

Christovam Barcellos¹

Lisiane Morelia Weide Acosta^{II}

Eugenio Lisboa^{II}

Francisco Inácio Bastos¹

Surveillance of mother-to-child HIV transmission: socioeconomic and health care coverage indicators

Vigilância da transmissão vertical do HIV: indicadores socioeconômicos e de cobertura de atenção à saúde

ABSTRACT

OBJECTIVE: To identify clustering areas of infants exposed to HIV during pregnancy and their association with indicators of primary care coverage and socioeconomic condition.

METHODS: Ecological study where the unit of analysis was primary care coverage areas in the city of Porto Alegre, Southern Brazil, in 2003. Geographical Information System and spatial analysis tools were used to describe indicators of primary care coverage areas and socioeconomic condition, and estimate the prevalence of liveborn infants exposed to HIV during pregnancy and delivery. Data was obtained from Brazilian national databases. The association between different indicators was assessed using Spearman's nonparametric test.

RESULTS: There was found an association between HIV infection and high birth rates ($r=0.22$, $p<0.01$) and lack of prenatal care ($r=0.15$, $p<0.05$). The highest HIV infection rates were seen in areas with poor socioeconomic conditions and difficult access to health services ($r=0.28$, $p<0.01$). The association found between higher rate of prenatal care among HIV-infected women and adequate immunization coverage ($r=0.35$, $p<0.01$) indicates that early detection of HIV infection is effective in those areas with better primary care services.

CONCLUSIONS: Urban poverty is a strong determinant of mother-to-child HIV transmission but this trend can be fought with health surveillance at the primary care level.

DESCRIPTORS: HIV Infections, prevention & control. Infectious Disease Transmission, Vertical. Health Services Accessibility. Socioeconomic Factors. Health Inequalities. Epidemiologic Surveillance Services. Ecological Studies. Basic Health services. Geographic information systems.

¹ Laboratório de Informações em Saúde. Instituto de Comunicação e Informação Científica e Tecnológica em Saúde. Fundação Oswaldo Cruz. Rio de Janeiro, RJ, Brasil

^{II} Coordenadoria Geral de Vigilância em Saúde. Secretaria Municipal de Saúde. de Porto Alegre, RS, Brasil

Correspondence:

Christovam Barcellos
Laboratório de Informações em Saúde
Instituto de Comunicação e Informação Científica e Tecnológica em Saúde
Fundação Oswaldo Cruz
Av. Brasil, 4365 – Manguinhos
21045-900 Rio de Janeiro, RJ, Brasil
E-mail: xris@fiocruz.br

RESUMO

OBJETIVO: Identificar áreas de concentração de crianças expostas ao HIV durante a gestação e sua associação com indicadores de cobertura da atenção básica à saúde, e de condições socioeconômicas saúde.

MÉTODOS: Estudo ecológico tendo como unidade de análise as áreas de abrangência de unidades básicas de saúde em Porto Alegre, RS, em 2003. Foram utilizados Sistema de Informações Geográficas e ferramentas de análise espacial para calcular indicadores de cobertura da atenção básica à saúde, condições socioeconômicas e prevalência de nascidos vivos expostos ao HIV durante a gravidez e perinatal. Os dados analisados foram obtidos em sistemas de informação nacionais. A associação entre os diferentes indicadores foi avaliada por meio de teste não-paramétrico de Spearman.

RESULTADOS: Observou-se associação entre infecção pelo HIV em gestantes com taxas de natalidade ($r=0,22$, $p<0,01$) e falta de assistência pré-natal ($r=0,15$, $p<0,05$). As maiores taxas de infecção por HIV em gestantes foram verificadas em áreas com piores condições socioeconômicas e dificuldades de acesso a serviços de saúde ($r=0,28$, $p<0,01$). No entanto, a relação observada entre a maior frequência de assistência pré-natal entre gestantes HIV positivas e maior cobertura vacinal nas áreas ($r=0,35$, $p<0,01$) indica a capacidade de detecção precoce da infecção pelo HIV em áreas com melhores serviços de atenção básica.

CONCLUSÕES: A pobreza urbana representa um forte condicionante da transmissão vertical do HIV mas a atuação de serviços de vigilância em saúde articulados com a atenção básica podem vencer essa tendência.

DESCRITORES: Infecções por HIV, prevenção & controle. Transmissão Vertical de Doença Infecciosa. Acesso aos Serviços de Saúde. Fatores Socioeconômicos. Desigualdades em Saúde. Serviços de Vigilância Epidemiológica. Estudos Ecológicos. Atenção básica de saúde. Geoprocessamento.

INTRODUCTION

One of the most significant advances in controlling the AIDS pandemic has been the actual opportunity to prevent or at least substantially minimize mother-to-child HIV transmission by means of timely proper prophylactic and therapeutic interventions. The milestones for these actions were the findings of the AIDS Clinical Trial Group⁷ (ACTG-076) which, in 1994, documented that antiretroviral prophylaxis considerably reduces mother-to-child HIV transmission.

In Brazil these evidences resulted in key public health policies. The Brazilian Ministry of Health STD/AIDS Program defined the control of mother-to-child transmission as a top priority. Brazil's strategy focuses on reinforcing its primary care system through training of health providers and managers, procurement, supply and monitoring of anti-retroviral drugs (ARVs) as well as defining "HIV-positive pregnant women and

exposed children" as a health event subject to compulsory notification^{15,a} requiring prompt intervention. These actions were decentralized at the municipal level in Porto Alegre, southern Brazil, as of September 2001. In 2002, the prevalence of HIV-infected pregnant women in the city of Porto Alegre reached 3% according to sentinel studies performed in maternity hospitals,¹³ which is substantially higher compared to 0.5% nationwide.¹¹

The Brazilian AIDS epidemic has been very dynamic and multifaceted, and is rather a combination of regional subepidemics, differing in magnitude, dynamics and at-risk populations that are most affected in each context and locality.³

Poverty is a critical health determinant in individuals and populations as it increases their vulnerability to different diseases and is a major barrier to equitable

^a Ministério da Saúde. Vigilância em Saúde. Dados e indicadores selecionados. Brasília, DF; 2003.

access to health care services, information and preventive measures.⁹ Previous studies of HIV-positive pregnant women in Porto Alegre documented clustering of areas with high prevalence rates and a substantial proportion of people living in shantytowns (*favelas*) along the city fringes.² Social inequalities in poor areas often comprise different components such as barriers to health service access⁵ and high rates of pregnancy among adolescents.⁴

Initiatives aiming to curb mother-to-child HIV transmission have to be comprehensive integrating health surveillance and care. An initiative was fully implemented in Porto Alegre after the 3rd Municipal Health Conference in 2001.^a This model promotes the integration between health care and health, epidemiological and environmental surveillance based on a process of decentralization and definition of coverage areas of primary care services. However, health surveillance is based on different, not necessarily integrated indicators. For instance, health care indicators refer to primary care units (PCU), whereas epidemiological indicators often refer to districts, and socioeconomic indicators are based on census tracts data. Health researchers and managers assessing health and socio-environmental indicators face the challenge of having to deal on a daily basis with a huge set of indicators from distinct spatial units.

PCU areas were recently established by local health administrators, tailoring the capacity of each health unit to the reference population in each coverage area. Although PCU areas do not represent a definitive impediment for the consultation of patients living outside their boundaries, each PCU preferentially provides care to the population living in its coverage area, and this is especially true for AIDS care and management, which involves counseling, long-term follow-up and provision of free medication for a relative large number of patients.

As there are no data originally assigned to these new spatial units, there is a pressing need to (re)define and calculate indicators for these new units. Geographical Information Systems (GIS) are useful tools that allow gathering data from different sources and formats, merging and integrating different information.¹⁰

The objective of the present study was to identify clustering areas of mother-to-child HIV transmission based on HIV epidemiological indicators associated with primary care indicators, as well as broad social and demographic indicators.

METHODS

An ecological study was conducted and data was organized and analyzed according to spatial clusters. The main unit of analysis was the area defined by each PCU. For this purpose, social, health care delivery and epidemiological indicators were estimated for these areas.

In Porto Alegre health surveillance is performed by the General Coordination of Health Surveillance. A thorough investigation of HIV-infected women and their offspring requires ongoing linkage of data generated from prenatal care services and updated information on delivery and follow-up of pediatric cases from different health units, e.g. hospitals, primary care units, and laboratories. Confirmed cases are reported as "HIV-positive pregnant woman and exposed child."

The local primary care network comprises 122 PCUs with their respective area and population. AIDS patient management and care, prenatal care of HIV-infected pregnant women and follow-up of children exposed to HIV are centralized in eight referral services, called Specialized Care Services. Three specialized services provide inactivated poliomyelitis virus (Salk) vaccines for children exposed to HIV or those living with AIDS.

Population and territorial data were obtained from the 2000 National Population Census.^b Data on live births in Porto Alegre were obtained from the National Information System on Live Births (SINASC) and data on newborns exposed to HIV during pregnancy and/or delivery was obtained from the National Communicable Disease Information System (SINAN). Additional data were obtained from Porto Alegre epidemiological surveillance.

In 2003, 394 cases of HIV-positive pregnant women and exposed children were notified, but seven cases of abortion and stillbirths were excluded. The final analysis included 387 cases of liveborn infants. Individual SINAN and SINASC records were geocoded to the level of street segment using the city digital map and GIS, constructed by the municipal information company. Using this database, 358 cases (92%) were fully geocoded.¹

The immunization database summarizes administrative information on vaccination coverage specifying doses administered at each primary care unit and calculating the proportion of children actually inoculated under the age of one to the population under one year of age of each given area. The tetravalent vaccine (diphtheria, pertussis, tetanus, and *Haemophilus influenzae*) was

^a Prefeitura Municipal de Porto Alegre. Conselho Municipal de Saúde. III Conferência Municipal de Saúde de Porto Alegre. Aprofundando o Controle Social. Caderno de resoluções. Porto Alegre: Conselho Municipal de Saúde, 2000. 94 p.

^b Instituto Brasileiro de Geografia e Estatística. Censo brasileiro 2000. Rio de Janeiro; 2001. [cited 2009 Oct 30] Available from: http://www.ibge.gov.br/home/estatistica/populacao/default_censo_2000.shtm

chosen as a tracer of immunization coverage due to the fact that this vaccine is part of the national basic immunization calendar, and is available at all PCUs. Therefore, immunization coverage was used as a proxy of PCU capacity to reach out to the reference population providing it primary care services.

Prenatal care data were extracted from SINASC live births forms with additional data on HIV-positive pregnant women available at SINAN. Attendance of prenatal visits was used as an indicator of population access to primary medical services as well as of the health unit capacity to detect and treat HIV-infected pregnant women.

Using a Geographic Information System, indicators were calculated by aggregating data from the original smaller spatial units into PCU areas. Data from PCUs, such as immunization coverage, were generalized to the corresponding polygon, i.e., the respective coverage area. Individual data, such as notification of HIV-positive pregnant women and live births were displayed as points in the map and summed to PCU areas. PCU areas were related to census tracts and their socioeconomic indicators were calculated according to the National Institute of Geography and Statistics (IBGE) data (2000 Population Census).

The following indicators were selected for analysis:

- Total population of PCU areas, calculated by summing up the population of the respective census tracts.
- Proportion of households located in shantytowns (*favelas*): ratio of the number of census tracts classified as “subnormal” in the 2000 Census by the total number of census tracts in each respective PCU area.
- Mean income of household heads living in PCU areas (in monthly minimum wages).
- Prevalence of HIV among pregnant women: ratio of the number of liveborn infants exposed to HIV by pregnancy and delivery to the number of live births in the respective PCU areas.
- Gross birth rate: ratio of the number of live births to the total population of each PCU area.
- Immunization coverage: ratio of three doses of tetraivalent vaccine actually applied to children under one year to the population in the respective PCU area.
- Proportion of liveborn infants with no prenatal care: ratio of the number of liveborn infants with no prenatal visit to the total live births in the respective PCU area.

- Proportion of liveborn infants exposed to HIV during pregnancy/delivery with no prenatal care: ratio of the number of liveborn infants exposed to HIV during pregnancy/delivery with no prenatal visits to the total number of live births exposed to HIV during pregnancy/delivery in the respective PCU areas.

Nonparametric correlation tests were used to assess the associations between the different indicators. Spearman's coefficient was calculated to assess the association between pairs of variables. Epi Info 6.04 and SPSS were used to perform basic tabulations and multivariate tests.

The study was approved by the Research Ethics Committees of *Grupo Hospitalar Conceição* and the Municipal Health Department of Porto Alegre. Patient information was kept confidential and private.

RESULTS

In 2003, a total of 17,802 live births were reported in the city of Porto Alegre, 2% of them among HIV-infected pregnant women. Most (96.5%) pregnancies were followed up during prenatal care visits as documented in live birth forms. However, a detailed analysis of these data reveals that prenatal care attendance was lower among HIV-infected pregnant women compared to all other women. Among 358 HIV-positive mothers, 44 (12.3%) did not receive any prenatal care. These numbers reveal an unequal primary health care between infected and non-infected women, which is a major challenge for proper control of mother-to-child HIV transmission.

Mean population of 121 PCU areas was 11,213, ranging from 927 in small communities to 140,921 in central areas.

The maps (Figures 1-3) show the distribution of selected indicators according to PCU areas. Low income areas are dispersed along the city periphery, i.e., in the semi-rural southernmost area and along the fringe around the city center. As depicted in the map, high income PCU areas are larger whereas small areas concentrate, in general, low-income households.

The high proportion of live births exposed to HIV with no prenatal care is a tracer of mother-to-child HIV transmission risk. This event is a combination of HIV exposure during pregnancy and difficult access to primary care services, indicating failure of health care programs and suggesting high risk of HIV exposure and transmission. The spatial distribution of this indicator shows that risk areas are clustered along the poor urban fringe. A comparison of the distribution of household income and risk maps shows specific conditions of

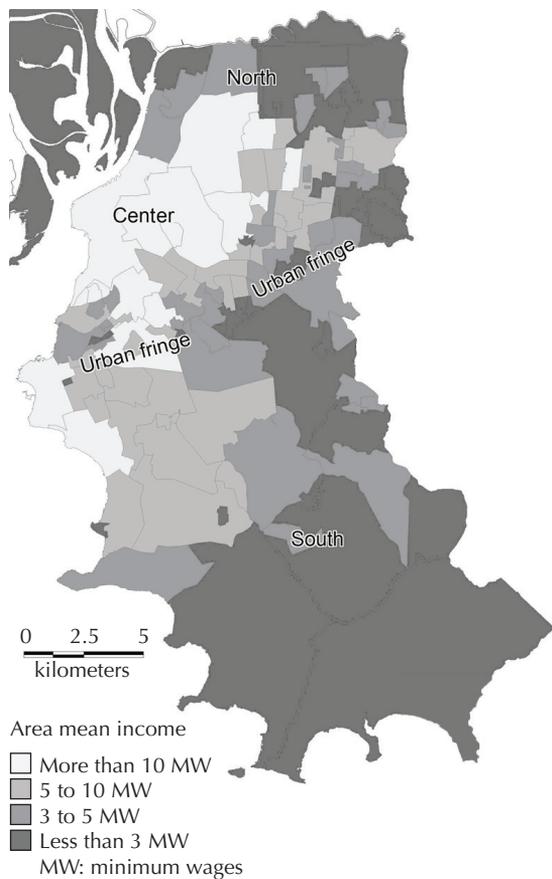


Figure 1. Income distribution in basic health unit areas in number of national minimum wages in 2000. Municipality of Porto Alegre, Southern Brazil.

risk of HIV transmission. Not all low-income areas have high mother-to-child HIV transmission rates. For instance, the semi-rural southernmost area is of low-risk, mainly because the overall HIV prevalence is low in this area. On the other hand, central and affluent areas have low mother-to-child HIV transmission risk due to adequate prenatal care, despite the relatively high HIV prevalence seen in that area.²

Immunization coverage was higher in small PCU areas scattered in the city periphery. The map showed a pattern of high immunization coverage in PCU small areas. Most of these small areas are served by Family Health Program.

Paired correlations between PCU area indicators are shown in the Table.

Significant inverse correlations were found between the proportion of households in shantytowns and mean income of household head. In these areas, high birth rates have been reported, as suggested by the inverse correlation between income and birth rate.

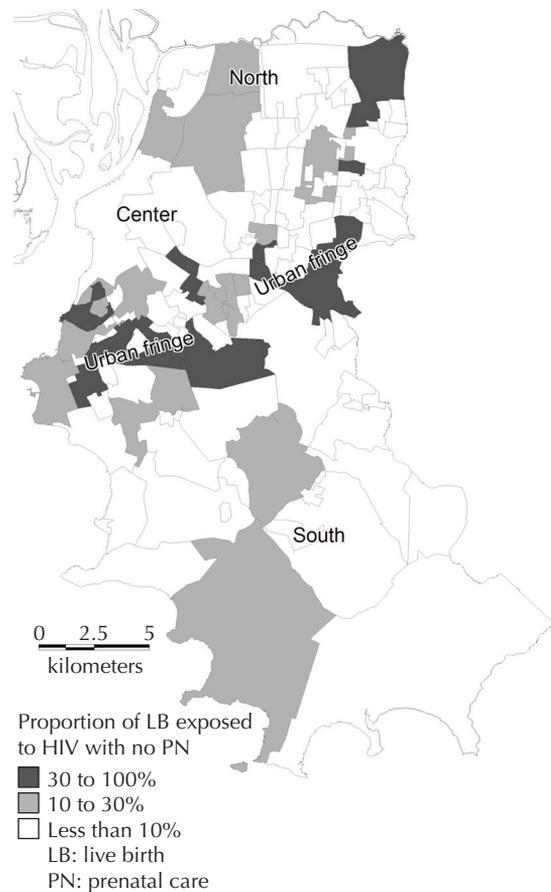


Figure 2. Proportion of live births exposed to HIV with prenatal care in primary care unit areas. Municipality of Porto Alegre, Southern Brazil, 2003.

On the other hand, mean household head income was inversely correlated to total population covered by each PCU, indicating that smaller coverage areas with scarce population are more common in low-income areas. The total population of PCU areas and mean income were inversely associated to immunization coverage.

The proportion of liveborn infants exposed to HIV with no prenatal care was strongly associated with low prenatal coverage and high prevalence of HIV in some low-income areas. This finding was expected since the variables used to calculate the indicators formulae share common terms. For instance, the denominator of incidence of liveborn infants exposed to HIV in those pregnant women who did not attend prenatal visits is the number of liveborn infants exposed to HIV, which is also the numerator of HIV prevalence in the area (see indicators list).

The indicator of vaccine coverage showed an inverse relationship to the proportion of liveborn infants exposed to HIV with no prenatal care, i.e., a primary care indicator was associated with the capacity of

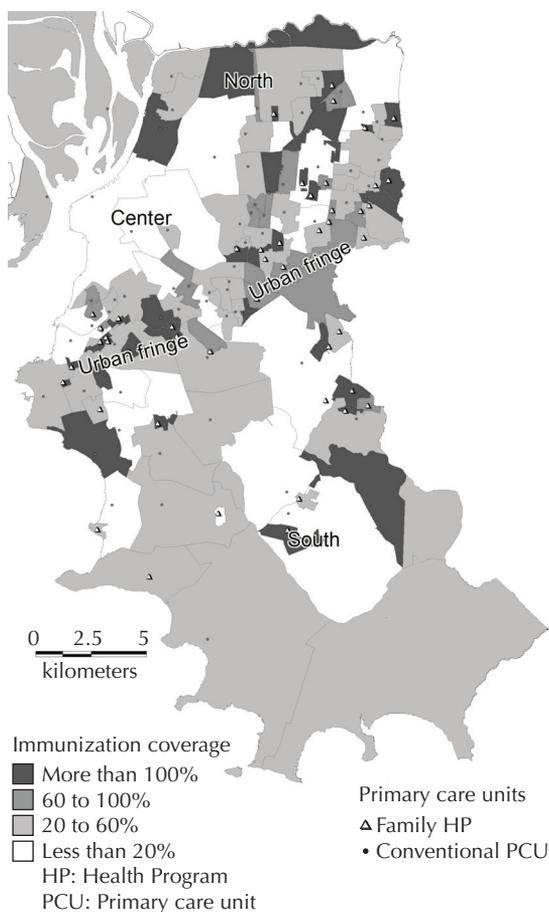


Figure 3. Immunization coverage in primary care unit areas. Municipality of Porto Alegre, Southern Brazil, 2003.

services to detect and treat HIV exposed children. However, vaccine coverage was not found to be associated with the prevalence of liveborn infants exposed to HIV, indicating that HIV infection among PCU population was not associated with the performance of primary care services.

DISCUSSION

The wide range of PCU populations is a consequence of two different primary care policies, one extensive serving a large number of people living in favorable socioeconomic conditions and other intensive strategically covering deprived urban populations, mainly located in shantytowns. The observed discrepancy of indicators among PCU areas is a result the spatial arrangement of these units.

General life conditions, such as low-income households and living in socially deprived areas (shantytowns) seem to be determinants of high birth rates, and this high birth rates were found to be associated with high HIV prevalence rates among pregnant women.⁶ Areas of high HIV transmission risk are located along the urban fringe of Porto Alegre, where shantytowns are concentrated.² These areas with high birth rates also have low prenatal care coverage.

The immunization coverage is higher in small PCU areas, and smaller coverage areas are commonly located in low-income areas. These indicators were associated with the proportion of HIV-infected pregnant women attending prenatal care. This finding suggests there is a potential for health services in the city of Porto Alegre to actively find HIV-exposed children and

Table. Nonparametric correlations matrix (Spearman test) among pairs of indicators calculated for primary care units areas (n=120). Municipality of Porto Alegre, Southern Brazil, 2003.

| Variable | Immunization coverage | Households in shantytowns | Mean income | Proportion of LB with no PN | Prevalence of LB exposed to HIV | Population | Birth rate |
|--|-----------------------|---------------------------|-------------|-----------------------------|---------------------------------|------------|------------|
| Immunization coverage | 1.000 | | | | | | |
| Households in shantytowns | 0.028 | 1.000 | | | | | |
| Mean income | -0.266 | -0.362 | 1.000 | | | | |
| Proportion of LB with no PN | -0.117 | 0.157 | -0.135 | 1.000 | | | |
| Proportion of LB exposed to HIV | -0.039 | 0.071 | 0.040 | 0.150 | 1.000 | | |
| Population | -0.715 | -0.146 | 0.601 | 0.084 | 0.019 | 1.000 | |
| Birth rate | 0.194 | 0.139 | -0.441 | 0.203 | 0.222 | -0.467 | 1.000 |
| Proportion of LB exposed to HIV with no PN | -0.350 | 0.042 | 0.284 | 0.289 | 0.285 | 0.407 | -0.057 |

Statistically significant correlations (p< 0.01) are highlighted as bold numbers.

LB: Live births

PN: Prenatal care

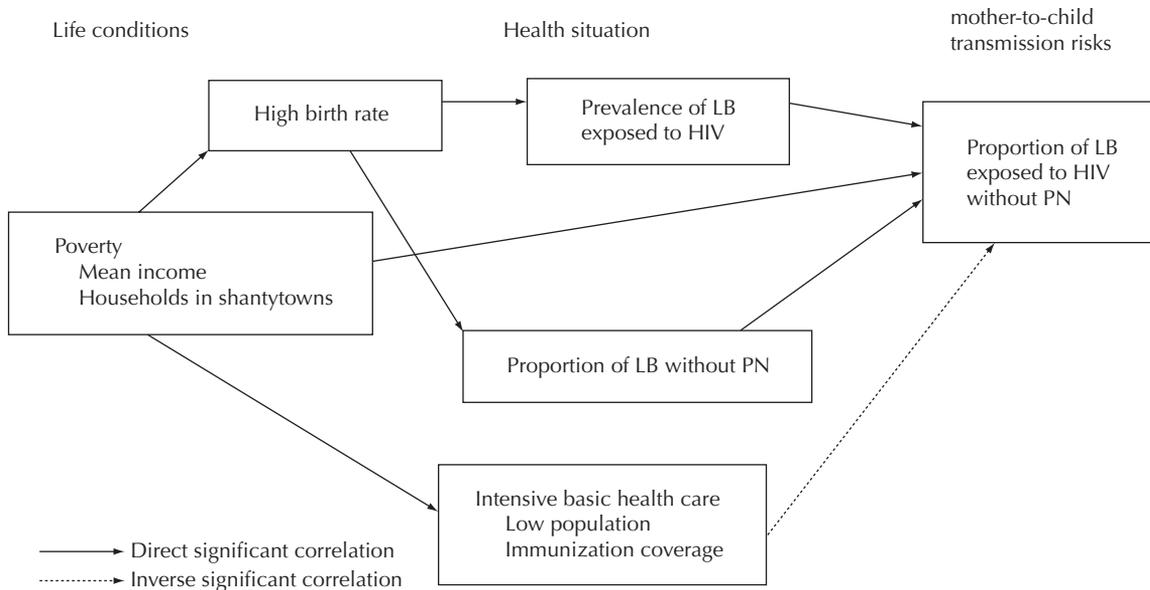


Figure 4. Graphic representation of the main relationships between basic health unit indicators. Municipality of Porto Alegre, Southern Brazil, 2003.

to engage women with risk pregnancies into basic prenatal care, providing specialized HIV/AIDS care. This pattern is probably explained by the important role of the Family Health Program in these areas. This is a community-based comprehensive primary care program involving regular household visits paid by health agents to promote treatment adherence and adoption of healthier behaviors and habits. This strategy was adopted in Brazil as a way to reinforce and extend primary care actions.⁸ The inverse association between the immunization coverage indicator and population size of PCU areas may indicate the strategic location of the initiatives aiming to minimize social inequality. On the other hand, immunization coverage is inversely associated to the incidence of children potentially exposed to HIV whose mother did not attend prenatal visits. Thus it indicates that primary care actions can strengthen the link between at-risk pregnant women and health services.

The association between PCU area population size and health indicators seems to be far from casual. The design of area boundaries modifies the values of aggregated social indicators and statistical associations among them.¹² Planning health services involves a choice of where services should be preferentially located and how many people should be targeted by a given service or initiative. Allocation of primary care units in low-income areas is an intentional strategy aiming to minimize health inequalities. The establishment of health services within smaller geographic areas, where underserved people cluster, highlighted such efforts.

Figure 4 illustrates the links among key indicators, according to the correlations found in the correlation matrix.

The analyses based on data collected for routine monitoring assess the different municipal areas from a global perspective, contributing to the definition of areas to be prioritized by public policies. This information may prove useful in the formulation and evaluation of health policies. Some important policies for controlling the AIDS epidemics have clear territorially based actions, such as the implementation of the Family Health Program in selected city areas. These are supported by information concerning the population profile and local socio-environmental characteristics. Other epidemiological study designs, based on individuals, can identify behavioral and subjective constraints acting as barriers of access to primary care services.¹⁴ However, in several instances, health managers need to analyze in an integrated way information obtained at the individual level and the contexts where these people live. In this sense, the present study presents specific limitations due to the lack of information obtained at the individual level and regarding these people's social networks, otherwise, it stresses the role of primary care services on facilitating population access to HIV testing and prophylaxis.

Poverty, especially in urban areas of a heterogeneous country such as Brazil, seems to be a strong determinant of mother-to-child HIV transmission as it is simultaneously associated with increased HIV infection rates and less than optimal pregnancy care and management. Preventive actions need to reinforce primary

care practices, such as household visits, counseling and on-site medication, especially in the most unfavorable social contexts. The effective results seen in comprehensive primary care units strongly suggest this is an appropriate strategy to prevent mother-to-child

HIV transmission. Also, full integration of routine surveillance with ongoing health care practices should be stimulated on a continuous basis and under permanent feedback.

REFERENCES

1. Acosta LMW. Determinando áreas prioritárias à assistência pré-natal em Porto Alegre através do georreferenciamento de gestantes HIV+. *Bol Epidemiol Porto Alegre*. 2004;5(20):4-5.
2. Barcellos C, Acosta LMW, Lisboa EP, Brito MRV, Flores R. Estimativa da prevalência de HIV em gestantes por análise espacial, Porto Alegre, RS. *Rev Saude Publica*. 2006;40(5):928-30. DOI:10.1590/S0034-89102006005000007
3. Bastos FI, Nunn A, Hacker MA, Malta M, Szwarcwald CL. AIDS in Brazil: the challenge and the response. In: Celentano DD, Beyrer C, editors. *Public health aspects of hiv/aids in low and middle income countries: epidemiology, prevention and care*. New York: Springer; 2008. p.629-54. DOI:10.1007/978-0-387-72711-0_29
4. Besculides M, Laraque F. Unintended pregnancy among the urban poor. *J Urban Health*. 2004;81(3):340-8. DOI:10.1093/jurban/jth122
5. Bostock L. Pathways of disadvantage? Walking as a mode of transport among low-income mothers. *Health Soc Care Community*. 2001;9(1):11-8. DOI:10.1046/j.1365-2524.2001.00275.x
6. Chan DJ. Fatal attraction: sex, sexually transmitted infections and HIV-1. *Int J STD AIDS*. 2006;17(10):643-51. DOI:10.1258/095646206780071018
7. Cooper ER, Charurat M, Mofenson L, Hanson IC, Pitt J, Diaz C, et al. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr*. 2002;29(5):484-94.
8. Escorel S, Giovanella L, Magalhães de Mendonça MH, de Castro Maia Senna M. The Family Health Program and the construction of a new model for primary care in Brazil. *Rev Panam Salud Publica*. 2007;21(2-3):164-76.
9. Filippi V, Ronsmans C, Campbell OM, Graham WJ, Mills A, Borghi J, et al. Maternal health in poor countries: the broader context and a call for action. *Lancet*. 2006;368(9546):1535-41. DOI:10.1016/S0140-6736(06)69384-7
10. Hanchette CL, Gibbs DA, Gilliam A, Fogarty KJ, Bruhn M. A national, geographic database of CDC-funded HIV prevention services: development challenges and potential applications. *Int J Health Geogr*. 2005;4:28. DOI:10.1186/1476-072X-4-28
11. Nogueira SA, Abreu T, Oliveira R, Araujo L, Costa T, Andrade M, et al. Successful prevention of HIV transmission from mother to infant in Brazil using a multidisciplinary team approach. *Braz J Infect Dis*. 2001;5:78-86.
12. Openshaw S, Taylor PJ. The modifiable areal unit problem. In: Wrigley N, Bennett RJ, editors. *Quantitative geography: a british view*. Oxford: Routledge; 1981. p.60-9.
13. Rigatti MFB. A vigilância epidemiológica da gestante HIV e criança exposta. *Bol Epidemiol Porto Alegre*. 2004;4(23):5-6.
14. Rodrigues CS, Guimaraes MDC, Cesar CC. Oportunidades perdidas na prevenção da sífilis congênita e da transmissão vertical do HIV. *Rev Saude Publica*. 2008;42(5):851-8. DOI:10.1590/S0034-89102008000500010
15. Santana R, Dhalia C, Barreira D, Barbosa A, Paz CA. Implantação da vigilância epidemiológica de gestantes HIV+ e crianças expostas [resumo]. *Rev Bras Epidemiol*. 2002;Supl.1:73. [Apresentado no 5. Congresso Brasileiro de Epidemiologia; 2002; Curitiba; BR]

The research study was funded by Centro de Estudos de Aids/DST do Rio Grande do Sul (CEARGS) and Center for Aids Preventions Studies, University of California-San Francisco (CAPS-UCS)/US Fogarty International Center ICOHRTA (Grant # 1D43TWO5799 CEARGS/CAPS), and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, Process No. 303798/2004).