

Assessment of HIV/Aids care in Croatia from 2007 to 2011

Nourry, Gaël Maxime

Master's thesis / Diplomski rad

2014

Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj: **University of Zagreb, School of Medicine / Sveučilište u Zagrebu, Medicinski fakultet**

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:105:117115>

Rights / Prava: [In copyright](#)/[Zaštićeno autorskim pravom.](#)

Download date / Datum preuzimanja: **2024-08-05**



Repository / Repozitorij:

[Dr Med - University of Zagreb School of Medicine Digital Repository](#)



**UNIVERSITY OF ZAGREB
SCHOOL OF MEDICINE**

Gaël Nourry

**Assessment of HIV/AIDS care in Croatia from
2007 to 2011**

GRADUATION THESIS



Zagreb, 2014

This graduate thesis was made at the University of Zagreb School of Medicine at the department of Infectious Diseases division HIV/AIDS, University Hospital Zagreb, mentored by professor Josip Begovac, M.D., PhD, and was submitted for evaluation in 2013.

List of abbreviations:

AIDS – Acquired immunodeficiency syndrome

CART – Combination antiretroviral therapy

HIV – Human immunodeficiency virus

MSM – Men who have sex with men

PCR – Polymerase chain reaction

UHID – University Hospital for Infectious Diseases

Contents:

Summary

Introduction 6

Objectives 7

Methods 8

Results 10

Discussion 18

Conclusions 22

Acknowledgments 23

References 23

Biography..... 25

Summary:**Title:**

Assessment of HIV/AIDS care in Croatia from 2007 to 2011

Author:

Gaël Nourry

Summary:

Background: Combination antiretroviral therapy (CART) for HIV infection has resulted in outstanding decreases in HIV-related morbidity and mortality. However, these achievements need to be translated into practice. HIV care is an important element of the response to HIV and encompasses a continuum from early diagnosis to treatment outcomes. Systematic monitoring of successful entry into HIV care, retention in care and monitoring treatment outcomes are important elements of a response to HIV/AIDS.

Objective: We evaluated several key indicators of the quality of care in adults living with HIV in Croatia.

Methods: In a retrospective analysis of reported data for 728 patients with HIV receiving medical care from 2007 to 2011, we determined performances for 6 HIV care healthcare indicators nationwide. These Indicators were: 1) patient access to HIV testing, 2) integration into care, 3) antiretroviral treatment guidelines compliance, 4) viral load suppression in patients starting CART, 5) retention into care and 6) success of care (survival after inclusion into care, viral suppression and CD4 cell count). A person was considered included into care if at least one CD4 cell count measurement was done in a calendar year. For the CD4 cell and viral load indicators the last measurement in a calendar year was used in the analysis.

Result: Of 316 entering care at UHID in the period 2007-2011, 186 (59%) were diagnosed late (CD4 cell count < 350 cells/mm³). Overall, 87% of were integrated into care within one month of diagnosis, the percentage ranged from 79 to 94% in individual calendar years. Among patients who ever had a CD4 cell count between 200 and 350 per mm³ and/or clinical AIDS the proportion of patients receiving CART was 82%, 89%, 89%, 91% and 94% for years 2007-2011 respectively. Of 228 patients who started CART in the period 2007-2010; 206 (90%) had a viral load measurement after 1-year (+/- 90 days) of therapy. An undetectable viral load was found in 88% (viral load < 50 copies/ml of HIV-1 RNA) and 97% (viral load < 400 copies/ml) of these patients. Retention in care was good as measured by the proportion of patients not seen in care in the next calendar year. The total number of patients in care ranged from 412 in 2007

to 637 in 2011, and lost to follow-up was 7.3% in 2007 and 6.2% in 2011. Survival after inclusion into care was 95%, 93% and 93% at one, two or three years respectively. The median CD4 cell count of all patients in care increased from 426 cells/mm³ in 2007 to 524 cells/mm³ in 2011. The proportion of patients in care with a viral load < 400 copies/ml increased over time.

Conclusion: The quality of HIV care in Croatia is very good. Late presenters remain a problem and efforts to promote earlier HIV diagnosis should be undertaken. Our data was generated on a national level, in the future, it can be used to monitor HIV public health policy and prevention.

Keywords: Health care interventions, HIV, AIDS, Croatia, HIV quality of care.

1. Introduction:

Without antiretroviral therapy (ART) most persons with human immunodeficiency virus (HIV) develop acquired immunodeficiency syndrome (AIDS) within 10-12 year after infection. AIDS results in important morbidity and premature death [1].

Antiretroviral treatment changed HIV from a fatal condition to a progressive chronic disease. As a chronic disease, HIV care became more complex; the need for standardization and guidelines became stronger. Standards of care for HIV are established by national and international guidelines [2-4]. In a resource limited setting, application of these guidelines can be challenging. This may have an impact on the quality of HIV care. State of the art care of HIV patients requires the use of multiple health care interventions such as disease monitoring, clinical interventions, and availability of antiretroviral drugs. Unfitting delivered care may have important implications for the health of HIV patients as well as for public health.

Croatia is an upper-middle/high income country with a population of 4.4 million. It has a centralized system of treatment and care for persons infected with HIV. All patients are treated in Zagreb at the University Hospital for Infectious Diseases (UHID). Regarding HIV treatment, Croatia can be considered a country with an individual approach to combination antiretroviral therapy (CART). Choice of drugs is limited; there are no single-tablet drugs available currently 14 drugs are used. Antiretroviral drugs are only given from the hospital pharmacy at UHID. Health care is free of charge for patients; costs of antiretroviral and monitoring are fully covered since 1998.

Individuals can be tested in 10 voluntary counseling and testing sites, tests are anonymous and free. All blood products are also tested since 1987.

Surveillance activities for HIV/AIDS epidemic are performed since 1985. Since 1997, there is a comprehensive electronic database on HIV infected patients available at UHID.

From 2007-2011, there was approximately an average of 64 new HIV diagnosis annually. In 2011, 76 persons were diagnosed with HIV in Croatia, 22 were diagnosed with AIDS. HIV incidence is 10-14 per million inhabitants, these values place Croatia in the category of countries considered to have a low HIV/AIDS level epidemic. Testing data suggest a low prevalence even in high risk group (< 5%) [5-7]. Croatia's HIV/AIDS epidemic started in 1985 when the first AIDS case was documented. The first cases were identified among labor migrants who returned from western European countries, a seafarers who acquired HIV in Africa and Eastern Asia [8]. Recent data suggest an emerging HIV epidemic among men who have sex with men (MSM) [5].

Quality of care measures and standard are now defined for many health care conditions. Efforts to measure and standardize the quality of care provided to persons infected with HIV had begun during 1990's. Several papers have been written to provide HIV care quality measures [9-10]. The World Health Organization (WHO) has developed a set of indicators to monitor the health systems response to HIV/AIDS without the capability to monitor laboratory management of patient such as their CD4 cell count and viral loads [11]. The advent of antiretroviral therapy resulted in a large decrease in hospitalization and length of hospital stays. Therefore our assessment of HIV care is more focused on outpatient settings.

Care of persons with HIV/AIDS is complex and require monitoring of quality indicators within different systems of clinical care provided to these patients. During the last few years, several institutions and countries have built their own cascade of care. Cascade of care is a visual representation of this continuum of care. It is a tool for clinicians as it enables them to quantify how their patients benefit from the care they received and also to help clinicians to identify deficiencies in continuum of care in order to improve HIV care [12]. It can also be used to monitor progress of HIV care in Croatia over time and possibly with other countries if similar methodology is used. To build our cascade of care we assessed 6 indicators. Our cascade begins with persons diagnosed with HIV, linked to care, retained in care, receiving CART, having undetectable viral load, and ends with success of care.

Suppression of the viral load through treatment cascade provide clinical benefit to patients as it can decrease morbidity and mortality, and on a public health perspective it may lead to a decrease HIV transmission. Some studies showed that having a low viral load in the community would result in a decrease in new HIV infection and that having a large portion of the HIV population with CART could have an impact on reducing HIV transmission [13-14].

2. Objectives:

Up to this date, no paper has been written, to evaluate HIV quality of care and treatment in Croatia. In this paper we decided to focus on care and outcome of HIV/AIDS treatment in Croatia. We propose strategies to define and assess HIV quality of care.

We analyzed 6 different indicators of care in adult patients (defined as 18 years old or older) living with HIV in Croatia for the 2007-2011 period.

3. Methods:

3.1 Study population:

Patient eligible for this analysis were seen in care at UHID from 2007 to 2011. Included in the analysis were Croatian citizens of 18 years of age or older. All patient data was obtained from an electronic database in use at UHID since 1997. A person was considered included into care if at least one CD4 cell count measurement was done in a calendar year. For this study, the following data was collected: Age, sex, risk group, date of HIV test, date of inclusion into care, CD4 cell counts, HIV-RNA measured, whether the patient is receiving CART, and date of CD4 counts and HIV-RNA measured since last follow-up results were used as proxy measure for medical visits.

3.2 Indicators

Health care measures delivered to HIV patient in Croatia were assessed for 6 quality of care indicators. Selected indicators regard timing of diagnosis (late diagnosis), integration into care, retention into care, virological and immunological indicator of treatment and success of care among HIV diagnosed patient. All indicators were defined with eligibility criteria for the measure.

3.3 Ethics statement:

The study is part of the project of the Ministry of Science and education for which Ethical Approval has been granted both by the University Hospital for Infectious Diseases (UHID), Zagreb, Croatia and University of Zagreb Medical School.

4. Definitions:

4.1 Early access to HIV testing for patients

To access early access to HIV testing, we used the proportion of late HIV diagnosis among newly diagnosed persons entering care at UHID. To further evaluate the state of immunosuppression of our HIV patient at diagnosis, we used two definitions to define late presentation. We discriminated late presentation from very late presentation. Late diagnosis was defined by a patient presenting with a CD4+ T-cells count <350 cells/mm³. Very late presentation was defined with a CD4 cell count <200 cells/mm³ or clinical AIDS.

In this analysis we also looked at the proportion of patients who had likely acute HIV infection or no seroconversion within 2 years. A clinical diagnosis of AIDS was made according to the European case definition [15].

We also excluded from this indicator patients who were already diagnosed or treated for HIV prior to receiving care in our hospital.

4.2 Rapid integration into care.

Integration into care is the active process of engaging newly diagnosed HIV infected patients into HIV primary care. To assess rapid integration into care, we measured the length of time between the HIV diagnosis and the first CD4 count, using data from our HIV diagnosis and CD4 laboratory count. Rapid integration into care was considered if the patient received his first CD4 count within one month following HIV diagnosis.

4.3 Compliance with current guidelines on when to start CART.

Guidelines recommend that all patient with a CD4 cell count <350 cells/mm³, or with a clinical diagnosis of AIDS to receive CART [2-3].

To assess guidelines compliance, we monitored the proportion of patient receiving CART who ever had a CD4 count ≤ 350 cells/mm³ or had been diagnosed with an AIDS defining illness. This analysis was done using the CD4 measurement closest to the end of the calendar year. CART was defined by at least two nucleo(s)tide reverse transcriptase inhibitors (NRTI) plus either one non-nucleoside reverse transcriptase inhibitor (NNRTI), protease inhibitor (PI) or raltegravir. Excluded from the analysis were patients with less than 3 month in care and a CD4 cell count 200-350 cells/ mm³ as were patient with less than 1 month in care and a CD4 cell count less than 200 cells/mm³.

4.4 Achieving viral load suppression,

We defined successful viral load suppression by the proportion of patient on CART with a viral load <50 copies/mL after receiving CART for a year. Viral load value was taken from the available measurement closest to the 12th month of therapy (± 3 months). We examined the HIV-1 RNA level collected from 2007 to 2011. Treatment failure was defined by a viral load >400 copies/mL. For the analysis, viral load levels were stratified as <50 or <400 copies/mL.

4.5 Retention into care

Integration into care and retention into care are distinct criteria on the engagement of care cascade. To assess the scope of HIV diagnosed patient attending UHID who are lost to follow up. We examined retention into care from 2007-2011. Retention was defined as being in care during one calendar year continuing care the following calendar year. We measured the proportion of patient not seen in care in the next calendar year using available CD4 count as proxy of engagement into care.

4.6 Successful care:

-Survival of HIV patient after inclusion into care:

Survival was estimated by the Kaplan-Meier plot. We evaluated survival for all patient included in HIV care at 1 year, 2 year, and 3 year after being diagnosed with HIV.

-Efficacy of viral suppression was estimated with the proportion of patients that have an undetectable viral load within one calendar year.

-Similarly, success of CD4 cell count increase was estimated with the proportion of patients that have a CD4 cell count >500 within one calendar year. The last CD4 count in a calendar year was used for this analysis. The sample population was clustered in 3 groups: CD4<200, CD4>200-349<, CD4>350. All patients included for HIV care were evaluated

All analyses were performed using the statistical software package SAS version 9.3.1 (SAS institute Inc, Cary, North Carolina, USA); the level of significance was set at 0.05.

5. Results:

Baseline characteristic

A total of 728 persons of 18 years of age or older were seen in UHID for HIV/AIDS care from 2007-2011, the majority of them were males (82-86%) and the median age for Adults (> 18 years of age) at last CD4 cell count measurement was 42.4 years (Table1).

Characterstics	Calendar year				
	2007	2008	2009	2010	2011
Patients in care	412	475	524	579	637
Age, median, years	42.2	42.2	42.4	42.1	42.4
Sex, male %	82	85	85	86	86
MSM transmission risk	47.1	50.5	53.4	57.5	59.0
Living in Zagreb, %	34.0	32.8	35.4	35.2	35.6
CD4 cell count, median, cells/mm ³	426	429	450	476	524
Receiving ART, %	78	80	80	82	85
Retention in care, %	93	94	93	94	94

Table 1. Main characteristic of patients in care at UHID, 2007-2011.

5.1. Early access to HIV testing for patients

Of the 314 persons newly diagnosed with HIV between 2007-2011, 187 (60%) were diagnosed late (CD4 cell count < 350 cells/mm³ or clinical AIDS); very late diagnosis (CD4 cell count < 200 cells/mm³ or clinical AIDS) was found in 132 (42%). In 2011, 66 patients entered care 70% of patient were diagnosed late and 45% were diagnosed very late. (Figure 1.)

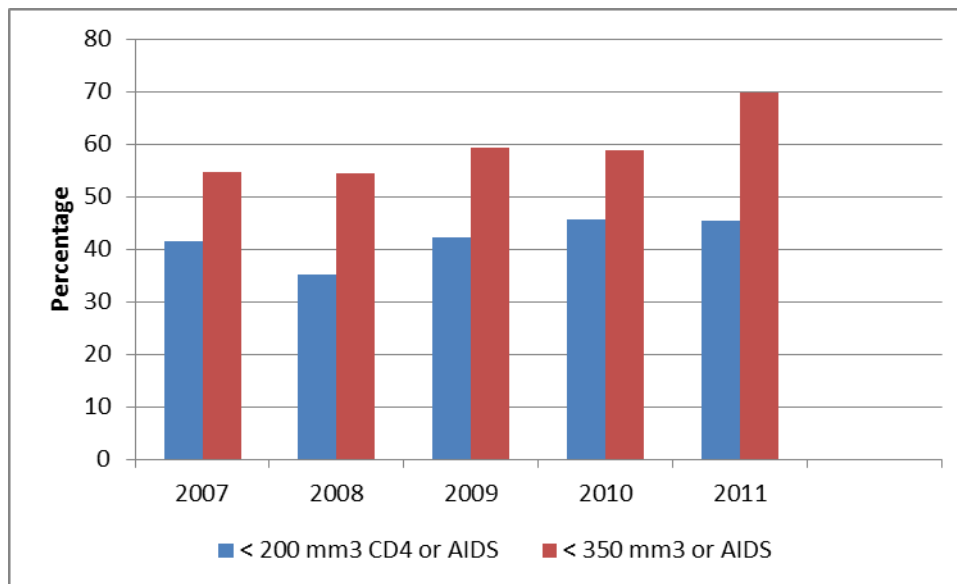


Figure 1. The problem of late presentation to care, Croatia, 2007-2011.

Of the 187 persons defined as having a late HIV diagnosis, 24 (12.8%) had acute HIV infection or reported a negative HIV diagnosis within the past 2 year prior to their HIV diagnosis.

5.2. Rapid integration into care

Between 2007 and 2011, 314 adults entered care with HIV infection. Among them 87% of persons diagnosed with HIV had a CD4 cell count within one month of HIV diagnosis. The percentage were 79%, 88%, 88%, 94%, 85% in year 2007-2011 respectively (Figure 2.)

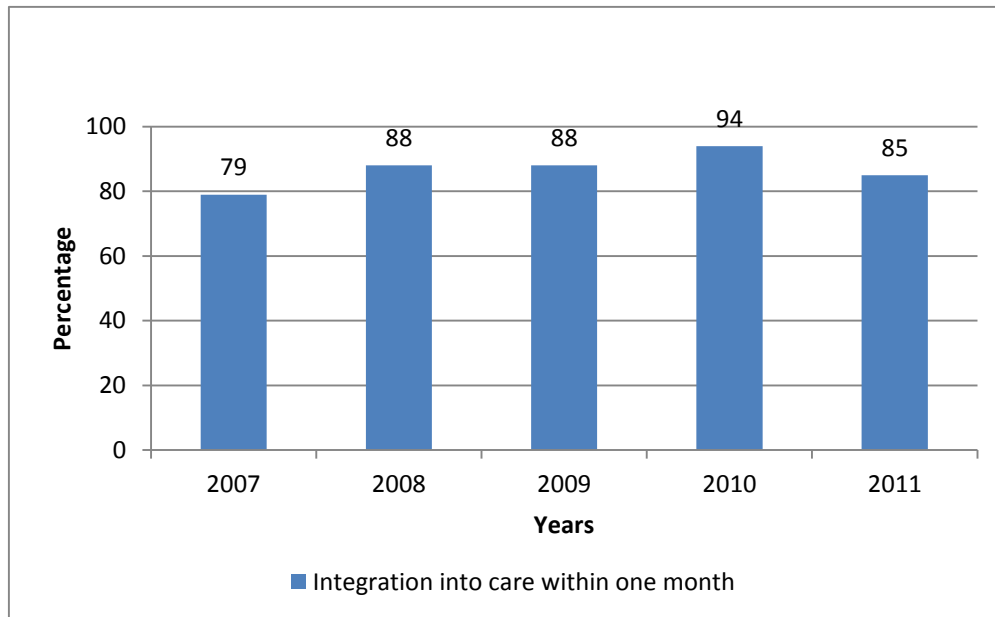


Figure 2. Time of first CD4 count within one months of HIV-diagnosis in Croatia 2007-2011.

Of 40 patients who did not link within one month, 32 (80%) had a CD4 cell count within a year after HIV diagnosis.

5.3. Compliance with current guidelines on when to start CART

Among patients who ever had a CD4 cell count between 200 and 350 cells/mm³ the proportion of patients receiving CART was 88%, 92%, 91%, 93% and 96% for years 2007-2011 respectively (Figure 3.). Compliance to guidelines increased progressively through the study period. In 2011, of the 479 patients with CD4 cell count <350 cells/mm³ or clinical AIDS, 20 were not receiving CART.

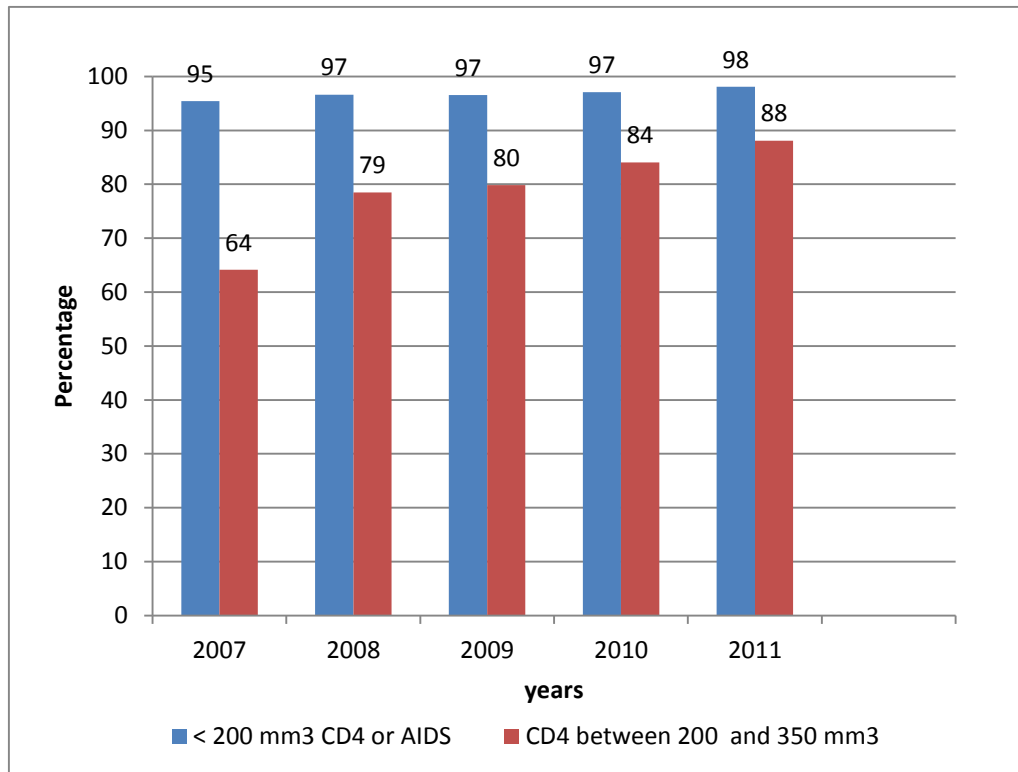


Figure 3. Compliance with treatment guidelines. The proportion of patients with a history of clinical AIDS or CD4 cell count <200 cells/mm³ or a CD4 cell count between 200 and 350/mm³ treated with CART in Croatia in the period 2007 to 2011. Included into the analysis were patients > 1 months in care (clinical AIDS or < 200 cells/mm³) or > 3 months in care (CD4 cell between 200 and 350 per mm³) in a calendar year.

5.4. Achieving viral load suppression after one year of CART

Among the 291 antiretroviral naïve patients who started CART in the period 2007-2011, 266 had a viral load measurement after one year of CART (+/- 90days). The following reasons for not having a measurement were observed (n=25): death (n=9), no test performed or unknown result (n=7), lost to follow-up (n=5), discontinuation (n=3), and treatment only during pregnancy (N=1).

Of 266 patients 257 (97%) had an undetectable viral load of < 400 copies/ml and 236 (89%) had <50 HIV-1 RNA copies/mL. (Figure 4.)

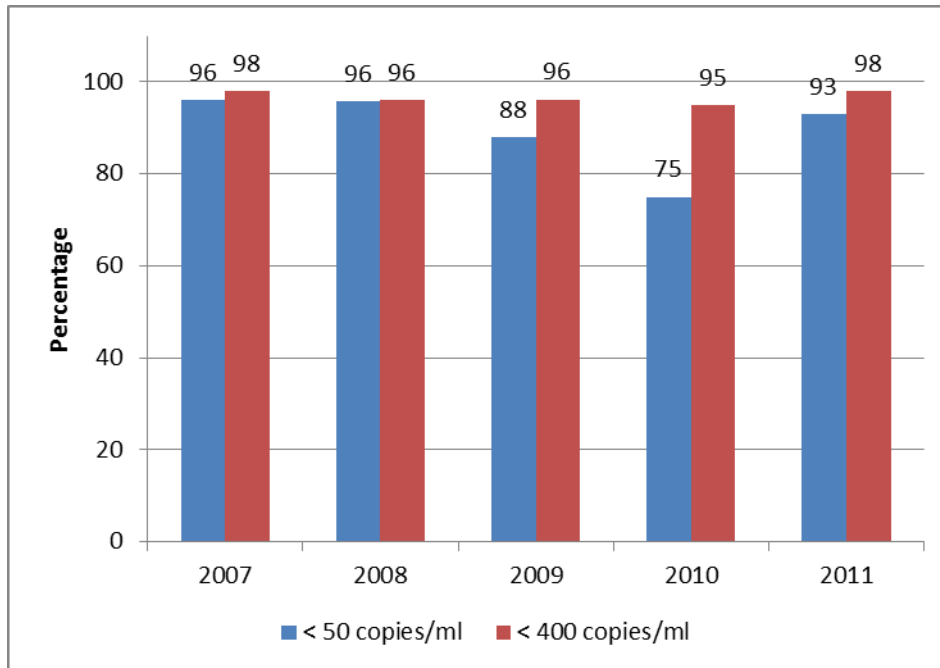


Figure 4. Viral load suppression after one year on CART, Croatia, 2007-2011

5.5. Retention into care:

The total number of patient engaged in care ranged from 410 in 2007 to 637 in 2011. Loss of follow up, defined as not in care during one calendar year while being in care in the previous calendar year, was 7.3% in 2007 and 6.4% in 2011. On average 93% of patient attending HIV care in one year attended care the following year. Cumulatively, over 5 years of observation, of 369 seen in 2006 by 2011 294 (79.7%) of patient were continuously in HIV care.

5.6. Successful care

Survival after inclusion into care was 95%, 93%, 93% at one, two, or three years respectively (Figure 5.)

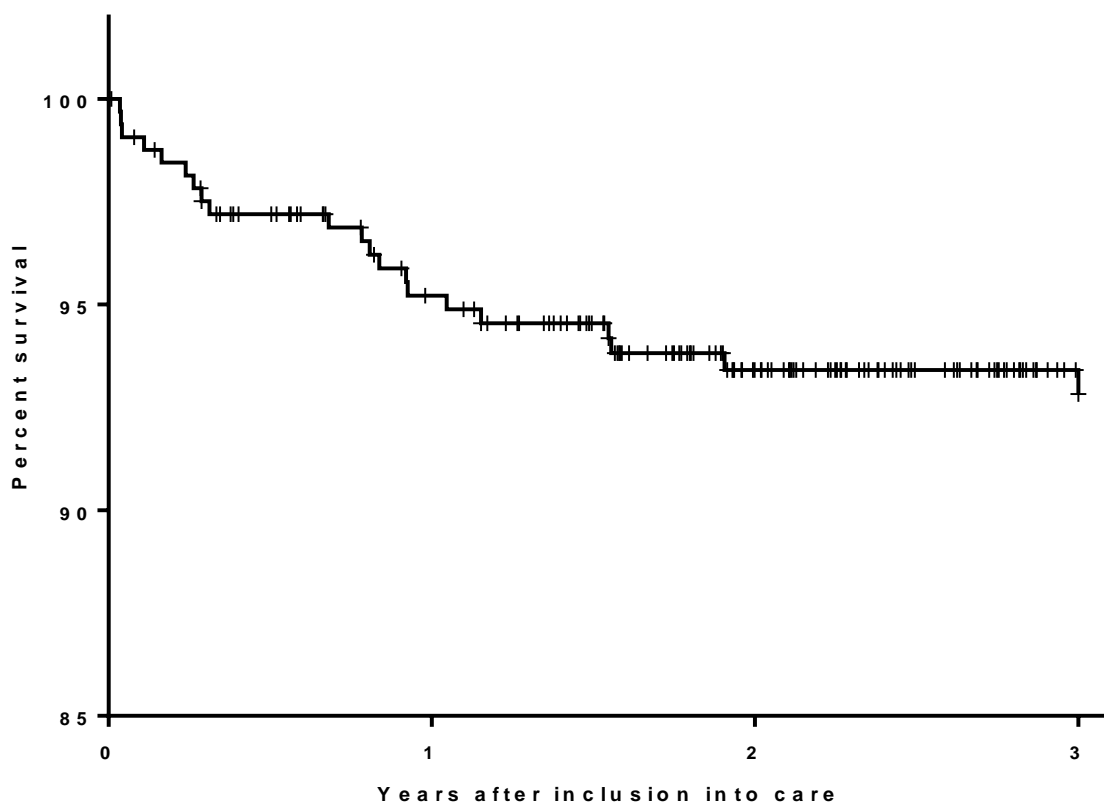


Figure 5. Survival after inclusion into care in the period 2007-2011.

The proportion of patient with a high viral load >10000 HIV-1 RNA copies/ml decrease over time (figure 6.)

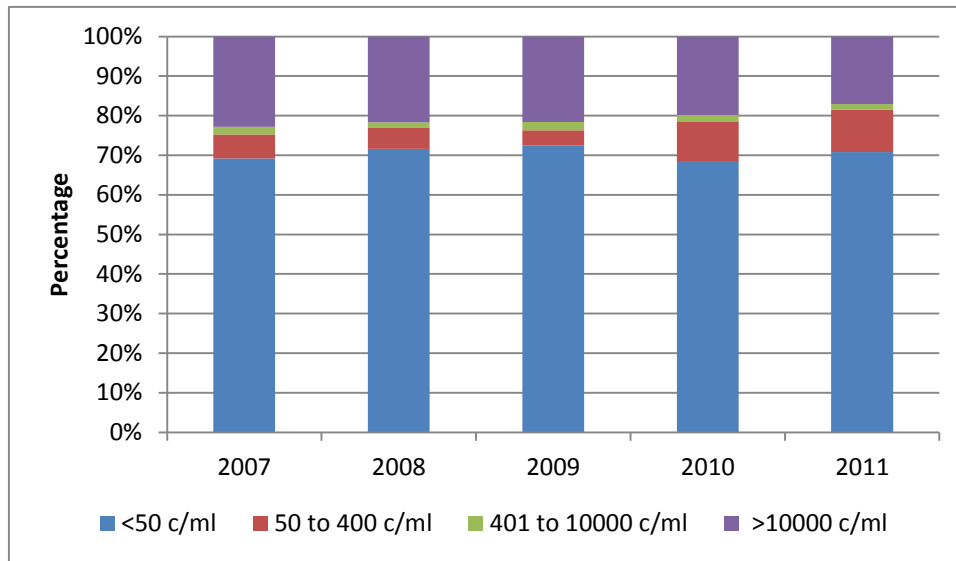


Figure 6. Viral load suppression in patients in care, Croatia, 2007-2011

The median CD4 cell count of all patient in care showed an increased trend from 426 cells/mm³ in 2007 to 524 cells/mm³ in 2011. This trend is consistent with the increase in suppressed viral load.

In 2011, among 637 adults in care (regardless of CART), 78% had a CD4 >350 per mm³ (Figure 7.).

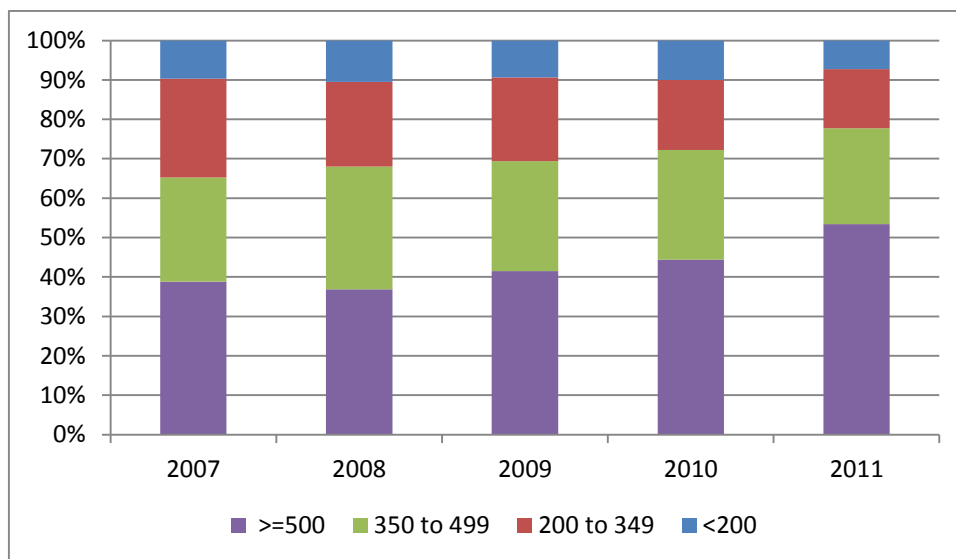


Figure 7. Different CD4 cell count strata for patient in care, Croatia, 2007-2011.

6. Discussion

6.1. Early access to HIV testing for patients

Over the natural course of an HIV infection CD4 count gradually decay. Median CD4 counts provide an indication of patient level of immunosuppression at diagnosis [16]. Testing and diagnose infected persons with HIV is the entry point to HIV care. Since 2007, UHID observed an increase in the proportion of patients presenting with advanced HIV infections, the proportion of very late presenter was stable. The high proportion of late presenter was considered to be the weakest point in our cascade of care.

Late HIV diagnosis is not only a tool to assess the efficiency of diagnostic procedure. It is also a major concern, such advanced disease present a poorer prognosis and it is associated with rapid progression to AIDS and an increase short term mortality compared to those diagnosed at an early stage of HIV [17]. A low CD4 count is also associated with an increased risk of non-AIDS related illnesses (cardiovascular, renal, hepatic, malignancies) [18-19].

Treating late presenter is also more challenging as they are more often associated with a higher rate of viral load failure [20]. Late presenters enter care at a stage of HIV where CART should have already begun. Efforts to decrease the proportion of late presenter could be translated into improved short term and long term mortality.

On a public health level, advance disease presents an increased transmission risk of HIV, increased health care cost [21]. Persons integrated into care are less likely to engage in risk transmission behaviour [22]. Posing an important barrier to reduction in incidence of HIV infection. Furthermore, the proportion of late presenter could also be considered as a reflection of persons unaware of their infection.

We can suppose that poor access to care might be due to cultural rather than financial reasons. As care is free of charge. Cultural reasons related to factor such as stigma, environment, and minority. More study are needed on our late presenter population to cluster and later on target this population.

The level of stigma toward MSM and patient with HIV/AIDS is still high in Croatia. [23-24].

The analysis of late presenters as limitations. For example, in early HIV infection a transient low CD4 ($<350/\text{mm}^3$) can be observed. In practice these patients are difficult to discriminate from late presenter in routine surveillance system. As a result, this overestimates the number of late presenters.

Several methods are available to expend our testing criteria to significantly decrease the rate of late presentation of HIV in Croatia: routine testing, targeted testing (STD), testing all patient aged 13-64 year's old, community based testing, oral testing at home.

In 2006, in order to respond to the high rate of undiagnosed HIV infections, the CDC published new HIV testing guidelines calling for routine testing in all health care settings [25]. By decreasing the proportion of late presenters, and thereby the proportion of patient unaware of their HIV status, our system will become increasingly representative of the HIV population in Croatia.

6.2. Rapid integration into care

From natural history of HIV infection, we know that a subclinical latent phase precedes the appearance of opportunistic infection. Monitoring the immune systems allows us to considerably decrease mortality by guiding clinician to start prophylactic drug against opportunistic infections and; it also indicates if antiretroviral treatments should be started.

It is recommended that all patients have their first CD4 count measured within two weeks of HIV diagnosis [26]. It is encouraging that almost nine out of ten patient with HIV had a CD4 count within one month of diagnosis. This demonstrates that CD4 count is usually requested at the time of diagnosis.

6.3. Compliance with current guidelines on when to start CART

AART in Croatia is available through the national health insurance system since 1998. In 2007 guidelines were modified to recommend the initiation of CART at a CD4-cell count ≤ 350 cell/mm³ [2-3]. Consequently, the proportion of patients starting CART at CD4-cell count < 350 cells/mm³ increased after 2007. During this study, most patients with a CD4 cell count < 350 cells/mm³ or clinical AIDS were receiving CART therefore compliance with current guidelines was not a barrier to HIV care in Croatia.

6.4. Achieving viral load suppression

Determination of HIV-1 RNA by PCR is available in Croatia since 1997. Between 2007 and 2011, our results show that most patients receiving CART achieved undetectable plasma HIV-RNA level.

The main goal of CART is to restore the immune system through the maximal suppression of viral replication. A consistently suppressed HIV viral load is associated with a decreased risk of developing AIDS, an improved survival, and a lower probability of transmitting HIV, particularly by sexual contact [27].

In developed countries, determination of plasma viral load is considered an essential part for monitoring effectiveness of CART and an excellent predictor of survival. The virological goal of CART is to reach less than 50 copies of HIV-1 RNA per milliliter of plasma measured by polymerase chain reaction (PCR) by week 24. According to BHIVA

guidelines, standard of care is defined as 85% of patient with a viral load <50 copies/mL after one year on CART[28].

Our results were considered to be satisfying as primary drug failure is common. One study showed that 24% of our patients failed to show a viral load reduction after 15 month on CART. Common factors associated with CART failure were: AIDS event, death, patient's poor compliance or absorption. Viral resistance is also often associated with CART failure but was not evaluated in this study.

Another indicator that we did not assess indicators is the frequency of VL testing. There is currently no consensus on the frequency of virological monitoring. Also, in a recent study, we did not observe that less frequent VL testing was associated with an increase in CART failure [29]. Therefore this indicator was considered less essential than achieving viral load suppression.

6.5. Retention into care

Retention in care is required for HIV patient's optimal outcomes. For patient who are not on CART, retention in care allows prompt initiation of CART once indicated, delivery of prophylactic medication for opportunistic infections and also prevention of mother to child transmission. For patients receiving CART, retention in care is essential to ensure provision of CART, identify potential side effects, and control effect of CART. For all patients, retention in care provide further assistance through ancillary services such as social support and psychological support [30].

Current data suggests that there is no clear gold standard to evaluate retention in care [31]. For example, patient on CART are expected to come more frequently than patient who are not. Visit frequency is frequently used as a measure of retention by public health department [32]. We used CD4 count as a proxy measure of patient visit and gap in care as a proxy for loss of follow-up. We found these measures to be convenient for our analysis, as they are easy to measure.

Our results show that the majority of HIV diagnosed adults in Croatia attended UHID regularly. About less than 1 in 10 adults were lost to follow up during the study period. Centralization of HIV care to UHID may account for high retention. Because of definition, it is common in other institutions to consider patient who moved to other facilities to be considered loss of follow up. One important limitation of our definition is that we cannot ensure that a patient lost to follow up is not actually included in care in another institution.

Similarly to access to care, we can suppose that HIV patient who stop coming to UHID do so because of cultural rather than financial reasons. As care is free of charge. Cultural reasons related to factor such as homophobia, stigma, environment, and minority, work responsibilities may limit retention in care. More studies are needed on our loss of follow up population to cluster and later on target this population.

6.6. Successful care

Monitoring of plasma HIV-1 RNA and determination of CD4 cell counts is related to the strategy of CART. Current recommendations on the frequency of VL testing after patients achieve an undetectable VL are mainly based on expert opinion and on the analysis. International Guidelines suggest VL testing every 3-4 month during the first and second year of CART, then extended to every half a year if viral load suppressed for a year and CD4 cell count are $>350/\text{mm}^3$ and adherence to CART is satisfactory [33]. Adequate monitoring of untreated patients is important in terms of appropriate initiation of CART and the prevention of AIDS, and also for survival. Determination of VL by PCR is available in Croatia since 1997.

Survival of HIV patient

The 1st year mortality rate of 5% in the study period reveals the consequences of late presentation. We believe that since the quality of care was good, if patients were to enter care earlier on this would have a direct impact on early mortality. We could improve this indicator. Approximately up to 10 people with AIDS die each year.

The mean CD4 count and proportion of suppressed HIV RNA level are increasing during the time period of the analysis, this result is consistent with the increase in the proportion of patients receiving CART over the same time period. We do not know if a decline in community HIV RNA level has contributed to our low HIV/AIDS level epidemic.

Some experts consider that a low VL among local HIV population should be enough to turn down an HIV epidemic.

We provided an overview of how Croatia is confronting the HIV continuum of care. This continuum of care can be used to inform of the efficacy of public health programs for HIV-positive people. And also to facilitate future quality improvement in the management of HIV infection in Croatia, by presenting visually where quality of care can be improved on a national level. Now that we presented our data, it also be possible to evaluate the effects of new policies and guidelines by looking at the outcome of changes on the cascade of care.

Other items were not included such as lipid screening, mental health screening, CART resistance test. In reviews, we found that compliance with current guidelines on initiation of *Pneumocystis jirovecii* Pneumonia (PCP) chemoprophylaxis was often used a criteria to evaluate HIV care. Very few patients received PCP chemoprophylaxis before 1992, today this is routinely done in our care. Therefore we didn't include this criterion. Furthermore, we considered that this criterion would relate more to AIDS patient quality of care more than the evaluation of care for our HIV population. These items could be included in a future evaluation

Standards of care are established to represent a clinically realistic level and at the same time exceed mean performance. It is unrealistic to define good care with 100% fulfillment of a particular measure. We showed that care of HIV patients improved from 2007 to 2011, larger proportion of patient are in care and on CART. However up to this day, many are not.

In theory, assessing quality of care could allow comparison of performance between institutions. However it is important to note that a wide difference in definition and methodology exist between institutions. Therefore looking at definitions is important before comparing them. Comparison is often not possible. Up to this date, there were no international guidelines regarding the definition and methodology of quality of care criteria. In future, standardized definition with similar numerator should allow comparison across studies. However this is not essential to evaluate HIV care in Croatia, as we considered that our definition should be sufficient to evaluate HIV care over time.

Our choice of indicators can be debated, but the need for monitoring is indisputable. Our assessment ensure that persons living with HIV/AIDS are diagnosed soon after acquiring HIV, successfully integrated into medical care, beginning effective antiretroviral therapy according to guidelines.

Also our finding on quality of HIV care in Croatia are encouraging, they do not minimize the key role of primary prevention such as condom use, clean needles program, and treatment of other STD in general.

Conclusion:

With the current paper we aimed to focus on public health attention on the HIV care situation in Croatia, by showing encouraging data on quality of care.

This is the first study that employs a brief panel of indicators based on current guidelines, to assess the quality of health care in Croatia on the whole HIV diagnosed population.

We investigated HIV care performance using available electronic surveillance data. The criteria we used in this evaluation of health care utilization of HIV patients were based on current HIV treatment guidelines. We analyzed a wide spectrum of simply measurable quality indicators, assimilating several aspects of HIV care from early diagnosis to care and survival. In the future, these criteria could be easily monitored up on a yearly basis.

Our findings suggest that the level of clinical HIV care received by HIV patient in Croatia was very good. However, the proportion of late presentation pose an important obstacle to reaching an optimal treatment outcome. This means that most patients in care, fully benefit of HIV treatment, however we need to be aware that an unknown proportion of non-diagnosed HIV infected people does not.

Competing interests

The authors declare that they have no competing interests.

Author's contribution

Funding

Acknowledgement

I wish to acknowledge the valuable help of all doctors, nurses, and personnel of the University Hospital for Infectious Diseases-Zagreb. Most ardently I wish to thank my mentor doc. dr. sc. Josip Begovac whose help and guidance proved invaluable.

7. References:

1. Hall HI, McDavid K, Ling Q, Sloggett A. Determinants of progression to AIDS or death after HIV diagnosis, United States, 1996 to 2001. *Ann Epidemiol.* 2006;16:824–33.
2. EACS Guidelines. Clinical Management and Treatment of HIV-infected Adults in Europe. 2011. x 5–4. 26-8-2011. Available at: <http://www.europeanaidsclicinalsociety.org/>
3. Gazzard BG, British HIV: Association Guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008. *HIV Med* 2008, 9(8):563–608.
4. HIV/AIDS Treatment and Care. Clinical protocols for the WHO European region. WHO Regional Office for Europe; 2009. Available at http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf
5. Bozicevic I, Lepej SZ, Rode OD, Grgic I, Jankovic P, Dominkovic Z, Lukas D, Johnston LG, Begovac J. Prevalence of HIV and sexually transmitted infections and pattern of recent HIV infection among men who have sex with men in Zagreb, Croatia. *Sex Transm Infect.* 2012 Nov;88(7):539-44.
6. Kolarić B. Croatia: still a low-level HIV epidemic?--seroprevalence study. *Coll Antropol.* 2011 Sep;35(3):861-5. Kolarić B, Stajduhar D, Gajnik D,
7. Rukavina T, Wiessing L. Seroprevalence of blood-borne infections and population sizes estimates in a population of injecting drug users in Croatia. *Cent Eur J Public Health.* 2010 Jun;18(2):104-9.
8. Ramirez-Piedad MK, Lepej SZ, Yerly S, Begovac J (2009) High prevalence of non-B HIV-1 subtypes in seamen and their sexual partners in Croatia. *J Med Virol* 81: 573–577.
9. Horberg MA, Aberg JA, Cheever LW, Renner P, O'Brien Kaleba E, Asch SM. Development of national and multiagency HIV care quality measures. *Clin Infect Dis* 2010; 51(6):732–738

10. Podlekareva DN, Reekie J, Mocroft A, Losso M, Rakhmanova AG, Bakowska E, Karpov IA, Lazarus JV, Gatell J, Lundgren JD, Kirk O; EuroSIDA study in EuroCoord. Benchmarking HIV health care: from individual patient care to health care evaluation. An example from the EuroSIDA study. *BMC Infect Dis.* 2012 Sep 25;12:229. doi: 10.1186/1471-2334-12-229.
11. A guide on indicators for monitoring and reporting on the health sector response to HIV/AIDS. Handbook of indicators for key HIV interventions in the health sector. WHO; 2011. Available at: http://www.who.int/hiv/data/UA2011_indicator_guide_en.pdf
12. Cheever LW. Engaging HIV-infected patients in care: their lives depend on it. *Clin Infect Dis* 2007; 44:1500–2
13. Das M, Chu PL, Santos GM, Scheer S, Vittinghoff E, McFarland W, Colfax GN. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS One.* 2010 Jun 10;5(6):e11068. doi: 10.1371/journal.pone.0011068.
14. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet.* 2009 Jan 3;373(9657):48-57. doi: 10.1016/S0140-6736(08)61697-9. Epub 2008 Nov 27.
15. Ancelle-Park R. Expanded European AIDS case definition. *Lancet.* 1993 Feb 13;341(8842):441.
16. Pantaleo, G, Graziosi C, Fauci AS. New concepts in the immunopathogenesis of human immunodeficiency virus infection. *N Engl J Med* 1993; 328(5): 327-35
17. Chadborn TR, Delpech VC, Sabin CA, Sinka K, Evans BG. The late diagnosis and consequent short-term mortality of HIV-infected heterosexuals England and Wales, 2000-2004. *AIDS* 2006; 20(18): 2371-9.
18. Lichtenstein KA, Armon C, Buchacz K, et al. Low CD4+ T Cell Count Is a Risk Factor for Cardiovascular Disease Events in the HIV Outpatient Study. *Clin Infect Dis* 2010; 51(40): 435-47.
19. Phillips AN, Neaton J, Lundgren JD. The role of HIV in serious diseases other than AIDS. *AIDS* 2008; 22(18): 2409-18.
20. Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: Risk factors for virologic failure and adverse drug reactions. *Ann Intern Med* 1999;131:81–87.
21. Marks G, Crepaz N, Janssen R. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. *AIDS.* 2006;20(10):1447–50
22. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: Implications for HIV prevention programs. *J Acquir Immune Defic Syndr* 2005;39:446–453.
23. Tesic V, Kolaric B, Begovac J (2006) Attitudes towards HIV/AIDS among four year medical students at the University of Zagreb Medical School—better in 2002 than in 1993 but still unfavorable. *Coll Antropol* 30 Suppl 2: 89–97.
24. Stulhofer, A., & Sandfort, T. G. M. (2005). Introduction: Sexuality and gender in times of transition. In A. Stulhofer & T. G. M. Sandfort (Eds.), *Sexuality and gen-*

- der in postcommunist Eastern Europe and Russia (pp. 1–25). New York: The Haworth Press
25. Centers for Disease Control and Prevention. Revised Recommendations for HIV Testing in Adults, Adolescents, and Pregnant Women in Health-Care Settings. *MMWR Morb Mortal Wkly Rep.* 2006;55(RR14):1–17.
 26. Helbert M, Breuer J. Monitoring patients with HIV disease. *J Clin Pathol* 2000; 53: 266–273.
 27. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011;365:493–505.
 28. Asboe D, British HIV Association guidelines for the routine investigation and monitoring of adult HIV-1-infected individuals 2011. *HIV Med.* 2012 Jan;13(1):1-44. doi: 10.1111/j.1468-1293.2011.00971.x.
 29. Plos One - Frequency of HIV-1 Viral Load Monitoring of Patients Initially Successfully Treated with Combination Antiretroviral Therapy.
 30. Messeri PA, Abramson DM, Aidala AA, et al. The impact of ancillary HIV services on engagement in medical care in New York City. *AIDS Care* 2002;14(Suppl 1):S15–S29. PubMed: 12204139.
 31. Mugavero MJ, Westfall AO, Zinski A, Davila J, Drainoni ML, Gardner LI, Keruly JC, Malitz F, Marks G, Metsch L, Wilson TE, Giordano TP; Retention in Care (RIC) Study Group. Measuring retention in HIV care: the elusive gold standard. *J Acquir Immune Defic Syndr.* 2012 Dec 15;61(5):574-80. doi:10.1097/QAI.0b013e318273762f.
 32. Zetola NM, Bernstein K, Ahrens K, et al. Using surveillance data to monitor entry into care of newly diagnosed HIV-infected persons: San Francisco, 2006–2007. *BMC Public Health* 2009; 9:17.
 33. Thompson MA, Aberg JA, Cahn P, Montaner JS, Rizzardini G, et al. (2010) Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society-USA panel. *JAMA* 304: 321–333.

8. **Biography:**

Education

University of Zagreb School of Medicine, *Medical Studies in English*, Zagreb Croatia 2008-2012

Pierre et Marie Curie University – Paris VI, Medical studies (first year – PCEM1), Paris France, 2005-2007

Lycée Molière, High School, Paris, 2004-2005

Clinical Experience in France

Elective/Medical student clerkship: Faculté de Médecine Paris-Descartes (Paris, France), January 2013, Internal Medicine and Tertiary referral center for Orphans Diseases, 3 months