Smooth Test of Goodness-of-Fit for Negative Binomial Distribution with Application to Unscheduled HIV Care Visits in a Tertiary Hospital

Collins Ojwang Odhiambo*

Institute of Mathematical Sciences, Strathmore University, Nairobi, Kenya

Abstract: Since the roll-out of antiretroviral therapy (ART) in Kenya, significant resource implications arising from regular treatment has attracted huge research interest, more specifically, unscheduled HIV care visits. Anticipating unscheduled HIV care visits for high-frequency regular groups is useful in helping clinics to focus efforts on reducing the burden of clinical appointments for families and facilities. In this paper, we fit data of unscheduled HIV care visits to a Negative Binomial Distribution and assess the fit using smooth tests of goodness-of-fit. The smooth tests applied here are an extension of Neyman's test where the score test is derived by embedding the null probability to form a larger class of alternative distribution. We conducted simulations by varying sample size and levels of dispersion for a negative binomial sample and compare performance of chi-square test, Kolmogorov- Smirnov test, Crammer-Von Misses test, Andersen-Darling and smooth test. We then utilized data on unscheduled HIV care visits, collected retrospectively from a tertiary referral hospital. The simulation results show that a smooth test does well under varying negative binomial conditions. Understanding patterns of unscheduled visits allows service providers to develop strategies to minimize this occurrence, particularly at a tertiary hospital.

Keywords: Unscheduled visit, HIV, Smooth test, Negative binomial, Tertiary hospital.

1. INTRODUCTION

There is a great need for studying unplanned clinical visits in a tertiary hospital, particularly when interested with assessing the likelihood of unscheduled hospital visits. Since the roll-out of antiretroviral therapy (ART) in Kenya, significant resource implications arising from regular treatment has attracted huge research interest, more specifically unscheduled HIV care visits [8, 9, 11]. Unplanned episodes of care visits; whether hospital readmission, emergency department evaluation, or unplanned hospitalization, course inconvenient for patients and are potential indicators of unsafe or inefficient practices [6, 7, 11]. Hospitals and health systems that provide HIV care services are particularly interested in determining the pattern of unscheduled HIV clinical visits in order to plan well. Detection of these unscheduled visits may occur at multiple facilities that do not routinely share patient-level data. This in event becomes difficult to determine, and hence remains a critical indicator of optimal care. Current methods of detecting re hospitalizations, unplanned episodes of care, and the symptomology associated with unplanned visits includes manual chart abstraction, query of claims databases, and analysis of hospital complaint lists [6-10]. These approaches of understanding the nature of unplanned care among patients in a typical HIV care clinic can be incomplete if data is not fitted to a distribution, primarily to determine the pattern. In this paper, we focus on unscheduled HIV Care clinical visits in a typical referral hospital in Kenya. We fit data of unscheduled HIV care visits to a negative binomial distribution and assess the fit using smooth tests of goodness- of- fit. The smooth tests applied here are an extension of Neyman's test where the score test is derived by embedding the alternative distribution in the null probability [2, 5]. Attempts to fit unscheduled clinical visits to a parametric distribution have not been given its due to its share of coverage in literature. Some of the articles that have utilized Neyman's test to assess goodness -of- fit include [2, 16-18]. Though there has been minimal community and societal level public health or policy interventions aimed at reducing unscheduled hospital visits, [1, 3, 4] no attempts have been made to fit these kinds of data to a distribution. The primary outcome measure of interest for fitting data to a distribution is to reduce the risk of unscheduled visits.

The smooth test considered here is a score test obtained by extending Neyman's goodness-of-fit approach [5] where the score test is obtained by nesting the null hypothesis in a larger class of probability distribution function [2]. Further, fitting Negative Binomial Distribution to complete samples simulated from several alternatives can be reliably assessed by smooth tests.

Patients started on ART are expected to regularly attend clinic for either continuous monitoring or drug

*Address correspondence to this author at the Institute of Mathematical Sciences, Strathmore University, Nairobi, Kenya;
Tel: +254 703 034 000/200/300 or (+254) (0) 730-734000/200/300;
Fax: +254 20 6007498;
E-mail: codhiambo@strathmore.edu

refill. For the purpose of planning, scheduled clinical visits enable the hospital to plan commodities, human resource and budget appropriately [10]. However, upsurge of unscheduled visits has compromised the quality of service and limited HIV clinical services in a typical Comprehensive Care Center (CCC). Testing for goodness- of- fit for unscheduled clinical visit data fitted to a parametric distribution is therefore important not only to determine which distribution best fits the data but also to enhance the accuracy in planning. In our formulation, we propose a score test for the null hypotheses that the unscheduled HIV care clinical visits follows a Negative Binomial Distribution.

To the best of our knowledge, there is no published article on fitting a parametric distribution to time to unscheduled HIV Care visit data of a typical tertiary hospital.

In the next section, materials and methods which include the data description, modelling of unscheduled HIV care visits, formulation of smooth goodness-of-fit for the Negative Binomial and simulations is presented. We discuss the performance of the smooth test in application and result section and then draw the conclusions of the test when fitted to unscheduled HIV Care visit data.

2. MATERIALS AND METHODS

2.1. Design and Setting

This is a retrospective data review of all patients who visited Kenyatta National Hospital between 1st March 2014, and 30th June 2017, using publicly available data from Health Information System (Version 2) (DHIS2). DHIS2 is a publicly available health information system used by many entities within the healthcare circles in Kenya. Clinicians and record officers at the hospital Comprehensive Care Center (CCC) are routinely required to fill a form which indicates if the interaction with a patient is scheduled or unscheduled. Patients with a scheduled clinical visit are usually given priority while the unscheduled are observed last unless the patient is in critical condition.

2.2. Data Description

Data for HIV care hospitalizations was reviewed between 1st March 2014 and 30th June 2017. Data was obtained from the country's health system (DHIS2). All re-admissions to Kenyatta National Hospital (Kenya's biggest referral hospital) were captured, regardless of department within CCC. The current patients receiving ART as at 30th June 2017 was 8,108. Of these patients 4,382 (54 %) had unplanned care visits during the at-risk period. Patients who had unplanned care visits tended to be older, had higher comorbidity index scores at discharge, and were more likely to have tuberculosis (TB) coinfection.

2.3. Motivation

Unscheduled HIV care visits to a tertiary hospital in resource-limited settings are a major source of pressure on health system resources. Whereas unscheduled hospital visit rates vary in different facilities, the difference in admission rates between emergency departments is even greater in HIV care settings. This situation is significant not only because of the unacceptable variation, but also because of the high and rising unit costs of unscheduled HIV care admissions compared to other forms of care, and because of the disruption emergency admissions cause to elective health care, most notably to in-patient waiting lists, and to the individuals admitted.

It is therefore important to manage unscheduled HIV care visits so as to reduce the burden on resource use in the long term. In order to do this, we need to fully understand which interventions are effective in order to reduce unplanned hospital admissions. In the HIV care settings, there have been community, population and policy level interventions aimed at reducing unscheduled visits but these have yielded little impact on admission rates. A gap is therefore identified for fitting the count data to a parametric distribution after studying a series of comprehensive and systematic literature reviews on the effectiveness of interventions that address the organization and delivery and access to care, with the purpose of reducing unscheduled hospital admissions.

2.4. Negative Binomial Distribution

The negative binomial (NB) distribution has been widely adopted for count responses because of its convenient implementation and flexible accommodation of extra-Poisson variability [12-14]. One of the important properties of the NB distribution is over dispersion.

The probability function of NB distribution with parameters (r-1 number of success) and x failures in $x+r-1$ trials, and success on the $(x+r)^{th}$ trial is given by

$$\Pr\{X = x\} = \left[\binom{x+r-1}{r-1} p^{r-1}(1-p)^{x}\right] p \qquad (1)$$

$$= \Pr\{X = x\} = \left[\binom{x+r-1}{r-1} p^r (1-p)^x\right]. \quad (2)$$

2.5. Goodness-of-fit

2.5.1. Smooth Test of Goodness-of-fit

Suppose we wish to test the null hypothesis that $X_1, X_2, \ldots, X_n$ is a random sample from a binomial distribution with the probability function $Pr\{X=x\}$. A smooth test can be constructed by extending Neyman's goodness-of-fit approach by nesting the null hypothesis in a larger class of probability distribution functions [2, 5].

The first step is to embed the null probability density function in an order *k* alternative as follows:

$$\varphi_k(x,\theta,\beta) = C(\theta,\beta)\exp\left\{\sum_{i=1}^{k}\theta_i h_i(x,\beta)\right\} f(x,\beta), \quad (3)$$

where $h_i(x,\beta)$ is orthonormal to $f(x,\beta)$, and $\beta = (\beta_1, \beta_2, \cdots, \beta_m)$ is vectors of real parameters and $C(\theta,\beta)$ is a normalizing constant that ensures $\varphi_k(x,\theta,\beta)$ integrates to one *i.e*.

$$\int_{-\infty}^{\infty} \varphi_k(x,\theta,\beta) = \int_{-\infty}^{\infty} C(\theta,\beta)\exp\left\{\sum_{i=1}^{k}\theta_i h_i(x,\beta)\right\} f(x,\beta) = 1 \quad (4)$$

Assuming that the partial derivatives of logarithm of the likelihood function together with their expectations exist, the derivation of score test statistics using maximum likelihood function for the observed random sample $X_1, X_2, \ldots, X_n$ have extensively been covered by [5, 19].

For *k* small, the alternative varies smoothly from the null. The score test is based on statistic $\hat{\varphi}_k = \sum_i^n \hat{\phi}_i^2$ [19] in which

$$\hat{\phi}_i = \sum_{j=1}^{n} \frac{h_j(X,\hat{\beta})}{\sqrt{n}}, \quad (5)$$

where $\hat{\beta}$ is the maximum likelihood estimate of β.

The first four orthonormal functions have been derived by Rayner and Best [2]

2.5.2. Other Goodness-of-fit Test

Since we are dealing with complete data, we employ other standard goodness-of-fit methods. The other goodness-of-fit tests considered here are Chi-square test (X^2), Anderson-Darling (A^2), Kolmogorov-Smirnov test (D_n) and Cramer-von-Mises (ω^2).

The X^2, A^2, D_n and ω^2 tests are based on departure between the empirical distribution function $\mathbf{F_n}$ and theoretical distribution function $\mathbf{F_0}$ of the sampled data. The null hypothesis is rejected when the difference is too large with a conclusion that the sampled data does not come from the underlying distribution [15].

Chi-square test

In Chi-Square goodness-of-fit test, the null hypothesis assumes that there is no significant difference between the observed and the expected value while the alternative hypothesis assumes that there is a significant difference between the observed and the expected value. The Chi-Square goodness-of-fit test uses the formula:

$$X^2 = \frac{(O-E)^2}{E}, \quad (6)$$

where, X^2 is the Chi-Square goodness-of-fit test, O is the observed value and E is the expected value.

Anderson-Darling test of goodness-of-fit:

$$A^2 = -n + \frac{1}{n}\sum_{i=1}^{n}\left[(2i-1) - 2n\ln(1-U_i^*) - 2(2i-1)\ln U_i^*\right]. \quad (7)$$

One-sample Kolmogorov-Smirnov test:

$$D_n = \sqrt{n}\ \sup|F_n(x) - F_0(x)| \quad (8)$$

$$= \sqrt{n}\ \max\left[\max\left\{\frac{i}{n} - U_i^*\right\}, \max\left\{U_i^* - \frac{i-1}{n}\right\}\right]. \quad (9)$$

Cramer-von Mises statistic (CM):

$$\omega^2 = \sum_{i=1}^{n}\left(\hat{U}_i^* - \frac{2i-1}{2n}\right)^2 + \frac{1}{12n}, \quad (10)$$

where $\hat{U}_i^* = F_0(\ln X_i)$.

2.5.3. Simulations

We conducted extensive simulations to assess the performance of a Chi-square test, Kolmogorov-Smirnov test, Crammer-Von Misses test and Andersen-Darling with that of smooth test. Let *x:* the number of trials required to produce *r* successes in a negative binomial experiment and *P*: the probability of success on an individual trial. All simulations were conducted using R. Because the NB random number generator in R does not allow non-integer values of *k,* NB random

variates were simulated using the fact that the NB distribution can be derived as a Poisson distribution with gamma-distributed intensity, *i.e*. a Poisson-gamma mixture. First, n values g_i was drawn from a gamma distribution with mean m and dispersion parameter k. Second, each of these values was used as the intensity parameter for a Poisson random variate to yield an NB-distributed value.

The bootstrapping procedure was applied 1,000 times to each generated dataset to obtain the significance level of the test. The size estimates were based on the proportion of replications that indicate acceptable fit, with a larger number of replications resulting in smaller CIs (higher power, more accuracy) around the estimates.

To investigate the performance of the different tests, we evaluated the exponential, Weibull and Gamma null hypothesis against their generalized alternatives for the initial distribution of failure ages. Hence, given the values of different parameters, values for each alternative were generated. Simulations were done for the 5% asymptotic level tests. We also performed simulations for values of the Negative Binomial Distribution and found the results to be consistent. Examining the performance of the directional tests, we again noticed that we are able to achieve required significance levels. Figures **1**, **2**, **3** and **4** summarize the percentage rejection of the tests for Chi-square, Kolmogorov-Smirnov, Cramer-Von Misses, Anderson Darling and Smooth Test of GOF. The fact that the test

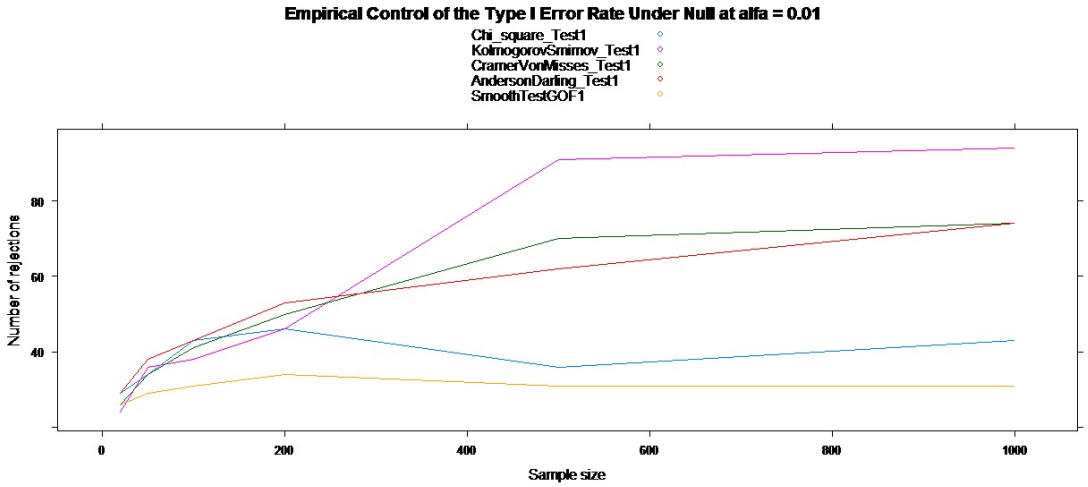

Figure 1: Graph of Empirical Control of the Type I Error Rate Under H_0 for Chi-square Test, Kolmogorov Smirnov Test, Cramer Von Misses Test1, Anderson Darling Test and Smooth Test of GOF at α=0.01, x (no. of trials to get r successes)=3 and P (probability of success)=0.4.

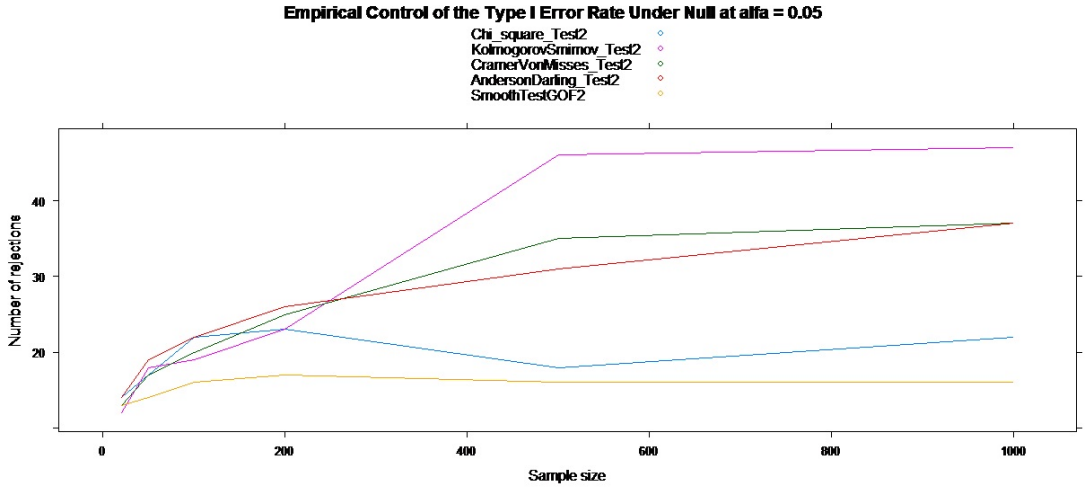

Figure 2: Graph of Empirical Control of the Type I Error Rate Under H_0 for Chi-square Test, Kolmogorov Smirnov Test, Cramer Von Misses Test, Anderson Darling Test and Smooth Test of GOF at α=0.05, x (no. of trials to get r successes)=5 and P(probability of success)=0.6.

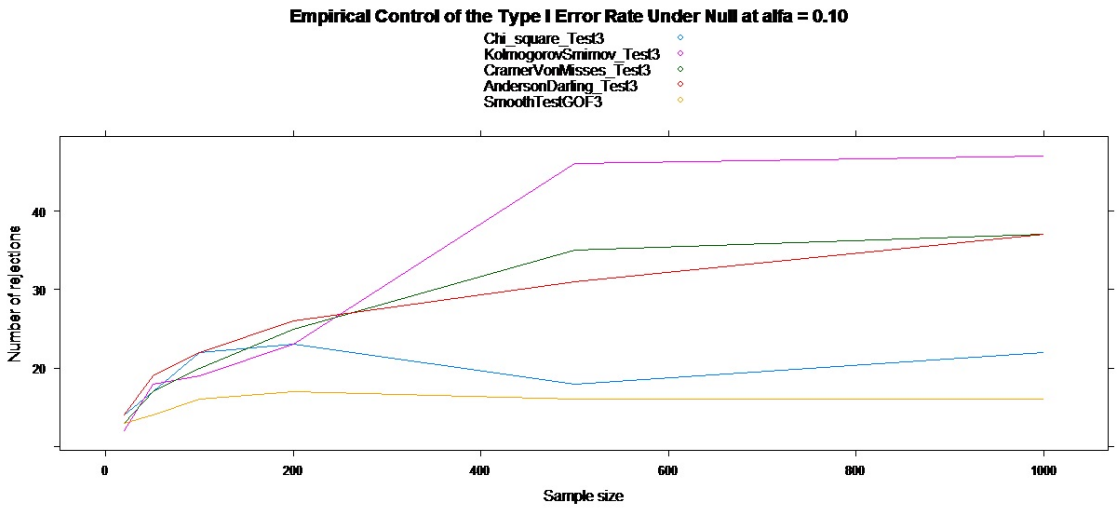

Figure 3: Graph of Empirical Control of the Type I Error Rate Under H_0 for Chi-square Test, Kolmogorov Smirnov Test, Cramer Von Misses Test, Anderson Darling Test and Smooth Test of GOF at α=0.10, x (no. of trials to get r successes)=10 and P (probability of success)=0.75.

is powerful for this alternative is expected because it was derived against such alternatives, whereas the observation that the 4 test is not powerful for this alternative is also expected because the normalized total-time-on-test statistic is invariant to changes in scale.

3. APPLICATION AND RESULTS

A total of 221,371 HIV clinical visits occurred between 1st March 2014, and 30th June 2017. 88,759 (40%) were unscheduled visits. The demographic characteristics of both scheduled and unscheduled HIV clinical visits are summarized in Table **1**. There were statistically significant differences between the two groups in relation to gender (p- value = 0.002), age (p - value = 0.001) and mode of arrival (p-value = 0.05). Univariate analysis revealed significant differences between the two groups of patients in relation to their mode of arrival, gender, age group and region of origin.

Analysis showed that some factors were associated with a higher risk of unscheduled HIV clinical visits (Table **2**). In terms of demographic variables, female patients had a relatively lower risk (RR 0.88; p-value =0.002) of unscheduled clinical visit than male patients. The age group (71-80 years) had a relatively higher risk (RR 1.59; p-value= 0.006) compared to those aged 21–30 years. Regions of patient's origin were not significant. Regarding variables related to mode of arrival to the hospital, patients who did not arrive by ambulance had a relatively lower risk (RR 0.88; p-value= 0.001) of an unscheduled clinical visit than patients who arrived by ambulance.

Table 1: Demographic Characteristics

	Scheduled Visits	Unscheduled Visits
Gender		
Male	49,111	77,121
Female	39,648	55,491
Total	88,759	132,612
Age group (Year)		
21–30	13,314	19,892
31–40	25,740	38,457
41–50	26,628	39,784
51–60	8,876	13,261
61–70	6,213	9,283
71–80	7,988	11,935
Total	88,759	132,612
Region		
Western Kenya	19,704	29,440
Rift Valley	10,651	15,913
Central Kenya	28,048	41,905
Eastern Kenya	12,426	18,566
Coast	17,929	26,788
Total	88,759	132,612
Mode of arrival		
Ambulance	52,550	67,669
Non-ambulance	36,209	64,943
Total	88,759	132,612

Table 2: Univariate Analysis using Logistic Regression with Gender, Age-group, Regional Area and Arrival Mode as Covariates

Variable	Adjusted RR	95% CI	p-value
Gender			
Male	1	ref	
Female	0.78	0.68, 0.88	0.002
Age group (years)			
21–30	1	ref	
31–40	1.33	1.12, 1.41	0.003
41–50	1.21	1.02, 1.33	0.006
51–60	1.31	1.18, 1.47	0.005
61–70	1.28	1.04, 1.35	0.003
71–80	1.42	1.2, 1.6	0.006
Region			
Western Kenya	1	ref	
Rift Valley	0.98	0.66, 1.12	0.423
Central Kenya	0.84	0.74, 1.11	0.331
Eastern Kenya	0.9	0.81,1.12	0.123
Coast	0.77	0.74, 1.11	0.221
Mode of arrival			
Ambulance	1	ref	
Non-ambulance	0.88	0.71, 0.88	0.0023

Rayner and Best [5] described how to calculate the components r^{th} component ϕ_r. This is a contrast in the differences observed minus expected standardized to be asymptotically independent and standard normal are not unique. If such a statistic is judged to be significant; interpretation would be that the r^{th} cell differs from its predecessors in the cell expectations and observations. For this data set we find corresponding p-values (from the ϕ_k) to be:

Table 3: Results of Smooth Goodness-of-fit Test of Sample Data for HIV Care Visits Fitted to Negative Binomial Distribution, using Order 4 with Method of Moment's Estimates. Nuisance Parameter Estimation is Computed using MME to get Parameter Estimates: 2.934074 0.001320519. Smooth Test Statistic ϕ_k= 0.1939066, p-value = 0.295. All p-values are obtained by the Bootstrap with 200 Runs

Order	ϕ_k	P-value
3rd	3th theoretically rescaled component ϕ_3 = -0.2203112	0.65
4th	4th theoretically rescaled component ϕ_4 = 0.	0.86

$$\phi_3 = -0.2203112$$

$$\phi_4 = 0.04347796$$

Since all the p-values are relatively large, the data has stood up to scrutiny of the negative binomial hypothesis and resoundingly confirmed analysis that non-rejection of the null hypothesis. See the results below.

CONCLUSION

The problem of testing that data of unscheduled HIV clinical visits fits a negative binomial distribution was considered. This problem is intrinsically related to that of validating whether NB is viable in light of the observed data. The goodness-of-fit procedures were derived as score tests obtained by embedding the null distribution in a larger family of probability distribution, with this family developed through smooth transformations. The resulting goodness-of-fit procedures are also related to model validation procedures.

Examination of the results suggests that the smooth goodness-of-fit test based on ϕ_i does provide a compromise between the omnibus tests and directional

tests. Clearly, k must be chosen without reference to the data in order to ensure a test of the desired size. Neyman [20] recommended that, in the absence of special knowledge about a particular problem, one should not select a value of k greater than four.

According to the results of this study, it can be concluded that unscheduled HIV care visits are imposing several burdens for health care systems. However, proper prediction is paramount to minimizing unplanned visits. Policy makers should thus consider fitting along with the evaluation of other aspects of readmission based on the fundamental researches.

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