Self-reported adherence to HAART in South-Eastern Nigeria is related to patients’ use of pill box

Chinwe Victoria Ukwe, Obinna Ikechukwu Ekunife, Obinna Patrick Udeogaranya, Ukamaka Ijeoma Iwuamadi

Abstract
The aim of this study was to assess levels of adherence and predictors of adherence to HAART in South-Eastern Nigeria. Self-reported adherence to HAART was assessed at 4-week intervals for a period of 3 months. A 10-item questionnaire was used to assess hypothesised factors in adherence to HAART. The average adherence score for the 3 months of follow-up was correlated with 10-item hypothesised factors and patient demographic variables. Linear regression was used to model the relationship between self-reported adherence and factors found to be correlated with adherence. The average adherence level of subjects that took part in the study was 86.1% ± 30.1%. Use of an adherence aid (pill box) was correlated with adherence (r=0.22, p<0.001, β=8.3%). The study revealed a slightly higher adherence level compared with most reports in Africa. Use of a pill box could help adherence to HAART, particularly in South-Eastern Nigeria.

Keywords: Human immunodeficiency virus (HIV), acquired immunodeficiency disease (AIDS), adherence, HAART.

Résumé
L’objectif de cette étude consistait à évaluer le niveau d’adhésion et des indices d’adhésion au traitement HAART dans le Nigeria du Sud-est. L’adhésion auto-déclarée au traitement HAART a été évaluée à 4 semaines d’intervalle sur une période de 3 mois. Un questionnaire à 10 éléments a été utilisé pour évaluer les facteurs supposés de l’adhésion au traitement HAART. La note d’adhésion moyenne pendant les 3 mois de suivi a été corrélée aux facteurs supposés des 10 éléments et aux variables démographiques des patients. Une régression linéaire a été utilisée pour modéliser la relation entre l’adhésion auto-déclarée et le facteur que l’on constatait être corrélé à l’adhésion. Le niveau d’adhésion moyen des sujets qui ont pris part à l’étude était de 86.1%± 30.1%. L’utilisation de l’aide à l’adhésion (la boîte à pilules) était corrélée à l’adhésion (r=0.22, p<0.001, β=8.3%). L’étude a indiqué un niveau d’adhésion légèrement supérieur par rapport à celui indiqué dans la majorité des rapports en Afrique. L’utilisation de la boîte à pilules pourrait favoriser l’adhésion au traitement HAART, en particulier dans le Nigeria du Sud-est.

Mots clés: Virus d’immunodéficience humaine (VIH), syndrome d’immunodéficience acquise (SIDA), adhésion, traitement HAART.

Introduction
HIV infection is a major public health problem. Around 33.2 million people are living with HIV, and each year around 2.5 million more people become infected with HIV, while 2.1 million die of AIDS (UNAIDS, 2008). Africa, with just over 10% of the world’s population, bears about 75% of this epidemic (Abdulsalami & Tekena, n.d.). Prevalence in West Africa is relatively low; however, in some large countries, rates are beginning to creep up, with Nigeria having an estimated 2.6 million adults and children living with HIV, and 170 000 persons who died due to AIDS in 2007 (WHO, 2008).

The HIV epidemic has huge economic consequences, both at the micro and macro levels, due to the loss of lives of many individuals during their productive years. Households face large financial burdens as a result of loss of income support from family members who die of the disease, as well as increasing costs of treatment of HIV/AIDS and associated opportunistic infections (NACP, 2002).

Adherence to antiretroviral therapy is the second strongest predictor of progression to AIDS and death, after CD4 count (Gifford et al., 2000; Matchtinger & Bangsberg, 2005). Available treatment for HIV can dramatically suppress viral load, enhance CD4 counts, and decrease morbidity and mortality related to HIV infection (Willard, 2005). Failure to adhere to prescribed regimens results in low drug levels, which can quickly render these combinations ineffective, because of rapid and irreversible selection of genetic variants with decreased drug susceptibility (Matchinger & Bangsberg, 2005). The impact of poor adherence is heightened by the fact that these variants are resistant to other drugs of the same class, and the limited numbers of drugs available are rapidly exhausted by cross-resistant variants, resulting in...
renewed HIV replication and immune destruction. Adherence rates approaching 100% are needed for optimal viral suppression (Gifford et al., 2000; Matchtinger & Bangsberg, 2005). Suboptimal adherence to ART may increase AIDS-related morbidity and mortality, decrease viral suppression, and leads to development of resistance (Gifford et al., 2000; Matchtinger & Bangsberg, 2005; NACP, 2002). Therefore, medication adherence is a fundamental concern in the management of HIV-infected patients.

Four types of factors have been found to predict problems with adherence to HAART: regimen characteristics, patient factors, the relationship between providers and patients, and system of care (WHO, 2003). These factors seem to be environment specific, due to different socio-medical backgrounds. For instance, in the southern part of Nigeria, Afolabi, Ijadunola, Fatusi and Olosode (2009) showed that HIV patients who did not pay for the preliminary ARV eligibility investigations, and those offered regular adherence counselling, adhered to their medication. In Benin City (Middle belt), adherence was dependent on adverse effects and the educational level of patients (Erah & Arute, 2008). In the Niger Delta region, the cost of antiretrovirals, educational status, medication adverse effects, occupational factors, and high pill burden of the prescribed regimen were factors supposed to be associated with non-adherence (Nwauche, Erhabor, Ejele & Akani, 2006). In a recent cross-sectional, single site study conducted in South-Eastern Nigeria, it was found that being female, under 35 years, single and having higher educational status were significantly associated with non-adherence (Uzochukwu et al., 2009). Understanding the predictors of adherence is the first step in trying to improve adherence to antiretroviral therapies. A detailed understanding of the possible factors that can contribute to non-adherence will greatly aid in the development of interventions to improve adherence, particularly for susceptible patients in different practice locations.

The aim of this study was to assess adherence to highly active antiretroviral therapy (HAART), and to determine predictors of adherence to a combination antiretroviral regimen using three HIV clinics in South-Eastern Nigeria.

**Methods**

This was a prospective and observational study with a 3-month assessment of adherence. It was carried out from May to September 2008. The study was conducted in HIV clinics of three health institutions located in two of the five states in South-Eastern Nigeria. The hospitals were St. Borromeo Hospital Onitsha, General Hospital Enugu-Ezike, and Bishop Shanahan Hospital Nsukka. A questionnaire administered through interview was used for the study. It was an exit study carried out by research pharmacists visiting the hospitals during the period of study. The 10 items in the questionnaire assessed factors hypothesised to affect adherence to HAART, derived from the World Health Organizations’ report on adherence (WHO, 2003). The 10 items consisted of nine closed-ended questions and one open-ended question. Three of the close-ended questions were dichotomously structured, while the other six items were designed as a 4-point Likert response scale. These factors included regimen characteristics, patient beliefs and provider factors. Items assessing patients’ demographic and clinical characteristics were also included in the questionnaire. The study instrument was face validated by some lecturers of the Department of Clinical Pharmacy and Pharmacy Management, and was pre-tested on 60 HIV patients to check its feasibility. The study instrument is shown in the Appendix.

All HIV-positive outpatients between 14 years and 65 years of age attending the three HIV clinics were approached to be included in the study. Only patients who consented to participate in the study were recruited. Patients who did not come to refill their prescriptions at the end of the 3-month period after recruitment were not included in the final analysis. Recruited patients were interviewed at the beginning of the study after they had refilled their prescription in a room in the pharmacy department. Demographic and clinical characteristics of the patients were obtained from the patients’ record. CD4 counts were recorded at baseline and at the end of the 3-month period.

Adherence to HAART was assessed using patients’ self report. Participants were asked non-judgmentally how often they had missed their doses in the last 3, 5 and 7 days, respectively. Adoption of this shorter period was to avoid ‘recall bias’. Adherence rates were therefore calculated as ‘pills taken over a specific period of time, divided by pills prescribed for that specific period of time’. Adherence was assessed at baseline, week 4, week 8 and week 12 (i.e. for a 3-month period). The average adherence score for the 3 months of follow-up served as the dependent variable, while the 10-item hypothesised factors and patient demographic variables were the independent variable.

All procedures were carried out according to a study protocol approved by the Local Ethics Committee of Federal Medical Centre, Owerri. The nature and objectives of the study were explained to patients who agreed to participate. Informed consent was formally obtained. The information about patients’ identity was not included with the other data, and only the principal investigator had access to this information. No reference to the patients’ identity was made at any stage during data analysis.

| Table 1. Demographic characteristics of participants (N=299) |
|-------------------------------------------------------------|
| **Variable**                  | **Frequency** | **Percentage (%)** |
| **Age (years)**          |               |                    |
| 16 - 25                   | 55            | 18.7               |
| 26 - 35                   | 148           | 50.3               |
| 36 - 45                   | 69            | 23.5               |
| 46 and above             | 22            | 7.5                |
| **Gender**                |               |                    |
| Male                      | 81            | 27.3               |
| Female                    | 216           | 72.7               |
| **Education**             |               |                    |
| No formal education      | 11            | 3.8                |
| Primary                   | 104           | 35.6               |
| Secondary                 | 133           | 45.5               |
| Tertiary                  | 44            | 15.1               |
| **Marital status**        |               |                    |
| Single                    | 91            | 33.8               |
| Married                   | 129           | 48.0               |
| Divorced                  | 5             | 1.9                |
| Widow/widower             | 36            | 13.4               |
| Separated                 | 8             | 3.0                |
| **Religion**              |               |                    |
| None                      | 2             | 0.7                |
| Moslem                    | 9             | 3.4                |
| Christian                 | 253           | 94.8               |
| African tradition religion | 3             | 1.1                |
Adherence to HAART is defined as patient taking 95% or more of his/her medication.

**Results**

Out of the 310 HIV patients enrolled in the study, adherence to HAART for the 3-month period was assessed in 299 patients (i.e. in 96.5% of the study population). Table 1 shows the patients’ demographic characteristics. The majority of the subjects were female and most of the patients had secondary education. More males declined to participate. Lack of time was the major reason most of them gave for their non-participation. Patients were largely Christians. Many of the patients were unemployed, while a minority were divorced or separated from their spouse.

In our study population, only a minority of the participants were in the last stage of HIV infection (i.e. HIV stage IV). Five types of HAART were used. Most patients in this study were treated with stavudine + lamivudine + nevirapine. At the end of the 3-month period there was an improvement in the average CD4 count, although a wide variance in average CD4 count improvement was obtained. Self-reported adherence level for the 3-month period was 86.1 ± 30.1%. The majority of subjects adhered to their medication (i.e. had up to or more than 95% adherence score). Details of the clinical characteristics of the study population are presented in Table 2.

In Table 3, bivariate associations between the independent variables and adherence are shown. Patients’ demographic factors which included age, gender, level of education, alcohol overindulgence, smoking and number of dependents were not correlated with the adherence score. Out of all 10 hypothesised predictors of adherence, only the use of an adherence aid was found to be correlated with adherence. Specifically, a pill box was the adherence aid used by the majority of patients. Since only one factor was correlated with adherence, linear regression was carried out to determine the effect of the use of an adherence aid on self-reported adherence to HAART. It was found that the use of an adherence aid increased the adherence score by 8.3%. Confidence limits were narrow, showing that we are 95% confident that change in adherence caused by the use of an adherence aid is between 1.5% and 15.1% increase in adherence.

**Discussion**

We conducted a prospective, observational study among patients on HAART regimen to assess objectively their adherence to HAART over a 3-month period. We also determined the predictors of adherence to a combination antiretroviral regimen based on documented factors that have been established to cause poor adherence. Since HAART is a long-term therapy, we assessed adherence for 3 months, to reflect better the participants’ drug-taking behaviour. On average, adherence to HAART was about 86%. This is slightly higher than the adherence level obtained. Self-reported adherence level was 86.1 ± 30.1%. The majority of subjects adhered to their medication (i.e. had up to or more than 95% adherence score).

### Table 2. Clinical characteristics of participants (N=299)

| Variable | Frequency (%) |
|----------|---------------|
| **HAART type** | |
| D4T + 3TC + NVP | 219 (73.2) |
| AZT + NVP + 3TC | 38 (12.7) |
| D4T + 3TC + EFV | 19 (6.4) |
| AZT + 3TC + NVP (Combivir®) | 15 (5.0) |
| Combivir + Efavirenz | 1 (0.3) |
| **Adherence to HAART** | |
| % Self-reported adherence level | 86.1 ± 30.1 |
| Non-adherent | 89 (29.8) |
| Adherent | 210 (70.2) |
| **Duration of diagnosis of HIV infection** | |
| 1 - 3 months | 49 (20.9) |
| 4 - 6 months | 27 (11.5) |
| 7 - 9 months | 75 (31.9) |
| 10 - 12 months | 30 (12.8) |
| >1 year | 54 (23.0) |
| **Stage of HIV Infection** | |
| Stage 1 | 60 (26.7) |
| Stage 2 | 86 (38.2) |
| Stage 3 | 69 (30.7) |
| Stage 4 | 10 (4.4) |
| **Baseline CD4 Count** | 206.0 (149.5 - 266.5) |
| **Last CD4 Count** | 271.0 (210.0 - 349.3) |
| **Change in CD4 Count** | 23.5 (8.0 - 93.5) |
| **Adherence** | |
| Non-adherent | 20.0 (3.0 - 107.5) |
| Adherent | 25.0 (8.5 - 88.0) |

*Adherence to HAART is defined as patient taking 95% or more of his/her medication.

### Table 3. Bivariate association between adherence and hypothesised variables

| Variable | r | p-value |
|----------|---|---------|
| **Patients demographics** | | |
| Age | 0.001 | 0.961 |
| Gender | 0.12 | 0.833 |
| Education | -0.035 | 0.556 |
| Alcohol overindulgence | -0.088 | 0.137 |
| Smoking | -0.039 | 0.508 |
| Number of dependants | 0.077 | 0.298 |
| **Regimen factors** | | |
| Regimen fits with lifestyle | 0.097 | 0.099 |
| Use of adherence aid | 0.220* | <0.001 |
| Medication change | 0.045 | 0.088 |
| **Patient beliefs** | | |
| ART are worth taking | 0.025 | 0.666 |
| Resistance can develop if ART is not taken | -0.087 | 0.139 |
| ART improves quality of life | 0.048 | 0.411 |
| You can fight HIV without ART | 0.088 | 0.135 |
| **Providers factors** | | |
| How often do you see your care provider | -0.110 | 0.071 |
| Trust in your care provider | 0.086 | 0.190 |
| Satisfaction with the level of care given | 0.091 | 0.153 |

r = Pearson correlation coefficient; two-tailed significance was judged by p<0.05

* Significant association.
reported by Mills et al. (2006), which found a higher level of adherence to antiretroviral regimens among Africans (77%) than North Americans (55%). Nevertheless some patients still had an adherence level lower than 95%, which is required for optimal viral suppression (Gifford et al., 2000; Willard, 2005). This underscores the critical need for interventions to help improve adherence to antiretroviral therapy in this group of patients.

As mentioned earlier in this paper, understanding the predictors of adherence will greatly help in the development of interventions to improve patient adherence to antiretroviral drugs. In our study we examined the relationship of factors that have been identified to affect adherence with adherence rate. However, the majority of these factors hypothesised to be associated with adherence were not correlated with adherence in the participants that we studied.

Only the use of an adherence aid was associated with adherence ($r=0.22, p<0.001$). Mostly, the adherence aid used by the subjects was a pill box. Improved adherence in patients who used a pill box may be because of the pill count conducted by pharmacists and pharmacy technicians during refill of ARTs. A pill box may have the added advantage of concealing the identity of the drug, and thus patients may feel comfortable carrying them around. This finding has been noted in another study (Chow, Chin, Fong & Bendayan, 1999). Other types of adherence aids have been shown to improve adherence to ARTs. In a pilot study of 55 patients, only those who received monetary reinforcement in addition to reminders and medication event monitoring system (MEMS) feedback were more adherent than controls (Liu, Golin & Millor, 2001). In another randomised trial of an online paging system, patients receiving paged medication reminders improved their adherence significantly more than controls over 4 weeks (Weilde & Ganera, 1999). Adherence aids such as pill boxes, clock, calendars, etc. could help adherence to HAART. The incorporation of these aids into clinical practice is necessary, as they have been shown to increase adherence. Including standardised patient education about adherence aids during antiretroviral therapy initiation is a practical way to introduce patients to these potentially valuable interventions. Further studies are needed to assess the long-term effects of medication reminder systems, and to compare the efficacy of different types of reminders to improve ART adherence. These studies should consider the use of a composite adherence measure in estimating adherence, i.e. patients’ self-report could be combined with pill count and pharmacy refill. This will ensure a more precise adherence estimate.

The findings of this study must be interpreted in the light of its limitations. Asking patients for their subjective ratings of adherence behaviour is fraught with some problems. Patients’ subjective reports have been showed to be a non robust predictor of adherence (Cramer & Mattson, 1991; Spector et al., 1986). Our study used a short follow-up period to assess adherence. However, studies of longer periods would give a better reflection of adherence rates since antiretroviral therapy is a chronic therapy.

Conclusion

The findings in this study revealed a slightly higher adherence level compared with most reports in Africa. The incorporation of adherence aids such as pill boxes during ART initiation could help adherence to HAART, particularly in South-Eastern Nigeria.

References

Abdulsalami, N., & Tekena, O.H. (no date). The epidemiology of HIV/AIDS in Nigeria. In: AIDS in Nigeria. Alujo (pp. 17-35). Federal Ministry of Health, Nigeria.

Adolabi, M.O., Ijadunola, K.T., Fatusi, A.O., & Olasode, O.A. (2009). Determinants of adherence to antiretroviral drugs among people living with HIV/AIDS in the Ille-Ijesa zone of Osun State, Nigeria. African Journal of Primary Health Care & Family Medicine, 1, 1-6.

Chow, R., Chin, T., Fong, I.W., & Bendayan, R. (1999). Medication use patterns in HIV-positive patients. Canadian Journal of Hospital Pharmacy, 46, 171-175

Cramer, J.A., & Mattson, R.H. (1991). Monitoring compliance with antiepileptic drug therapy. In: J.A.Cramer & B. Spiller (eds), Patient compliance in medical practice and clinical trials (pp. 123-137). New York: Raven Press.

Erah, P.O., & Arute, J.E. (2008). Adherence of HIV/AIDS patients to antiretroviral therapy in a tertiary health facility in Benin City. African Journal of Pharmacy and Pharmacology, 2(7), 145-152.

Gifford, A.L., Bornmann, J.E., Shiverly, M.J., Wright, B.C., Richman, D.D., & Bozzette, S.A. (2000). Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. Journal of Acquired Immune Deficiency Syndromes, 23(5), 386-395.

Liu, H.H., Golin, C.G., & Millor, L. (2001). A comparison study of multiple measures of adherence to HIV protease inhibitors. Annals of Internal Medicine, 134, 968-977.

Machtinger, E.L., & Bangsberg, D.R. (2005). Adherence to HIV antiretroviral therapy. HIV Insite knowledge base chapter. Retrieved September 13, 2008 from http://hivinsite.ucsf.edu/InSite/page=kb-03-02-099

Mills, E.M., Nachega, J.B., Buchan, I., orbinski, I., Attaran, A., & Rachlis, B. (2006). Adherence to antiretroviral therapy in sub-Saharan Africa and North America. JAMA, 296(6), 679-690.

National AIDS Council Publication (1997-2002). Botswana HIV and AIDS. Second Medium Term Plan. Ministry of Health, Republic of Botswana.

Nwauh, C.A., Erhabor, O., Ejele, O.A., & Akani, I. (2006). Adherence to antiretroviral therapy among HIV-infected subjects in a resource-limited setting in the Niger Delta of Nigeria. African Journal of Health Sciences, 13(3-4), 13-17.

Spector S.L., Kinsman, R.A., Miall, M., Siegel, S.C., Rachelefsky, G.S., Katz, R.M. et al., (1986). Compliance of patients with asthma with an experimental aerosolised medication: implications for controlled clinical trials. Journal of Allergy Clinical Immunology, 77, 65-70.

UNAIDS (2008). Report on the global AIDS epidemic. Geneva. Retrieved October 17, 2008 from http://data.unaids.org/pub/GlobalReport/2008/ JC1511_GR08_ExecutiveSummary_en.pdf

Unochukwu, B.S.C., Orwujekwe, O.E., Onuwa, A.C., Okoli, C., Ugura, N.P., & Chukwugwo, O.I. (2009). Determinants of non-adherence to subsidised antiretroviral treatment in southeast Nigeria. Health Policy and Planning, 24(3), 189-196.

Weidle, P.J., & Ganera, I. (1999). Adherence to antiretroviral medications in an inner city population. Journal of Acquired Immune Deficiency Syndromes, 22, 498-502.

Willard, S. (2005). Managing side effects and promoting adherence in patients with HIV disease: a nurse’s role. The nurse’s role CE.2005. Retrieved November 8, 2008 from www.medscape.com/viewprogram/4573.pnt

WHO (2008). Epidemiological fact sheet on HIV and AIDS in Nigeria. Retrieved September 8, 2008 from http://www.who.int/globalatlas/predefinedReports/ EFS2008/full/EFS2008_NG.pdf

WHO (2003). Adherence to long term therapies: Evidence for action. Retrieved October 10, 2008 from http://apps.who.int/medicinedocs/collection/ medicinedocs/pdf/s4883e/s4883e.pdf
Appendix: Study Instrument

**PART A To be conducted at baseline**

Patient’s ID __________ Date ___________ Hospital Name ____________________________

Age _______ Sex _______ Stage and Duration of Diagnosis of HIV infection _________________________

Viral load ___________________ CD4 count _______________________

Level of education No formal education [ ] Primary [ ] Secondary [ ] Tertiary [ ]

Occupation Trader [ ] Civil Servant [ ] Self employed [ ] Business executive [ ] Not employed [ ]

Number of dependants (adults and children) _______________________

Do you take alcohol? [ ] Yes [ ] No [ ]

Do you smoke? [ ] Yes [ ] No [ ]

---

### The number of ARVs and non ARVs prescribed

| No | DRUG | FREQUENCY | DURATION (days) |
|----|------|-----------|-----------------|
| 1. |      |           |                 |
| 2. |      |           |                 |
| 3. |      |           |                 |
| 4. |      |           |                 |
| 5. |      |           |                 |
| 6. |      |           |                 |

| No | DRUG | FREQUENCY | DURATION (days) |
|----|------|-----------|-----------------|
| 1. |      |           |                 |
| 2. |      |           |                 |
| 3. |      |           |                 |
| 4. |      |           |                 |
| 5. |      |           |                 |
| 6. |      |           |                 |

### Associated opportunistic infections

1. 4.
2. 5.
3. 6.

### HIV related symptoms

1. 4.
2. 5.
3. 6.
**PART B To be conducted at baseline**

| Question                                                                 | Yes | No |
|--------------------------------------------------------------------------|-----|----|
| 1. Does your regimen fit with your lifestyle (daily activities)?          |     |    |
| 2. Do you use adherence aids e.g. pill box, calendar e.t.c. to help you remember to take your medication? |     |    |
| 3. Did you have any medication change since the last visit?               |     |    |

| Question                                                                 | Strongly agree | Agree | Disagree | Strongly disagree |
|--------------------------------------------------------------------------|----------------|-------|----------|-------------------|
| 4. Antiretroviral are worth taking                                        |                |       |          |                   |
| 5. You can fight HIV without antiretroviral drugs                          |                |       |          |                   |
| 6. One may develop resistance if antiretroviral drug is not taken as prescribed |                |       |          |                   |
| 7. Antiretroviral drug improves quality of life                           |                |       |          |                   |
| 8. You agree totally with your medical care provider on everything he tells you |                |       |          |                   |
| 9. You are satisfied with the level of care given to you by your medical provider |                |       |          |                   |

10. How often do you see your care provider? (Average per month) __________

**PART C To be conducted at baseline, week 4, week 8 and week 12**

Please tick [✓] where appropriate

1. Over the past 7 days, how many times did you miss your medication?

| ARV Med Name, Dosage, Frequency | 3 days ago (Doses missed) | 5 days ago (Doses missed) | 7 days ago (Doses missed) |
|----------------------------------|--------------------------|--------------------------|--------------------------|
| 1.                               |                          |                          |                          |
| 2.                               |                          |                          |                          |
| 3.                               |                          |                          |                          |
| 4.                               |                          |                          |                          |
| 5.                               |                          |                          |                          |
| 6.                               |                          |                          |                          |

2. Did you experience any side effects while taking your medication?  Yes [ ] No [ ]

3. If your answer to the above question is Yes, Can you identify the side effects you experienced. Tick where applicable: Nausea [ ] Diarrhea [ ] Headache [ ] Fatigue [ ] Depression [ ]

4. Specify any other problem you experienced while taking your drugs

5. CD4 count ____________________________