Evaluation of Patients Adherence to HIV Medication Based on Pharmacy Records

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Introduction: Adherence is the extent to which a person's behaviour is consistent with health care recommendations[1]. Adherence to a certain therapeutic regime will determine an illness clinical outcome; indeed, treatment strategies must be sustainable to be successful[2]. But how can we quantitatively measure adherence? Some consider that good adherent patients are those who carry out about 80 % of the recommended behaviour[1], while others believe that an adherence of 95% is the required standard[3]. Actually, adherence is a multifactorial variable depending upon determinants such as population features and the complexity of therapeutic regime[4]. However some argue that those taking more pills in a daily basis do not seem to differ in terms of compliance from the ones who take simpler regimens[5].
The fact that complex and expensive antiretroviral therapeutics are currently at use makes it important to acknowledge its efficacy which is highly correlated with adherence. Investigating the compliance to such therapies should be a priority on any clinical setting where HIV patients are followed up[6]. Various methods to measure adherence have been used such as patient-report adherence; pill count; serum concentration of antiretroviral; assisted medication taking[7]. Each one of these methods has its pros and cons, thus using them isolated seem to lack scientific value[8]. However, and despite its limitation, there is one method which is refill compliance using pharmacy records very useful in predicting patient behaviour towards their medication[9]. This latter method allows the identification of those individual who will not certainly have successful treatment duo to lack of medication acquisition[10, 11].

Objective: Assessment of HIV patient compliance to antiretroviral therapy based on Pharmacy files.

Methods: This is a six-month longitudinal prospective descriptive study starting in January 2004. Our sample population consisted of HIV patients undergoing antiretroviral therapy, except pregnant women and HIV patient while in haemodialysis, who received medication from the Pharmacy Department of Hospital Fernando Fonseca during the study's first month. Hospital Fernando Fonseca is a Public General Hospital within the National Health System Hospital Network. This health unit serves a population of about 600.000 individuals and has approximately 678 inpatients beds.
After a previous pilot project to certificate the quality of this study, the authors and other pharmacists collected data that were gathered in the pharmacy records for each patient. These data included demographic variables (age, race and gender) therapeutic regimens features and refill compliance features (dates of pharmacy department visits and number of pills obtained in each visit).
Based on refill compliance using pharmacy records we assessed a Continuous Measure of Medication Acquisition (CMA = Cumulative days' supply obtained /Total days to next fill or end of observation period). This index will ultimately give us the adherence of our population to HIV therapy dispenses. We decided to include in our project the number of days spent in the hospital ward to increase CMA's probability to be the actual adherence to antiretroviral therapies.
Data were gathered in the Microsoft Excel 2000 and analysed using the Statistical Package for Social Science 9.0 program.

Results and Discussion :

In the beginning of 2004 we had roughly 700 patients who carried out their HIV therapies. During the recruitment period we obtained a sampled population of 522 individuals including 9 patients who started their treatment in this stage.

1.- Demographic Variables

As we can observe in our population, the number of Caucasian individuals is higher (n=336; 64,4%) than the number of non Caucasian (n=186; 35,6%) (**Table 1**). Equally interesting is the fact that there seems to be no significant difference between the number of male and female in the non Caucasian patients.
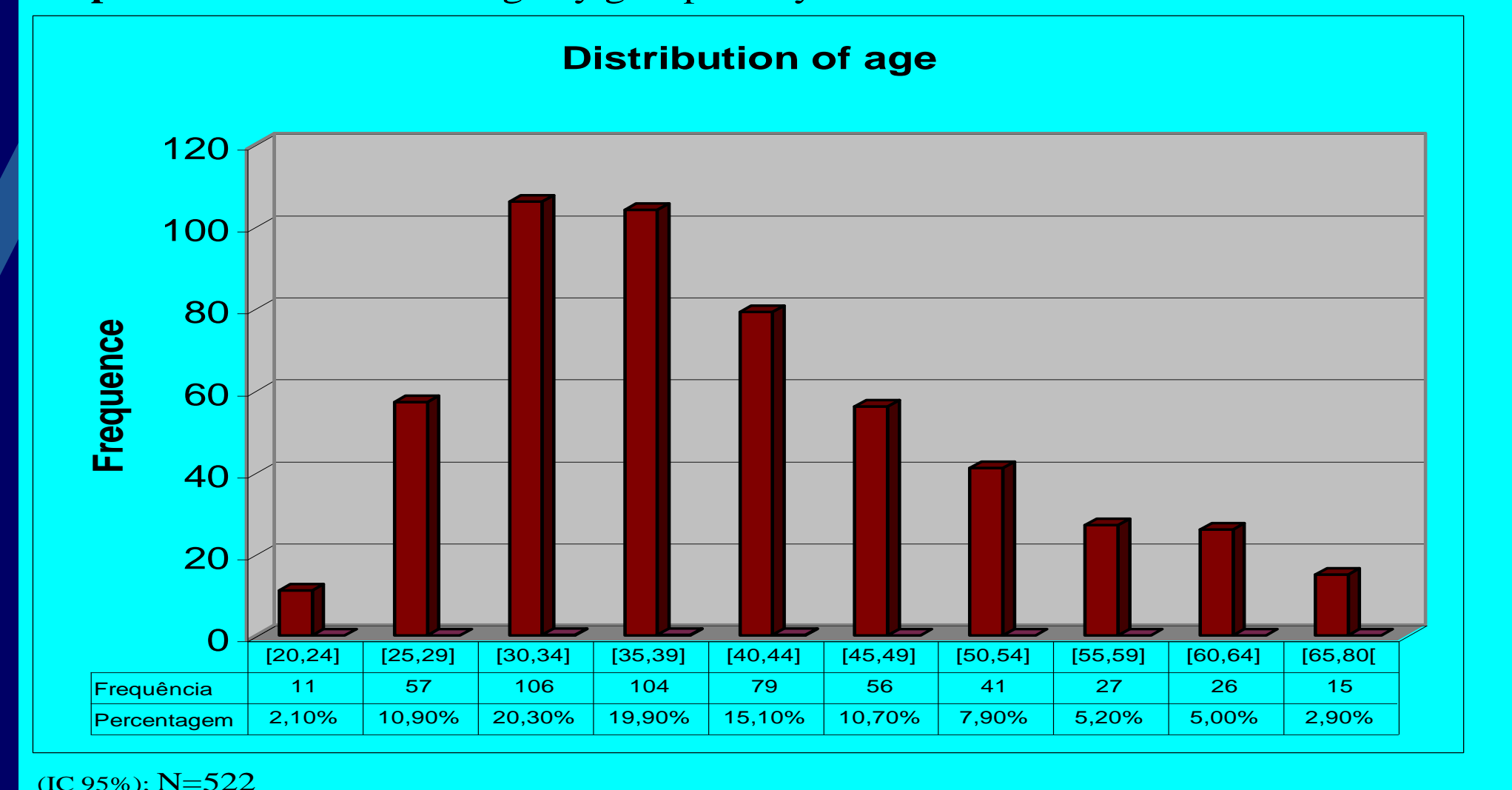
Table 1: Distribution of race by sex.

Race	Sex Male n	Male %	Female n	Female %	Total n	Total %
Caucasian	236	45,2	100	19,2	336	64,4
Non-caucasian	94	18,0	92	17,6	186	35,6
Total	330	63,2	192	36,8	522	100,0

n – number; % - percentual value; (IC 95%); N=522.

The majority of our patients, 40,2% (n=210) has between thirty and forty years old (**Graphic 1**). A highly proportion of our studied subjects are older than we had previously thought.

Graphic 1: Distribution of age by group of 5 years.

Distribution of age

	[20,24]	[25,29]	[30,34]	[35,39]	[40,44]	[45,49]	[50,54]	[55,59]	[60,64]	[65,80]
Frequência	11	57	106	104	79	56	41	27	26	15
Percentagem	2,10%	10,90%	20,30%	19,90%	16,10%	10,70%	7,90%	5,20%	5,00%	2,90%

(IC 95%); N=522

2.- Therapeutic Regimens

The most frequent therapeutic regimens are those which included 2 NRTIs (Nucleoside Reverse Transcriptase Inhibitors) + 1 NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitors) (51,3%; n=268) and 2 NRTIs + 1 IP (Protease Inhibitors) (29,3%; n=153) (**Table 2**). Some individuals of our target population use others highly diverse regimens possibilities.

Table 2: Distribution of Therapeutic Regimens during the recruitment period

Therapeutic Regimens	n	%
2 NRTI + NNRTI	268	51,3
2 NRTI + IP	153	29,3
2 NRTI + 2 IP	49	9,4
3 NRTI	17	3,3
Others[(*)]	35	6,7
Total	522	100,0

NRTI – Nucleoside Reverse Transcriptase Inhibitors; NNRTI - Non-Nucleoside Reverse Transcriptase Inhibitors; IP –Protease Inhibitors; [(*)] – 2 NRTI + NtRTI (Nucleotide Analog Reverse Transcriptase Inhibitors), NRTI + IP + NtRTI, NRTI + NNRTI + NtRTI, NRTI + 2IP + NNRTI + NtRTI, 2IP + NNRTI + NtRTI among others; n – number; % - percentual value; (IC 95%); N=522.

Taking into account the number of pills consumption in a daily basis **Table 3** clearly puts forward that 55,9% (n=292) of our patients consume between tree to six pills per day.

Table 3: Number of pills per day distribution.

Number of pills/day	n	%
2	10	1,9
3 a 4	184	35,2
5 a 6	108	20,7
7 a 8	85	16,3
9 a 10	55	10,5
11 a 12	49	9,5
13 a 14	31	5,9
Total	522	100,0

n – number; % - percentual value; (IC 95%); N=522.

From the analysis of data regarding the number of takings on a daily basis we can verify that the number of takings was between 1 and 5 takings per day, even though there was a higher incidence when 2 (30,7%; n=160), 3 (44,4%; n= 232) and 5 (22,0%; n=115) takings per day were considered (**Table 4**) .

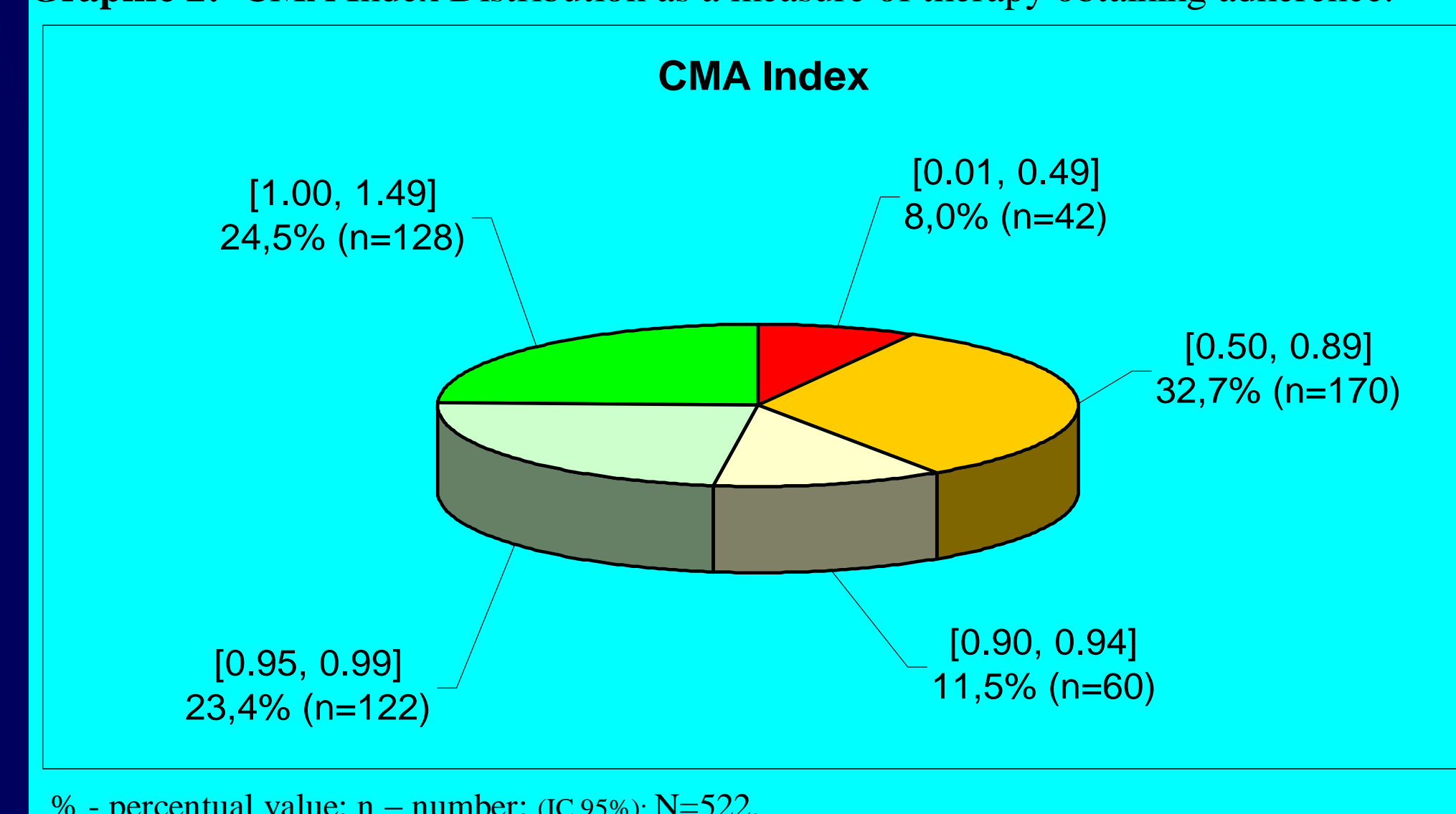**Table 4:** Number of takings per day distribution.

Number of takings/day	n	%
1	6	1,1
2	160	30,7
3	232	44,4
4	9	1,7
5	115	22,0
Total	522	100,0

n – number; % - percentual value; (IC 95%); N=522.

3.- CMA Index

Approximately 24,5 % (n=128) of our population has a CMA ≥ 1 and 23,4% (n= 122) has a 0,99 < CMA > 0,95 (**Graphic 2**).

Graphic 2: CMA Index Distribution as a measure of therapy obtaining adherence.

CMA Index

- [1.00, 1.49] 24,5% (n=128)
- [0.01, 0.49] 8,0% (n=42)
- [0.50, 0.89] 32,7% (n=170)
- [0.90, 0.94] 11,5% (n=60)
- [0.95, 0.99] 23,4% (n=122)

% - percentual value; n – number; (IC 95%); N=522.

These results are not what we expected according to the previous pilot study results.
Having in mind that CMA is an index obtained from pharmacy refill data, which eventually allow us to speculate about the adherence to HIV therapies, and that CMA = 1 would mean supposedly one hundred percent adherence, therefore we can assume that our sampled population is just 24,5 % absolutely adherent to their antiretroviral therapies.

Data Analysis seems to indicate that there are more male individuals (represented by 33,5% of the studied population and 53,0% of the sampled male population) having a CMA > 0,95 when compared to the female individuals (represented by 14,5% of the studied population and 39,1% of the sampled female population) (**Table 5**).

Table 5: CMA Index distribution by gender.

CMA Index n(%)	Sex Male	Female	Total
[0.01, 0.49]	20 (3,8)	22 (4,2)	42 (8,0)
[0.50, 0.89]	97 (18,6)	73 (13,9)	170 (32,5)
[0.90, 0.94]	38 (7,3)	22 (4,2)	60 (11,5)
[0.95, 0.99]	82 (15,7)	40 (7,8)	122 (23,5)
[1.00, 1.49]	93 (17,8)	35 (6,7)	128 (24,5)
Total	330 (63,2)	192 (36,8)	522 (100,0)

n – number; % - percentual value; (IC 95%); N=522.

As far as race is concern, results seem to demonstrate that there are more Caucasian individuals (represented by 33,5% of the studied population and 52,1% of the sampled Caucasian population) having CMA> 0,95 when compared to the non Caucasian individuals (represented by 14,3% of the studied population and 40,3% of the sampled non Caucasian population) (**Table 6**).

Table 6: CMA Index distribution by race.

CMA Index n(%)	Race Caucasian	Non Caucasian	Total
[0.01, 0.49]	26 (5,0)	16 (3,1)	42 (8,1)
[0.50, 0.89]	90 (17,2)	80 (15,2)	170 (32,5)
[0.90, 0.94]	45 (8,6)	15 (2,9)	60 (11,5)
[0.95, 0.99]	77 (14,7)	45 (8,6)	122 (23,3)
[1.00, 1.49]	98 (18,8)	30 (5,7)	128 (24,5)
Total	336 (64,4)	186 (35,6)	522 (100,0)

n – number; % - percentual value; (IC 95%); N=522.

Aging seems to influence adherence. As a matter of fact data displayed give the impression that as long as age of the studied population is augmenting we verify an accompanying increase in the percentage of the individuals with CMA ≥ 1, if we consider the number of individuals inside each age group (**Table 7**).

Table 7: CMA Index distribution by age.

CMA Index n(%)	[20,29]	[30,39]	[40, 49]	[50, 59]	[60, 69]	[70, 79]	Total
[0.01, 0.49]	4	18	12	5	2	1	42 (8,0)
[0.50, 0.89]	33	71	37	21	4	4	170 (32,6)
[0.90, 0.94]	11	19	19	4	5	2	60 (11,5)
[0.95, 0.99]	10	53	32	17	7	3	122 (23,4)
[1.00, 1.49]	10	49	35	21	12	1	128 (24,5)
Total	68	210	135	68	30	11	522 (100,0)

n – number; % - percentual value; (IC 95%); N=522.

Looking into **Table 8** we can not state that therapeutic regimen would influence adherence to HIV therapies.

Table 8: CMA Index distribution by therapeutic regimen.

CMA Index n(%)	2 NRTI + NNRTI	2 NRTI + IP	2 NRTI + 2IP	3 NRTI	Others[(*)]	Total
[0.01, 0.49]	20	11	7	3	1	42 (8,0)
[0.50, 0.89]	85	52	16	3	14	170 (32,6)
[0.90, 0.94]	30	21	3	2	4	60 (11,5)
[0.95, 0.99]	69	33	9	4	7	122 (23,4)
[1.00, 1.49]	64	36	14	5	9	128 (24,5)
Total	268	153	49	17	35	522 (100,0)

NRTI – Nucleoside Reverse Transcriptase Inhibitors; NNRTI - Non-Nucleoside Reverse Transcriptase Inhibitors; IP –Protease Inhibitors; [(*)] – 2 NRTI + NtRTI (Nucleotide Analog Reverse Transcriptase Inhibitors), NRTI + IP + NtRTI, NRTI + NNRTI + NtRTI, NRTI + 2IP + NNRTI + NtRTI, 2IP + NNRTI + NtRTI among others; n – number; % - percentual value; (IC 95%); N=522.

Having in mind the plausible impact of pill burden over the adherence to HIV medication, results don't allow us to declare what we had long thought, that a small number of pills consume per day would be associated with a slightly elevated CMA Index (**Table 9**).

Table 9: CMA Index distribution by number of pills per day.

CMA Index n(%)	2	3 a 4	5 a 6	7 a 8	9 a 10	11 a 12	13 a 14	Total
[0.01, 0.49]	1	15	7	7	5	4	3	42 (8,0)
[0.50, 0.89]	3	50	40	34	20	18	5	170 (32,6)
[0.90, 0.94]	1	21	12	13	5	3	5	60 (11,5)
[0.95, 0.99]	2	49	25	17	10	11	8	122 (23,4)
[1.00, 1.49]	3	49	24	14	15	13	9	128 (24,5)
Total	10	184	108	85	50	49	30	522 (100,0)

n – number; % - percentual value; (IC 95%); N=522.

It is not clear at all whether the number of takings is influent or not in adherence to antiretroviral therapies (**Table 10**).

Table 10: CMA Index distribution by number of takings per day.

CMA Index n(%)	1	2	3	4	5	Total
[0.01, 0.49]	1	15	17	1	8	42 (8,0)
[0.50, 0.89]	1	55	70	2	42	170 (32,6)
[0.90, 0.94]	-	17	23	1	19	60 (11,5)
[0.95, 0.99]	3	39	55	2	23	122 (23,4)
[1.00, 1.49]	1	34	67	3	23	128 (24,5)
Total	6	160	232	9	115	522 (100,0)

n – number; % - percentual value; (IC 95%); N=522.

Conclusions: Whether we consider antiretroviral therapeutic regimens or demographic features we are not able to conclude anything regarding their relationship towards adherence. The same is applied to the individuals that started their HIV therapy in the period of recruitment of our sampled population; we are in absolutely no condition of saying that those are more or less adherent.

Acknowledging that our patients are highly non-adherent to HAART and that there are apparently no demographic or medication reasons for that we may ask how can we improve our patient's compliance to antiretroviral therapies so important to determine their own quality of life and progression of disease? We reckon we might begin by developing a system of continuous health assistance to this kind of population as a whole regardless of their demographic or medication profile determinants. **Education** is in our point of view the tool with which to guide our patients towards a positive behaviour and attitude in what their HIV illness is concern.

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