





## 5.1. Non-occupational post exposure prophylaxis

Non-occupational exposure to HIV is defined as coming into accidental contact with blood and/or other biological fluids either through sexual or parenteral contact outside of a strictly defined health environment, whereas occupational exposure to HIV is defined as when health professionals accidentally come into contact with blood or biological fluids whilst they are working [1].

The belief that non-occupational post exposure prophylaxis (NPEP) to HIV can avoid infection is based on biological plausibility. There is data which indicates the efficiency and effectiveness of NPEP for HIV in animal models [2-3], in VT [4] and in the health environment [5]. Due to the fact that for ethical reasons it is not possible to perform authorised controlled clinical tests on NPEP, various observational studies have been carried out which suggest that it can be effective [6-7]. Currently, in this environment, there are state recommendations on the management of these exposures [1].

In 2001 a state project financed by “La Marató de TV3” Foundation was initiated in Spain with the aim of evaluating the viability of the efficiency of NPEP for HIV, as an integral part of an European register (NONOPEP project), financed by the European Commission and coordinated by CEEISCAT [8]. Once the project was finalised in 2005, in Catalonia a registry of non-occupa-

Table 5.1.1. Distribution of notified cases by centre, 2001-2008.

Center	N	%
Hospital Clínic i Provincial de Barcelona	905	56.1
Hospital del Mar	261	16.2
Hospital General Universitari Vall d'Hebron	173	10.7
Ciutat Sanitària Universitària de Bellvitge	141	8.7
Hospital Universitari Joan XXIII	29	1.8
Hospital General de Granollers	28	1.7
Hospital Verge de la Cinta	22	1.4
Hospital Universitari Germans Trias i Pujol	18	1.1
Hospital de Mataró	10	0.6
Hospital de Terrassa	10	0.6
Hospital Universitari Arnau de Vilanova	8	0.5
Hospital Creu Roja de Barcelona	3	0.2
Hospital Mutua de Terrassa	2	0.1
Creu Roja de Catalunya	1	0.1
Hospital Provincial de Santa Caterina	1	0.1
<b>Total</b>	<b>1,612</b>	<b>100.0</b>

tional exposures to HIV has been maintained voluntarily [9].

The registry includes non-occupational exposures to HIV, whether or not they have received ART, and information is collected anonymously and voluntarily on the characteristics of those individuals exposed and the sources of infection, along with the characteristics of the exposure, categorising infection according to risk (low, medium, high), serology and clinical monitoring, the ART prescribed, and tolerance and adherence to these treatments.

The objectives of the registry are:

- Report the demand and the practice of NPEP with antiretroviral drugs in HIV negative people.
- Monitor the suitability of clinical practice for the existing recommendations regarding the use of NPEP.

- Report the adherence and the side effects of ART in HIV negative people who have received NPEP.

This section reports the cases reported in Catalonia from 2001-2008.

During the period 2001-2008 1,612 cases were reported in the registry, of which 59.1% were men. **Table 5.1.1** indicates the distribution of cases according to the notifying centre. The average age was 30 (interquartile range (IQR) 24-38) and the average time between exposure and first consultation was 12.4 hours (IQR 60-60). In 909 cases (56.4%) NPEP was prescribed. In 63% (1,015) the accidental exposure was through sexual contact, in 31.6% (509) it was through parenteral contact and in 5.4% (88) through other types of exposure (**table 5.1.2**). The source was identified in 1436 cases (89.1%). Of these, in 82.1% the initial serological status with regards to HIV was unknown. Of the total exposures, the

Table 5.1.2. Distribution of notified exposure types.

	N	%
<b>Sexual</b>		
Anal reception	67	6.6
Anal insertion	99	9.8
Vaginal reception	66	6.5
Vaginal insertion	125	12.3
Oral sex	44	4.3
Unspecified	614	60.5
<b>Subtotal</b>	<b>1,015</b>	<b>63.0</b>
<b>Parenteral</b>		
Accidental pricking	394	77.4
Aggression	42	8.3
IDU material sharing	3	0.6
Unspecified	70	13.8
<b>Subtotal</b>	<b>509</b>	<b>31.6</b>
<b>Others</b>		
Blood contact with non intact skin	22	25.0
Human bite	12	13.6
Blood contact with mucosae	9	10.2
Blood contact with intact skin	12	13.6
Unspecified	33	37.5
<b>Subtotal</b>	<b>88</b>	<b>5.5</b>
<b>Total</b>	<b>1,612</b>	<b>100</b>

Table 5.1.3. Distribution of treatments and patterns by exposure risk category.

TAR	Risk category							
	Alt		Mig		Baix		Desconegut	
	N	%	N	%	N	%	N	%
<b>No</b>	<b>47</b>	<b>21.5</b>	<b>101</b>	<b>27.4</b>	<b>405</b>	<b>64.3</b>	<b>150</b>	<b>38.0</b>
<b>Yes</b>	<b>172</b>	<b>78.5</b>	<b>267</b>	<b>72.6</b>	<b>225</b>	<b>35.7</b>	<b>245</b>	<b>62.0</b>
Single therapy	3	1.7	11	4.1	15	6.7	13	5.3
Double therapy	89	51.7	112	41.9	108	48.0	170	69.4
Triple therapy	72	41.9	135	50.6	95	42.2	58	23.7
Four drugs	7	4.1	8	3.0	7	3.1	4	1.6
More than four	1	0.6	1	0.4	0	0.0	0	0.0
<b>Total</b>	<b>219</b>		<b>368</b>		<b>630</b>		<b>395</b>	

evaluation of grade of risk carried out by the notifying doctor was stated in 1217 cases (75.5%), distributed in the following way: 630 (51.7%) low risk cases, 368 (30.3%) medium risk cases

and 219 (18%) high risk cases.

The guidelines of ART prescribed were 2 drugs in 52.7%, 3 drugs in 39.6% and 4 or more drugs in 3.1%.

Table 5.1.3 indicates the distribution of treatment guidelines according to the grade of risk. It should be stressed that ART was prescribed in 62% of cases where no evaluation of risk is stated. It was also prescribed in 35.7% of low risk cases.

71.3% of the 1,037 who received ART and 55.7% of those untreated attended the follow up visit which took place one month after the first visit. 714 cases (44.3%) attended six months later, 45% of those who received treatment and 43.5% of those who did not receive it, respectively. In relation to adherence to ART, amongst those receiving treatment with proof of a subsequent visit, 22 cases (3.5%) interrupted the treatment. In the table 5.1.4 we can see the causes of the treatment interruption. Amongst those people exposed who received treatment and who visited subsequently, 169 (16.3%) presented some kind of adverse side effect. Gastro-intestinal symptoms were the most frequent (66.1%), followed by non-specific symptoms such as generally feeling unwell and fatigue (11.3%) and effects on the nervous system (10.2%). The rest of the side effects (12.4%) were fever, skin changes, and distortions in results of laboratory tests of the genitourinary system (table 5.1.5).

During this period, 3 HIV seroconversions were identified (0.3%) in 2003, 2004 and 2005 respectively. They occurred in MSM with unprotected sexual relations which gave a negative result for HIV at the time of the consultation. The 3 cases received the triple combination of AZT

Table 5.1.4. Causes of interrupted treatment in treated persons and one-month follow-up.

Causes	Interruptions	%
Negative effects	7	31.8
HIV source person negative once PEP had started	3	13.6
Patient's own decision	5	22.7
Other causes*	7	31.8
<b>Total</b>	<b>22</b>	

\* Reevaluation of the doctor, pregnancy, interactions with other drugs.

Table 5.1.5. Number and type of side effects in ART treated persons that come to a following visit.

Number of side effects per person	N	%
One	84	49.4
Two	62	36.9
Three or more	23	13.7
Type of side effects		
Nausea and / or vomiting	90	31.8
Diarrhea	62	21.9
Malaise and fatigue	32	11.3
Headache	19	6.7
Abdominalgia	18	6.4
Other gastrointestinal alterations	17	6.0
Other nervous system alterations	10	3.5
Others *	35	12.4

\* Anorexia, fever, renal colic and laboratory alterations.

+ Lamivudine and Nelfinavir for four weeks without treatment interruptions. The time between the visit made due to the exposure and the initiation of the prophylaxis was 2, 24 and 40 hours respectively. Each case had all had previous exposures, one case before and two cases after the exposure which lead to the consultation. In all three cases the HIV status of the source was unknown.

## 5.2. Project for the computerisation of clinical epidemiological monitoring of HIV

### infection and AIDS (PISCIS Cohort)

2011 marks three decades of the reporting of the first cases of opportunistic infections in previously healthy people which lead the world's scientific community to consider the appearance of a new disease, which until that moment had been unknown [10]. Since then, observational studies have played a fundamental role in HIV infection and AIDS. Important issues such as understanding the natural history of the infection, trying to resolve the question of the best moment

to begin ART as well as how to explain the progression of the disease in the age of HAART, amongst other things, have been considered through the development of this type of epidemiological study.

The PISCIS Project was created with the aim of resolving these types of questions and understanding the performance of the epidemic using the advantages that cohort studies offer. This project was initially conceived with the design of a computer programme which, like a systemised clinical history, collected the necessary information which it was able to translate using special computer programmes (FIPSE, 3084/99). Within this the creation of a network of clinical epidemiological information was attempted between the main hospitals which offer specialised clinical attention to patients living with the infection (FIPSE; 36354/02) in Catalonia and the Balearics.

From that time, the PISCIS project has been made up of a prospective multicentre cohort study made up of seropositive patients over 16 years of age and who have been seen for the first time in some of the main hospitals (9 in Catalonia and 1 in the Balearics) starting from 1<sup>st</sup> January 1998 [11]. Since 1998 data has been collected retrospectively and from 2000 the main data in the cohort has been collected prospectively.

Since 1<sup>st</sup> January 1998 until 31<sup>st</sup> October 2009 the PISCIS Cohort has recruited a total of 11,359 people, monitoring for an average of 51 months. Amongst the total of people recruited, 8,778 were men (77.2%),

Table 5.2.1. Description of patients at the time of inclusion. PISCIS cohort January 1998-October 2009.

	Total PISCIS Cohort (n=11,359 n (%))	New diagnoses (n=7,023) n (%)
<b>Sex (male)</b>	8,778 (77.2)	5,515 (79.1)
<b>Age on inclusion</b>		
<35	4,942 (43.5)	3,248 (46.3)
35-55	5,766 (51.0)	3,259 (46.4)
> 55	568 (5.0)	442 (6.3)
<b>Mode of transmission</b>		
MSM	3,652 (32.4)	2,743 (39.4)
Heterosexual	3,122 (27.7)	2,297 (33.0)
IDU	3,504 (31.1)	1,327 (19.0)
Others	991 (8.8)	586 (8.4)
<b>Naive on inclusion</b>	6,934 (61.0)	5,320 (75.8)
<b>CD4+ baseline</b>		
<200	2,692 (32.0)	1,737 (32.8)
200-350	1,794 (21.3)	1,106 (20.9)
>350	3,932 (46.7)	2,451 (46.3)
<b>CD4+ baseline (average) (1)</b>	325 [152-525]	322 [141-521]
<b>HIV1-RNA baseline (log<sub>10</sub>) (average) (1)</b>	4.4 [3.0-5.1]	4.6 [3.7-5.2]
<b>HCV coinfection</b>	2,684 (37.3)	1,279 (27.0)
<b>HBV coinfection*</b>	659 (6.9)	438 (7.5)
<b>AIDS diagnosis at the time of inclusion</b>	2,352 (20.7)	1,287 (18.3)
<b>Person-years of follow-up</b>	47,936	29,446
<b>On follow-up</b>	7,167 (63.4)	4,857 (69.7)
<b>Deaths</b>	1,041 (9.2)	502 (7.2)

\* Excluding Son Dureta Hospital. / (1) Interquartile range.

the most frequent group of informed transmission was (32.4%), followed by the drug users (31.1%) and heterosexual groups (27.7%).

Amongst the total of patients recruited, 7,023 patients (61.8%) were newly diagnosed with HIV/AIDS, these being the patients with the time period between diagnosis and the date of inclusion in the cohort of less than one year. The main epi-

demiological and clinical characteristics of the total of patients recruited in the PISCIS Cohort and the group of new diagnoses is seen in **table 5.2.1**.

### 5.2.1. Progression of HIV Infection

**Figure 5.2.1** shows the clinical evolution of HIV infection to diagnosis of AIDS and death. Of the total of

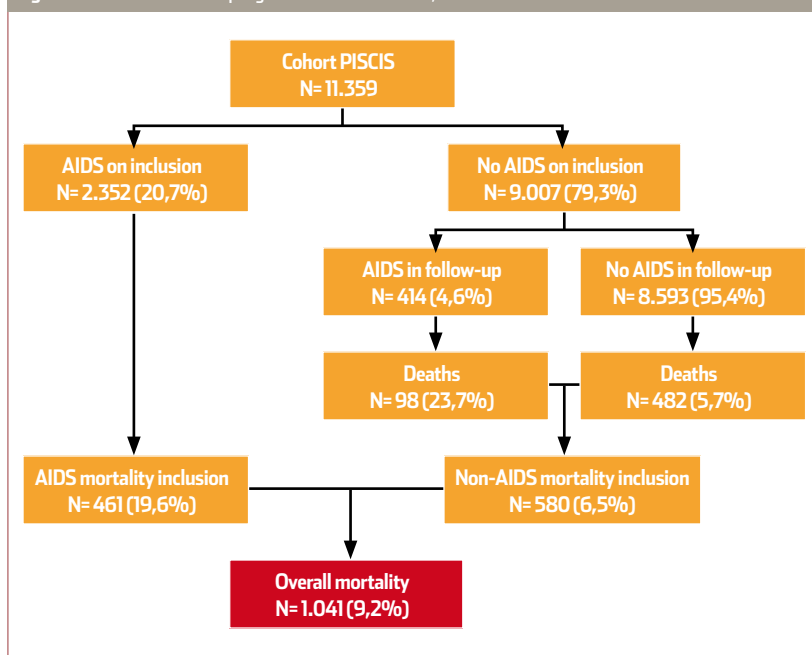
11,359 patients, 2,352 (20.7%) had at that time or had previously had an AIDS defining condition. Of the 9,007 (79.3%) patients who did not present AIDS defining symptoms at the time of inclusion in the cohort, 414 (4.6%) developed an AIDS defining illness during the monitoring. A total of 1,041 people (9.2%) died during the study period, the highest level of mortality being amongst those who had AIDS at the time of inclusion (19.6%) compared to those who were asymptomatic (6.5%).

### 5.2.2. Treatment for HIV Infection

Since the mid-1990s, with the initiation of HAART, diverse observational studies have shown the favourable change in the natural history of the infection. However, the optimum moment to initiate treatment has always been subject to debate. In the last 15 years, international HIV management guidelines have oscillated between proposing very early initiation of treatment, stimulated mainly by the publication of the first proposed models of the eradication of the infection in the short term [12], and deferring treatment for as long as possible. This last fact can be highlighted by two probable motives: the appearance of serious side effects to ART and the necessity of having to continue this treatment practically indefinitely due to persistent viral replication in cellular reservoirs [13].

Currently, the improved profile of toxicity in certain treatment guidelines [14], the higher effectiveness of the new medications, and the epi-

Figure 5.2.1. HIV infection progression. PISCIS cohort, 1998-2009.



dence gathered in studies showing similar mortality rates of seropositive patients who respond adequately to treatment compared to the general uninfected population [15], has determined that early initiation of treatment is once again proposed. The PISCIS cohort has contributed to this discussion and a recent publication, via specific statistical analysis, concluded that the best moment to start HAART is before the CD4+ cell count falls below 350 [16].

Amongst the total of patients recruited in the cohort, 9,178 (80.7%) received ART at some time during their monitoring. Amongst these, 5,447 (59.4%) were treatment naïve and initiated it for the first time in a PISCIS participating hospital. Although with the appearance of new, stronger medications in recent years, it is becoming more and more difficult to use the classic

definition of HAART (a minimum of three medications from at least two different classes), if we maintain this concept, we find that 96.2% of treatment naïve patients used a regimen which fulfilled these HAART criteria.

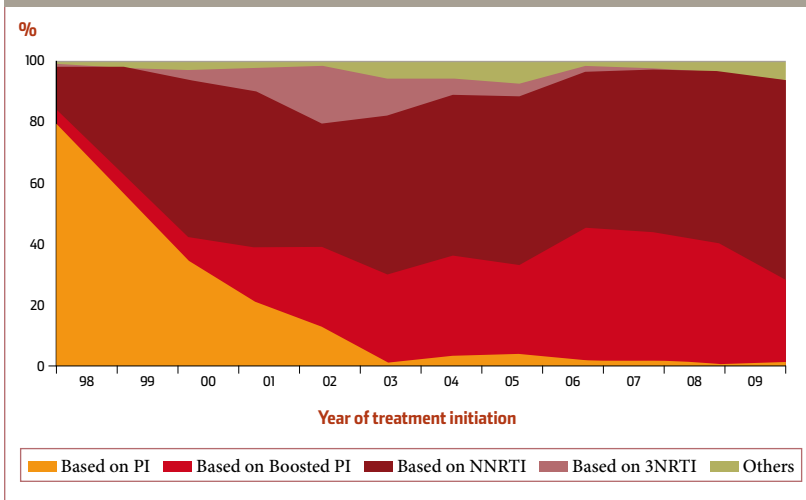
75% of patients initiated ART with a baseline CD4+ count below 350 and 21.3% had already had an AIDS defining condition. The preferred regimen for the initiation of treatment was based on non-nucleoside reverse transcriptase inhibitors (NNRTI), at 45.7%, followed by the regimen based on Protease inhibitors (PI) (25.9%), adding both regimens with the backbone consisting of 2 Nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) (table 5.2.2). Figure 5.2.2 shows the evolution of the first line treatment regimen used in the cohort year by year.

Table 5.2.2. Description of naive patients initiating treatment. PISCIS cohort, January 1998 - October 2009.

	Naive initiating treatment (n=5,447) n (%)
<b>Sex (male)</b>	4,273 (78.6)
<b>Age on inclusion</b>	
<35	2,502 (45.9)
35-55	2,585 (47.5)
>55	341 (6.3)
<b>Mode of transmission</b>	
MSM	1,940 (35.7)
Heterosexual	1,722 (31.7)
IDU	1,407 (25.9)
Others	366 (6.7)
<b>CD4+ on treatment initiation</b>	
<200	1,665 (42.9)
200-350	1,425 (32.8)
>350	1,056 (24.3)
<b>CD4+ on treatment initiation (average) (1)</b>	231 [103-346]
<b>HIV RNA on treatment initiation (log 10) (average) (1)</b>	4.9 [4.3-5.4]
<b>HCV coinfection</b>	1,036 (31.0)
<b>HBV coinfection*</b>	455 (7.6)
<b>AIDS diagnosis on inclusion</b>	1,160 (21.3)
<b>Initiating HAART</b>	4,924 (96.2)
<b>HAART regimen on inclusion</b>	
Based on PI	1,036 (21.0)
Based on Boosted PI	1,276 (25.9)
Based on NNRTI	2,252 (45.7)
Based on 3NRTI	247 (5.0)
Others	113 (2.3)
<b>Person-years of follow-up</b>	26,583
<b>On follow-up</b>	3,972 (72.9)
<b>Deaths</b>	464 (8.5)

\* Excluding Son Dureta Hospital. /  
(1) Interquartile range.

Figure 5.2.2. Annual evolution of the regimen of starting ART in naive patients. PISCIS cohort (1998-2009).



### 5.3. Clinical epidemiological study of mothers and children exposed to HIV and/or antiretroviral drugs (NENEXP Project)

The NENEXP Project (FIPSE 36535/05) is a multicentre cohort study of pregnant HIV positive women and their children, coordinated by CEEISCAT, which began in January 2000 and has received the support of FIPSE in successive renewals (FIPSE 3081/99, FIPSE 36352/02). This project has contributed to awareness about the evolution of VT of HIV in Catalonia, as well as the progress of the infection in pregnant women in recent years.

The main objectives of NENEXP Project are:

- Identify and monitor the apparition of adverse side effects from the use of ART during the pregnancy, birth and neonatal period on mother, foetus and new born baby, in the short, mid and long term.
- Describe the socio-demographic profile of the women infected with HIV who do not receive prenatal attention until the time of the birth.
- Identify the maternal factors of the pregnancy and the newly born related to the appearance of adverse effects of ART in the children exposed during the pregnancy, birth and the first weeks of life.

Currently, the participating hospitals are: Hospital San Joan de Déu (Esplugues de Llobregat), HUGTiP (Badalona), Hospital Valle d'Hebrón (Barcelona), Hospital del Mar (Barcelona), Hospital de Mataró (Mataró), Hospital Granollers (Granollers), Hospital Arnau de Vilanova (Lleida), Hospital Parc Taulí (Sabadell), and

during 2008 Hospital Joan XXIII (Tarragona) and the University Hospital Joan de Reus. Together, the obstetric and paediatric units of these centres attend to the majority of pregnant mothers infected with HIV and their children.

In this study information is collected on all new born babies in the participating centres which have been exposed to HIV and/or to therapeutic or prophylactic treatment with antiretroviral drugs during the pregnancy, the birth or the 28 days after the birth, as well as their respective mothers. The data collected refers to the ART and to the clinical monitoring of the pregnancy and birth of HIV infected women, along with the ART (be it prophylactic or not), and the long term clinical and analytical monitoring of their children. The children receive medical check-ups at regular intervals (at birth, 2 and 6 weeks, 3, 6, 12, 18 and 24 months and later, one control each year), where information relevant to the antiretroviral prophylaxis, and the state of health (growth and illnesses) and also the results of the complementary tests). The corresponding results of the 10 hospitals in Catalonia which participated in the study until 2009 are presented here. Up until 31<sup>st</sup> December 2009, data on 803 children from 806 pregnancies of 683 women has been collected in Catalonia.

With regards to the country of origin of the mothers, 61% were Spanish, 21% were from elsewhere and 18% were of unidentified origin. Amongst the foreign mothers, 69% were from

Figure 5.3.1. VT rate evolution in Catalonia, NENEXP Project 2000-2009.

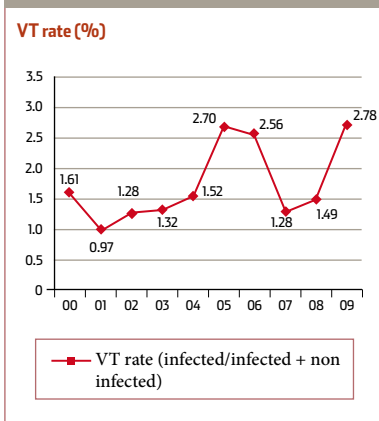
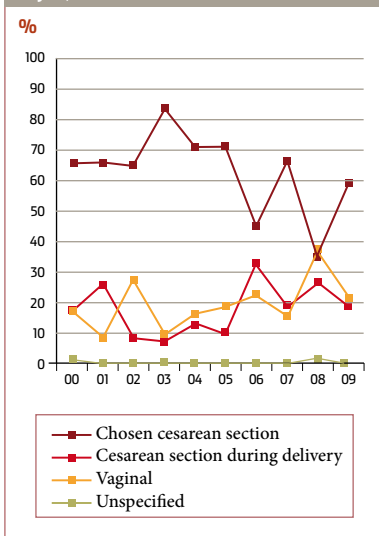


Figure 5.3.2. Evolution of the mode of delivery in HIV-positive mothers newborns. NENEXP Project, 2000-2009.



Sub-Saharan Africa, 34% were from Latin America and 13% were from EU countries.

The rate of transmission in the group of children included was 2.26%. **Figure 5.3.1** shows the evolution of the rate of VT in the last 9 years in Catalonia. It is important to stress that there are still women who are diagnosed with the infection at the moment of

Table 5.3.1. Time of diagnosis of HIV infection in the mother.

Time of diagnosis	Number of pregnancies	%
Before pregnancy	624	80.31
During pregnancy	128	16.47
During delivery	11	1.42
Post-delivery	12	1.54
Without information	2	0.26
<b>Total pregnancies</b>	<b>777</b>	<b>100.00</b>

childbirth or after and therefore, have not taken any of the prenatal measures to prevent HIV transmission. Up until 2009, cases of 23 women were reported, of whose children 6 (26%) were infected with HIV.

ART was administered during the pregnancy to 597 of the 683 pregnant women (87.4%), of whom 85% were given HAART. The average gestational age at birth was 37.08 weeks, with an IQR between 36.92 and 37.25 weeks. Four hundred and ninety two children (61.2%) were born by elective caesarean section. One hundred and thirty eight (17.1%) were born by caesarean section performed during the course of the birth and 151 (18.1%) by natural vaginal birth, with no definite trends appearing over the period studied (**figure 5.3.2**). Antiretroviral prophylaxis after the birth was initiated within the first 48 hours of life in 753 children (95%). Eight of the new born babies were breastfed.

During the first 5 days of life congenital anomalies were diagnosed in 50 (6.22%) of the new born babies included in the cohort. The 9<sup>th</sup> edition of the International Classification of Diseases was used to define these anomalies. The majority of the anomalies detected were mild or

corrected themselves spontaneously over time. By groups, the most frequent problems were musculoskeletal, genitourinary and the closure of the foramen ovale. These findings are not significantly more important than in the general population, and do not differ from those reported in similar groups [17-18]. They have to be interpreted in the context of the tests performed on these children, a fact which aids the diagnosis of anomalies which could have gone undetected.

#### 5.4. Recent HIV Infections: AERIVIH (2006-2007)

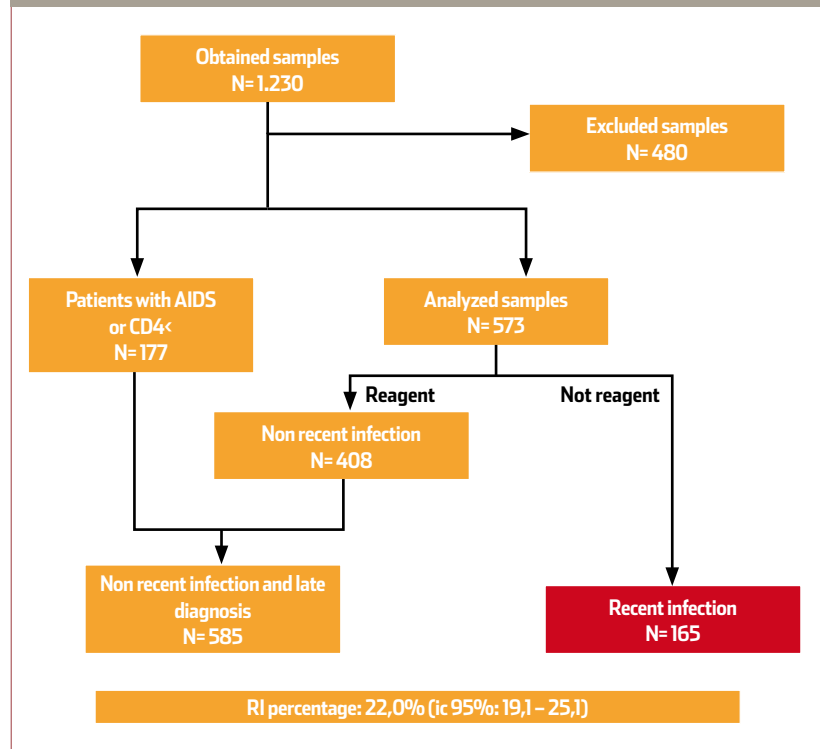
The identification of new infections provides a more precise estimation of the current dynamic of the epidemic, the information being more useful to design appropriate intervention strategies. Given that new HIV diagnoses can include infections which occurred some years before the diagnosis, these diagnoses do not reflect the extent and characteristics of new infections. With this objective, in 1998 the standardized algorithm for the recently infected was defined (STARHS: Serological Testing Algorithm for Recent HIV Seroconversions) as a means of differentiating

recent infections (RI) of less than 170 days from seroconversion (with a CI 95% of 144 to 200 days), from the non-RI [19].

Since it was defined for the first time in Europe, many countries have incorporated the STARHS technique into their HIV surveillance systems [20-25]. In the United States, the CDC has also implemented a national surveillance system for the HIV epidemic [26] incorporating the STARHS technique. Since 2001, CEEISCAT and the Microbiology Service of the HUGTiP participate in the external quality assurance for STARHS, run by CDC, with 100% satisfactory results.

On the other hand, CEEISCAT has coordinated the AERIVIH project (Standardized Algorithm for Recent HIV Infections Study Group), a study in which the STARHS technique has been used (Vironostika-LS) to identify those individuals who were recently infected amongst those recently diagnosed with HIV. The samples analyzed were new known HIV diagnoses, during the period from 2003 to 2005, and came from laboratories from primary health centres, hospitals and alternative screening centres/NGOs, and an STI clinic (Project number: 022.010 Marató TV3) [27]. In accordance with the results of this study, the percentage of recently infected (RI) amongst the new HIV diagnoses was 19.2%. The majority of RI patients were men (79.8%), with a median age of 33.1 years, and 62.5% were MSM. Immigrants made up 26.5% of RI cases, the majority being from South America. Amongst the RI cases, at least 16.5%

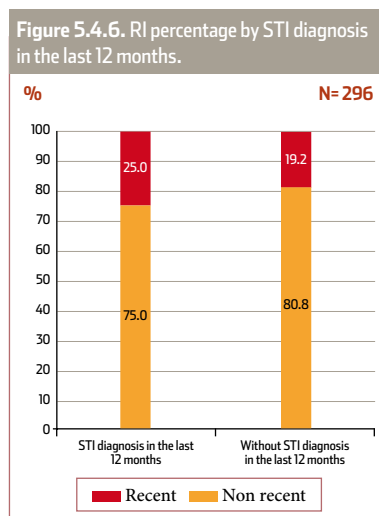
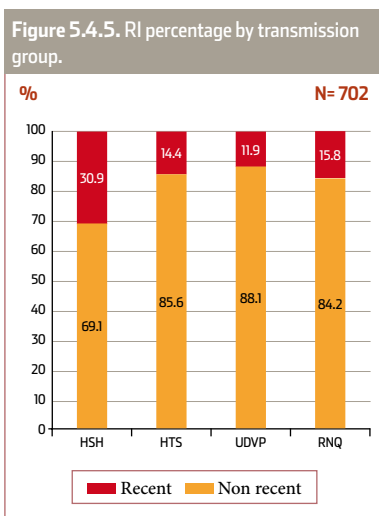
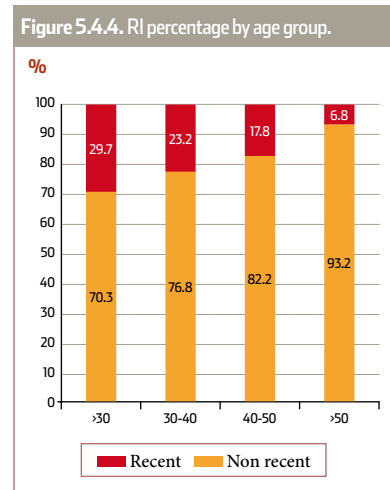
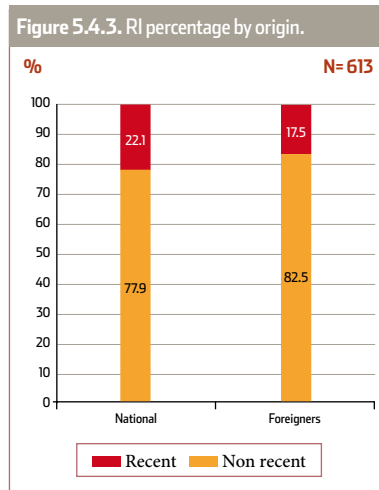
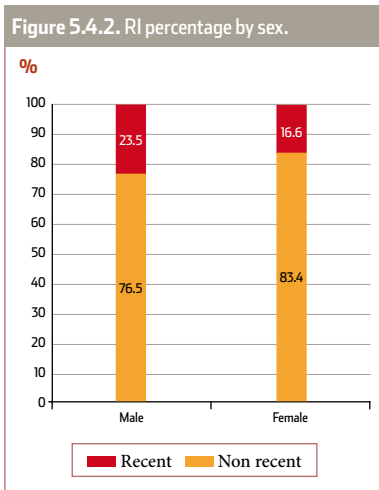
Figure 5.4.1. Algorithm for the identification of samples with recent infection.



reported the diagnosis of another STI during the year previous to their HIV diagnosis. This study demonstrated that the implementation of STARHS in our area was feasible and, as a consequence, from 2006 it has been included in SIVES. The monitoring of RI has been systematically implemented in the centres which participated in the AERIVIH project (2003-2005) and those which, voluntarily have decided to maintain participation since 2006. The Microbiological Department of HUGTiP continues to carry out analyses of samples in this new period. There are 14 Catalonian hospitals and 8 screening centres participating in the new AERIVIH project. Of the 14 hospitals, 9 already participate in the

PISCIS project. Meanwhile, the 8 alternative screening centres also form part of the network of centres participating in the HIVDEVO project (voluntary declaration of HIV) and which, along with counseling, offer free HIV tests voluntarily, anonymously and confidentially [28].

During 2006 and 2007 1,230 HIV positive samples were collected, of which, 480 samples were excluded for not fulfilling the inclusion criteria. Of the samples which were not excluded, 177 cases were patients diagnosed late (CD4+ counts lower than 200, or with clinical criteria indicating AIDS), therefore they were not analyzed. In total, 573 samples were analyzed, of which 408 were not recent diagnoses and 165



were more frequent amongst MSM (23.5%) (figure 5.4.2), the native patients (22.1%) (figure 5.4.3), patients under 30 years of age (29.7%) (figure 5.4.4) MSM (30.9%) (figure 5.4.5) and patients diagnosed with an STI in the 12 months prior to HIV diagnosis (25%) (figure 5.4.6). The differences in proportions were statistically significant in the variable ages and risk groups.

### 5.5. Monitoring the resistances transmitted to antiretrovirals in patients recently infected with HIV (2003 - 2005)

In spite of the success of ART against HIV-1 [29], there is still a group of individuals with treatment failure who are potentially at risk of transmitting resistant viruses. The phenomenon of transmitted resistance, when an individual is infected by a strain of HIV-1 with one or more mutations associated with resistance

were RI. The overall percentage of RI cases was 22% (CI95%: 1.19 – 1.25) (figure 5.4.1). For each year of diagnosis, the percentage of RI cases was 18.7% (CI95%: 14.6 – 23.4), and in 2007 it was 24.5% (CI95%: 20.5 – 28.9). The characteristics of new diagnoses, according to RI cases are described in table 5.4.1. 78.3% of new diagnoses were men, 19.6% were immigrants (44.2% coming from South America) and 48.8% of cases were MSM. The median age was

35.6 (IQR: 29.4 – 43.4) and 39.7% of new diagnoses were in the age group ranging from 30 – 40 years old. Information on STI diagnoses during the 12 months previous to the HIV diagnosis was obtained in 296 cases, and 12.2% had been diagnosed with some type of STI during the 12 months before their HIV diagnosis.

Those cases identified as RI with HIV, according to the STARHS technique,

Table 5.4.1. Characteristics of new HIV diagnoses, according to have been identified as RI (N=750).

	Total	Recent	P
	N (%)	N (%)	
<b>Sex</b>			
Male	587 (78.3)	138 (23.5)	0.106
Female	163 (21.7)	27 (16.6)	
<b>Origin (N=613)</b>			
<b>National</b>	<b>493 (80.4)</b>	<b>109 (22.1)</b>	0.540
<b>Foreigners</b>	<b>120 (19.6)</b>	<b>21 (17.5)</b>	
South America	53 (44.2)	13 (24.5)	
Central and Western Europe	12 (10.0)	0 (0.0)	
North Africa and Middle East	5 (4.2)	1 (20.0)	
Sub-Saharan Africa	16 (13.3)	1 (6.3)	
Eastern Europe and Russia	4 (3.3)	0 (0.0)	
Asia	2 (1.7)	2 (100.0)	
Unknown	27 (22.5)	4 (14.8)	
<b>Age*</b>			
<30	212 (28.3)	63 (29.7)	<0.005
30 - 40	298 (39.7)	69 (23.2)	
40 - 50	152 (20.3)	27 (17.8)	
>50	88 (11.7)	6 (6.8)	
<b>Transmission group (N=702)</b>			
MSM	343 (48.8)	106 (30.9)	<0.005
HTS	298 (42.5)	43 (14.4)	
IDU	42 (6.0)	5 (11.9)	
Risk undefined	19 (2.7)	31 (15.8)	
<b>STI** (N=296)</b>			
Yes	36 (12.2)	9 (25.0)	0.503
No	260 (87.8)	50 (19.2)	

\* Median and IQR. / \*\* Having had a STI in the last 12 months.

to antiretroviral drugs, implies a threat to treatment [30].

Population level surveillance of transmitted resistance in RI patients is an essential element in the global evaluation of resistance to ART [31]. The RI patients with transmitted resistance act as sources of the transmission of resistant HIV variants. The prevalence of resistance is high-

er in RI patients, provoked by the gradual disappearance of transmitted resistance of the dominant quaspecies over the course of time. For this reason, the prevalence of transmitted resistances in RI patients is a clear indicator of the rate of current transmitted resistances [30]. The epidemiologic surveillance of transmitted resistances provides us with relevant information to evaluate and adapt

the therapeutic recommendations in the context of HAART.

In Spain, as in other Western European countries and North America, B was the most prevalent subtype of HIV-1, although recent articles describe the rapid progression of subtypes other than B [32]. Awareness of the prevalence of subtypes other than B in our area will permit the estimation of what problems exist when using diagnostic tests and measurements of viral load (VL) validated for subtype B. The objectives of this study were to estimate the prevalence of transmitted resistances, and identify the HIV-1 subtypes in a group of RI VIH-1 patients who had been identified using STARHS, in Catalonia between 2003 and 2005.

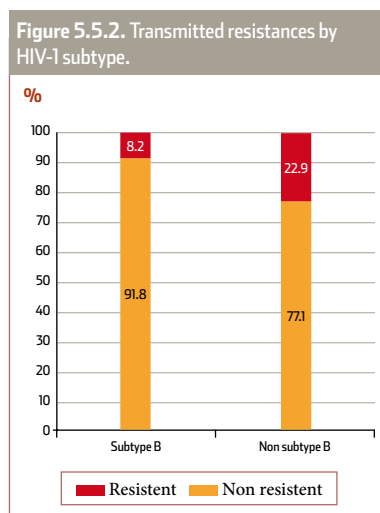
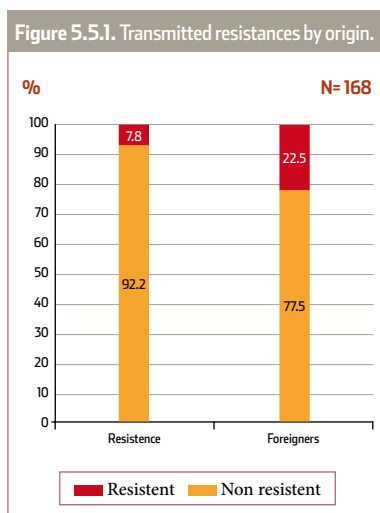
The study group consisted of 182 samples identified as RI, of which 20 cases (11%) showed mutations associated with resistance. Table 5.5.1 describes the characteristics of the RI cases. The prevalence of transmitted resistances was highest amongst immigrants (22.5% vs 7.8% in native cases,  $p = 0.019$ ) (figure 5.5.1) and in patients with non B subtypes (22.9% vs 8.2% in subtype B,  $p = 0.030$ ) (figure 5.5.2). Ten individuals (4.9%) had evidence of transmitted resistances to NRTI; six (3.3%) to NNRTI, two (1.1%) to PI, and only two individuals (1.1%) showed mutations associated with more than one type of drug. The most prevalent mutations were found in the reverse transcriptase gene: A62V (2.7%), K103N (2.7%) and M41L (1.6%) (figure 5.5.3).

Regarding HIV-1 subtypes, of the 182 sequences analyzed, 35 (19.2%) were

Table 5.5.1. Epidemiological characteristics of patients with mutations associated to resistances.

	Total	Resistant	P
	182	20 (11.0) 95% CI: 6.8–16.5	
<b>Sex*</b>			
Male	147	18 (12.2)	0.374
Female	35	2 (5.7)	
<b>Age (years) (N=181) §</b>			
<30	69	7 (10.1)	0.571
30 - 40	78	8 (10.3)	
40 - 50	21	2 (9.5)	
>50	13	3 (23.1)	
<b>Transmission group*</b>			
MSM	88	9 (10.2)	0.053
Heterosexual	41	6 (14.6)	
IDU	24	5 (20.8)	
Risk undefined	29	0 (0.0)	
<b>Origin* (N=168) †</b>			
National	128	10 (7.8)	0.019
Foreigners	40	9 (22.5)	
<b>Subtype VIH-1*</b>			
B	147	12 (8.2)	0.030
Non-B	35	8 (22.9)	
<b>Geographical area*</b>			
Barcelona metropolitan area	165	16 (9.7)	0.098
Rest of Catalonia	17	4 (23.5)	

\*N (%). / † P value calculated for 168 patients with available information. / § Median and IQR. Metropolitan area of Barcelona (Àmbit Metropolità: Barcelona, l'Hospitalet de Llobregat, Badalona, Sabadell, Mataró, Cornellà i Granollers. Rest of Catalonia: Lleida, Tortosa, Reus, Vic i Palamós.



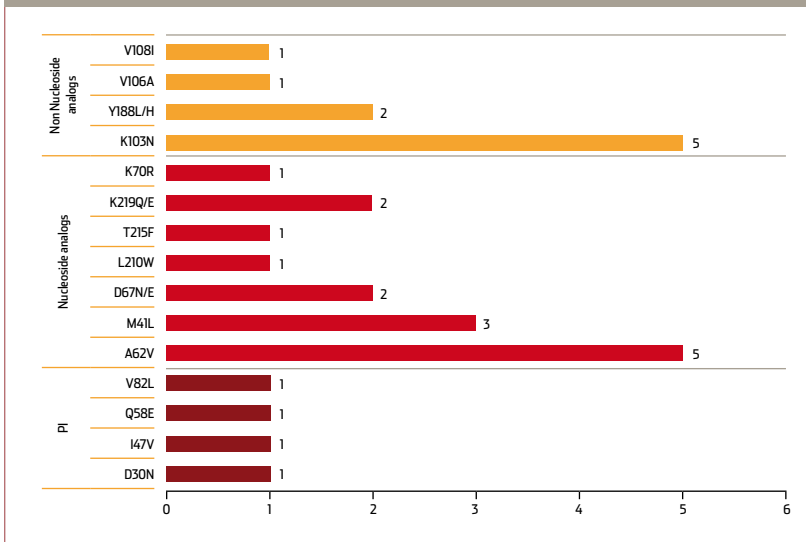
identified as subtype B. In age groups, the individuals aged between 40 and 50 years displayed a higher prevalence of non-B subtypes (47.6%) (figure 5.5.4) compared to other groups. In transmission group, IDUs showed a higher prevalence of non-B subtypes (41.7%) (figure 5.5.5). Amongst immigrant patients, 30% were infected by a non-B subtype (figure 5.5.6).

## 5.6. Project: “Synergies between HIV infection and the Human Papillomavirus: Cervical cancer and its prevention in HIV infected women”

The Human Papillomavirus (HPV) is considered to be a cause of pre-malignant lesions and cervical cancer. The DNA of HPV has been detected in more than 99% of all cases of cervical cancer [33]. HPV is an STI, and has been associated with risk factors similar to other STIs (multiple sexual partners, premature initiation of sexual activity, and sexual relations with highly promiscuous men, low socio-economic status, and the non-use of barrier contraceptives). The papillomaviruses are classified in accordance with their oncogenic potential or the relation they have with cancer of the cervix and its precursor lesions.

Thus, those related with invasive cervical cancer are named as high-risk (HR-HPV) and those which have been isolated more frequently from low-grade squamous intraepithelial lesions (LSIL) and from the

Figure 5.5.3. Number of mutations associated to resistances by drug family.



acuminate warts are designated as low-risk (LR-HPV). The most common types of LR-HPV are 6 and 11, which are detected more frequently in benign genital and cervical warts. HPV types 16, 18, 31 and 45 are detected more frequently in high-grade squamous intraepithelial lesions (HSIL) and cervical cancer, HPV type 16 being the predominant

type in the cases of invasive cancer of the cervix [34-36].

Premalignant precursor cervical cancer lesions continue to be an unresolved public health problem in HIV positive women. Invasive cervical carcinoma is an AIDS defining condition, incorporated into the new classification of 1993.

HIV positive women have a higher prevalence of HPV infection and a higher prevalence of multiple type infections, compared to HIV negative women [37-40].

In 2007 CEEISCAT started a project with the aim of studying the synergies between HIV and HPV in order to improve the prevention of cancer of the cervix, through the establishment of a cohort of women infected with HIV. It received funding from FIPSE (32620/06) and the Institute for Women which belongs to the Ministry of Work and Immigration (81/06)

The objectives of the project were:

- Estimate the prevalence of HR-HPV in HIV positive women.
- Estimate the prevalence of cervical lesions in HIV positive women.
- Report the frequency and distribution of the types of HR-HPV in HIV positive women.

Figure 5.5.4. Distribution of HIV-1 subtypes, by age group.

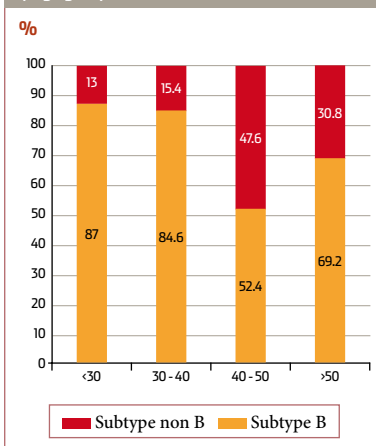


Figure 5.5.5. Distribution of HIV-1 subtypes, by transmission group.

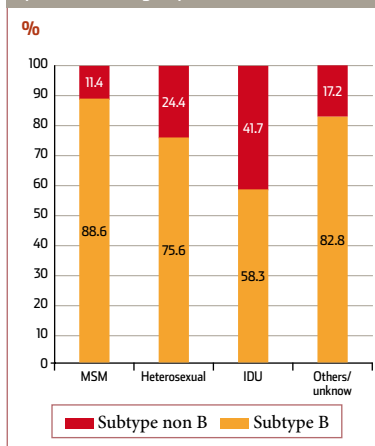
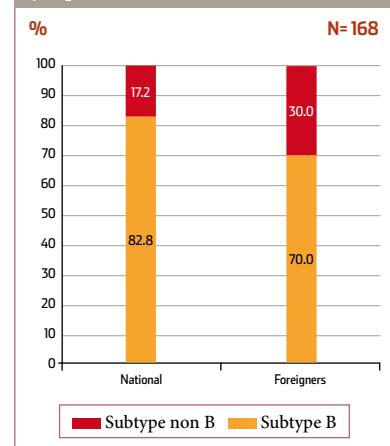


Figure 5.5.6. Distribution of HIV-1 subtypes, by origin.



- Describe the clinical-epidemiological characteristics of HIV positive women infected with HR-HPV.
- Report the screening history of HIV positive women.
- Identify the factors associated with HR-HPV infection and the development of cervical lesions.

A closed multicentre cohort established for the prospective monitoring of HIV/AIDS infected women was embedded in the PISCIS cohort monitoring the HIV infected patients. For the purpose of the proposed objectives, a transverse analysis was carried out. The study group was taken from the participating hospitals which were:

Hospital Clínica-IDIBAPS (Barcelona), University Hospital of Bellvitge (Hospitalet de Llobregat), Hospital Consorci Sanitario Parc Taulí (Sabadell), HUGTiP (Badalona), Hospital General de L'Hospitalet (Hospitalet de Llobregat), Hospital de Palamós (Palamós), Hospital Comarcal del Alt Penedès (Vilafranca del Penedès) and Hospital de la Santa Creu i Sant Pau (Barcelona). Between September 2007 and March 2009, 479 HIV positive patients were recruited. Recruitment was carried out in the HIV units of each one of the participating hospitals and the patients referred to the gynecological service where they were seen at least once and a maximum of twice a year. The diagnostic algorithm defined for the study was followed (based on the proposal for the DS of the Catalanian Parliament). In each visit a clinical-epidemiological survey was carried

out. A gynecological revision was performed on all the patients and an endocervical sample was taken for a smear test, to determine the presence of HPV DNA (Screened with second generation Hybrid Capture, HC2, Digene) and viral genotyping (Roche Linea Array). In the cases where necessary, a colposcopy and cervical biopsy were also carried out. **Figure 5.6.1** shows the algorithm followed during the study.

479 endocervical samples were analyzed (100% of the samples collected) which were obtained during

the first visit of the patients participating in the study. 159 samples were positive for HR-HPV infection (33.2% prevalence) and 320 samples were negative (**figure 5.6.1**). This prevalence is considerably higher than in the general population and is consistent with other studies performed on HIV positive women in Catalonia [38]. We can see a high prevalence of cervical lesions both LSIL and HSIL, 13.8% and 3.8% respectively (**figure 5.6.2**). Amongst the HIV positive women, those who were HPV positive had a higher prevalence of cervical le-

**Figure 5.6.1.** Algorithm for detection of HPV infection and cervical lesions in HIV positive women participating in the study.

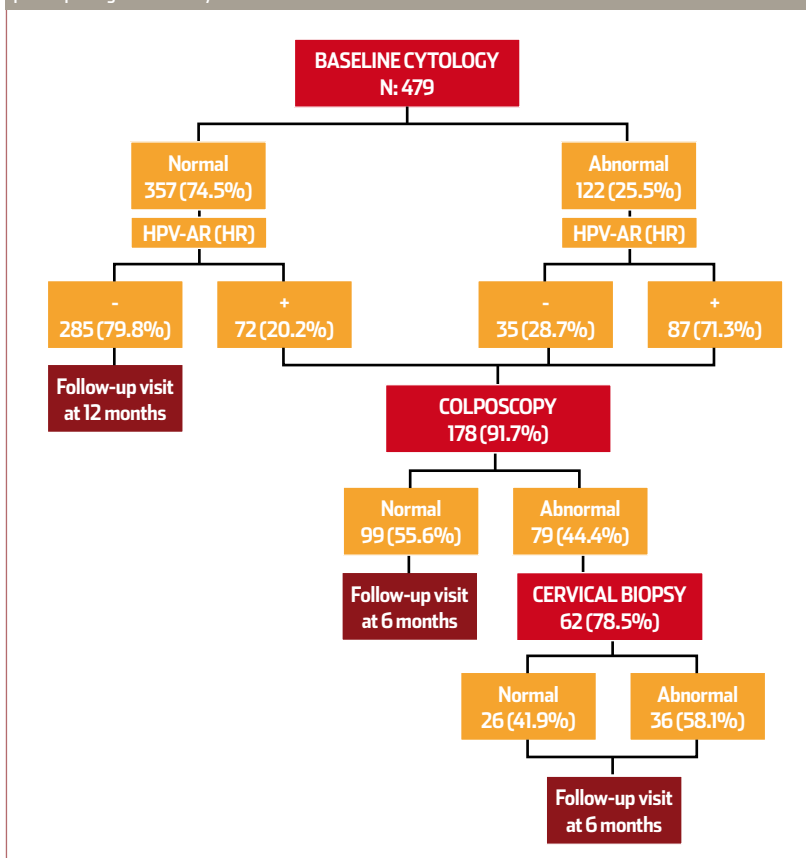


Table 5.6.1. Distribution of HPV types.

High Risk HPV types	
16	34 (23.0)
18	15 (10.1)
31	19 (12.8)
33	10 (6.8)
35	15 (10.1)
39	11 (7.4)
45	12 (8.1)
51	18 (12.2)
52	24 (16.2)
56	17 (11.5)
58	21 (14.2)
59	15 (10.1)
68	8 (5.4)
73	6 (4.1)
82	4 (2.7)
Probable High Risk HPV types	
53	30 (20.3)
66	15 (10.1)

sions, 35.2% of LSIL and 11.3% of HSIL. 78% of women co-infected with HIV and HPV had multiple infections. The types of HR-HPV most prevalent were 16, 52 and 53 with 23%, 16.2% and 20.3% respectively (table 5.6.1).

By 31<sup>st</sup> March 2010, 331 patients (69.1%) had attended a follow up visit. The prevalence of HR-HPV infection at the second visit was 33.53% (111/331). The prevalence of cervical lesions detected in the follow up visits was: 12.1%, 17.9% and 2.7% for atypical squamous cells of undetermined significance (ASCUS), LSIL and HSIL respectively.

The socio-demographic characteristics of the patients co-infected with HR-HPV and HIV are resumed in table 5.6.2. The majority of women infected with HR-HPV

Table 5.6.2. Main sociodemographic, behavioural, and clinical characteristics of the HIV and HPV co-infected women.

Sociodemographic Characteristics	Total n (%)	HPV+ (HR) n (%)
Age (years)		
<30	37 (7.7)	22 (13.8)
30-40	164 (34.2)	57 (35.8)
>40	278 (58.0)	80 (50.3)
Place of birth		
Spain	348 (72.7)	116 (73.0)
Other	131 (27.3)	43 (27.0)
Marital status		
Single	133 (27.9)	51 (32.3)
Stable partner	220 (46.2)	65 (41.1)
Widow	53 (11.1)	21 (13.3)
Divorced/separated	70 (14.7)	21 (13.3)
Study level		
Without studies	32 (6.7)	9 (5.7)
Primary Education	206 (43.2)	70 (44.3)
Secondary Education	113 (23.7)	30 (19.0)
Vocational training	71 (14.9)	29 (18.4)
Higher Education	55 (11.5)	20 (12.7)
Employment situation		
Unemployed	206 (43.0)	77 (48.4)
Businesswoman	22 (4.6)	6 (3.8)
Professional	36 (7.5)	7 (4.4)
Salaried	215 (44.9)	69 (43.4)

were aged over 40 (50.30%). The percentage of foreign women was 27% and most of the co-infected patients were married or had a partner (41.1%). 50% had a level of infection no higher than basic level and as for the type of work they carried out, 48.4% reported not being in work at that time.

82.3% of the HR-HPV positive women had begun sexual relations before 18 years of age. The majority

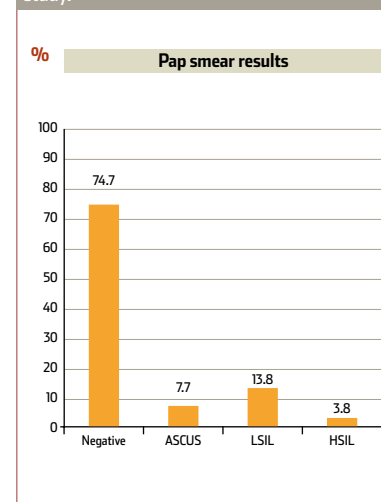
had only one sexual partner during the last 6 months (63.3%). The frequency of the use of condoms, both with the regular and sporadic partner, was similar; 33.1% and 33.3% respectively (table 5.6.3).

The lack of adherence to screening programs for cervical cancer has been identified as one of the most common contributing factors in the development of cervical cancer.

The Protocol for the Screening for Cervical Cancer in Catalonia recommends that HIV positive women take an annual smear test [41-43]. A shorter interval may be considered, if CD4 are below than 500 cel/mm<sup>3</sup>, or if there is abnormal cytology. In this study, the proportion of women who was screened for cervical cancer was low.

In this study, 54.9% of coinfecting women did not take an annual smear test, 41.2% of women with no pre-

Figure 5.6.2. Cervical lesions prevalence of the HIV positive women participating in the study.



**Table 5.6.3.** Behavioural characteristics of women co-infected with HIV and HR-HPV.

behavioural characteristics	Total n (%)	HPV+ (HR) n (%)
<b>Age at first sexual intercourse (years)</b>		
≤18	379 (79.5)	130 (82.3)
>18	98 (20.5)	28 (17.7)
<b>Number of sexual partners lifetime</b>		
1	46 (9.7)	9 (5.8)
2-3	121 (25.6)	39 (25.2)
4-5	89 (18.8)	34 (21.9)
6-10	76 (16.1)	27 (17.4)
11-20	74 (15.6)	22 (14.2)
>20	67 (14.2)	24 (15.5)
<b>Number of sexual partners during the last 6 months</b>		
None	127 (27.3)	43 (27.9)
1	308 (66.1)	98 (63.6)
2-3	28 (6.0)	11 (7.1)
4-5	2 (0.4)	1 (0.6)
6-10	1 (0.2)	1 (0.6)
<b>Use of condom in last 6 months with stable partner</b>		
Always	175 (58.7)	58 (61.1)
Regularly	30 (10.1)	6 (6.3)
Occasionally	36 (12.1)	11 (11.6)
Never	57 (19.1)	20 (21.1)
<b>Use of condom in last 6 months with occasional partner</b>		
Always	39 (63.9)	13 (61.9)
Regularly	6 (9.8)	2 (9.5)
Occasionally	4 (6.6)	1 (4.8)
Never	12 (19.7)	5 (23.8)

vious smear test were infected with HR-HPV and 23.5% showed smear test abnormalities (table 5.6.4).

The main route of transmission of 77.3% of co-infected HIV positive women was heterosexual. The average time of HIV infection was 89 months. 90.3% of the women were taking HAART and the average time on treatment was 63 months. The average CD4 count and VL was 409

**Table 5.6.4.** History of cervical cancer screening for women coinfecting with HIV and HR-HPV.

History of cervical cancer screening	Total n (%)	HPV+ (HR) n (%)
<b>Number of pap smear lifetime</b>		
0	24 (5.2)	11 (7.2)
1	22 (4.8)	10 (6.5)
2-5	137 (29.7)	66 (43.1)
6-10	109 (23.6)	20 (13.1)
+11	169 (36.7)	46 (30.1)
<b>Age at first pap smear (years)</b>		
<25	297 (75.0)	102 (77.3)
25-35	75 (18.9)	23 (17.4)
>35	24 (6.1)	7 (5.3)
<b>Pap smear frequency</b>		
Once a year	210 (50.6)	60 (45.1)
One every 2-3 years	105 (25.3)	30 (24.1)
One every 4-5 years	39 (9.4)	16 (12.0)
One every 6-10 years	34 (8.2)	14 (10.5)
Less than one every 10 years	27 (6.5)	11 (8.3)

cells/mm<sup>3</sup> and 50 copies/ml, respectively (table 5.6.5).

The factor associated with HPV infection was age (Odds Ratio (OR): 0.9 CI 0.94-0.99), with women younger than 35 years having a higher prevalence of infection than those who were older. The factors associated with the existence of cervical lesions (ASCUS, LSIL and HSIL) were: Having started sexual relations before 18 years of age (OR: 2.3 CI: 1, 1-5, 0) as opposed to having started after 18 years of age. Having CD4 levels lower than 200 cells/mm<sup>3</sup> (OR 5.7 CI: 2.2-14.8) and between 200 and 500 cells/mm<sup>3</sup> (OR: 1.8 CI: 10, 1-3, 4) compared with those women with a count of CD4> 500 cells/mm<sup>3</sup>. A HIV VL of > 10,000copies/ml (OR 3.1 CI: 1.4-6.9) compared with those women who had a VL of <400 copies/ml.

**Table 5.6.5.** Clinical characteristics of women co-infected with HIV and HR-HPV.

Clinical characteristics	Total n (%)	HPV+ (HR) n (%)
<b>CD4 T lymphocyte count (cells/mm<sup>3</sup>)</b>		
<200	43 (9.5)	27 (17.9)
200-500	196 (43.1)	68 (45.0)
>500	216 (47.5)	56 (37.1)
<b>Mean time on treatment (months)</b>	<b>90</b>	<b>63</b>
<b>VL</b>		
<400	313 (74.5)	88 (64.7)
400-5.000	45 (10.7)	17 (12.5)
5.000-10.000	13 (3.1)	5 (3.7)
>10.000	49 (11.7)	27 (19.9)
<b>Currently on treatment</b>	<b>413 (86.2)</b>	<b>134 (84.3)</b>
<b>On HAART +</b>	<b>354 (85.7)</b>	<b>121 (90.3)</b>
<b>No on HAART</b>	<b>59 (14.3)</b>	<b>13 (9.7)</b>
<b>Time on treatment (months)</b>		
<60	139 (33.7)	65 (48.5)
60-120	139 (33.7)	32 (23.9)
>120	135 (32.7)	37 (27.6)
<b>Mean CD4 T lymphocyte count (cells/mm<sup>3</sup>)</b>	<b>480 (RIQ: 331-702)</b>	<b>409 (RIQ: 267-570)</b>
<b>Average of time on treatment (months)</b>	<b>90 (RIQ: 43-132)</b>	<b>63 (RIQ: 24-131)</b>
<b>Mean HIV-1 viral load (copies/mL)</b>	<b>50 (RIQ: 40-584)</b>	<b>50 (RIQ: 40-4320)</b>
<b>Mean time since HIV infection</b>	<b>119 (RIQ: 59-191)</b>	<b>89 (RIQ: 34-185)</b>

## 5.7. Cohort of HIV negative men who have sex with men (MSM) for the study of early HIV and STI diagnosis and their determining factors

The ITACA project is a longitudinal study which began in 2008 with the collaboration of BCN Checkpoint, a community based alternative centre for the detection of HIV and other STIs for MSM. The purpose of the study is to establish a cohort of seronegative MSM from which to prospectively collect socio-demographic, behavioural and clinical data, also facilitating and encouraging the taking of a regular HIV test as promoted by other similar studies [44-45]. In 2008, the project was co-financed by the Ministry of Health and Consumer Affairs/ National Plan

Image 5.1. Rapid tests for detection of antibodies against HIV.



for AIDS thus forming part of the programmes for the prevention and control of HIV/AIDS in 2008. From 2009 and until the end of 2010, the main source of funding is the pharmaceutical company Gilead.

The general objectives to be considered are:

- Contribute to the activities for the prevention of HIV and other STIs in BCN Checkpoint.
- Facilitate the early diagnosis of HIV.
- Evaluate the impact of peer counselling in the changing of risk behaviours and identifying potentially effective preventative interventions.
- Create a stable platform of seronegative MSM for the development of preventative interventions and investigative programmes directed at this group.
- Carry out a pilot study in Catalonia to monitor serostatus and behaviour of MSM that will be extrapolated to other geographical areas within Spain.

In the basal visit, and every 6 or 12 months in the follow up visits, biological information is collected for the detection of HIV antibodies and of syphilis through rapid blood tests (Determine® HIV-1/2 and Determine® Syphilis TP, respectively) and socio-demographic and behavioural data along with the information from the participants in the cohort gained from a specific questionnaire which

Image 5.2. The highest percentage of RI is observed among MSM. Continuing to promote HIV testing in this group is essential.



the assessor completes subsequent to the HIV test and the counselling session.

Since the introduction in 2006 of the rapid HIV test in alternative community based centres in Catalonia, the demand for the HIV test has continued to rise and BCN Checkpoint is a good exponent, the number of annual tests having increased from 281 to 1,513 (2006 and 2009 respectively). In 2007 10% of all HIV positive test results reported in Barcelona were from tests taken at BCN Checkpoint.

The total number of HIV tests carried out in the ITACA cohort from 1<sup>st</sup> December 2008 until 31<sup>st</sup> December 2009 was 2,323, with the corresponding retention of follow up visits from December 2009 of 77.9%. The total of HIV positive participants who could not continue in the cohort was 4 by the end of 2009.

Based on the current data available, it is important to highlight both the notable increase of the number of HIV tests carried out at BCN Checkpoint since the introduction of the rapid HIV test in 2006 and the high retention of the ITACA cohort of seronegative MSM.

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➤ Longitudinal studies are a necessary complement for a thorough knowledge of the natural history of HIV and other STIs.

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➤ The clinical monitoring of patients is one of the weak points in the compliance with the current recommendations of NPEP, as only half of the cases (independent to the risk of exposure and the indication of ART) attend the test at the six month stage. Measures to assure the complete monitoring of all cases must be reinforced.

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➤ During the study period, three seroconversions were identified which, after detailed and thorough study, could not be attributed to an error in the PEP prescribed. It is essential to remember that this practice is only to be used in exceptional circumstances. It must not at any time be used instead of first line HIV prevention, which has to continue to be the priority in both community and individual interventions.

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➤ The most frequent route of transmission amongst the patients

included in the PISCIS cohort is sexual, with the MSM group the most common group both in total in the cohort and in new diagnoses. Therefore it is important to strengthen prevention measures in this group by promoting condom use, as well as access to the HIV test.

---

➤ One fifth of the patients recruited in the PISCIS cohort already had an AIDS defining condition or had previously had one at the time of inclusion in the cohort. Early diagnosis of the infection must be promoted to be able to access treatment and to adopt preventative measures to avoid the transmission of the virus and possible reinfections.

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➤ After the decrease which the introduction of antiretroviral prophylaxis and other preventative measures implied during pregnancy, the rate of VT has stabilised in the last few years, with a rate of 2%. Despite all this, and with the resources available in the health field, there is room for improvement and therefore maintaining preventative measures will be necessary.

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➤ The arrival of immigrant populations from countries with a high prevalence of HIV may introduce subtle variations in the context of VT in Spain. New efforts must be made to identify vulnerable groups and interventions which guarantee access to preventative measures.

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➤ The congenital anomalies found in children exposed to ART during pregnancy do not appear to justify, neither by their frequency nor their seriousness, a change in the guidelines for antiretroviral prophylaxis or ART in the mother.

---

➤ The results obtained from the integration of STARHS in the integrated system of HIV surveillance has shown that the algorithm is a useful tool to be able to describe the epidemiological characteristics of the infections which are being produced in our area. On the other hand, the identification of the factors associated with the RI can be incorporated into the different programmes and campaigns for the prevention and control of HIV and STIs, thus contributing to the decrease in the number of new infections for these pathologies.

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➤ The highest percentage of RI was found in the MSM group (30.9%). The greater risk of RI amongst MSM may have a double interpretation: on the one hand it is a known fact that this group takes more HIV tests (increasing the probability of being identified as RI), but an increase in risk behaviour and STIs has also been observed, a fact which would indicate a higher incidence of HIV in this group. A key piece of information to interpret the results would be to know the testing pattern of our study population.

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➤ The prevalence of transmitted resistances in RI patients in Catalonia (11%) is similar to those observed in other studies carried out in other regions of Spain and Europe. It will be important to reinforce prevention messages in HIV positive patients and assure the correct adherence to treatments to decrease this percentage in the future.

➤ Immigrant patients and those infected with non B subtypes have a higher prevalence of associated mutations and resistances, and this suggests that these are already circulating in the environment under study.

➤ The systematisation of epidemiological surveillance resistances to ART is the key to the correct monitoring of these parameters (prevalence of transmitted resistances and of subtypes).

➤ The high number of HIV positive women incorrectly screened for cervical cancer, along with the high prevalence of HR-HPV cervical lesions, means that it is vital to promote the screening of this group. The screening should be complemented with diagnostic techniques which allow for the detection of asymptomatic HPV infections in HIV positive women.

➤ Taking into consideration the high prevalence of the detection

of HPV 16, the genotype which causes 60% of the cases of cervical cancer in HIV positive women, once the effectiveness, safety and immunogenicity of the HPV vaccine has been demonstrated, the vaccination of HIV positive women is recommended.

➤ In spite of the fact that the concluding results of the ITACA project are not available, the high retention of the cohort corroborates the potential of alternative centres in the promotion of the rapid HIV test and the introduction of counselling as strategies, the aims of which are the early diagnosis of HIV and the reduction of risk behaviours.

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