Adherence to Antiretroviral Therapy by People Accessing Services from Non-governmental HIV Support Organisations in Three Caribbean Countries

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ABSTRACT

Objective: To identify factors associated with antiretroviral therapy (ART) adherence in order to guide the development of strategies to improve the situation.

Design and Methods: A cross-sectional survey was conducted with people living with HIV (PLHIV) who receive services from non-governmental organisations affiliated to the Caribbean Regional Network of People Living with HIV/AIDS (CRN+) in Antigua and Barbuda, Grenada and Trinidad and Tobago. PLHIV, from CRN+, traced potential participants, administered informed consent procedures and carried out structured interviews. The main outcome measure was 95% to 100% adherence over the previous seven days. Multiple logistic regression was conducted to identify associations with demographic characteristics, psychological status, health and support service use, sexual behaviour and substance abuse.

Results: Of 394 respondents, 69.5% were currently taking ART. Of these, 70.1% took 95% to 100% of their prescribed pills. One in 20 took more pills than prescribed, all of whom were prescribed fewer or equal to the median pill number. Factors independently associated with adherence were use of a counselling service (OR 3.20; 95% CI 1.55, 6.61), revelation of HIV status without consent (OR 2.31; 95% CI 1.13, 4.74), alcohol consumption (OR 0.47; 95% CI 0.23, 0.96) and side effects (OR 0.32; 95% CI 0.15, 0.68). Drug resistance to ART was reported by 6% of users.

Conclusion: Improvements in ART adherence may be achieved by counselling, focussed attention to alcohol users and developing drugs with reduced side effects. Such measures are critical to maintain PLHIV quality of life gains and prevent the proliferation of drug resistant HIV strains.

Keywords: Adherence, antiretroviral therapy, counselling, HIV

La Adhesión a la Terapia Antiretroviral por Personas que Acuden a los Servicios de Organizaciones no Gubernamentales de Apoyo a la Lucha Contra el VIH en tres Países del Caribe

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RESUMEN

Objetivo: Identificar los factores asociados con la adhesión a la terapia antiretroviral (TAR) para guiar el desarrollo de estrategias encaminadas a mejorar la situación.

Diseño y Métodos: Se llevó a cabo un estudio transversal con personas que viven con VIH (PVVIH), y que reciben los servicios de organizaciones no gubernamentales afiliadas a la Red Regional del Caribe de Personas que Viven con VID/SIDA (CRN+) en Antigua y Barbuda, Granada, y Trinidad y Tobago. La PVVIH de CRN+ se dio a la búsqueda de participantes potenciales, aplicó los procedimientos de consentimiento informado, y llevó a cabo entrevistas estructuradas. La principal medida de resultado fue de 95% a 100% de adhesión durante los últimos siete días. Se llevó cabo una regresión logística múltiple con el propósito de identificar las asociaciones con características demográficas, estado psicológico, salud y uso del servicio de apoyo, conducta sexual y abuso de sustancia.

Resultados: De 394 encuestados, el 69.5% se hallaban tomando TAR actualmente. De éstos, 70.1%

tomaron de 95% a 100% de las píldoras prescritas. Uno de cada 20 tomó más píldoras que las prescritas, a todos los cuales se les prescribió un número menor o igual a la mediana de las píldoras. Los factores independientemente asociados con la adhesión fueron: uso de un servicio de aconsejamiento (OR 3.20; 95% CI 1.55, 6.61), revelación de la condición de VIH sin consentimiento (OR 2.31; 95% CI 1.13, 4.74), consumo de alcohol (OR 0.47; 95% CI 0.23, 0.96) y efectos colaterales (OR 0.32; 95% CI 0.15, 0.68). Resistencia al medicamento con relación a TAR fue reportada por 6% de usuarios.

Conclusión: *Las mejoras en la adhesión a la TAR pueden lograrse mediante aconsejamiento, atención focal a los consumidores de alcohol y desarrollo de medicamentos con efectos colaterales reducidos. Tales medidas son de importancia fundamental si se quiere mantener ganancias para la calidad vida de las PVVIH y prevenir la proliferación de cepas de VIH resistentes a los medicamentos.*

Palabras claves: Adhesión, terapia antiretroviral, aconsejamiento, VIH

INTRODUCTION

In the Caribbean, access to antiretroviral therapy (ART) by people living with HIV (PLHIV) has expanded dramatically (1), increasing life expectancy, reducing morbidity and reducing AIDS incidence (2).   However, these benefits have been accompanied by concerns related to adherence. Breaks, inconsistency and cessation of ART can result in viral load resurgence, greater susceptibility to re-infection and development of drug-resistant HIV strains, leading to health deterioration and amplifying difficulties in containing the epidemic (3).

Studies on ART adherence in the Caribbean reflect these concerns. Various methods have been used to measure adherence and associations with sociodemographic variables measured. Respondents have also been asked to explain why they did not adhere (4−7).

The variables explored in these studies are unlikely to capture the range of factors that could impact on treatment adherence. We present an analysis of adherence based on the ecological framework for health, according to which a range of individual, relationship, community and societal factors influence health outcomes (8, 9). At the individual level, a range of biological and personal factors may affect adherence, such as side effects, psychological status, income and substance abuse. At the relationship level, experiences with partners, other PLHIV, family members, healthcare and other service providers could influence adherence. Community contexts may be important, such as healthcare settings, household and neighbourhood features. At the societal level, legislation, policies and social norms associated with HIV stigma may be influential.

This study examines factors at various levels in the ecological framework to identify influences on adherence among PLHIV who receive services from non-governmental organisations (NGOs) affiliated to the Caribbean Regional Network of People Living with HIV/AIDS (CRN+). Available funding allowed a survey in Antigua and Barbuda, Grenada and Trinidad and Tobago in 2007.

SUBJECTS AND METHODS

People eligible to participate were PLHIV who were members of or accessed services from the NGOs affiliated to CRN+. Because the number of eligible people in several of the NGOs was small (range: 17 − 250), we aimed to include all those eligible rather than select a sample. Non-governmental organisations gave estimates of numbers of eligible people in their organisations.

Data were collected *via* structured face-to-face interviews and thus did not include biological measures or capture societal factors such as legislation that might be considered using the ecological framework. The questionnaire covered demographics, socio-economic status, psychological well-being, healthcare utilisation, health-seeking behaviours, experiences as a result of being HIV+ (including stigma and discrimination), NGO activities, HIV status disclosure, sexual behaviour and substance abuse. Most questions were developed in consultation and piloting with CRN+ members. A few questions on psychological status were included from other instruments (10, 11).

To maximize trust and build PLHIV research capacity, CRN+ NGOs selected personnel who were trained to trace potential participants, provide study information, request informed consent and carry out interviews. Most of these people were PLHIV themselves; others were trusted HIV professionals. A person in each NGO maintained the list of people interviewed and their code numbers; people conducting data entry and analysis did not have access to the study participants' identities. Each NGO established a referral system for interviewees who experienced distress. Financial compensation was provided for participant expenses incurred. All participants provided informed consent. The study received ethical approval from the Chief Medical Officers, Ministries of Health of participating countries.

Adherence to ART was measured over the past seven days. Respondents were asked to state the daily number of pills their doctor had prescribed. They were then asked to state the number of pills they took yesterday, the day before that, three days ago and so on until pill intake was counted

for each of the past seven days. The number of pills taken was divided by seven and compared with the number prescribed per day. If the numbers matched, there was 100% adherence. The main outcome measure was 95% − 100% adherence because 95% adherence is thought to be adequate to ensure efficacy and prevent the emergence of resistance (5, 7).

As this was an exploratory analysis, seeking to identify any factor that might help explain adherence, potential associations between adherence and the range of variables in the questionnaire were explored. Data analysis was conducted using Statistical Packages for Social Sciences (SPSS) version 12 (SPSS Inc., Chicago). For categorical data, cross-tabulations were used and statistical significance of associations initially assessed using the Fisher's exact test (2-sided) for 2 x 2 tables or the Pearson chi-square statistic. Associations between the number of pills prescribed and whether the person adhered or took more or less pills than prescribed was conducted using non-parametric methods including the Kruskal-Wallis test. Unadjusted odds ratios (ORs) were calculated for associations between categorical variables and adherence. Multivariate logistic regression was used to produce adjusted ORs. All factors that were found significant at the 5% level in univariate analyses were included in the multivariate analysis, using Forward (Conditional) Stepwise Logistic Regression, to identify the factors independently associated with adherence. Non-governmental organisations were included as dummy variables in the multivariate analysis, to account for clustering of research participants by membership of individual NGOs.

RESULTS

Of 574 people estimated to be eligible, 394 participated (70%). Reasons for non-participation included difficulties in tracing potential respondents, non-attendance at scheduled interview, and illness of potential respondents or research staff. No person refused to participate.

Respondents were predominantly female (56%). About a quarter of males reported that they had been infected *via* sex with men. Respondents were mostly of lower socio-economic status. Most (82%) were interviewed in Trinidad because this island has the largest number of PLHIV and NGOs affiliated to CRN+ in the countries studied (Table 1).

Of 394 respondents, 295 (74.8%) had ever taken and 274 (69.5%) were currently taking ART. Most (56%) had experienced side effects and 6% reported experiencing drug resistance. Of those currently taking ART, 264 provided information enabling adherence to be measured. Two-thirds of them (66.3%) reported that they adhered to their prescription exactly over the past seven days. A further 3.8% took between 95% and < 100% of their prescription, 9.2% were 80 − 94% adherent and 15.9% were < 80% adherent. Almost one in 20 (4.9%) took more pills than prescribed. Respondents took an average of 93.1% of their prescribed dose of pills (95% confidence interval: 89.1%, 97.0%).

Table 1:   Sociodemographic characteristics of respondents (n = 394)

Characteristic	Number of respondents	Percentage of respondents[a]
Country/island where interview took place		
Antigua and Barbuda	23	5.8
Grenada	15	3.8
Tobago	35	8.9
Trinidad	321	81.5
Gender		
Male	170	43.1
Female	222	56.3
Means of transmission		
Men who had sex with men	38	9.6
Men who had sex with women	110	27.9
Women who had with men	202	51.3
Men or women: other means of transmission	12	3.1
Age group		
Under 25	46	11.7
25–34	127	32.2
35–44	108	27.4
45 and over	113	28.7
Income level of family		
Family does not have enough to live	113	28.7
Family has enough money to live, but we do so by making many sacrifices	195	49.5
Family has sufficient money to live without making many sacrifices	27	6.9
Family has enough so that we do not have to go without anything of importance	19	4.8
Highest level of education attained		
Primary or never went to school	121	30.7
Secondary	182	46.2
Technical/vocational	65	16.5
University	23	5.8
Employment status		
Employed	196	49.7
Unemployed	198	50.3
Main source of income or financial support		
Salary/wage	172	43.7
Casual work	14	3.6
Disability benefit	60	15.2
Public assistance	41	10.4
Partner	20	5.1
Friends/family	40	10.2
Non-governmental, community or faith-based organisation	12	3.0
Other	27	6.9
Marital status		
Unmarried	318	80.7
Married	37	9.4

Where percentages do not add up to 100, some data are missing. These data include respondents who stated "Prefer not to answer the question" or "Don't know".

The number of pills prescribed per day ranged from 1 to 14 with a median of 4 and a mode of 3 pills (Fig. 1). Table 2 shows that the median number of pills prescribed was lower among those who took more than prescribed (3 pills), but was the same for those who took the same number or less than prescribed [4 pills] (chi-square statistic = 12.41; *p* = 0.002 according to the Kruskall-Wallis test). The narrowest range (2 to 4 pills prescribed) was among the respondents who took
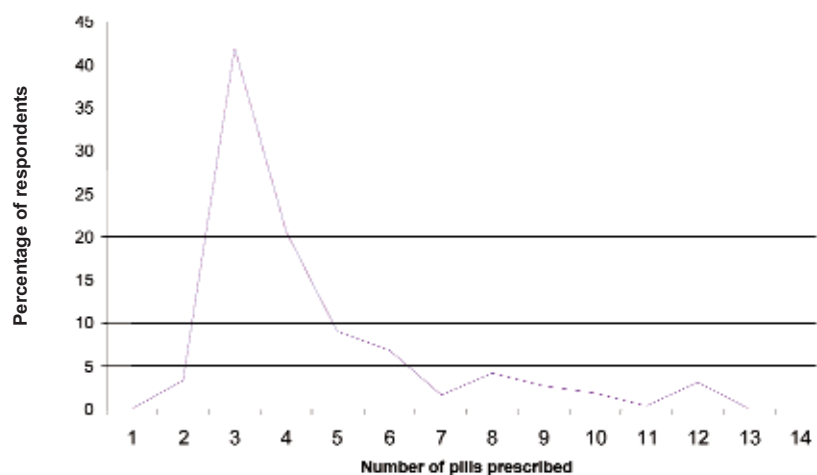
Fig. 1:   Distribution of number of pills prescribed.

Table 2:   Relationship between adherence and number of pills prescribed per day

		Number of pills prescribed		
	n	Median	Minimum	Maximum
Took **same** number as prescribed	175	4	2	13
Took **fewer** pills than prescribed	76	4	3	14
Took **more** pills than prescribed	13	3	2	4
Total	**264**	**4**	**2**	**14**

more pills than prescribed. The small number of people who took more pills than prescribed (n = 13) prevented further detailed analysis of possible reasons for taking more than prescribed.

Table 3 shows the factors significantly associated with adherence. Of factors identified in univariate analysis, having had a treatment break over the past 12 months was conceptualised as being associated with rather than explaining adherence over the past seven days and so was excluded

Table 3:   Factors significantly associated with 95 to 100% adherence to number of antiretroviral pills prescribed in the past 7 days: unadjusted odds ratios and results of multivariate logistic regression

Variable[a]	n	Percentage of respondents with 95% to 100% adherence	Unadjusted Odds Ratio	95% CI	p[b]	Adjusted Odds Ratio	95% CI	p[c]
Provided information on adherence (of 274 currently taking antiretroviral therapy)	264	70.1						
Experienced side effects (n = 260)					0.008			0.003
No	109	78.9	1.00			1.00		
Yes	151	63.6	0.47	0.27–0.82		0.32	0.15–0.68	
Difficulty taking so many pills every day (n = 258)					0.006			
No	201	73.6	1.00					
Yes	57	54.4	0.43	0.23–0.79				
Had a treatment break in past 12 months, where stopped taking ARV medication for a while (n = 264)					0.001			N.A.
No	216	74.5	1.00			N.A.	N.A.	
Yes	46	50.0	0.34	0.18–0.66		N.A.	N.A.	
Ever had a viral load test (n = 240)					0.012			
No	29	93.1	1.00					
Yes	211	67.3	0.15	0.04–0.66				

Table 3 cont'd: Factors significantly associated with 95 to 100% adherence to number of antiretroviral pills prescribed in the past 7 days: unadjusted odds ratios and results of multivariate logistic regression

Variable[a]	n	Percentage of respondents with 95% to 100% adherence	Unadjusted Odds Ratio	95% CI	p[b]	Adjusted Odds Ratio	95% CI	p[c]
Used HIV specialist service in past 12 months (n = 261)					0.045			
No	18	94.4	1.00					
Yes	243	67.9	0.12	0.02–0.95				
Used a counselling service in past 12 months (n = 260)					0.002			0.002
No	133	60.9	1.00			1.00		
Yes	127	78.7	2.38	1.37–4.12		3.20	1.55–6.61	
Shared experiences of living with HIV with another HIV+ person in past 12 months (n = 235)					0.007			
No	114	62.3	1.00					
Yes	121	78.5	2.21	1.24–3.94				
Learned about new treatment opportunities for PLHIV in past 12 months (n = 241)					0.014			
No	139	64.7	1.00					
Yes	102	79.4	2.10	1.16–3.80				
Received improved HIV treatment, care and support in past 12 months (n = 241)					< 0.001			
No	105	58.5	1.00					
Yes	135	80.0	2.83	1.60–5.03				
Participated in exercise or sports activities in past 12 months (n = 241)					0.007			
No	185	66.5	1.00					
Yes	56	85.7	3.02	1.35–6.79				
Someone disclosed that respondent is HIV+ without consent (n = 230)					0.004			0.023
No	102	59.8	1.00			1.00		
Yes	128	77.3	2.30	1.29–4.07		2.31	1.13–4.74	
Disclosed HIV+ status to his/her child or children (n = 252)					0.047			
No	158	58.9	1.00					
Yes	94	75.5	1.80	1.01–3.20				
Alcohol use in past 12 months (n =260)					0.048			0.039
No	119	71.6	1.00			1.00		
Yes	141	59.7	0.58	0.34–0.99		0.47	0.23–0.96	

NOTES:

Shaded area indicates that this variable was not independently associated with adherence.

N.A. = Not applicable

a. Numbers in brackets are those with full data on BOTH the adherence variable and the exposure variable in question. Persons who responded "Don't know", or "Prefer not to answer" were excluded.

b. Significance of Wald statistic

c. Adjusted for all variables in the final model. Forward (Conditional) Stepwise Regression was used to analyse all variables in the table with the exception of, "Had a treatment break in past 12 months". Membership of individual NGOs was included in the analysis. Analysis was conducted for 177 cases with full data on all variables. Significance was assessed using the multi-parameter Wald test.

from multivariate analysis. Once all the other variables found to be significantly associated with adherence, plus the NGO variable, were included in the multivariate logistic regression model, adherence was found to be independently positively associated with use of a counselling service and unwanted disclosure of HIV status and negatively associated with side effects and alcohol use. These four factors were found to be associated with other variables that emerged as significantly associated with adherence in univariate analysis. For instance, use of counselling was positively related with improved care, treatment and support, learning about new treatment opportunities and participating in sports and exercise. It was negatively associated with alcohol use and having had a viral load test.

DISCUSSION

Interpreting the results of this study *via* the ecological frame-work, some individual factors were associated with ad-herence, such as alcohol use and side effects, as found in other studies (12, 13). Other domains relating to individuals, including socio-economic status, had no discernible impact. Our research corroborates findings (4 − 7, 12) that demo-graphic characteristics are not associated with ART ad-herence.

At the relationship level, if the respondent had ex-perienced unwanted HIV status disclosure they were more likely to adhere. At the community level, HIV care, treat-ment and support settings and actions appear important, such as number of pills prescribed and counselling provision. Other contexts such as household composition and facilities were not associated with adherence. Our methodology did not allow the assessment of most societal influences. Some of our questions indicated the presence of stigma and dis-crimination, recording issues such as less favourable treat-ment by service providers. However, none of these variables was associated with treatment adherence.

A meta-analysis of adherence studies showed adequate adherence in 77% (95% CI 68, 85%) of patients in Africa and 55% (CI 49, 62%) in North America (14). In the present study, 70.1% of patients were 95 − 100% adherent, this level being similar to those in Africa and higher than North America. The seven-day estimate compares favourably with that of 54.8% in a survey of PLHIV attending government treatment facilities in Jamaica (7) and 58.4% in the Centre for HIV/AIDS Research, Education and Services (CHARES) at the University Hospital of the West Indies in Jamaica. The mean level of adherence (number of prescribed pills taken) in the present study was 93.1%, compared with 87.7% at CHARES (6).

Having interacted with an adherence counsellor was not associated with adherence in Jamaica (7), while coun-selling increased the likelihood of adherence in our study. It may be that the quality of counselling differs between the CRN+ NGOs and the government sector in Jamaica. The benefits of counselling in the present study are suggested by its association with learning of new treatment opportunities; participating in sports and exercise and its negative associa-tion with alcohol use. Further research should examine coun-selling and personalised HIV care in different service settings. In Haiti, community health-workers have been employed to provide individual case management and assistance in ART adherence. This intervention has been recommended for adherence promotion in resource-poor settings (15) but not widely used in the English-speaking Caribbean.

There is still substantial room for improvement in the level of adherence suggested in the present study. Alcohol users may require focussed attention and personalised care in developing adherence promotion strategies. Our results also stress the need to develop drugs with reduced side effects (13).

Taking more pills than prescribed has not been recorded in other Caribbean studies. The fact that this was associated with being prescribed a small numbers of pills makes this finding plausible and suggests that further re-search be conducted on patient perceptions of pill quantities necessary for effective treatment.

The positive association of adherence with unwanted disclosure of HIV status is unexpected and challenging to understand. It may indicate that fear of ridicule, blame and discrimination from people who may know their HIV status is a powerful stimulus that drives PLHIV to attend more carefully to their health. When combined with the finding that adherence was more likely with counselling, it suggests that adherence is encouraged on the one hand by perceived support and on the other by fear. An ethical approach would be to build supportive services and relationships rather than to add to the fears of PLHIV *via* unwanted disclosure.

The respondents have a similar socio-economic profile to PLHIV in the Jamaican study in government healthcare settings. In the index study, 50% were unemployed, com-pared with 52% among PLHIV in Jamaica, and 9% in the general population in that country (7). The clientele of CRN+ NGOs and government healthcare settings may be of lower socioeconomic status than people who obtain HIV care elsewhere. The findings of this study should not be regarded as representative of PLHIV across social classes. The sample was not selected randomly, further challenging generalisa-tion.

In summary, estimates of adherence in this study among NGO service recipients in three Caribbean countries compare favourably with estimates from elsewhere in the Caribbean and North America. Improvements in ART adherence in the Caribbean may be achieved by improved counselling, focussed attention to alcohol users and develop-ing drugs with reduced side effects. Such measures are cri-tical to maintain PLHIV quality of life gains and counteract the real prospect of proliferation of drug resistant strains of HIV.

REFERENCES

1. UNAIDS. A study of the Pan Caribbean Partnership Against HIV/AIDS (PANCAP): Common goals, shared responses. UNAIDS and CARICOM; 2004.
2. UNAIDS. Report on the global AIDS epidemic. Geneva: Joint United Nations Programme on HIV/AIDS; 2008.
3. Jack N. Implementation of HIV drug resistance monitoring in the Caribbean. 10th Meeting of Caribbean National Epidemiologists and Laboratory Directors; October 12–16; Hyatt Regency Hotel, Port of Spain, Trinidad and Tobago 2009.
4. Armstrong D, Thompson K, Persaud N. Adherence to antiretroviral therapy in HIV-infected patients: implications for enhancing current practices. West Indian Med J 2004: 21–24; **53 (Suppl 2):** 21.
5. Adomakoh N, Emtage M, Borysiewicz K, Abayomi A, Roach T. The impact of adherence to highly active antiretroviral therapy on virologic outcome at a national HIV/AIDS treatment centre in Barbados. West Indian Med J. [Abstract] 2003 April 30–May 3; **52 (Suppl 3):** 18.
6. Williams M, Clarke T, Williams P, Barton EN. The mean levels of adherence and factors contributing to non-adherence in patients on highly active antiretroviral therapy. West Indian Med J 2007; **56:** 270−4.
7. Harvey K, Carrington D, Duncan J, Figueroa J, Hirschorn L, Manning D. Evaluation of adherence to highly active antiretroviral therapy in adults in Jamaica. West Indian Med J 2008; **57:** 293−7.
8. Heise LL. Violence Against Women: An Integrated, Ecological Framework. Violence Against Women 1998; **4:** 262−90.
9. World Health Organization Global Campaign for Violence Prevention. The ecological framework. Geneva: WHO; 2009 [cited 2009 12 November]; Available from: http://www.who.int/violenceprevention/approach/ecology/en/index.html.
10. Grierson J, Thorpe R, Pitts M. HIV Futures Five: Life as We Know It. La Trobe University; 2006 [2009 12 November]; Available from: http://www.latrobe.edu.au/hiv-futures/HIV%20Futures%205%20Report.pdf.
11. World Health Organization. WHOQOL-HIV BREF. Geneva: World Health Organization; 2002 [cited 2009 12 November]; Available from: http://www.who.int/mental_health/evidence/WHOQOL-HIV%20BREF.pdf.
12. Haubrich RH, Little SJ, Currier JS, Forthal DN, Kemper CA, Beall GN, et al. The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response. AIDS 1999; **13:** 1099−107.
13. Vervoort S, Borleffs J, Hoepelman A, Grypdonck M. Adherence in antiretroviral therapy: A review of qualitative studies. AIDS 2007; **21:** 271−81.
14. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, et al. Adherence to Antiretroviral Therapy in Sub-Saharan Africa and North America: A Meta-analysis. Jama 2006; **296:** 679−90.
15. Mukherjee JS, Ivers L, Leandre F, Farmer P, Behforouz H. Antiretroviral therapy in resource-poor settings. Decreasing barriers to access and promoting adherence. J Acquir Immune Defic Syndr 2006; **43 (Suppl 1):** S123−6.