

# A Foothold for Subtype C in the Americas: Associations with C and Non-C HIV Infection in South Brazil

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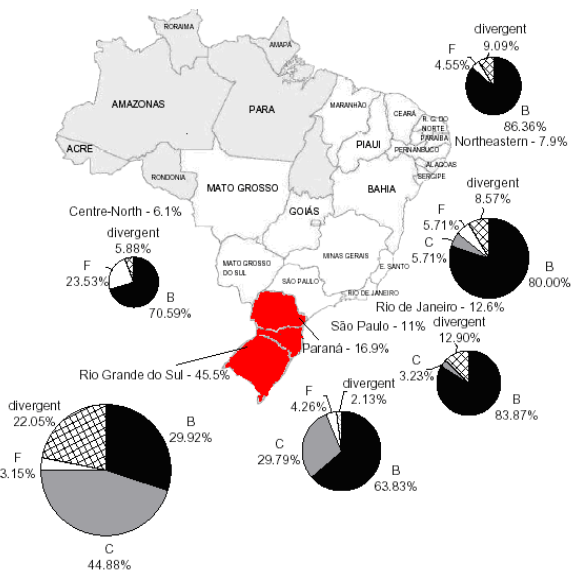
## Background

- HIV epidemic in Brazil is has stabilized, with nationwide seroprevalence <1%.
- AIDS incidence overall declined 40% between 2000 and 2006.
- But recently, the Southern states of Rio Grande do Sul, Paraná, and Santa Catarina surpassed São Paulo and Rio de Janeiro as the regions most affected by the epidemic.
  - In 2006, AIDS incidence was 17 cases/100,000 in the South, vs. 11.5 in the Southeast (São Paulo and Rio de Janeiro), and 10.1 nationally.
- HIV subtype C is now the dominant circulating HIV strain in the south, whereas HIV subtype B still predominates elsewhere in Brazil (Figure 1).
- It is unknown whether the co-circulation of subtypes C and B is due to differences in risk behavior, social or sexual mixing, or viral-host interactions such as tissue tropism.

## Objective

To better understand the epidemiology of infection and the differential spread of HIV subtypes in Southern Brazil, especially the rapid expansion of HIV subtype C infection. We examine prevalent HIV infection, recently acquired HIV, and HIV subtypes in associations with sociodemographic and risk behavior data in a large population of persons attending HIV counseling and testing (VCT) centers in Rio Grande do Sul.

Figure 1. Southern Brazil is the Epicenter of a Subtype C Epidemic



Brindeiro RM, Diaz RS, Sabino EC, et al. Brazilian Network for HIV Drug Resistance Surveillance (HIV-BResNet): A survey of chronically infected individuals. AIDS 2003, 17:1063–1069

## Methods

- Projeto AMPLIAR** studies the epidemiology of HIV transmission in South Brazil.
- Population:** HIV testing clients >16 years old from 4 VCT centers covering 65% of the testing population in Rio Grande do Sul.
- Data collection:** Pre-test sociodemographic and risk behavior data from consenting VCT clients using a modified version of the national risk assessment questionnaire.
- Laboratory tests:** HIV status determined by a reference standard including a 4<sup>th</sup> generation EIA with confirmatory Ab testing, HIV NAAT if 4<sup>th</sup> gen-negative (Roche Amplicor 1.5 Ultra pooled 1:20), and follow-up serology (if initially positive). Recent infections assessed using the BED CEIA assay (Calypte; ODn cutoff=0.8). Subtyping by population sequencing of *pol* (ViroSeq; Abbott) and phylogenetic analysis.

- Statistical analyses:** Assessed associations between sociodemographic and behavioral variables and the principal outcomes (HIV infection [prevalent and recent] and HIV subtype) in bivariate analyses using chi-square and Fisher’s exact tests, and in multivariate logistic regression (STATA version 9).

## Summary of Results

### Population:

- 1210 AMPLIAR participants, enrolled between October 2006 and August 2007.
- 46% were female; 50% aged 24 to 40 years; 45% were married. Few reported sex work (7.3%) or injection drug use (0.5%).

### HIV infection:

- HIV seroprevalence was 12.4% (Table 1).
- HIV infection positively associated with being non-white, <8 years of education, age, ever married, and being MSM (Table 1); and negatively associated with sex work.
- Variables independently associated with HIV included: sexual partner choice (MSM vs.non-MSM; AOR 3.4, 95% CI 1.89–6.2), <8 years of education (AOR 1.6, 95% CI, 1.13–2.35), and sex work, which was protective (AOR 0.07, 95% CI 0.01–0.49) (Table 3).

### Recent/acute HIV infection:

- 29 participants (2.4%) classified as recently or acutely infected (Table 2).
- Recent/acute HIV infection associated with being MSM, and <8 years of education (Tables 2 and 3).

### HIV subtype:

- 110 (72%) of 152 HIV-infected participants were subtyped: 62% were C, 29% B, and 9% other (F and recombinants) (Figure 2).
- Subtype C infection was associated with age ≥40 and being a heterosexual male vs. MSM (Table 4).

Table 1. Participant Characteristics and Bivariate Associations with HIV Infection

Characteristic	N (%)	HIV+ (%)	OR	95%CI	P
All	1210(100)	152(12.4)			
HIV Stage					
chronic		123(10.0)			
acute & recent HIV		29(2.4)			
Female (vs. male)	560(46)	71(12.7)	1.02	0.72-1.43	0.93
Nonwhite (vs. white)	333(28)	54(16)	1.54	1.07-2.21	0.02
<8 yrs schooling	456(38)	75(16)	1.73	1.23-2.44	0.002
Age (year)					
16-23	310(25)	24(8)	1		
24-40	588(50)	87(15)	1.96	1.22-3.16	0.005
40+	310(25)	41(13)	1.76	1.03-3.0	0.04
Married (vs. not)	547(45)	82(15)	1.47	1.05-2.08	0.03
Sex work	88(7.3)	1(1)	0.074	0.01-0.54	0.0008
MSM (vs. all others)	90(7)	20(22)	2.13	1.25-3.63	0.004
MSW (vs. MSM)	558(86)	61(11)	1		
MSW	90(14)	20(22)	2.33	1.32-4.11	0.003
IDU	6(0.5)	1(17)	1.40	0.16-12.07	0.80

Table 2. Bivariate Associations with Recent Infection

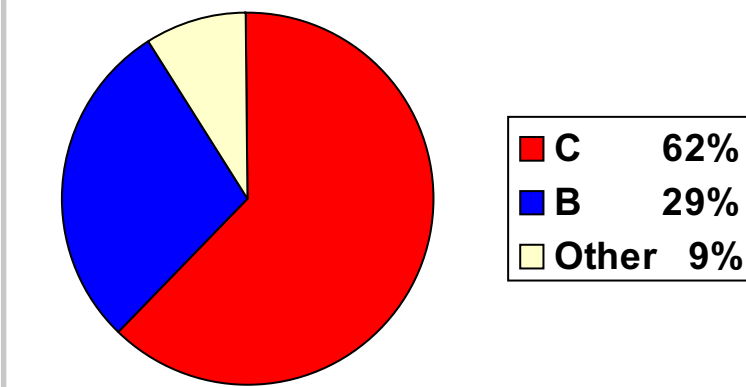
Participant Characteristic	N(%)	Ac/Recent HIV+(%)	OR	(95%CI)	P
Uninfected + Recent/Acute	1085(100)	29(2.7)			
Female	503(46)	14(3)	1.08	0.52-2.27	0.83
Not white vs. white	287(26)	8(2.8)	1.06	0.47-2.43	0.88
Age (years)					
16-23	285(26)	8(2.8)	1		
24-40	525(48)	13(2.5)	0.87	0.36-2.15	0.78
40+	277(25)	8(2.9)	1.03	0.38-2.79	0.95
<8 years schooling	401(37)	20(5)	4.0	1.79-9.0	0.003
Social exclusion	12(1)	1(8.3)	3.51	0.44-28.25	0.21
Sex work	87(8)	0			
MSM (vs. all)	77(7)	7(9.1)	4.48	1.84-10.92	0.0003
MSM vs. MSW					
MSW	505(87)	8(1.6)	1		
MSM	77(13)	7(9.1)	6.21	2.15-17.92	0.0001

Table 3. Independent Associations with HIV Infection

Characteristic	Odds HIV-infection* (all)			Odds Acute/Recent HIV Infection^		
	AOR	95%CI	P	AOR	95%CI	P
Female	1.27	0.87-1.84	0.2	1.79	0.96-1.03	0.6
Nonwhite	1.34	0.92-1.95	0.1	0.91	0.39-2.12	0.8
<8 yrs schooling	1.63	1.13-2.35	<0.01	4.83	2.10-11.1	<0.001
Sexwork	0.07	0.01-0.49	<0.01	--	--	--
MSM	3.42	1.89-6.2	<0.001	8.17	2.78-24.02	<0.001

\* Adjusted for age, sex, race, schooling (<or>8 yrs), sexwork, msm (vs. msw or woman).  
^ Adjusted for age, sex, race, schooling (<or>8 yrs), msm (vs. msw or woman).

Figure 2. Prevalence of HIV-1 Subtypes (chronic and acute/recent infections)



Of the 110 HIV-infected participant samples available for subtyping, 68 were subtype C and 31 were subtype B. The remaining 11 consisted of F (4), BF recombinants (5), CB recombinant (1), and AG recombinant (1).

Table 4. Bivariate Associations with C vs. Non-C HIV Infection

Characteristic	Reporting(%)	Non-C(%)	C(%)	OR	95% CI	P
Subtyped	110(100)	42(38)	68(62)	--	--	--
Age (years)						
16-23	14(13)	8(57)	6(43)	1	--	--
24-40	65(60)	26(40)	39(60)	2	0.6-6.6	0.2
40+	29(27)	7(24)	22(76)	4.2	1.0-17.9	0.04
Female	50(46)	19(38)	31(62)	1	0.5-2.2	1
Ever married (vs. never)	73(68)	25(34)	48(66)	1.6	0.7-3.7	0.3
Nonwhite (vs. white)	39(36)	15(38)	24(62)	1	0.4-2.2	0.9
<8 yrs schooling	51(47)	16(31)	35(67)	1.8	0.8-3.8	0.2
MSM vs. MSW	58(100)					
MSW	43(74)	13(30)	30(70)	3.5	1.02-11.7	0.05
MSM	15(26)	9(60)	6(40)	1		
MSM vs. all subtyped	108(100)					
MSW & Women	93(86)	32(34)	61(66)	1	--	--
MSM	15(14)	9(60)	6(40)	0.3	0.1-1.1	0.06

## Conclusions

- There is an association between subtype C and being heterosexual (vs. MSM) in Southern Brazil.
  - No evidence of heterosexual and MSM populations being socially and sexually isolated.
  - Thus, findings suggest that subtype C may be more efficiently transmitted female-to-male, perhaps by preferential shedding in vaginal mucosa (John-Stewart 2005). Alternatively, there may be sexual mixing patterns not captured by behavioral measures.
  - More specific behavioral data (e.g., at partner and network level), linked to subtyping, is required to understand better the relationship between HIV subtype, partner choice, and type of intercourse.
- Analysis of recent infection data suggest that MSM and persons with less formal education continue to be at risk and in need of increased prevention efforts.
- Very low rate of HIV infection among sex workers, despite a median of 51/2000 partners over 12 months (data not shown), may indicate that this group has more effectively adopted prevention strategies, and warrants future study.

## Limitations

- Results obtained from persons seeking HIV testing at VCTs and, as such, are not generalizable to the overall population.
- Underreporting of risk behaviors may result in conservative estimates of excess risk associated with HIV infection.
- Small sample size of this interim analysis limits our ability to identify associations with subtype C vs. non-C HIV infection.
- Some populations at risk of HIV infection may not present for testing at the VCT sites that participated in this study (e.g., sex workers, IDU). Low numbers of IDU are particularly concerning as IDU is a well-recognized risk factor for HIV infection and a prevalent behavior in Rio Grande do Sul.