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Full Length Research

The use of Semi-Markov Model to determine the efficacy of CDC staging criterion in Nigeria (A case study of General Hospital Minna, Niger State)

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ABSTRACT: Semi-Markov model in discrete state and time to study the trajection among the various defined HIV/AIDs stages has been presented in this paper. The model was used to determine the staging of HIV- infected clients reported at heart-to-heart clinic of General Hospital Minna, Niger State, Nigeria for a period of 10 years. The result shows that there is no transition from asymptomatic stage of HIV to late/advance AIDs such that $\varphi_{14}(n) = 0$; which led to gradual increment in the graphs of interval transition probabilities for all $n \in N$.The study shows that there are some increments in the transition probabilities from stages 2, 3 and 4 to stage 1 from about 0.05745, 0.01055 and 0.00379 in the first month (n = 1) to about 0.37163, 0.17821 and 0.05862 in the forty four months (n = 44) and in the forty five months (n = 45) respectively. From the virtual transition probabilities, the graph is gradually decreasing after forty-five (45) months. The result show that $\varphi_{11}(n)$, $\varphi_{22}(n)$, $\varphi_{33}(n)$ and $\varphi_{44}(n)$attained the values of about 0.56516, 0.50353, 0.53343 and 0.65623 respectively for the first few months or years. The percentage decrease is about 37.1%, 17.8% for stages 2, 3 in forty-four months and 5.8% for stage 4 in forty-five month duration. However, client's transitions dropped slowly and attain stability of stage at infinity. In compliance to the medical view, all HIV-naïve patients transit to AIDs stage especially when therapeutic intervention is lacking. The model established in this study could assist the Medical Personnels' (MP), Health Care Providers (HCP), Epidemiologists, Medical Statisticians and other funding organizations to plan for the treatment, tracking and intervention for the ever increasing scourge of HIV/AIDs.

Keywords: Discrete time, HIV-naives, holding time, interval transition probability, semi-Markov process, waiting time.

INTRODUCTION

With the pandemic spread of AIDs, a universally applicable staging system for HIV infection and disease is needed. World Health Organization (WHO) staging system solely depends on clinical investigations as they manifest on HIV-naïve individuals; before staging them into any of WHO four staging thresholds (stage 1, 2, 3 and 4). In Nigeria and other developing nations, it is WHO staging system that is in place because it is easier to implement. However, with the availability of FACS machine used for CD4 counts in most settings, clinicians encourage the counseled and tested HIV-naïves to go for CD4 count before staging. This clearly indicates strong inclination to United States Centre for Disease Control (US-CDC) approach. It could be the surer method because machine measuring is involved. The CDC defined a set of guidelines and recommendations for HIV-infected adolescents and adults on the basis of clinical conditions associated with the HIV infection and CD4+ T-lymphocyte counts (CDC, 1997). Kay (1986) reported in cancerology that, disease dynamic can be

defined through various states: life without diseases, appearance of symptoms, mastitis and eventual death.

Chronic diseases are always characterized by their long duration and generally their slow progression. Gillaizeau et al. (2014) asserted that many chronic and non-chronic diseases, except few exhibit clinical events which are stochastic in nature. These events may denote disease incidences, progression, relapse, remission, recovery etc. The biomedical dynamic processes can be stationary, progressive or non-progressive with respect-tive to the adopted medical interventions and time index. Stochastic processes entails the trajectories within and among the various states within time t. The changes and duration among the diseased states are often unknown. Stochastic modeling then becomes imperative to model such dynamic process in order to understand the underlying mechanism inherent in disease progression.

Welte et al. (2006) showed that a semi-Markov process with sojourn times given as a general lifetime distribution can be approximated by a conventional Markov process with exponentially distributed sojourn times. This means that the general lifetime distribution is replaced by a sum of exponentially distributed times. One way to estimate the general lifetime distribution in the semi-Markov model is the use of expert opinion. Basta et al. (2008) used a cross sectional self-report data collected from 208 HIV sero-positive individual to determine the accuracy of Transtheoretical model (TTM) constructs to predict the stages of change for exercise behaviors in individual living with HIV/ AIDS. They discovered based on their sample that predictive discriminant analysis classified HIV- naive individuals into the correct stages substantially better than chance alone except that no one was accurately predicted in one of stages out of four.

Cox (1972) asserted that Markov models are widely used in medicine, particularly in the study of chronic diseases, extending classical survival models to the analysis of multi-state processes. In literature, conventional survival analysis has been used as a gold standard in modeling time to single event. Here, one terminal event may be onset of diseases or death. In these situations, time to event data may incorporate the comparison of hazard rates, intensities or survival function between states. Laird et al. (2013) asserted that, the natural history of disease can be modeled using a variety of approaches that fall under the general framework of multi-state modes, including Markov processes, non-homogenous Markov processes, semi-Markov processes and hidden Markov processes. However, in order to model the complex and stochastic duration-dependent processes usually encountered in epidemiology and biomedicine; the rigid Markovian assumption may be unrealistic and has to be relaxed. In this paper, semi-Markov model in continuous state and time was used to study the transition and prediction of HIV/AIDs naïve patients in order to improve the surveillance of HIV/AIDS management.

MATERIALS AND METHODS

Study area and data source

The data used in this paper work, were collected at the heart–to-heart clinic of General Hospital Minna, Niger State, Nigeria. It is WHO staging system currently in place in Nigeria because of easier implementation. However, with the availability of FACS machine used for CD4 counts in most settings whereby clinicians encourage the counseled and tested HIV-naïves to go for CD4 counts before staging. This clearly indicates strong inclination to CDC approach. It could be the surer method because machine measuring is involved.

Semi-Markov model

Semi-Markov process is a stochastic process in which changes of state occur according to a Markov chain and for which the time interval between two successive transitions is a random variable of interest whose distribution may depend on the present state from which the transition takes place (Bellman, 1957).

Model formulation

The transition of HIV/AIDs staging was modelled according to US-CDC staging threshold and stage the HIV/AIDs-naive clients into four stages using the principle of Markov chain. The stages was defined as follows:

Stage 1: ≥ CD4 500
Stage 2: CD4 350 – CD4 499
Stage 3: CD4 200 – CD4 349
Stage 4: < CD4 200

It was observed that the stages 1, 2 and 3 communicates while stage 1 and stage 4 are transients, and all possible transitions of the process are made between the stages 1, 2, 3, 4 (Figure 1). We would like a transition to occur at a time the duration of stay in a stage is completed, even if the new stage is the same as the old. Such transitions are called virtual transition and are represented by loops in the transition diagram.

From the Figure 1, we record the transition probability matrix P for the process as shown in equation 1.

$$P = \begin{pmatrix} p_{11} & p_{12} & p_{13} & 0 \\ p_{21} & p_{22} & p_{23} & p_{24} \\ p_{31} & p_{32} & p_{33} & p_{34} \\ p_{41} & p_{42} & p_{43} & p_{44} \end{pmatrix} \quad (1)$$

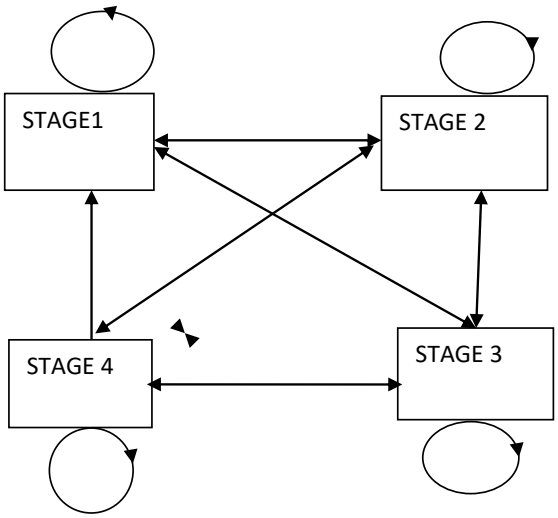

Figure 1. The transition diagram for the US-CDC staging criterion based on CD4 counts.

The semi-Markov process technique was used to analyses the process with the above set of stage. The transitions can be readily identified from the transition probability matrix P. To study this process, the probabilistic nature of the transition was specified. In addition, think of this process as a process whose successive stage occupancies are governed by the transition probabilities of a Markov chains, but whose stay in any stage is described by a random variable that depends on the stage to which the next transition is made.

Holding time and waiting time

Let (P_{ij}) be the probability that the HIV-naïve client that is in stage i on its last transition will enter stage j on its next transition $i, j = 1, 2, 3,4$. The transition probabilities must satisfy the following:

$$\left.\begin{array}{l} p_{ij} \geq 0 \\ \sum_{j=1}^{4} p_{ij} = 1 \end{array}\right\} \quad ij = 1,2,3,4. \qquad (2)$$

Whenever the HIV-naïve client enters stage i it remains there for a time T_{ij} in stage i before making a transition to stage j. T_{ij} is called the holding time in state i. The holding times are positive integer valued random variables each governed by a probability distribution function $f_{ij}(\ )$ called the holding time distribution function for a transition from stage i to stage j (Howard 1971).

Thus, $P(T_{ij} = m) = f_{ij}(m)\ i, j = 1, 2, 3,4 \qquad (3)$

It was assumed that the means μ_{ij} of all holding time distribution are finite and that all holding times are at least one month in length. That is, $f_{ij}(0) = 0$.

To completely describe the semi-Markov process, the holding time distribution functions in addition to the transition probabilities must be specified.

For a fixed value of i, T_{ij} is the same for each value of j, $(i, j = 1, 2, 3,4)$.

Let $F_{ij}(\cdot)$ be the probability distribution of T_{ij}

$$F_{ij}(n) = P(T_{ij} \leq n) = \sum_{m=0}^{n} f_{ij}(m) \qquad (4)$$

And $\bar{F}_{ij}(\ )$ be the complementary probability distribution of T_{ij}.

$$\bar{F}(n) = 1 - F_{ij}(n) = p(T_{ij} > n) = \sum_{m=n-1}^{\infty} f_{ij}(m) \qquad (5)$$

Suppose the HIV-naïve client enters stage $\boldsymbol{i}$. Let Y_i be the time it spent in stage $\boldsymbol{i}$ before moving out of the stage $\boldsymbol{i}$. Then Y_i is called the waiting time in state $\boldsymbol{i}$.

Let $W_i(\ )$ be the probability distribution function of Y_i

Then, $W_i(m) = p(Y_i = n) = \sum_{j=1}^{4} p_{ij}\, f_{ij}(m) \qquad (6)$

The probability distribution $W_i(\ )$ and the complementary probability distribution $\bar{W}_i(\ )$ for the waiting times are given as follows:

$$W_i(m) = P(Y_i \leq n) = \sum_{m=1}^{4} W_i(m) \qquad (7)$$

$$= \sum_{m=1}^{n} \sum_{j=1}^{4} P_{ij}\, f_{ij}(m) \qquad (8)$$

$$= \sum_{j=1}^{4} p_{ij} F_{ij}(n) \quad (9)$$

$$\bar{W}(n) = p(Y_i > n) = 1 - W_i(n) = \sum_{m=n+1}^{\infty} w_i(m) \quad (10)$$

$$= \sum_{m=n+1}^{\infty} \sum_{j=1}^{4} p_{ij} f_{ij}(m) \quad (11)$$

$$= \sum_{j=1}^{4} p_{ij} \bar{F}_{ij}(n) \quad (12)$$

Interval transition probability in discrete time

$\phi_{ij}(n)$ was defined to be the probability that the condition of HIV-naïve client will be in stage j in day n given that the client entered stage i in month zero. This is called the interval transition probability from stage i to stage j in the interval $(0, n]$. Then,

$$\phi_{ij}(n) = \delta_{ij} \overline{W}_i(n) + \sum_{k=1}^{4} P_{ik} \sum_{m=1}^{n} f_{ik}(m) \phi_{kj}(n-m) \quad (13)$$

$$\delta_{ij} = \begin{cases} 1 & i = j \\ 0 & i \neq j \end{cases} \; i, j = 1,2,3,4 \; n = 1,2,3,4.... \quad (14)$$

This is the interval transition probability from stage i to stage j in the interval $(0, n]$

Application

Heart-to-Heart popularly known as VCT/H2H clinic at General Hospital Minna is one of the comprehensive HIV/AIDs referral site. The clinic is responsible for data collation on HIV/AIDs clients of General Hospital Minna and other three feeder sites within Minna and its environs. The study was conducted on the available data for the period of ten (10) years i.e from July 2009 to February 2019. Out of over thousands patients files, 219 randomly selected ART-naïve HIV-seropositive patients were included at various stages of diseases progression based on the US-CDC staging system that have substantial complete retrospective follow-up data on CD4 counts. The reported data is summarized in Table 1, 2 and 3.

The transition probability matrix of the Table 2 is presented as:

Table 1. A summary of the HIV/AIDs-naïve patients according to CDC staging criterion from 2009-2019.

Class interval (MW)	Stages	Frequency
≥ 500	1	71
350-499	2	40
200-349	3	57
>200	4	51
Total		219

Table 2. The transition count matrix for the CDC stages among HIV/AIDS-naive from 2009 – 2019.

	Stage 1	Stage 2	Stage 3	Stage 4	Total
Stage 1	41	7	5	0	53
Stage 2	13	19	4	3	39
Stage 3	13	10	31	11	65
Stage 4	4	4	17	37	62
Grand total					219

Table 3. Mean holding time in the stages.

Stage	Mean holding time
Stage 1	13
Stage 2	10
Stage 3	17
Stage 4	16

$$P = \begin{bmatrix} 0.7736 & 0.1321 & 0.0943 & 0 \\ 0.3333 & 0.4872 & 0.1026 & 0.0769. \\ 0.2000 & 0.1538 & 0.6419 & 0.1693 \\ 0.0645 & 0.0645 & 0.2742 & 0.5968 \end{bmatrix}$$

Exponential holding time in stages (discrete time)

Suppose that the holding times in each stage before making a transition to another stage follows the exponential distribution with parameter λ. This implies that the mean holding time in each stage is $1/\lambda$ (in months). The mean holding time in each stage is shown in Table 3. The table shows that HIV/AIDs clients recorded the highest mean holding time in stage 3 then followed by stage 4, stage 1 and stage 2 respectively.

RESULTS

Table 4 presents the values of interval transition probabilities in continuous time from stage 1 to stage 2,

Table 4. Interval transition probabilities for $\varphi_{12}(n)$, $\varphi_{13}(n)$, $\varphi_{21}(n)$, $\varphi_{23}(n)$, $\varphi_{24}(n)$ and $\varphi_{31}(n)$.

n	$\boldsymbol{\varphi_{12}(n)}$	$\boldsymbol{\varphi_{13}(n)}$	$\boldsymbol{\varphi_{21}(n)}$	$\boldsymbol{\varphi_{23}(n)}$	$\boldsymbol{\varphi_{24}(n)}$	$\boldsymbol{\varphi_{31}(n)}$
1	0.01812	0.01293	0.05745	0.01768	0.00696	0.01055
2	0.02618	0.01869	0.08214	0.02529	0.01325	0.02054
3	0.03365	0.02402	0.10448	0.03216	0.01895	0.02998
4	0.04057	0.07339	0.1247	0.03839	0.02411	0.0389
5	0.04697	0.09105	0.14299	0.04402	0.02457	0.04735
6	0.0529	0.10333	0.15954	0.04911	0.02499	0.05533
7	0.05839	0.13725	0.17452	0.05566	0.02538	0.06288
8	0.06347	0.15883	0.18807	0.05983	0.02572	0.07002
9	0.06819	0.18449	0.20033	0.0636	0.02603	0.07678
10	0.07254	0.19756	0.23366	0.06702	0.02632	0.08317
11	0.07658	0.20273	0.2437	0.07011	0.02657	0.08921
12	0.08032	0.21539	0.25278	0.07291	0.02681	0.09492
13	0.08378	0.22486	0.261	0.07544	0.02701	0.10032
14	0.08699	0.23015	0.26744	0.07773	0.0272	0.10543
15	0.08995	0.23227	0.27517	0.0798	0.02738	0.11026
16	0.0927	0.23464	0.28125	0.08167	0.02753	0.11483
17	0.09525	0.23646	0.28676	0.08336	0.02767	0.11916
18	0.0976	0.23814	0.29175	0.0849	0.02774	0.12324
19	0.09979	0.2397	0.29626	0.08443	0.02757	0.12711
20	0.10181	0.24114	0.30034	0.08568	0.02767	0.13075
21	0.10368	0.24248	0.31533	0.08682	0.02776	0.13421
22	0.10541	0.24371	0.31938	0.08785	0.02785	0.13748
23	0.10702	0.24486	0.3264	0.08878	0.02786	0.14057
24	0.1085	0.24592	0.33934	0.08962	0.02792	0.14349
25	0.10988	0.2469	0.35161	0.09038	0.0278	0.14671
26	0.11015	0.24781	0.35385	0.09107	0.02786	0.14933
27	0.11133	0.24865	0.35588	0.0917	0.02791	0.1518
28	0.11242	0.24943	0.35771	0.09226	0.02795	0.15414
29	0.11343	0.25165	0.35937	0.09277	0.028	0.15635
30	0.11466	0.25232	0.36087	0.09323	0.02804	0.15844
31	0.1158	0.25394	0.36223	0.09365	0.02807	0.16042
32	0.11683	0.25451	0.36346	0.09403	0.0281	0.1623
33	0.11727	0.25504	0.36457	0.09437	0.02813	0.16407
34	0.11816	0.25653	0.36558	0.09468	0.02816	0.16574
35	0.11953	0.25799	0.36649	0.09496	0.02818	0.16732
36	0.12014	0.25841	0.36731	0.09522	0.02818	0.16882
37	0.1219	0.25908	0.36806	0.09545	0.0282	0.17023
38	0.12296	0.26116	0.36873	0.09565	0.02822	0.17157
39	0.12357	0.2625	0.36934	0.09584	0.02823	0.17284
40	0.12499	0.26344	0.3699	0.09601	0.02824	0.17404
41	0.12601	0.26473	0.3704	0.09617	0.02826	0.17517
42	0.12773	0.26597	0.37085	0.0963	0.02827	0.17624
43	0.12918	0.26724	0.37126	0.09644	0.02828	0.17725
44	0.13137	0.26947	0.37163	0.09654	0.02829	0.17821

stage 1 to 3, stage 2 to stage 1, stage 2 to stage 3, stage 2 to stage 4 and stage 3 to stage 1 respectively using Equation (11), for $n = 1, 2$…….44. It is illustrated in Figure 2.

Table 5 presents the values of interval transition probabilities in continuous time from stage 3 to stage 2, stage 3 to 4, stage 4 to 1, stage 4 to stage 2, stage 4 to stage 3 respectively using equation (11), for $n = 1, 2, \ldots, 45$. This is graphically shown in Figure 3.

Table 6 presents the values of virtual interval transition

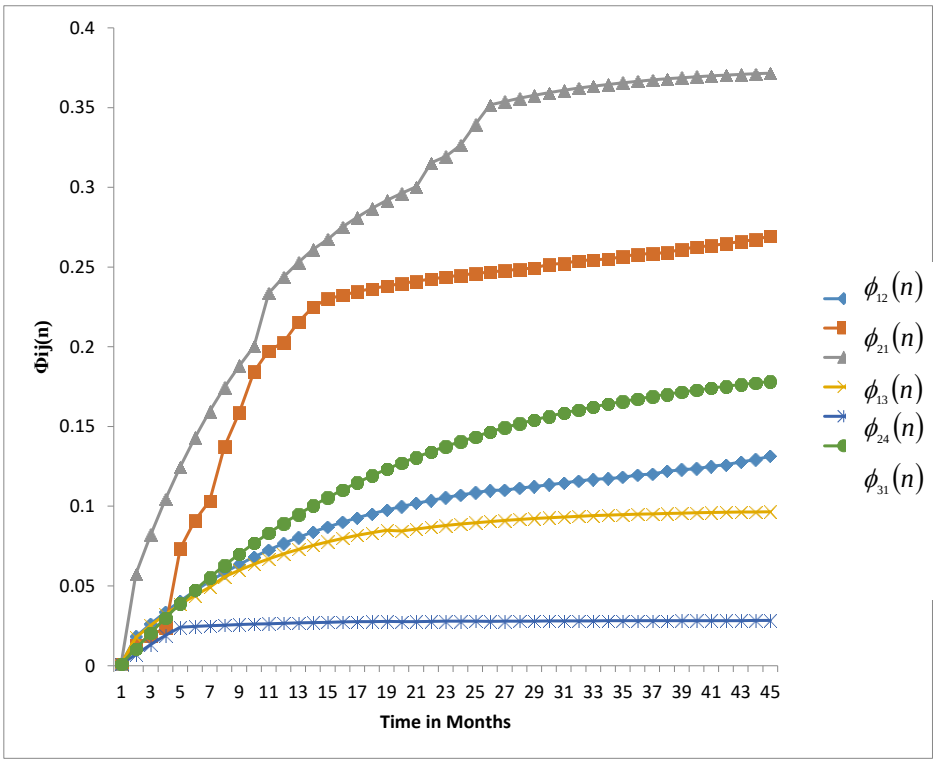

Figure 2. The graph of interval transition probabilities for $\varphi_{12}(n)$, $\varphi_{13}(n)$, $\varphi_{21}(n)$, $\varphi_{23}(n)$ $\varphi_{24}(n)$ and $\varphi_{31}(n)$

Table 5. Interval transition probabilities for $\varphi_{32}(n), \varphi_{34}(n), \varphi_{41}(n), \varphi_{42}(n)$ and $\varphi_{43}(n)$.

n	$\varphi_{32}(n)$,	$\varphi_{34}(n)$	$\varphi_{41}(n)$	$\varphi_{42}(n)$	$\varphi_{43}(n)$
1	0.02518	0.02772	0.00379	0.0161	0.00379
2	0.0458	0.05042	0.00735	0.03122	0.00735
3	0.06269	0.069	0.01069	0.04543	0.01069
4	0.07651	0.08422	0.01383	0.05746	0.01383
5	0.08782	0.09667	0.01678	0.07	0.01678
6	0.09709	0.10687	0.01955	0.07118	0.01955
7	0.10467	0.11522	0.02215	0.07229	0.02215
8	0.11088	0.12206	0.02459	0.08268	0.02459
9	0.11597	0.12765	0.02676	0.09244	0.02676
10	0.11653	0.13224	0.02891	0.10162	0.02891
11	0.11994	0.13599	0.03094	0.11024	0.03285
12	0.12273	0.13906	0.03285	0.11833	0.03285
13	0.12501	0.14158	0.03463	0.12594	0.03463
14	0.12689	0.14363	0.03632	0.13308	0.03632
15	0.12842	0.14532	0.03789	0.13979	0.03789
16	0.12967	0.1467	0.03938	0.14609	0.03938
17	0.1307	0.14783	0.04077	0.15202	0.04077
18	0.13154	0.14876	0.04208	0.16092	0.04208
19	0.13223	0.14951	0.04331	0.16144	0.04331
20	0.13279	0.15013	0.04446	0.16535	0.04445
21	0.13325	0.15064	0.04555	0.17096	0.04555
22	0.13363	0.15106	0.04657	0.1753	0.04657
23	0.13394	0.1514	0.04752	0.17937	0.04752

Table 5. Contd.

24	0.13419	0.15168	0.04842	0.18319	0.04842
25	0.1344	0.15191	0.04927	0.18678	0.04927
26	0.13457	0.15209	0.05006	0.19016	0.05006
27	0.13471	0.15224	0.05081	0.19333	0.05087
28	0.13482	0.15237	0.05151	0.19631	0.05151
29	0.13491	0.15247	0.05217	0.1991	0.05217
30	0.13499	0.15258	0.05279	0.20173	0.05279
31	0.13505	0.15264	0.05337	0.2042	0.05337
32	0.1351	0.1527	0.05391	0.20652	0.05391
33	0.13514	0.15275	0.05443	0.2087	0.05443
34	0.13518	0.15278	0.05491	0.21075	0.05491
35	0.13521	0.15281	0.05536	0.21267	0.05536
36	0.13523	0.15285	0.05579	0.21448	0.05579
37	0.13525	0.15287	0.05619	0.21617	0.05619
38	0.13526	0.15288	0.05656	0.21777	0.05656
39	0.13528	0.1529	0.05691	0.21926	0.05691
40	0.13529	0.15211	0.05725	0.22067	0.05725
41	0.1353	0.15212	0.05756	0.22199	0.05756
42	0.1353	0.15213	0.05785	0.22323	0.05785
43	0.13531	0.15213	0.05812	0.2244	0.05812
44	0.13531	0.15214	0.05884	0.2255	0.05838
45	0.13532	0.15214	0.05862	0.22652	0.05862

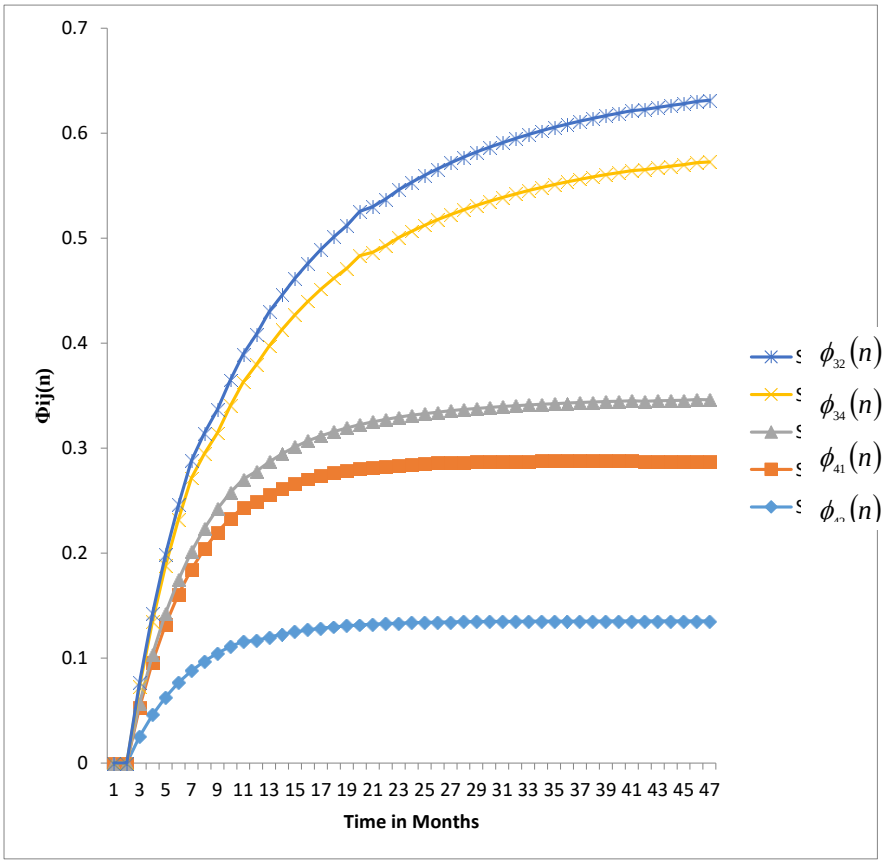

Figure 3. Graph of interval transition probabilities for $\varphi_{32}(n), \varphi_{34}(n)$, $\varphi_{41}(n)$ $\varphi_{42}(n)$ and $\varphi_{43}(n)$.

Table 6. Virtual transition probabilities $\varphi_{11}(n)$, $\varphi_{22}(n)$, $\varphi_{33}(n)$ and $\varphi_{44}(n)$.

n	$\varphi_{11}(n)$	$\varphi_{22}(n)$	$\varphi_{33}(n)$	$\varphi_{44}(n)$
1	0.98388	0.9536	0.93654	0.97633
2	0.96895	0.91162	0.88324	0.95408
3	0.95513	0.87363	0.83837	0.9332
4	0.94233	0.83925	0.80037	0.91489
5	0.88604	0.81235	0.76816	0.89645
6	0.86392	0.788	0.74071	0.88973
7	0.84377	0.72847	0.71722	0.88342
8	0.81436	0.74411	0.69704	0.86813
9	0.80564	0.70975	0.6796	0.85404
10	0.76732	0.67533	0.66807	0.84055
11	0.7319	0.67275	0.65487	0.82788
12	0.71069	0.65939	0.64329	0.81598
13	0.69429	0.6473	0.63309	0.8048
14	0.68836	0.63636	0.62405	0.79429
15	0.68287	0.62646	0.62362	0.78442
16	0.67736	0.6175	0.60881	0.77515
17	0.67266	0.6094	0.60232	0.76644
18	0.6683	0.60213	0.59646	0.75493
19	0.66426	0.59579	0.59115	0.75194
20	0.66052	0.59165	0.58633	0.74472
21	0.65705	0.58622	0.5819	0.73794
22	0.65385	0.58253	0.57784	0.73157
23	0.65088	0.57092	0.5741	0.72558
24	0.64813	0.5669	0.57064	0.71996
25	0.64558	0.55547	0.56699	0.71468
26	0.64322	0.54015	0.56402	0.70972
27	0.64104	0.53717	0.56125	0.70506
28	0.63902	0.52447	0.55867	0.70068
29	0.63715	0.52203	0.55626	0.69656
30	0.63892	0.51983	0.55399	0.6927
31	0.63002	0.51783	0.55188	0.68907
32	0.62926	0.51602	0.5499	0.68566
33	0.62666	0.51438	0.54805	0.68244
34	0.62269	0.5129	0.5463	0.67943
35	0.62131	0.51156	0.54466	0.67661
36	0.61948	0.51037	0.54311	0.67395
37	0.61616	0.50927	0.54165	0.67146
38	0.6123	0.50828	0.54028	0.66911
39	0.59688	0.50738	0.53899	0.66691
40	0.59585	0.50657	0.53857	0.66484
41	0.59044	0.50584	0.53742	0.6629
42	0.58626	0.50517	0.53633	0.66107
43	0.58223	0.50457	0.53531	0.65936
44	0.57858	0.50402	0.53434	0.65775
45	0.56516	0.50353	0.53343	0.65623

probabilities in continuous time from stage 1 to stage 1, stage 2 to 2, stage 3 to stage 3 and stage 4 to stage 4 respectively using Equation (11), for $n = 1, 2, 3 \ldots 45$. This is graphically shown in Figure 4.

DISCUSSION

The paper presented Semi- Markov model to study the efficacy of the hitherto CDC staging system of the

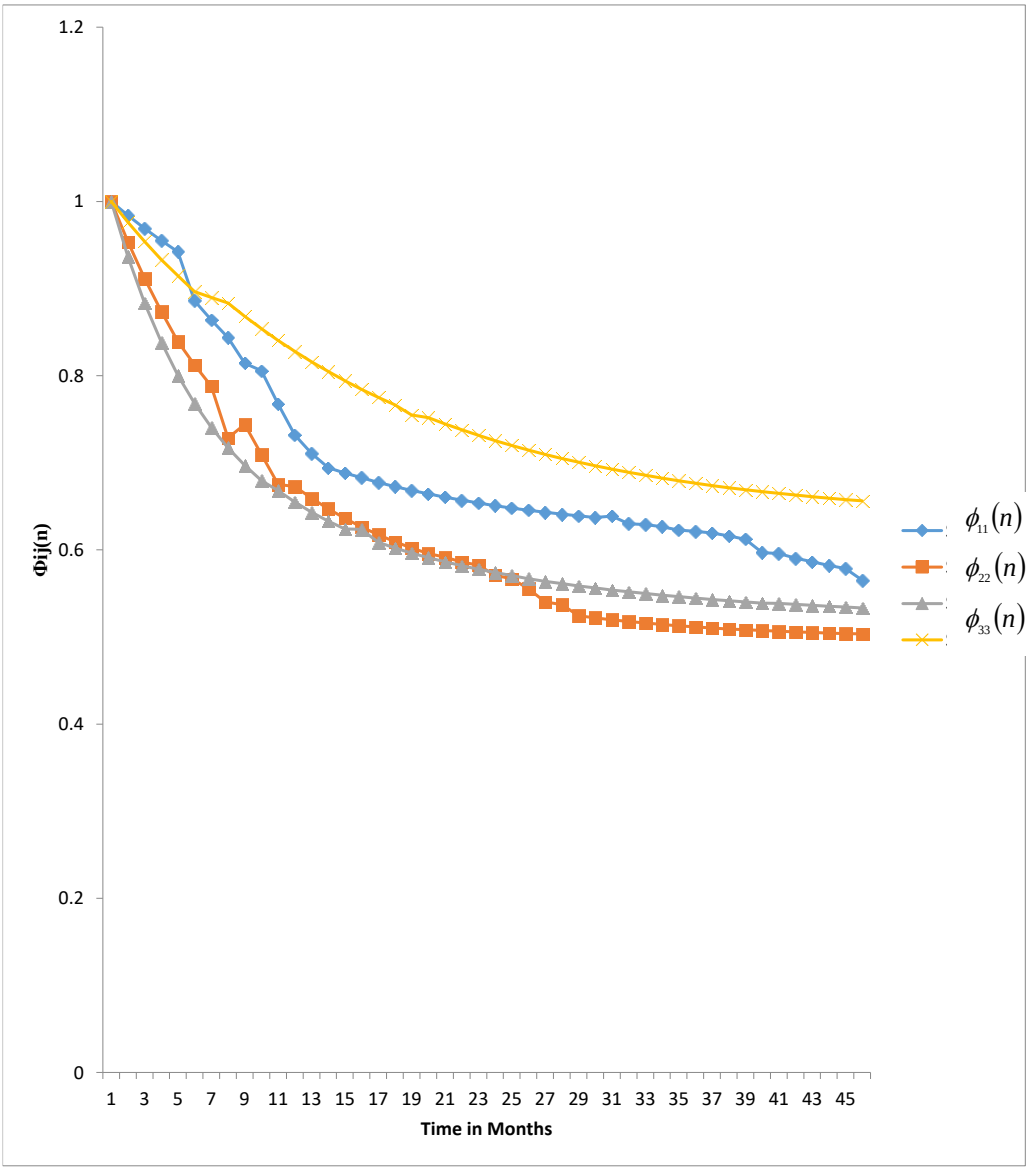

Figure 3. The graph of virtual transition probabilities$\varphi_{11}(n)$,$\varphi_{22}(n)$, $\varphi_{33}(n)$ and$\varphi_{44}(n)$.

reported cases of HIV/AIDs–naïves patients in Nigeria using continuous time semi-Markov model. From the empirical analysis of the data collected, the result shows that there is no transition from stage 1 to stage 4: that is $\varphi_{14}(n)=0$ for all n. In other words, there is no transition from asymptomatic stage of HIV to late/advance AIDs. Additionally, when HIV-naïves clients were in stage 1, they transits to stage 2 most time than stage 3 and incidentally there is no transition to stage 4. This is reasonable in medical sense, as there is rarely a case of HIV-naïve patient shunting directly to advance AIDs stage 4. Also, when HIV/AIDs patients were in virtual stages (i.e transiting to same stage), patients are intransient stages most of time than any other stages.

In the discrete time, from Tables 4 and 5 and Figures 2 and 3 the result shows that there were some increments in the transition probabilities from states 2, 3 and 4 to state 1 from about 0.05745, 0.01055 and 0.00379 in the first day $(n=1)$ to about 0.37163, 0.17821 and 0.05862 in the forty-four days $(n=44)$ and in the forty five days $(n=45)$ respectively. The percentage decrease is about 37.1%, 17.8% for stages 2, 3 in forty-four months and 5.8% for stage 4 in forty-five months duration.

Table 6 and Figure 4 show that $\phi_{11}(n),\phi_{22}(n),\phi_{33}(n)$ and $\phi_{44}(n)$ attained the values of about 0.56516, 0.50353, 0.53343 and 0.65623 respectively for the first few months or years. They all however dropped slowly

and diminish to zero at infinity. These show that in compliance to the medical view, all HIV-naïve patient's transit to AIDs stage especially when therapeutic intervention is lacking. The result also suggests that if the patients were staged in any of these stages, they remains/persists in that HIV/AIDs stage for some days before a change of real or virtual stage could occur. Thus, change of stage occurs less frequently over the time. The behavior of $\phi_{11}(n), \phi_{22}(n), \phi_{33}(n)$ and $\phi_{44}(n)$ for $n = 1, 2, 3, \ldots$ are very interesting. This is because they produced almost the same values of probabilities. This is very clear in the graphs as they almost form a straight line along $y = 1$.

Therefore, the discrete time semi-Markov models could be used to ascertain the prognostic and therapeutic adherence of HIV infected individuals on the treatment schedules. The model can also be used to predict expected stage(s) a newly infected HIV-naïve client is likely to be placed. The prediction model information could be useful in the tracking, surveillance and management of HIV/AIDs individual undergoing treatment.

Conclusion

A semi-Markov model in discrete time to determine the efficacy and staging of HIV/AIDs naïves using US-CDC criterion has been presented. The model has been able to ascertain long-run staging of HIV/AIDs patients. Prediction of their respective stages during retrospective cohort study has also been shown to be adequately captured according to the threshold values. The study was able to show the HIV-naïve clients remain in that stage for longer period if the therapeutic intervention is not readily available. The expected future stages is readily obtainable by the application of the model derived in this study.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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