Send Orders for Reprints to reprints@benthamscience.ae

BENTHAM OPEN

CrossMark

The Open Biomedical Engineering Journal

Content list available at: www.benthamopen.com/TOBEJ/

DOI: 10.2174/1874120701610010012

The Pratt Pouch Provides a Three-Fold Access Increase to Antiretroviral Medication for Births outside Health Facilities in Southern Zambia

Alexander P. Dahinten and Robert A. Malkin*

[1] *Developing World Healthcare Technologies Lab, Duke University, Durham, USA*

Abstract:

Introduction:

Modern day antiretroviral therapy allows HIV+ pregnant women to lower the likelihood of viral transmission to their infants before, during, and after birth from 20-45% to less than 5%. In developing countries, where non-facility births may outnumber facility births, infant access to safe antiretroviral medication during the critical first three days after birth is often limited. A single-dose, polyethylene pouch ("Pratt Pouch") addresses this challenge by allowing the medication to be distributed to mothers during antenatal care.

Methods:

The Pratt Pouch was introduced as part of a one year clinical feasibility study in two districts in Southern Province, Zambia. Participating nurses, community health workers, and pharmacists were trained before implementation. Success in achieving improved antiretroviral medication access was assessed *via* pre intervention and post intervention survey responses by HIV+ mothers.

Results:

Access to medication for HIV-exposed infants born outside of a health facility increased from 35% (17/51) before the introduction of the pouch to 94% (15/16) after ($p<0.05$). A non-significant increase in homebirth rates from 33% (pre intervention cohort) to 50% (post intervention cohort) was observed ($p>0.05$). Results remained below the national average homebirth rate of 52%. Users reported minimal spillage and a high level of satisfaction with the Pratt Pouch.

Conclusion:

The Pratt Pouch enhances access to infant antiretroviral medication in a rural, non-facility birth setting. Wide scale implementation could have a substantial global impact on HIV transmission rates from mother to child.

Keywords: ARV Access, developing countries, HIV, homebirth, non-facility birth, PMTCT.

INTRODUCTION

Mother to child transmission (MTCT) of HIV accounts for more than 90% of new HIV infections in children [1]. In Sub-Saharan Africa, where 92% of worldwide HIV at-risk births occur, this results in over 200,000 new pediatric infections every year [1, 2]. Infections can occur antenatally, during birth or postnatally throughout breastfeeding. Because newborns with undeveloped immune systems are particularly susceptible to infections, it is vital they be medicated immediately after birth. Over 35% of HIV infected infants die before their first birthday and more than half

* Address correspondence to this author at the Department of Biomedical Engineering, Duke University, Hudson 136, Box 90281, Durham, NC 27708, USA; Tel: 919-660-8266; Fax: 919-684-4488; Email: robert.malkin@duke.edu

do not survive past the age of two [3]. Antiretroviral therapy (ART) has been shown to effectively lower MTCT from 20-45% to less than 5% [4]. In the past, the United Nations and the global health community, building on the Millennium Development Goals, have set the ambitious aim to "achieve universal access to treatment for HIV/AIDS" by providing ART to 15 million people, including newborns, by the end of 2015 and claim to be on target to achieve this goal [5].

Although antiretroviral (ARV) medication is effective, in low-resource countries mothers and infants often lack access. The obstacles that contribute to limited ARV access are numerous, including: supply chain distribution challenges; lack of trained community health care providers and high home birth rates. Most notably, medicine distribution networks in developing countries struggle to keep hospitals and clinics in rural communities supplied with the necessary medication. In Zambia, an estimated 88% of HIV+ pregnant women (PW) and 38% of HIV+ children under the age of fifteen receive ARVs [6]. Additionally, 52% of births in Zambia occur outside of a health facility (hospital or clinic) making it difficult for mothers to access medication for their infants immediately after birth [7]. Although often available in-country, ARV medication is not reaching mothers who have a high likelihood of giving birth outside of a hospital or clinic environment.

In 2006, PATH (Seattle, WA, USA) piloted a technology to optimize medication distribution by pre-dosing Exacta-Med oral syringes with Nevirapine (NVP) and packaging them into adhesive foil bags. PATH conducted a successful four month pilot in five provinces in Kenya, however the technology never reached large-scale distribution. Furthermore, the drug was only predicted to remain effective for two months due to moisture and preservative loss; contain choking hazards in the form of a removable tip and suffered from leaky syringes [8]. In developing countries, pregnant women may only come to a health facility once before birth, and hence any packaged ARV provided antenatally must remain active for much longer than two months.

Building upon the idea of providing pre dosed medication, the Pratt Pouch (Fig. **1**). was designed to package ARVs in single use, heat sealed polyethylene pouches [8 - 11]. This solution addresses newborn ARV access challenges by optimizing the amount of medication provided to mothers antenatally, and hence eliminating wastage. Furthermore, user and stability testing has shown that the Pratt Pouch preserves the active ingredients for all three commonly prescribed infant ARV drugs (NVP, AZT, 3TC) for at least one year [8, 9]. These storage properties allow pouches to be packaged, stored and distributed in rural communities over an extended period of time once a bottle of medication has been opened. The pouch has also been shown to be a highly accurate delivery vehicle for mothers at home [12].

Importantly, the Pratt Pouch is easily incorporated into the current medical supply chain and can be either used as a "bridge" or a "full" intervention. In the full intervention, the entire postnatal infant ARV regiment is packaged into pouches and distributed to mothers after giving birth either at home or at a health facility [12]. In the bridge intervention, a pre-determined number of pouches are distributed to all HIV+ pregnant women who come to a health center for antenatal care. If birth occurs outside of a health facility, the mother is able to dose her infant immediately.

Fig. (1). The pratt pouch.

This feasibility study documents the first district-wide clinical implementation of the Pratt Pouch's bridge model in two rural districts of Zambia. The impact on access and user acceptability is discussed, in addition to the training and distribution processes.

METHODS

This operational study was approved by the Zambian Ministry of Health; the Zambian PMTCT Technical Working Group; the Pharmaceutical Regulatory Authority of Zambia and the UNZA Biomedical Research Ethics Committee.

A total of four cohorts of women participated in this study; one cohort provided pre intervention data and three overlapping cohorts provided post intervention data. In September of 2013, a Pratt Pouch team member with the help of a local interpreter collected survey only control data from all known, consenting HIV+ mothers who had delivered a live child in the previous three years. Data was collected from women who presented in Siavonga District, Zambia (Chaanga and Sianyoolo Health Centers) and Chirundu District, Zambia (Chipepo, Kapululira, and Lusitu Health Centers). These mothers had not received the Pratt Pouch intervention, and were considered part of the "pre intervention" control cohort (cohort 1). Participating women were asked: (1) if they had a live birth in the last three years; (2) if they had a live birth, did they give birth in a health facility and (3) did their child receive ARVs within the first three days of life. No additional questions were asked and no identifying information was recorded. Each clinic was visited only once.

In October of 2014, a post intervention survey was conducted by a Pratt Pouch team member with the help of a local interpreter. All consenting HIV+ women who presented in Siavonga District, Zambia (Chaanga, Kariba, and Sianyoolo Health Centers) and Chirundu District, Zambia (Chipepo, Kapululira, and Lusitu Health Centers) and who delivered a live child in the previous year were asked to participate. These mothers had received the Pratt Pouch intervention, and were considered part of the "post intervention" experimental cohort (cohort 2). Participating women were asked: (1) if they had a live birth in the last year; (2) if they had a live birth, did they give birth in a health facility; (3) did their child receive ARVs within the first three days of life; (4) what method was used to deliver the first dose of ARV and (5) if they delivered outside of a health facility, why they did so. No additional questions were asked and no identifying information was recorded. Each clinic was visited only once.

Data on candidate and enrolled HIV positive, pregnant women was collected throughout the year long intervention. The third cohort (candidate mothers) was defined as all HIV+, pregnant women who were identified by trained staff at selected clinics or on outreach visits to surrounding villages during the duration of the study. The fourth cohort (enrolled mothers) consisted of all candidate women who came to a health clinic and agreed to be enrolled in the study during the intervention.

The Pratt Pouch intervention occurred between the two surveys and began with training pharmacists, nurses, and community health workers (CHW). This training was subcontracted to IntraHealth International who collected and anonymized both the patient and survey data. In November of 2013, each healthcare worker cadre was classroom trained by an American HIV specialist. Nurses and CHWs completed a half-day training. Pharmacists completed a full day training that was complemented with an in service training by a Zambian in December of 2013. All cadres' training was validated in February of 2014 with oral test questions. Additionally, pharmacist filled pouches were spot-checked (weight and burst testing) in February of 2014.

After successful validation, pharmacists at Siavonga District and Mtendere (Chirundu) District Hospital filled, sealed, and stockpiled pouches for use during the study. Each pouch was filled with 2.2ml of Nevirapine (50mg/5ml; Cipla, Mumbai (India)). Pouches were individually filled using a 3ml syringe (Norm-Ject, A3) with a 14 gauge dispensing tip (Metcal, TT14-DHUV-PK). Once a pharmacist opened a bottle, they continued to fill pouches until the bottle was empty. Filling procedures were identical to a 2012 study in Tanzania [9]. All pouches were marked with a single 3/4' x 1' laser inkjet label (Gaylord, 341L) that included: medication name, dose, pouch fill date, expiration date and batch number. Once labelled, seven pouches and a pictorial user instruction sheet were packaged into small, transparent plastic bags and stockpiled.

CHWs performed paid outreach trips to rural villages surrounding: Chaanga, Chipepo, Kapululira, Kariba, Lusitu, and Sianyoolo Health Clinics. On these trips, workers identified HIV+ pregnant women and introduced them to the Pratt Pouch. These candidate women were encouraged to visit the local clinic for antenatal care and to enroll in the study. CHWs worked closely with the nurses, informing them about newly identified mothers. Nurses requested a bag of pouches for each candidate mother from the pharmacist. All candidate women who were seen by nurses at the clinics were eligible for enrollment. Not all mothers who were identified as candidates were enrolled. Enrolled mothers received a bag containing seven filled Pratt Pouches and a user instruction sheet. They were also orally instructed how to correctly use the pouch and given the opportunity to ask questions. Mothers were not given test pouches to practice with nor shown how to use the pouch with demonstration pouches. Enrolled women were encouraged to give birth at a

health facility. If they were unable to give birth at a health facility, they were instructed to orally administer one pouch per day to their newborn and to return to the clinic as soon as possible, but no later than seven days after birth.

After giving birth, enrolled women returned to the clinic for a postnatal visit. At this point, all mothers returned used and unused pouches and completed a "user feedback survey" about their experience. Mothers were asked: (1) how long after birth their infant received the first ARV dose; (2) whether they used the pouch as instructed by the nurse and (3) if they found the included instructions helpful. Mothers were also asked to (4) estimate the amount of spillage that occurred and (5) if they liked the pouch and would use it to give other medication to their infant. Only women who delivered live babies were surveyed.

All candidate women who delivered live babies but were not enrolled during the study for whatever reason were defined as "missed". There was no way to accurately predict whether missed mothers delivered outside of a facility or not (since they never enrolled). To approximate the number of mothers who were missed and gave birth outside of a facility, the pre intervention non facility birth rates were used. Using this number allowed for an approximate ARV access rate recorded during intervention to be calculated ("in study estimated ARV access rate"). Mothers who gave birth at a health clinic or returned for a postnatal visit received a full 240ml bottle of liquid formulation ARV for their infant and were told to continue dosing their child in accordance to national PMTCT guidelines.

RESULTS

There were 51 HIV+ mothers surveyed at clinics prior to pouch intervention and 32 HIV+ mothers surveyed at clinics after the pouch intervention. During the study, 169 HIV+, pregnant women were identified as candidates of which 160 were enrolled and 67 gave birth during the study. Nine women were missed.

Pre intervention survey data found that only 35% (6/17) of HIV+ mothers who had non-facility births were able to medicate their newborn within three days. Of the post intervention mothers surveyed, 94% (15/16) had medicated their child within three days ($p<0.05$). This is nearly a three-fold increase in access to ARVs for non-facility births.

During the study, nine women were missed. Candidate women were missed due to: a national liquid formulation NVP shortage (6); mothers denying their HIV status (2) and refusing to use pouches for religious reasons (1).

The in-study estimated ARV access rate was 27/30, *i.e.*, 90% of candidate women who gave birth at home were able to medicate their infant within three days during the study, very close to the post intervention survey results.

There was some increase in the rate of non-facility births among all HIV+ mothers surveyed before and after the study from 33% (17/51) to 50% (16/32) - though the difference was not statistically significant. The user feedback survey data reported a non facility birth rate of 45% (30/67). As a reference, the national average non-facility birth rate is 52% [7]. The results are summarized in (Table **1**).

Table 1. Summary of the collected pre intervention, in-study, and post intervention data.

	Pre intervention	**In-study (Estimated)**	**Post intervention**
HIV+ women	51	67	32
HIV+, non-facility births	17 (33%)	30 (45%)	16 (50%), *p>0.05*
HIV+, non-facility births where infant was unable to access NVP < 3 days	6 (35%)	27 (90%)	15 (94%), *p<0.05*

When asked why they gave birth outside of a facility, 69% of mothers in the post intervention cohort stated they did not have access to transportation. A further 19% had an unexpected, sudden delivery and 12% gave birth on the way to a facility. No woman mentioned that the Pratt Pouch influenced her decision.

The pouch was primarily used as a bridge: 73% of mothers used at least 3 pouches and 88% used less than 7 pouches before visiting a clinic. This indicates that while women could have used more pouches they did not. Using the Pratt Pouch did not discourage women from returning to a health facility with their infant after birth for a postnatal follow up visit.

Survey responses were collected from 26/30 enrolled mothers who had non-facility births. All 26 reported: (i) no problems using the pouches as instructed by the nurse; (ii) finding the instructions useful and (iii) finding the pouch easy to use. While dosing their infants, 38% (10/26) mothers did not spill any medication and 62% spilled "a little/ a few drops". No mother spilled "a lot of medication". All infants (25/25) accepted the medication in the pouch. Finally, 92% (24/26) of mothers "liked using the pouch" and 100% (25/25) would "use it in the future to give other medication to their infant".

DISCUSSION

Within one year, the Pratt Pouch significantly increased access to ARV medication for HIV exposed infants born outside of a health facility from 35% to 94% ($p<0.05$). Expansion of the use of the Pratt Pouch could dramatically increase access to ARV's for children born at home globally.

Despite this remarkable success, there remain barriers to universal access. Access depends on the ability of healthcare workers to perform HIV testing and subsequent availability of liquid formulation ARVs. In this study, we could have approached 100% access if there had not been a national medication shortage, a circumstance that is not uncommon in low resource countries. In 2013, more than 20% of national health facilities in South Africa reported a stock out or shortage of ARV and/or TB medication in the preceding three months, with provincial percentages ranging from 4.4% to 53.9% [13]. Over the past 20 years, extensive investment in national health systems mainly by foreign organizations in the form of effective supply chain managements and Global Health Initiatives has significantly improved access to health services and medication in Sub-Saharan countries [14, 15]. However, reaching rural, underserved populations still poses a significant challenge to achieving universal access. Widely implementing the Pratt Pouch will help.

During the study, it was important to align the need for ARV access intervention with encouraging facility births because giving birth outside of a clinic exposes both the mother and the infant to risks beyond HIV [16, 17]. Although the post intervention, non facility birth rate saw an increase (from 34% before to 45% during), it was not significant and remained below the national average of 52% [7].

In addition, no mothers stated the pouch as a reason for having a non facility birth. On average, HIV+ women who had non-facility births lived almost 4km further away from a health facility than ones who had births at a clinic. This suggests that barriers to clinic access such as cost and time are far more predictive of facility birth than the provision of medication in advance [18]. This finding is supported by studies on advanced distribution of Misoprostol in developing countries which found no related increase in non-facility births and even some decrease [19, 20].

In this study, mothers successfully used the Pratt Pouch as a bridge before accessing health facilities. All enrolled mothers brought their infant to a clinic within seven days of being born, indicating that the end of the pouch supply was not the reason they returned to the clinic. Since 73% used at least three pouches, this suggests that mothers needed to recover before returning to the clinic. At the clinic, mothers were given a bottle of NVP by the nurse and instructed to continue dosing their infants with the included syringe. In future interventions, Pratt Pouches could also be used as a substitute for syringe dosing. In Ecuador, pharmacists package enough pouches to allow mothers to administer 30 days' of ARV to their infants [12]. By replacing the syringe, the ARVs are stored in a more controlled environment and mothers are not required to measure, leading to more accurate dosing.

Accurately dosing ARV medication is important because overdosing can cause life threating side effects and underdosing can lead to viral drug resistance [21, 22]. A related study in Mozambique reported that approximately 50% HIV+ mothers deviated from a reference dose by greater than 20% when measuring ARV medication using either a cup or a syringe [23]. Enrolled mothers in Ecuador have previously been shown to administer an average of 101% of the intended dose when using the Pratt Pouch [12]. Based on the spillage reported by mothers enrolled in this study, we expect similar accuracy to that reported in Ecuador.

Training is an important component of the effective use of the Pratt Pouch. Within one year, a total of 41 health care workers at eight different facilities were successfully trained; 16 nurses, 18 community health workers and 7 pharmacists. Initially, all three cadres were trained in classrooms by an American HIV specialist who had not previously worked in the country. Three months after training, a follow up quiz confirmed information retention in nurses (8) and CHW (11).

Pharmacist training validation follow up was conducted two weeks after training. At first, 6/7 (86%) pharmacists were not able to accurately fill or seal pouches. In response, these six pharmacists were individually re trained and tested on the job by a Zambian. This study only began after the second training.

Although a total of seven pharmacists were trained, only three ended up participating in the study *i.e.* actually filling and sealing pouches at their respective hospitals. This was due to three pharmacists accepting new jobs at different hospitals and one pharmacist taking maternity leave. Two months after follow up training, pouch weight and burst testing validation for the three participating pharmacists confirmed that they had been successfully trained and retained the information.

We suggest that nurses and CHW can be successfully trained in groups because the training required is minimal. Pharmacists, on the other hand, probably require local, in-service training because the tasks required to fill and seal pouches accurately are unfamiliar, subtle, and complex.

CONCLUSION

A major challenge of preventing pediatric HIV infection in low resource countries is access to safe liquid formulation ARV medication. The challenge becomes even more difficult to address in rural communities with high non facility births. Within one year, the Pratt Pouch was able to significantly raise access to safe ARV medication for infants born to HIV+ mothers outside of a facility. The intervention was successfully integrated into the Zambian healthcare system and mothers were able to accurately dose without any reported difficulties.

As an example, of the roughly 41,000 infants born to HIV+ Zambian women outside of a clinic in 2012 [6, 7], only about 14,000 were medicated with ARVs immediately after birth. With the Pratt Pouch, a further 24,000 at-risk infants could have received treatment. Increasing infant access to ARVs *via* the Pratt Pouch globally could prevent hundreds of thousands from becoming HIV+ every year.

LIST OF ABBREVIATIONS

ART	=	Antiretroviral therapy
ARV	=	Antiretroviral (medication)
CHW	=	Community health workers
MTCT	=	Mother-to-child transmission (of HIV)
Pratt Pouch	=	A single-dose, polyethylene pouch used to enhance access to antiretroviral medication in rural communities *via* antenatal distribution.
PW	=	Pregnant women

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Joy Ekuta and Jania Arcia-Ramos for collecting the pre- and post-intervention survey data. Furthermore, thanks go to following IntraHealth International staff members who were involved with overseeing on-the-ground implementation and training: Annie Malumo; Kate Stratten; Robert Dodge; Jonas Chanda; Dorothy Chikampa; Thomas Banda and Yonas Asfaw.

These efforts associated with the Pratt Pouch are made possible by the generous support of the Saving Lives at Birth partners: The United States Agency for International Development (USAID); Government of Norway; Bill & Melinda Gates Foundation; Grand Challenges Canada and World Bank.

REFERENCES

[1] UNAIDS, *Regional Fact Sheet: Sub-Saharan Africa.* Geneva, Switzerland, 2012.

[2] UNAIDS, *Regional Fact Sheet: Sub-Saharan Africa.* Geneva, Switzerland, 2013.

[3] M-L. Newell, H. Coovadia, M. Cortina-Borja, N. Rollins, P. Gaillard, and F. Dabis, "Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis", *Lancet,* vol. 364, no. 9441, pp. 1236-1243, 2004. [http://dx.doi.org/10.1016/S0140-6736(04)17140-7] [PMID: 15464184]

[4] K.M. De Cock, M.G. Fowler, E. Mercier, I. de Vincenzi, J. Saba, E. Hoff, D.J. Alnwick, M. Rogers, and N. Shaffer, "Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice", *JAMA,* vol. 283, no. 9, pp. 1175-1182, 2000. [http://dx.doi.org/10.1001/jama.283.9.1175] [PMID: 10703780]

[5] U. Nations, "The millennium development goals report 2014", Available at: http://www.un.org/millenniumgoals/2014%20MDG%20report/MDG%202014%20English%20web.pdf

[6] UNAIDS, *Progress Report on the Global Plan towards the Elimination of New HIV Infections among children by 2015 and keeping their Mothers Alive.* Geneva, Switzerland, 2013.

[7] C. S. O. (CSO), M. O. H. (MOH), T. D. R. C. (TDRC), U. O. Zambia, and M. I. Inc., *Zambia Demographic and Health Survey 2007.* CSO and Macro International Inc: Calverton, Maryland, USA, 2009.

[8] R. Malkin, "Foilized pouches can prevent the transmission of HIV from mother to child using multi-drug therapies", *J. Biomed. Sci. Eng.,* vol. 7, pp. 45-47, 2014.
[http://dx.doi.org/10.4236/jbise.2014.71007]

[9] R. Malkin, and C. Howard, "A foilized polyethylene pouch for the prevention of transmission of HIV from mother to child", *Open Biomed. Eng. J.,* vol. 6, pp. 92-97, 2012.
[http://dx.doi.org/10.2174/1874120701206010092] [PMID: 23028405]

[10] R. Malkin, and K. von Oldenburg Beer, "Diffusion of novel healthcare technologies to resource poor settings", *Ann. Biomed. Eng.,* vol. 41, no. 9, pp. 1841-1850, 2013.
[http://dx.doi.org/10.1007/s10439-013-0750-5] [PMID: 23377566]

[11] R. Malkin, "A pouch may be prevent the transmission of HIV from mother to child", *J. Biomed. Eng. Res.,* vol. 2, pp. 66-70, 2013.
[http://dx.doi.org/10.5963/BER0202002]

[12] A. Choy, M. Ortiz, and R. Malkin, "Accurate dosing of antiretrovirals at home using a foilized, polyethylene pouch to prevent the transmission of HIV from mother to child", *Medicine (Baltimore),* vol. 94, no. 25, p. e1030, 2015.
[http://dx.doi.org/10.1097/MD.0000000000001030] [PMID: 26107673]

[13] SSP Stockouts National Survey, *Stock Outs in South Africa: A National Crisis.,* 2013. Available from: http://stockouts.org/uploads/3/3/1/1/3311088/stop_stockouts_report_2013pdf_1.pdf

[14] M.A. Tolle, B.R. Phelps, C. Desmond, N. Sugandhi, C. Omeogu, D. Jamieson, S. Ahmed, E. Reuben, L. Muhe, S.E. Kellerman, and Child Survival Working Group of the Interagency Task Team on the Prevention and Treatment of HIV infection in Pregnant Women, Mothers and Children, "Delivering pediatric HIV care in resource-limited settings: cost considerations in an expanded response", *AIDS,* vol. 27 (suppl. 2), pp. S179-S186, 2013.
[http://dx.doi.org/10.1097/QAD.0000000000000105] [PMID: 24361627]

[15] A.E. Warren, K. Wyss, G. Shakarishvili, R. Atun, and D.D. Savigny, "Global health initiative investments and health systems strengthening: a content analysis of global fund investments", *Global Health,* vol. 9, no. 1, p. 30, 2013.
[http://dx.doi.org/10.1186/1744-8603-9-30] [PMID: 23889824]

[16] T.R. Feyissa, and G.A. Genemo, "Determinants of institutional delivery among childbearing age women in western ethiopia, 2013: unmatched case control study", *PLoS One,* vol. 9, no. 5, p. e97194, 2014.
[http://dx.doi.org/10.1371/journal.pone.0097194] [PMID: 24810609]

[17] C. Ronsmans, J.F. Etard, G. Walraven, L. Høj, A. Dumont, L. de Bernis, and B. Kodio, "Maternal mortality and access to obstetric services in West Africa", *Trop. Med. Int. Health,* vol. 8, no. 10, pp. 940-948, 2003.
[http://dx.doi.org/10.1046/j.1365-3156.2003.01111.x] [PMID: 14516306]

[18] D. Montagu, G. Yamey, A. Visconti, A. Harding, and J. Yoong, "Where do poor women in developing countries give birth? A multi-country analysis of demographic and health survey data", *PLoS One,* vol. 6, no. 2, p. e17155, 2011.
[http://dx.doi.org/10.1371/journal.pone.0017155] [PMID: 21386886]

[19] L. Grenier, J. Smith, S. Currie, and S. Suhowatsky, *Advance Distribution of Misoprostol for SelfAdministration: Expanding Coverage for the Prevention of Postpartum Hemorrhage.* Jhpiego: Baltimore, MD, 2013.

[20] J.M. Smith, S.D. Baawo, M. Subah, V. Sirtor-Gbassie, C.J. Howe, and G. Ishola, "Advance distribution of misoprostol for prevention of postpartum hemorrhage (PPH) at home births in two districts of Liberia", *BMC Pregnancy Childbirth,* vol. 14, p. 189, 2014.
[http://dx.doi.org/10.1186/1471-2393-14-189] [PMID: 24894566]

[21] M. Nikanjam, D. Kabamba, T.R. Cressey, D. Burger, F.T. Aweeka, E.P. Acosta, S.A. Spector, and E.V. Capparelli, "Nevirapine exposure with WHO pediatric weight band dosing: enhanced therapeutic concentrations predicted based on extensive international pharmacokinetic experience", *Antimicrob. Agents Chemother.,* vol. 56, no. 10, pp. 5374-5380, 2012.
[http://dx.doi.org/10.1128/AAC.00842-12] [PMID: 22869579]

[22] I. Boehringer Ingelheim, *Pharmaceuticals, "Viramune: Medication Guide".* 2005. Available at : http://www.fda.gov/downloads/Drugs/DrugSafety/ucm089818.pdf

[23] L.M. Howard, J.A. Tique, S. Gaveta, M. Sidat, R.L. Rothman, S.H. Vermund, and P.J. Ciampa, "Health literacy predicts pediatric dosing accuracy for liquid zidovudine", *AIDS,* vol. 28, no. 7, pp. 1041-1048, 2014.
[http://dx.doi.org/10.1097/QAD.0000000000000197] [PMID: 24463393]

Received: March 31, 2015 Revised: October 27, 2015 Accepted: October 27, 2015