method involves estimating the number of cases in a defined population using

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multiple sources of information assuming that each source alone may under-count the population (Morrison and Stone, 2000).Applications of capture recapture has not received much attention in Nigeria and none at all in Taraba State, especially in the aspect of hidden populations such as HIV/AIDS amongst pregnant women. This study will help in presenting the capture-recapture technique as a more appropriate approach to use in estimating the number of populations that are difficult to count through the classical counting methods. It is also a useful method for researchers who do not have the money to carry out surveys or time to rely on government funded surveys or some other agencies for data collection.The objectives of this study is to show how capture-recapture method can be applied toestimate the prevalence of HIVin pregnant women and also evaluate the number of those multiple registered. To illustrate the method, secondary data obtained from three health facilities in Gembu from 2013 – 2015 were used.

Review of Related Literature

Historically, capture-recapture method can be said to be first used by Graunt in 1662 (Cochran, 1978;Van Hest, 2007) who used it to estimate the population of London, Laplace also used it 150 years later in an attempt to estimate the population of France and laid out its mathematical foundations (Laplace 1786 and Laska,2002). Petersen in 1896 applied the technique in the study of fish populations. He used the simplest capture-recapture model, which is the 2 sample method to estimate the unknown size of a population of plaice in the Limfjord in Denmark. In this case, animals are captured from the population and marked. Those animals are then released back into the population, after a certain interval, another batch is captured from the same population. The numbers of those marked animals that have been re-captured are noted. Using the number of recaptures and the numbers of animals caught in both the first and the second samples, it is possible then to estimate the total population size by making certain assumptions. In epidemiology, capture recapture is applied in population estimation by merging several lists of names and removing the overlap in the list. Its application to human epidemiology is made possible by the following assumptions;
All members of the population can be matched on all lists (every individual in the register must have a unique identification and there should be at least one common identifier)

There should be no significant changes during the given time period, example by migration or death,

All members of the population have the same probability of being captured and recaptured and also the registers are independent of one another. This method has also been used to estimate population size in a variety of health applications including for example infants born with birth defects, women with preclinical cancer, and persons with severe and persistent mental illness, drug abusers and persons with sexually transmitted infections. It has also been used to evaluate the degree of ascertainment of various disease monitoring systems. (Laska, 2002).Sekar and Deming (1949) applied the capture-recapture methods to estimate birth and death rates in an area near Calcutta, this started a development of the capture-recapture methodology in demography and social science in general. Other interesting applications include the estimation of plant populations (Alexander, Slade and Kettle 1997; Chao 2001), rare and elusive populations (e.g. Homeless persons, disabled patients or mentally people) and the number of species in a community (Colwell and Coddington 1994; Boulinier, Nichols, Sauer Hines and Pollock, 1998; Chao 2001). In 1993, Damiano D. Abeni, Giovanna Brancato and Carlo A. Perucci used capture-recapture methods to estimate the size of the population with HIV -1 infection in Lazio, Italy.Pezotti *et al* (2003) used the four source capture-recapture to estimate the number of people infected with HIV in the Venetto region in Italy and the completeness of case ascertainment using a data coverage from 1983-2000.In 2013, Ligia *et al*, estimated the number of HIV positive pregnant women in the state of Sergipe, Brazil using capture-recapture.

MATERIALS AND METHODS

Ethics Statement

The data collection process in the facilities was carried out under the supervision ofthe office of the Association of Women living With HIV/AIDS in Nigeria (ASWAN), Taraba Chapter and New Generation and Social Initiative Development, (NEWGAP) Gembu. Due to the sensitive nature of the research, patient's names, age and addresses are not included in this study.

Data Sources

Sardauna local government in Taraba state, Nigeria, has three major health facilities which caters for the needs of HIV/AIDS patients, which are: Gembu Centre of HIV/AIDS Advocacy in Nigeria (GECHAAN), Mambilla Baptist Hospital (MBH) and General Hospitals Gembu and Warwar (GH).

Methodology and Individual Identifiers

Pregnant women usually visit the three health facilities for routine antenatal check-up where they are usually tested for their HIV/AIDS status. When a woman is confirmed positive, her name, address, age and year of diagnosis is recorded in the Prevention of Mother To Child Transmission (PMTCT) register. The individual identifiers that was used for matching people from each list or register are the identifier's surname, middle initials, the first name, the local government of origin, the date of birth, and address. A database was constructed for each facility with those six identifiers and was put into a spreadsheet using excel 2013 with the names arranged alphabetically, surname first. The three databases were cross linked and each individual identifier is compared one facility list with the other. Individuals are considered as matched, when at least five of the identifiers are the same.

Capture Recapture Method Employed

After matching the lists (record linkage) and removing the overlap between the lists, a three-source log-linear capture-recapture analysis was performed by fitting eight log-linear models to the data arranged in a 2x2x2 contingency table, where each of the two's corresponds to the number of registered cases in each of the health facilities. The dependent variable for each model was the logarithm of the number of cases in each of the 7 non empty cells of the contingency table. The eight possible models are;

Model 1; GECHAAN+MBH+GH

It assumes independence as it has no interaction terms while models 2 – 7 assume the 2 by 2 interactions terms and these are;

Model 2; GECHAAN+MBH+GH+GECHAAN*MBH + GECHAAN*GH;
Model 3: GECHAAN+MBH+GH+GECHAAN*MBH+MBH* GH
Model 4: GECHAAN+MBH+GH +GECHAAN*GH+MBH* GH;
Model 5: GECHAAN+MBH+GH+GECHAAN*MBH
Model 6: GECHAAN+MBH+GH +GECHAAN*GH;
Model 7: GECHAAN+MBH+GH +MBH*GH
Model 8: GECHAAN+MBH+GH+ GECHAAN* MBH+ GECHAAN *GH +MBH*GH+GECHAAN *MBH*GH.

Model 8 is the saturated model as it involves fitting the seven data points to the seven observed points. The analyses was performed using the public domain statistical package R for statistical computing (R foundation for Statistical Computing Vienna Australia), the model incorporates the expected value of the random variable, the total population size, the probabilities of being on each list, and an interaction parameter that accounts for list dependency(IWGDMF):1995,a &b). The model analysed the frequency of individuals appearing in one, two or three lists, thus determining the unknown frequency (those appearing in none of the lists.).The output of the analysis produced an estimate of the population size, confidence interval and the Akaike Information Criterion (AIC). The AIC was used for selecting of the most appropriate model.

Validation of the Capture Recapture Log-linear Models with other Alternative Models

Van Hest *et al*, (2008) showed that validity is particularly useful for the estimation of hidden populations due to heterogeneity. A software for the analysis of capture recapture data, the package Rcapture written in R, produced by Baillargeon and Rivest (2007) was used to validate our results. The Rcapture package, incorporates three types of models; Chao (1987) model, estimates a lower bound (LB) with abundance, both with a time effect (Mth Chao) and without time effect (Mh Chao). Darroch's models of time effect (Mth) and without time effect (Mh) are considered by Darroch et al (1993) and Agresti (1994).The Poisson and Gamma models by Rivest and Baillargeon (2007). The Rcapture has a log-linear component: they are fitted by carrying out a Poisson regression with the R function 'glm', the log-linear parameters are then transformed to demographic parameters. The fit focused on the frequency of the individuals appearing in one, two or three registers simultaneously. It displayed the observed and predicted statistics by each model using the function closedp. The predicted and observed statistics were compared using chi-square statistics. The functions closedp, closedp. Mx are then used to produce the customised log linear model for closed populations capture recapture experiments. The function generated the total missing population estimate, the Akaike Information Criterion (AIC), deviances, degrees of freedom and its standard error. The best fitted model was selected and compared with the log linear capture recapture selected model to determine its validity.

Data Presentationand Discussion of Results

Capture recapture estimates

Using capture recapture, Figure 1 shows that, out of the six hundred and twelve (612) HIV Positive pregnant women identified in the three registers, 149 cases were captured in GH only; 159 cases were captured from MBH only; and 219 cases from GECHAAN only were captured. 33 persons were captured in MBH and GH facilities only, 27 persons were identified in GECHAAN and GH only, while 8 persons were captured in MBH and GECHAAN ,cumulatively 68 persons were captured in more than one list while 17 persons were captured in all the three lists simultaneously.

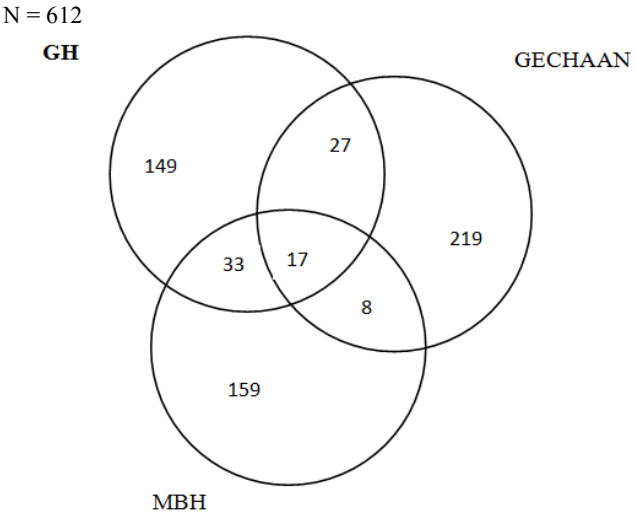

Figure 1. Venn diagramof matched cases

Model Fitting of the Capture Recapture Estimates Using R

The R software for statistical computing was used to fit the eight log-linear modelling frame work of the capture recapture estimates, the result of the analysis is shown in Table 1.

Table 1. Summary of the Capture Recapture Estimation Models

Model	AIC	Population Estimate	Confidence Interval	Deviance	Degrees of freedom
Model 1	95.9	963	754 -1237	47.844	3
Model 2	90.91	736	502 -1113	38.834	1
Model 3	78.79	1221	817-1914	27.723	1
Model 4	59.929	4723	2274-9767	7.852	1
Model 5	88.894	766	578 -1023	38.908	2
Model 6	96.484	1102	813-1515	46.407	2
Model 7	78.028	1455	1069-2015	27.951	2
Model 8	54.0	12392	4621-35693	2.1982e-14	0

In general, even though the saturated model has the lowest AIC, it will not be selected as it is saturated, complex and has no degrees of freedom left and in the log-linear capture-recapture estimation procedure, the least complex, i.e. the least saturated (in other words the most parsimonious) model, who sefit appears adequate, is preferred (Papoz, Balkau, and Lellouch, 1999). Model 4, has the next lowest AIC with the value at 59.9, it also has the lowest deviance residual of 7.852 on 1 degree of freedom. Model 4 was then selected.The R output of the selected model shows the estimated population of infected pregnant women in the study area as 4372 cases, indicating that 3760 cases have not been registered in any of the health facilities. See Table 2.

Table 2. R Output of the Selected Log-linear Model

Model	Population Estimate	Confidence Interval	cases cases (n)	No of registered	Unregistered	AIC	Degrees of Freedom
GECHAAN +MBH+GH +GECHAAN*GH +MBH*GH	4372	2274 -9767	612	3760	59.9	1	

The Population estimate (4372) is used to compute the total data coverage of HIV Positive women in the area;

Total estimated data coverage $= \frac{No\ of\ Observed\ cases}{No\ of\ estimated\ cases} * 100$

The number of estimated cases = 4372
The number of registered cases = 612
The number of unregistered cases = 3760

This indicates that data coverage stood at 14%, indicating that 86% of the HIV positive pregnant women in Sardauna are not identified, see Figure 2.

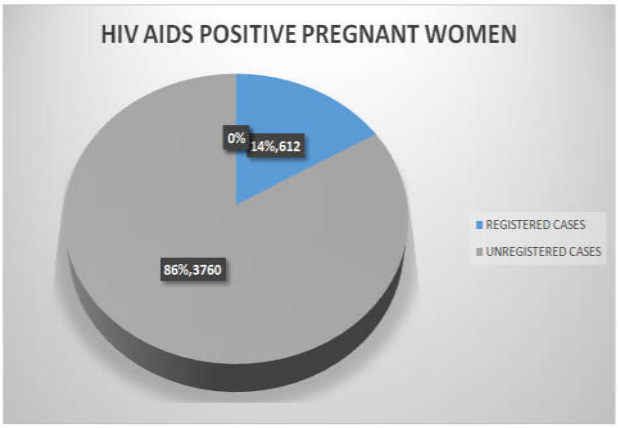

Figure 2. Registered and Unregistered cases (2013 -2015)

Alternative Models and Model fit

A summary of the results produced from the output of the Rcapture software from the alternative models is shown in Table 3.It contains, the Abundance (estimated population), models deviance, degrees of freedom (df), the Akaike Information Criterion (AIC) and the customised log linear model for closed populations. Where;

N= the estimated population size (abundance)

M_0: the probability of being registered is not affected by any factor
M_t: the probability of being registered is affected by time
M_h Models: the probability of registrations is affected by heterogeneity alone
M_{th}: the probability of registrations is affected by time and heterogeneity
M_b: the probability of the registration process is affected by individual's behaviour
M_{bh}: the probability of the registration process is affected by individual's behaviour and heterogeneity.

Table 3. Summary of Results of Alternative Models

	Abundance	deviance	Degrees of Freedom	AIC
M0	1582.5	56.001	5	100.077
Mt	1575.1	47.844	3	95.921
Mh Chao (LB)	1973.4	33.383	4	79.460
Mh Poisson2	3894.3	33.383	4	79.460
Mh Darroch	8525.2	3.383	4	79.460
Mh Gamma3.5	19909.9	33.383	4	79.460
Mth Chao (LB)	1963.6	25.083	2	75.160
Mth Poisson2	3880.8	25.083	2	75.160
Mth Darroch	8517.6	25.083	2	75.160
Mth Gamma3.5	19952.7	25.083	2	75.160
Mb	1023.8	47.431	4	93.508
Mbh	1128.3	47.164	3	95.241
Customized Log-linear Rcapture	4964.6	7.852	1	59.929

Number of captured units: 612
Abundance Estimations and Model Fits.

DISCUSSION

The customised log linear model for closed populations capture recapture experiments corroborates with the log linear model for capture recapture experiments, both having the same deviance, AIC and degrees of freedom. This results confirms the validity of our population estimate (N) and is therefore selected as the best model based on thelog-linear capture-recapture estimation procedure that has the least complex, i.e.the least saturated (in other words the most parsimonious) model, whose fit appears adequate (Papoz, Balkau and Lellouch, 1999). Based on cross matching of the identification codes, 102 HIV positive pregnant women were multiple registered in the study area. This is explained in;

Model 4: GECHAAN+MBH+GH +GECHAAN*GH+MBH* GH. This result shows that the two way interactions: the MBH*GH interaction and GECHAAN* MBH interaction are both positive. This means that there is a positive dependence between MBH* GH, and a positive dependence between GECHAAN* GH. For a real life situation such as this, the positive dependence between the interactions means that patients are constantly referred from GH to MBH, and also referrals take place from GH to GECHAAN. With the three facilities all located in the same town, it is easy for patients to get tested in a facility, never return and get tested in another facility due to the proximity. This accounts for the number of multiple registrations. Our findings shows the total prevalence of HIV in pregnant women stood at 4372 cases, while only 612 cases were recorded by the three health facilities. Maternal statistics from the records as obtained from the hospital registers shows that only 28% of the women from the rural areas have been tested and registered. From the records, it was observed that most of the population of pregnant women tested reside in the urban centre (Gembu town) where all the health facilities are sited. This may account for the high estimate of the numbers of those not registered.

Recommendations and Conclusion

It can be seen from the results of the study that capture-recapture is a useful method that can be used in the evaluation of information systems, it may also serve to improve the reporting practices and the coverage of health and surveillance systems (Ligia, *et al.,* 2013). The capture recapture method is recommended as a more appropriate method of estimation for elusive populations, and as alternative to population based survey method (which has to do with voluntary participation rather than obligatory participation of persons and may constitute a bias) because it is cost effective and near accurate as data is collected directly as well as verified from hospital registers of those tested and confirmed infected. The merging of four or more data sources for capture recapture is proving to be a strong method for estimating populations that are hard to access, particularly where data are poorly kept.Hence, this method should be extended to the estimation of the incidence and prevalence of such elusive populations. Capture recapture method incorporating tag loss is recommended for use in estimating this hard to access populations as it minimises the number of multiple registrations. This methods can be used to estimate other elusive populations like the female sex workers (FSW), Men that have Sex with Men (MSM), Injecting Drug Users (IDU) and the general population of HIV/AIDS. In conclusion, this study shows that capture recapture procedure has the potential to provide reliable and accurate estimate of HIV positive pregnant women and other difficult-to-access

population. Also results of the research is relevant to NGOs, Epidemiologists and governments at both state and federal levels to initiate policies that is aimed at reducing the number of those infected in orderto allow planning for health services for this population and reduce its transmission.

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REFERENCES

Abeni. D. D., Brancato, B. and Perucci,C.A. 1993. Capture Recapture to Estimate the Size of the Population with Human Immunodeficiency Virus Type Infection. *Epidemiology* 5(4).

Adah Abbah 2015.Gembu: Home of Tourism. Retrieved from Leadership Online Newspaper on 21/08/2015 at 3:58 am.

Alexander H.M. ,Slade N.A. ,Kettle W.D.,(1997) .Application of Mark Recapture Models to Estimation of the Population of Plants. Ecology 78: 1230 -1237

Baillargeon S and Rivest L.P. 2007. Rcapture: Log Linear Models for Capture Recapture Experiments R Package Version, 1.2 -0, http://Cran R project.org/Package =Rcapture.

Bouliniear .T, Nicholls J.D., Sauer J .R, Hines .J. E., Pollock K.H. 1998. Estimating Species Richness; The Importance of Heterogeneity in Species Detectability. Ecology 79(3); 1018 -1028.

Chao A. 2001. An Overview of Closed Capture-recapture Models. *Journal of Agricultural, Biological and Environmental Statistics*. 6(2), 158-175.

Cochran W. G. 1978.Laplace Ratio Estimator, Contributions to Survey Sampling and Applied Statistics. New York Academic Press, pp 3- 10

Colwell R.K., and Coddington J.A 1994.Estimating Terrestrial Biodiversity through Extrapolation.*Journal of Plant Ecology.*5 (1):3 -21.

Core Team. R. 2012. *R*: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna Austria .URL,http//www.R.Project.org

Darroch J.N, Fienberg S.E, Gloneck G.F.V, and Junker B.W 1993. A Three Sample Multiple Recapture Approach to Census Population Estimation and Heterogeneous Catchability. *Journal of Statistical Association*. 88:1137 -1148.

Hest N. A.H, Grant, A. D., Smit, F., Story, A., and Richardus, J. H. 2008 Estimating Infectious Disease Incidence: Validity of Capture Recapture Analysis and Truncated Models for Incomplete Count Data, *Epidemiol Infect*.136 (1):14 -22.

Hest, N.A.H. 2007. Capture-Recapture Methods in Surveillance of Tuberculosis and Other Infectious Diseases.

International Perspectives on Sexual and Reproductive Health 2013, 39(2)

International Working Group for Disease Monitoring and Forecasting (IWGDMF) 1995. Capture-Recapture and Multiple Record Estimation 1; History and Theoretical Development. *American Journal of Epidemiology*.142, 1047-1058.

International Working Group for Disease Monitoring and Forecasting (IWGDMF) 1995. "Capture –Recapture and Multiple –Record System Estimation II: Applications in Human Diseases". In: *American journal of epidemiology*; 142.10,

Laplace SP 1786. Sur Les naissances, *le mariages et le morts. In historaire d' l acadaime royale de sciences Anee* 1783: Paris, p693

Laska, E. 2002.The Use of Capture-Recapture Methods in Public Health .Bulletin World Health Organisation, 80(11), Geneva.

Lebreton, J.D., Burnham K.P., Clobert J and Anderson D.R 1992.Modelling Survival and Testing Biological Hypothesis Using Marked Animals. A Unified Approach with Case Studies. Ecological Monographs 62:67 -118.

Ligia, M. D. L., Duarte G.S., Gurgel R.Q., Martins, N.G.R., Pinto da Silva, F. J. C., and Ilozue, C. 2013. Estimating the Number of HIV-Positive Pregnant Women in Sergipe, Brazil, Using Capture-Recapture, AIDS Care: Psychological and Socio-Medical Aspects of AIDS/HIV.

Morrison, A. and Stone D.H. 2000. Capture-Recapture: A Useful Methodological Tool for Counting Traffic Related Injuries? Injury Prevention; 6:299-304.

Papoz, L., Balkau, B. and Lellouch, J. 1999. Case Counting in Epidemiology: Limitation of Methods Based on Multiple Data Sources. *International Journal of Epidemiology*. 25:474-478.

Petersen C.G. 1896.The Yearly Immigration of Young Plaice into the Limford from the German Sea. Rep .Dan .Biol .Stat. (6) 1 – 48.

Pezotti, P., Piovesin, C., Michieletto, F., Rezza, G., and Gallo, M.2003. Estimating the Cumulative Number of Human Immunodeficiency Virus Diagnoses by Cross Linking from Four Different Sources: International Journal of Epidemiology, 32:778-83

Rivest, L. P. and Baillargeon, S. 2007. Applications and Estimation of Chao Moments Estimation for the Size of a Closed Population. *Journal of Biometrics* 63(4): 999-1006.

Sekar C.C, and Deming W.E. 1949.Methods of Estimating Birth and Death Rates and the Effects of Registration. Journal of American Statistic Association (44):101 – 15.

Stephen, C. 1996. Capture-Recapture in Epidemiological Studies. Infect Control Hospital Epidemiology. 17, 262-266.

Taraba State Ministry of Health: Taraba State Strategic Health Development Plan. (2010-2015)

Van der Heidgen P.G.M., Zwane. E, and Heissen David. 2008. Structurally Missing Data Problems in Multiple List Capture Recapture .*Adv.Stat.Anal*, 93:5-21

Zaba, B., Calvert, C., Marston, M., Isingo R., Naleingi-Miro, J., Lutalo, Tet al 2013. Effect of HIV Infection on Pregnancy Related Mortality in Sub-Saharan Africa; Secondary Analysis of Pooled Community Based Data from the Network for AnalysingLongitudinal Population - Based HIV/AIDS Data on Africa (AlPHA).Lancet.381 (9879):1699

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