Time series analysis comparing mandatory and voluntary notification of newly diagnosed HIV infections in a city with a concentrated epidemic

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Abstract

Background: In Catalonia, a law was passed in 2010 to incorporate HIV infection as a mandatory disease and to reduce under-reporting, perform follow-up and to improve prevention. Currently, there are studies that describe the surveillance of new diagnoses of HIV infection. However, there are no studies that compare the change from voluntary to mandatory notification. This study evaluates the impact of mandatory notification on the registered cases of newly diagnosed HIV infections in a city with a concentrated epidemic.

Methods: We analysed newly diagnosed HIV infections that were included in the city register. A descriptive analysis compared the number and the epidemiological characteristics of cases that were declared in two different periods (when notification was voluntary in 2001–2009 and when mandatory in 2010–2011). Time series analysis was conducted, evaluating trends and changes by fitting a Poisson regression model. The Epidemiology Service from the Public Health Agency was responsible for gathering and analyzing data and producing reports on communicable disease for the city. The data used in this study is openly available.

Results: Overall, 4510 cases of HIV infection were registered, 81.9% were men and 74.5% of them aged over 30. Among men, 55.6% were men who had sex with men (MSM), and among women, the most common route of transmission was heterosexual (HTS) with 65.4%. An annual average of 560 cases was registered between 2010 and 2011. This represents an increase of 33% from the annual average over the previous period (p<0.001). Time series analysis showed that the probability of notification was 2.8 (95% confidence interval 2.4–3.3) times higher with mandatory notification than in the earlier period. There was a statistically significant decrease of missing values in the period of mandatory notification (p<0.001).

Conclusions: Mandatory notification of HIV has resulted in an increase in detection of newly diagnosed infections, reduced the levels of missing data and has provided a more realistic picture of the epidemiology of HIV. This information also helps to improve the suitability of interventions aimed at HIV prevention and control.

Keywords: Mandatory reporting, Disease notification, Population surveillance, HIV

Background

With the introduction of highly active antiretroviral treatments (HAART) in 1996, when HIV tests were largely available, the Acquired Immunodeficiency Syndrome (AIDS) ceased to be a good epidemiological marker for HIV infection [1]. A change occurred in the natural course of the infection, prolonging the period between infection and development of AIDS, as well as an important reduction in mortality [1]. As a consequence, data from AIDS registries no longer reflected the magnitude nor the characteristics of the epidemic [1,2]. Since 1999, the World Health Organisation (WHO) has promoted the implementation of population-based surveillance systems, for the new HIV cases in developed countries [3]. Since the notification is used in only some areas, this does not allow...
describing the general epidemiological characteristics of the infection [4].

Despite being one of the most affected Western European countries in terms of HIV infection rates, Spain does not have state-wide population-level data on HIV infection [2,5,6]. Epidemiological surveillance has been carried out voluntarily, based on the notification of new diagnoses of HIV infection by the various Autonomous Communities [7] and among them, Catalonia, which began notification of new cases in January 2001. It should be taken into account that levels of under-reporting could be around 15 to 30% [8]. Moreover, voluntary notification systems cannot ensure the elimination of duplicates and there is no follow-up until the development of AIDS or death. In 2010, Catalonia passed a law which incorporates HIV infection as an individually name-based mandatory disease [9] with the aim of reducing under-reporting, performing follow-up and improving prevention in the same way that AIDS had been since 1987 [10,11].

A total of 28 of the 30 countries belonging to the European Union were notifying new cases of HIV in 2009. In 2000, 13 of these countries had national notification systems and in 8 of them, notifications were mandatory [12,13]. Despite the existence of these reporting systems, there are no studies published evaluating the impact of the change from voluntary to mandatory notification.

The objective of this study was to evaluate the impact of mandatory notification on the numbers of new diagnoses of HIV infections reported in a large city with a concentrated epidemic; comparing the epidemiological characteristics of those cases registered before to those registered after the mandatory notification came into effect.

Methods
Study design and study population
The city of Barcelona is situated in the northeast of Spain. It had a population of 1,619,337 inhabitants in 2010 [14]. AIDS rates were 46.7 per 100,000 inhabitants in 1994, before the introduction of HAART, and 4.5 per 100,000 inhabitants in 2010 [10,11]. This city has a low-level of concentrated epidemic (where high levels of infection are found only in specific groups) and estimates that HIV prevalence is mainly based on data collected from populations most at risk – especially men who have sex with men (MSM) [3].

We analysed registered cases of new diagnoses of HIV infection in Barcelona over the period from 1 January 2001 to 31 December 2011, excluding AIDS diagnoses.

A structured questionnaire was used to collect clinical and epidemiological information: sex, age, region of birth, route of transmission, CD4 cell count and reporting centre. Doctors reported new diagnoses of HIV. The Epidemiology Service from the city’s Public Health Agency was responsible for gathering and analyzing data and producing reports on communicable disease for the city, therefore the data used in this study is openly available. Other changes, such as testing policy, campaigning to promote HIV testing or change of case definition, were not accompanied in the switch from voluntary to mandatory notification.

Statistical methods
A descriptive analysis was carried out, comparing the number and epidemiological characteristics of cases registered voluntarily from 2001 to 2009, with those corresponding to the period of mandatory notification from 2010 to 2011, by means of the chi-squared test. A Poisson regression model was fitted to analyse the time series. Quarter was considered as a unit of time, taking the first period as reference. In order to test trend, a linear component was fitted, adding a quadratic function that allows for attenuation of trend over time. A dummy variable indicating the mandatory period was then included, in order to evaluate the magnitude of the effect of the law coming into force on the number of newly notified diagnoses. Finally, an interaction term was included to allow a change in the incidence trend in the second period. The analysis was conducted on the total number of cases, as well as stratified by demographic variables, transmission route and reporting centre. Furthermore, interactions between quarter and the stratifying variables were tested. The likelihood test was used to compare models, and only statistically significant results were included in the final models. 95% confidence intervals (CI) and p-values < 0.05 were considered statistically significant. All analyses were carried out with SPSS version 18 [15] and STATA version 11.0 [16].

Results
During the study period, 4510 new diagnoses of HIV infection were notified, representing an average of 410 cases annually. The epidemiological characteristics of new diagnoses reported are showed in Table 1. 81.9% were men, and 74.5% were aged over 30 years. By sex, only 43% of the men and 32.5% of the women were born in Spain. Among men, 45.5% were MSM, 10.8% were heterosexuals (HTS), and 9.3% were intravenous drug users (IDU). Among women, the most common route of transmission was HTS (65.4%), followed by IDU (15.2%). At the time of their diagnosis, 39.3% had CD4>350 cell/ul, 14.7% between 350 and 200 cell/ul, 12.9% under 200 cell/ul and 33.3% unknown. The most common reporting centre was a hospital, accounting for 64.6% of all reported cases.

The annual average of notifications over the period 2001–2009 was 376.6, while that for 2010–2011 was 560, representing a 33% increase in the annual number of notifications (p <0.001). The epidemiological characteristics of the cases by period are showed in Table 1. It
Table 1 Epidemiological characteristics of HIV new diagnoses reported in Barcelona (2001 – 2011)

|                          | 2001-2011 n=(4510) | 2001-2009 Voluntary period n=(3390) | 2010-2011 Mandatory period n=(1120) | P-value* |
|--------------------------|---------------------|--------------------------------------|--------------------------------------|----------|
| Sex                      | n=4510              | n=3390                               | n=1120                               |          |
|                         | N                   | %                                   | N                                    | %        |
| Sex                      | Men                 | 3692                                 | 81.9                                 |          |
|                         | Women               | 818                                  | 18.1                                 |          |
| Age (<30 and >30 years age) | <30 years of age    | 619                                  | 13.7                                 |          |
|                         | >30 years of age    | 3358                                 | 74.5                                 |          |
|                         | Unknown             | 533                                  | 11.8                                 |          |
| Age groups               | 14-19 years of age  | 9                                    | 0.2                                  |          |
|                         | 20-29 years of age  | 474                                  | 10.5                                 |          |
|                         | 30-39 years of age  | 1562                                 | 34.6                                 |          |
|                         | 40-49 years of age  | 1306                                 | 29.0                                 |          |
|                         | 50-59 years of age  | 418                                  | 9.3                                  |          |
|                         | > 60 years of age   | 208                                  | 4.6                                  |          |
|                         | Unknown             | 533                                  | 11.8                                 |          |
| Region of birth          | Spain               | 1854                                 | 41.1                                 |          |
|                         | Western Europe and North America | 281 | 6.2 | 174 | 5.1 | 107 | 9.6 |
|                         | Latin America and Caribbean | 849 | 18.8 | 561 | 16.5 | 288 | 25.7 |
|                         | Eastern Europe and Central Asia | 145 | 3.2 | 86 | 2.5 | 59 | 5.3 |
|                         | North Africa and Middle East | 54 | 1.2 | 37 | 1.1 | 17 | 1.5 |
|                         | Sub-Saharan Africa | 198                                  | 4.4                                  |          |
|                         | Unknown             | 1129                                 | 25.0                                 |          |
| Route of transmission    | HTS men             | 487                                  | 10.8                                 |          |
|                         | HTS women           | 536                                  | 11.9                                 |          |
|                         | MSM                 | 2052                                 | 45.5                                 |          |
|                         | IDU men             | 419                                  | 9.3                                  |          |
|                         | IDU women           | 124                                  | 2.7                                  |          |
|                         | Unknown             | 892                                  | 19.8                                 |          |
| CD4 count                | > 350 cell/ul       | 1773                                 | 39.3                                 |          |
|                         | < 350–200 cells/ul  | 665                                  | 14.7                                 |          |
Table 1 Epidemiological characteristics of HIV new diagnoses reported in Barcelona (2001 – 2011) (Continued)

| Reporting centre | <200 cells/ul | 12,9 | 436 | 12,9 | 144 | 12,9 |
|------------------|---------------|------|-----|------|-----|------|
| Unknown          | 1492          | 33,1 | 1228| 36,2 | 264 | 23,6 |

Comparison between voluntary notification period with mandatory notification period. (2001–2009 versus 2010–2011).

HTS: Heterosexual contact, MSM: Men having sex with men, IDU: Injecting drug Users.

* Chi² test.
was observed that there was a change in the percentage composition by sex, with an increase in the proportion of notifications corresponding to men. The majority of cases were aged over 30 years. However, a change was seen in the proportion of notifications among individuals aged under 30, which rose from 8.1% to 29.5% (p<0.001). With regard to region of birth, those born in Spain presented a decline in notifications, which led to an increase in the relative proportions of foreign-born individuals, the most common of which were people born in Latin American and Caribbean countries. The rate of notification corresponding to cases of sexual transmission rose from 64.2% to 80.4% (p<0.001), particularly among MSM whereas among IDU, there was a decline from 12.9 to 9.5%. There was a significant decline in the proportion of missing values for most of the variables during the period of mandatory notification, especially region of birth and route of transmission, comparing with the voluntary period (p<0.001).

As shown in Table 2, the probability of notification increased by 2.8 times (CI 2.4-3.3) with the introduction of mandatory HIV notification, compared to the period when notification was voluntary. Figure 1 shows a rise in the number of cases of HIV notified up to the year 2006, a year in which a change in the trend may be seen, after which cases began to decline. With the introduction of mandatory notification, an increase is observed in the level of cases notified. However, the decreasing trend of series of quarters is not altered by the change in notification, since the interaction between the trend and the law coming into force was not significant.

Figure 2 illustrates the increase in HIV notified cases, following the introduction of the law, in terms of sex, age, region of birth, route of transmission and reporting centre. Only the interaction between sex and quarter was statistically significant (p <0.001), suggesting that the trend differs between men and women and that, in men, the decrease in HIV reporting was greater than in women in the period of voluntary notification.

Discussion
In Barcelona, AIDS has been a mandatory notified disease since 1986, and HIV was included in the registry as a voluntary notifiable disease only until 1996 [8]. During the HIV/AIDS epidemic there was, and continues to be, controversy over whether HIV infection should be notified. Following a long debate over many years, in 2010 Catalonia passed a law making a mandatory registry of HIV infection [8]. Such a mandatory registry permits better characterisation of the infection, avoidance of duplication, the study of sexual partners, effectiveness of therapy, and follow-up of cases of infection until the appearance of AIDS, or death [17]. However, some studies have suggested that the introduction of this type of notification could diminish the number of persons who undergo the test; however these predictions have not been reflected in significant declines in testing in the United States [18].

In our study, both the results of bivariate analysis and of time series analysis showed that the introduction of mandatory notification of new diagnosis of reported HIV infection led to an increase in such notification of almost three times. This increase in the completeness of notification results in a more precise description of the epidemiological situation regarding HIV infection. The epidemiological characteristics are similar in both periods, although some proportions have changed, new diagnoses being more common among men with higher risk of sexual transmission; particularly MSM and those aged over 30 years. There is a notable percentage increase of groups at risk following the introduction of the law, such as individuals aged under 30 and people born outside Spain. Regarding the notifying centre, hospitals are the main sources of notifications in both periods.

Table 2 Effect of the introduction of mandatory notification of new HIV diagnoses in Barcelona

|                          | RR        | CI  95%     | P-value |
|--------------------------|-----------|-------------|---------|
| Linear Trend             | 1.09      | 1.08-1.10   | <0.001* |
| Quadractic adjustment term | 0.99     | 0.99-0.99   | <0.001* |
| Indicator of introduction of mandatory notification | 2.79     | 2.39-3.25   | <0.001* |

Poisson Regression N cases= α+β1(Quarter from origen) + β2(Quarter from origen)^2 + β3(mandatory notification indicator).

RR: relative risk; CI: confidence interval.

* Poisson Regression.
Comparison of the epidemiological characteristics against data available at national level (2003–2010) revealed differences with respect to the proportions in the different categories of transmission. It is important to stress that national-level data cover 71% of the population (32,843,416 inhabitants in 2010) [19], making it difficult to extrapolate to the rest of the country, since the degree and patterns of HIV transmission differ between the different Autonomous Communities. It should also be noted that amongst them, the notification of new cases of HIV is voluntary and that some proportion of these cases have probably not been notified [19]. This reveals the need to have a notification system that permits more exhaustive surveillance of the epidemic, in order to obtain appropriate quality and quantity of information. Thus, this information will allow the estimation of the magnitude of the infection and to monitor its trends [20], especially in the large cities, which is where cases tend to be concentrated. Comparing with the data of HIV diagnoses that were reported by the EU/EEA countries in 2011 (rate of 5.7 per 100000 in the population), 10% of all HIV diagnoses were reported among young people aged 15 to 24 years, and 30% among MSM [21]. These trends are similar to those observed in Barcelona, describing a concentrated epidemic especially by sexually transmitted infection, mainly in MSM.

Studies with regard to the switch from voluntary to mandatory notification were not possible to find. However, in other settings, it has been observed that appropriate and exhaustive systems of surveillance of transmissible infections, not only HIV, generate more precise information at population level, presenting a more realistic picture of the infection situation [22,23]. Accurate information has helped large scale efforts in eradicating smallpox [24] and reducing dracunculiasis in Asia and Africa [25,26].

Reporting of HIV infection must be interpreted with caution however, taking into account other available epidemiological data, because these reports do not provide a direct measurement of the incidence or prevalence of HIV infection [12,13]. The proportion of HIV infected individuals, who are diagnosed and reported, varies according to the phase of the epidemic [27], HIV testing patterns [28], and characteristics of surveillance systems.
Therefore, new diagnoses of HIV infection, reported into a registry, varies despite of their mandatory or voluntary state. But with a mandatory notification registry, all cases that have been diagnosed are reported, despite their infection state. HIV mandatory reporting is helping to improve assessment of the scale and extent of recent HIV transmission in the population [12], to visualize a better picture of HIV endemic situation in the city and to describe the epidemiological characteristics of emerging risk groups. It is important to stress that with mandatory notification, elimination of duplicate reports and the ability to match reports of HIV infection with other data sets are accomplished [31]. These are two characteristics [3], which are essential requirements, for an effective HIV reporting system. Another important advantage of mandatory notification is that it is possible to recover data by active surveillance; therefore there might be a decrease in missing data as it was observed in our analysis.

**Strengths and limitations**

Time series analysis has permitted the description and estimation of the evolution in trends affecting the notification of new diagnoses of HIV infection [29,30]. Thus, while on the one hand we observe an increase in the number of mandatory notifications, the slope of the overall trend persists in both periods.

Among the limitations of this study, one is the short period of follow-up of mandatory notification. This raises the issue of the need to continue its evaluation, in order to determine whether the changes and the rise in number of notifications persist over time.

Another aspect to be taken into account is that the analysis was conducted with the start date of mandatory notification as January 2010, despite the fact that the law only came into force in July 2010, and the publication of the 2010 manual of notifiable diseases and mandatory notification of HIV infection was also included [31]. Consequently, some centres, not notified when this was voluntary, began to do so at the beginning of 2010. We decided that the first two quarters of 2010 were included in the analysis, as the impact of mandatory notification starts from the second quarter of this year, despite the law only coming into force in July 2010.

**Conclusions**

In conclusion, while the voluntary system of notification was useful in order to describe global trends of the infection, HIV mandatory notification increased the number of new diagnoses notified, made visible a change in the relative proportions of epidemiological characteristics of the HIV infection, such as greater representation of men (particularly the MSM group), has led to the appearance of certain groups that were formerly not so strongly represented, such as individuals aged under 30 years. This information, more exhaustive and of a higher quality than that obtained with the voluntary notification system, will serve to improve evaluation and design of prevention programmes allowing more effective control of HIV infection.

**Abbreviations**

AIDS: Acquired Immunodeficiency Syndrome; CI: confidence intervals; HAART: highly active antiretroviral treatments; HIV: Human immunodeficiency virus; HTS: heterosexuals; IDU: intravenous drug users; MSM: men who have sex with men; RR: relative risk; WHO: World Health Organisation.

**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

JMR, as the main author, made substantial contributions to the conception, design and interpretation of the data. PGO, SPH and JAC have all been involved in the designing of the study, drafting the manuscript, or revising it critically for important intellectual content. All authors read and approved the final manuscript.

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