Journal of Public Health in Africa ...research and practice

Time series analysis of Nevirapine syrup consumption in prevention of mother-to-child transmission and optimal supply chain model in Oshana region, Namibia.

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Contributions: The authors contributed equally.

Conflict of interest: The authors declare no potential conflict of interest.

Funding: none

Acknowledgements: The authors wish to thank all staffs from Oshana health directorate who plays a key role in the supply chain of essential medicines for their support with the study. No funding was received for the study. There is no conflict of interest in this study.

Key words: Nevirapine syrup; Mother to Child Transmission, HIV/AIDS

This article has been accepted for publication but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the final one.
Please cite this article as doi: 10.4081/jphia.2020.1029

Abstract

Introduction. HIV/AIDS continue to be serious communicable disease whose impact on public health in Namibia is massive. It is estimated that the prevalence rate of HIV in Namibia is 17.2%, ranking the country as the fifth highest in sub-Saharan Africa (SSA). Some improvement in reducing the number of cases of HIV/AIDS has been made in the country, but the sporadic shortage of medicines continues to slow down government efforts to foster the emergence of an HIV-free generation of Namibians
Objective of the study. Develop and demonstrate a mathematical supply-chain model, which can establish parameters to prevent stock-outs of NVP suspension.
Method: The study adopted retrospective approach to acquire data from 2012-2016.
Results. Gamma supply chain model was developed as the optimal model for NVP syrup and forecasted consumption for 2017-2018 was determined.
Conclusion and recommendation. It is a recommendation of this study that new guidelines for implementation of optimal supply-chain models at the regional medical store, health centers and clinics be implemented for Nevirapine syrup.

Introduction

Strengthening of supply chain of Anti-retroviral therapy (ARVs) is very crucial in order to make essential medicines available[1.] In Namibia, several efforts have been done to strengthen supply chain of ARVs, including strengthening Prevention of Mother to Child Transmission (PMTCT) programs, but sporadic shortage has been reported [1, 2] The situation may be caused by the absence of a clear picture of aggregation of consumption figures of Nevirapine (NVP) syrup in medical stores and within health facilities which has not been given much attention. This study has examined the supply-chain system in Oshana region and has developed an optimal mathematical supply-chain models which is needed to ensure achievement of optimal conditions to prevent stock-outs of NVP syrup. The supply chain models help in determining the optimum level of inventories that should be maintained in managing the frequency of ordering, deciding on quantity of medicines to be stored, tracking the flow of supply chain to provide uninterrupted service to customers without any delay in delivery [3.]
The study done in various countries on inventory control with gamma probability distribution encompasses both normal and negative exponential probability distribution models to represent the lead time demand of fast- and slow-moving items respectively, as a special case but also covers the gap left by them. [5] These models play an important part in defining the optimal ordering and pricing policies. [4]
The study conducted in Eastern Uganda on strengthening the program for the prevention of mother to child transmission of HIV, noticed that there was no consistency of NVP syrup supply to the facilities[6]

Study design

A retrospective, quantitative, descriptive design was appraised over a five-year period (2012-2016).

Study setting.

The study was conducted at Oshakati Multi Regional medical depot (OMRMD) and all primary health care (PHC) facilities in Oshana region except Eloolo clinic.

Sampling technique for health facilities

Oshakati Multi Regional medical depot (OMRMD) and all PHC facilities in Oshana region was selected in sampling.

Data collection procedures.

Data of NVP syrup, on initial stock, quantity ordered, received, consumed and expired as from 2012-2016 were collected from all PHC facilities and OMRMD, by examining existing data from Syspro database for inventory management, Baby mother follow up monthly reports, NVP syrup register and Electronic dispensing tools (EDT).

Data analysis.
The data were then analyzed by SPSS version 24 software, in which probability distribution of consumption for NVP syrup was determined. Simple linear regression was applied for time-series analysis to forecast consumption and predict when stock-out would occur. The significance level was set at < 0.05
Assumptions and notations in order to develop an optimal mathematical supply chain model

Assumptions
- Daily demand is stochastic, i.e. daily demand is independent of each other
- Inflation rate is constant.
- Single supplier is considered.
- Health facilities use periodic review inventory policy.
- Transport cost from OMRMD to all PHC facilities is constant.
- The supply of NVP syrup is greater than the demand.
- Storage capacity is the same to all PHC facilities.
- The service level is 98%
- Lead time for each level of the supply chain is constant
- OMRMD deliver the same lot size when the PHC facilities write requisition.
- Shortage of NVP syrup is not allowed.

Notations
- AMC= Total average monthly consumption of NVP syrup for all PHC facilities.
- Q_o=Optimal reorder quantity of NVP syrup.
- S_o=Stock on hand at order point.
- D_i= Monthly demand.
- L = Lead time in days.
- rf = Optimal reorder frequency per year in days.
- SS =Optimal safety stock of NVP syrup.
- 1-α = Probability of no stock out of NVP syrup during lead time.
- μD=Mean demand of NVP syrup
- $\sigma^2 D$= Standard deviation demand
- μL=Mean lead time
- σ^2L=Standard deviation lead time.
- Qmax = Optimal maximum stock level of NVP syrup.

Formulation of mathematical supply model.
Cycle inventory = AMC (L+rf) and safety inventory is Zσ (AMC (L + rf).
AMC=μD-------------------------- (i).
Therefore *μD(L+rf)* and the safety stock level(ss) is
SS= zσ (μD (L+rf) ------------------------(ii)
The demand during lead time, plus review period DL =$\sum_{i=1}^{L+r} Di$ follows a normal distribution, whose expectation and variance can be calculated similarly as before

Expected demand (E)

$E[DL+rf] = E[\sum_{i=1}^{L+r} Di] = (rf + \mu L)\mu D$……………………. (iii) The Variance (V) =

$V[DL+rf] = V[\sum_{i=1}^{L+r} Di] = (rf + \mu L)\sigma^2 D + \sigma^2 L \mu^2 D$………. (iv). Qmax = (iii) + (iv)

$Qmax = \mu D(\mu L + rf) + z\alpha\sqrt{(\mu L + rf)\sigma 2D + \mu 2D\sigma 2L}$ --------------------------- (v)

To prevent a stock out of NVP syrup during the lead time, the service level (1- α) should be 98%.

Therefore $Qmax = \mu D(\mu L + rf) + 2.05\sqrt{(\mu L + rf)\sigma 2D + \mu 2D\sigma 2L}$ -----------------------(vi)

The quantity to order (Q_o) is replenishment level minus quantity on hand.

$Q_o = Qmax - S_o$-------------------------------(vi)

Ethical consideration

The ethical approval was obtained from the University of Namibia (UNAM), School of Public Health, Ministry of Health and Social Services (MoHSS) and from respective study sites.

Results

The optimal supply chain model was calculated, based on the frequency distribution of NVP syrup consumption for PHC facilities and OMRMD combined, which was adjusted to specific distribution using chi square goodness of fit test. Forecasting was used to determine future consumption of NVP syrup. Reorder point and frequency were also calculated based on collecting data.

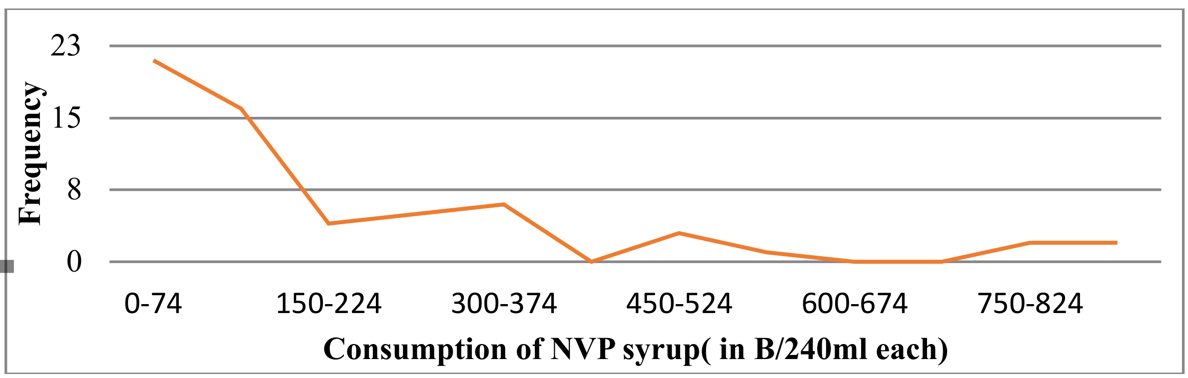

Figure 1 Frequency polygon curve of consumption of NVP syrup for health facilities from 2012-2016 (N = 60)

Figure 1, depicts a frequency polygon in which the distribution is positively skewed with high kurtosis. Resemble as gamma distribution

Null (H_o) and alternative (Ha) hypothesis was stated that the frequency distribution of NVP syrup consumption follows gamma probability distribution and does not follow gamma probability distribution respectively.

Table 1 Observed and expected frequency of NVP syrup consumption for all health facilities (N=60)

Frequency			
	Observed frequency	**Expected frequency**	**Residual**

6.0	6	21.0	-15.0
8.0	8	16.2	-8.2
9.0	9	9.0	.0
16.0	16	6.0	10.0
21.0	21	7.8	13.2
Total	60		

Test Statistics	
	Frequency
Chi-Square	53.87
df	4
Asymp. Sig.	0.16

$\chi 2(4) = 53.87$, $p= 0.16 > 0.05$. Therefore, there is statistically significant, enough evidence that the distribution of consumption of NVP syrup at PHC facilities and OMRMD follows a gamma distribution.

Table 2 Quarter year consumption of NVP syrup and forecasting for all health facilities (N=60)

			Y_t		Baseline	Y_t/CMA		Y_t/S_t	T_t	
t	Year	Quarter	C_p	MA (4)	CMA (4)	S_t, I_t	S_t	Deseasonalize		Forecasting
1	**2**	1	354				0.83	426	302	251
2		2	738				0.81	911	339	275
3		3	253	560.75	569.62	0.44	0.72	351	377	271
4		4	898	578.5	556.87	1.61	1.37	655	414	567
5	**3**	1	425	535.25	524.25	0.81	0.83	512	451	374
6		2	565	513.25	460.12	1.23	0.81	697	489	396

7		3	165	407	403.5	0.41	0.72	229	526	379
8		4	473	400	359.37	1.32	1.37	345	563	771
9	**4**	1	397	318.75	357.62	1.11	0.83	478	601	499
10		2	240	396.5	417.25	0.57	0.81	296	638	516
11		3	476	438	442.37	1.08	0.72	661	676	487
12		4	639	446.75	465.62	1.37	1.37	466	713	977
13	**5**	1	432	484.5	475.75	0.91	0.83	520	750	622
14		2	391	467	450.62	0.87	0.81	482	788	638
15		3	406	434.25	421.5	0.96	0.72	563	825	594
16		4	508	408.75	429.9	1.18	1.37	370	863	1182
17	**6**	1	330	451	687.5	0.48	0.83	397	900	747
18		2	560	924	1014.6	0.55	0.81	691	937	759
19		3	2298	1105.3			0.72	3191	975	702
20		4	1233				1.37	899	1012	1386
21	**7**	1					0.83		1049	871
22		2					0.81		1087	880
23		3					0.72		1124	809
24		4					1.37		1161	1591
25	**8**	1					0.83		1199	995
26		2					0.81		1236	1001
27		3					0.72		1274	917
28		4					1.37		265	363

The classic multiplicative model (Y_t=S_t x I_t x T_t) was used to derive seasonal and irregular components, while a simple linear regression was used to forecast and assess the fitness. Year 2-8, represent 2012-2018. MA (4) is a moving average of four periods. CMA (4) is a centered, moving average of four periods. S_t is the seasonal trend, it is irregular trends, C_p is the forecasted consumption of Nevirapine syrup in over a quarter and T_t is the time trend.

Table 2 indicates that in quarter 1, 2 and 3 the consumption of NVP syrup is below the baseline by 17%, 19% and 28% respectively and quarter 4 is above the baseline by 37%. Consumption of NVP syrup in year 2017-2018 was forecasted

Table 3 Replenishment time for NVP syrup at PHC facilities and OMRMD

Year	Quarter	Actual replenishment time (days)	Expected replenishment time (days)	Variance	C_p
2012	1	0	0	0	251
	2	56	30	26	275
	3	49	30	19	271
	4	141	30	111	567
2013	1	53	30	23	374
	2	37	30	7	396
	3	17	30	-13	379
	4	71	30	41	771
2014	1	21	30	-9	499
	2	16	30	-14	516
	3	33	30	3	487
	4	33	30	3	977
2015	1	20	30	-10	622
	2	27	30	-3	638
	3	32	30	2	594
	4	9	30	-21	1182
2016	1	37	30	7	747
	2	42	30	12	759
	3	38	30	8	702
	4	0	0	0	1386
Total				**192**	**12393**

For a month = 9.6/3= 3.2 days, therefore replenishment time is 10+3 = 13. Hence the standard deviation of lead time (σLT) = 13 days. This is also the amount of time that safety stock will have to hold at all health facilities combined. For the demand average (μD) = AMC =12393/60= 206 B/240ml of NVP syrup= μD. For the daily demand of NVP syrup =12393/ 20 x 60 =10B/240ml of NVP syrup. The safety stock (ss) is 13 x 10= 130 B/240ml of NVP syrup. The safety stock level = ss = Z × ΣLT × μD =2.05 x 13 x 10 =266 B/240ml of NVP syrup as a safety stock.

Reorder point of NVP syrup (ROP)
ROP = 13 x 13 +266 = 435 B/240ml of NVP syrup.

Optimal reorder frequency
= 60 orders needed /32 orders requested = 1.8 months, which is equivalent to 1.8 x 4 weeks = 7 weeks. Optimal reorder frequency is 7 weeks.

Gamma supply chain model for consumption of NVP syrup
For the consumption of NVP syrup at health facilities, the mathematical model proposed is a gamma probability distribution model with probability density function as follows,
$f(\mathrm{x}, \gamma, \beta) = \frac{\left(\frac{10-206}{233}\right) exp\left(\frac{-10-206}{233}\right)}{\beta\Gamma(\gamma)}$.x ≤ μ;$\beta$ >0. The equation above can be rewritten as the equation below
$\Gamma(x) = \int_0^{\propto} t^{x-1} e^{-t}\, dt$ where $\Gamma(x)$=gamma function.
$\beta$is scale parameter = variance /consumption of NVP syrup with non-zero observation = 48092/206 ~ 233. ∝ is shape parameter = consumption of NVP syrup with non-zero observation/standard deviation =$206/219 \approx$ 1. From the formula above $\Gamma(x)$= 0.0018~ 0.18%.

Table 4 Simulation for gamma probability distribution model

	1-month interval	2-month interval	3-month interval
Mean demand	88	198.84	200.36
SD	0.015	0.012	0.010
Random demand	120	180	226

From the table above, it shows that simulation of 2-month reorder interval is not far from the mean demand of 206.
In this study Monte Carlo simulation technique was used to assess the performance or the impact of gamma supply chain model at 1-month interval, 2-month interval and 3-month interval. The table 4 shows the impact of the supply chain model by a reorder interval of 1 months, 2 months and 3 months. In gamma probability distribution model 1000 cases were simulated. Note that exponential and normal distribution are the special cases of gamma distribution probability models.

Discussion
Figure 1, show that consumption of NVP syrup follows gamma distribution and this was confirmed by chi-square goodness of fit test as indicated in table 1. In the consumption forecasting (table 2) indicate

that in every fourth quarter, there is an increase of NVP syrup consumption by almost 37%, while the first three quarters are 17%, 19% and 28% below baseline consumption respectively. Forecasted consumption of NVP syrup has considered all the irregularities or unexpected in NVP syrup consumption.[10,11] Gamma supply chain model for NVP syrup was proposed based on the consumption distribution of Nevirapine syrup as indicated in table 2. The model suggested help to accommodate the fluctuation of the demand of NVP syrup. The fluctuation can be due to seasonalities, irregularities etc. as indicated in table 2. The traditional method is ineffective in estimating consumption/demand, because it does not consider the effects of seasonality or irregularities in consumption of NVP syrup. This method assumes that the demand is normal distributed.[13] As a results the sporadic shortage of medicines, including NVP syrup have been reported in public health facilities[1,2].
Gamma supply chain model has been used in different field, to predict different events which might occur, hence appropriate measures can be taken, including inventories in pharmaceutical sector [13]. Gamma model is fit to inventory of medicines as it is a flexible, which means it has characteristics of other probability distributions like normal, exponential and Poisson [3,5] Therefore, all these distribution models mentioned are part of gamma model.[7] Different studies have shown efficiency of gamma model in strengthening inventories both in pubic and private health facilities. [8,9] Gamma supply chain model was validated by simulation at 1, 2 and 3 month reorder interval as indicated in table 4. The results show that the mean simulated is not far from mean demand of 206 B/240ml. Therefore, the gamma supply chain model is an appropriate fit in preventing stock out of NVP syrup by optimally estimated the demand of NVP syrup at reorder frequency of 7 weeks. In case of traditional method the ordering frequency is 6 weeks. [12].

Limitation

The study conducted in Oshana region only, and exclude the supply chain at the national level.

Conclusion and recommendation.

Optimal gamma supply-chain model developed helps to prevent stock-outs of NVP syrup by predicting when a stock-out might occur, which enables appropriate measures for its prevention. Further studies are needed, which comprises the components of supply chain from all the levels from nation level.

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