

Cohort profile update: The Swiss HIV Cohort Study (SHCS)

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Key features

- The Swiss HIV cohort study (SHCS), a national, multicenter cohort, is continuously enrolling HIV-infected adults since 1988 to monitor the HIV epidemic in Switzerland.
- After 30 years of follow-up, changing characteristics and behavior of the HIV-infected population in Switzerland as well as the availability of novel drugs and computational and laboratory methods open up new research areas.
- By the end of 2019, 9 816 participants at the median age of 52 [43-58] years were under follow-up.
- A biobank containing 1.7 million blood samples, collected over more than 30 years, allows modern laboratory analyses.
- The SHCS is focusing on the following research topics: Co-medication and co-morbidities, impact of new treatment strategies, sexual transmitted diseases, host genomic and precision medicine, HIV transmission, evolution of broadly neutralizing antibodies and vaccine development, HIV cure and health economic assessments and cost-effectiveness analyses.
- Information for interested collaborators can be found on the SHCS website (<http://www.shcs.ch/132-who-can-submit>).

Key words:

HIV, cohort, epidemiology, antiretroviral therapy, biobank, observational study

The original cohort

The Swiss HIV Cohort Study (SHCS) provides a unique research platform for clinical, translational, epidemiological, social and basic research. The SHCS was established in 1988. It is an ongoing, multicenter, clinic-based, prospective longitudinal observational study including HIV-infected adults in Switzerland. The study design provides continuous enrollment and semiannual study visits, where socio-demographic and clinical and laboratory information is collected. Patients are recruited by all university hospitals in Switzerland, by numerous regional hospitals and private physicians. In the participating institutions, all HIV infected patients are asked to participate in the SHCS. The participation is voluntary and an informed consent is needed. The SHCS has a growing biobank including over 1.7 million aliquots of plasma and peripheral blood mononuclear cells (PBMCs), which were collected over the last 32 years. Today, the SHCS is a powerful tool to study different aspects of the HIV infection such as challenges of antiretroviral treatment, including drug resistance and drug-drug interactions, co-infections, co-medications and co-morbidities, social and gender aspects of the disease, virus-host interactions in particular determinants of the development of broadly neutralizing antibodies, viral reservoir studies, cell biological and virus and host genetic mechanisms of the disease, transmission of HIV on a population level, and pregnancy outcomes. By the end of 2019, a total of 20 845 individuals were included in the SHCS, of whom 9 816 patients were still under follow-up.

What is the reason for the new focus (or new data collection)?

We update the SHCS cohort profile, published in 2009, because of changing characteristics of the HIV-infected population in Switzerland and due to changes in the focus of research within the SHCS ¹.

In the last decade, the care of HIV-infected patients improved substantially in Switzerland.

Long-term treatment success, with suppressed viral load, is achieved among the vast majority of patients. Modern combination antiretroviral therapies (ART) are highly effective, less toxic and better tolerated. Potent ART led to a reduction of the pill burden and simplified therapies such as mono/dual therapies or long-acting agents. The long-term efficacy and tolerability of these new treatment strategies need to be assessed in population based real life cohorts. In addition, in the last few years generic antiretroviral drugs were introduced. The SHCS aims to study the acceptance, tolerability and effectiveness of these drugs.

Key patient characteristics of the HIV population are changing. The SHCS is dealing with an aging population, mainly because of the strongly increasing life expectancy of the HIV-infected population in Switzerland which comes close to the life expectancy of the HIV-uninfected population ²⁻⁴. Along with increasing age, other factors are increasing such as the median body mass index, number of co-morbidities and the number of co-medications (Figure 1).

In recent years, the SHCS also observed behavioral changes ⁵. A higher rate of SHCS participants have condomless sex. The number of sexually transmitted diseases increased in recent years, which shifted the research focus to co-infections, such as hepatitis C, syphilis, gonorrhea and chlamydia ⁶⁻⁹. The availability of HIV pre-exposure prophylaxis among non-infected individuals might lead to additional behavioral changes within the HIV-infected population ¹⁰.

Moreover, new computational and laboratory methods, such as machine learning and full genome sequencing, have opened new research fields and generate a need for an adapted dataset ^{11, 12}.

What will be the new areas of research?

The SHCS is shifting the focus towards the following topics:

- i) Co-medication and co-morbidities: A better understanding of the management of drug-drug interactions (DDIs) in clinical practice is crucial as polypharmacy represents an increasing issue in the context of the aging HIV population. Polypharmacy increases the need for therapeutic drug monitoring (TDM) in routine clinical follow-up of people living with HIV and for research purposes..
- ii) Impact of new treatment strategies: The SHCS aims to further study the beneficial and adverse effects of new treatment strategies, in particular the effect of simplified treatments and generic drugs.
- iii) Sexual transmitted diseases: The epidemiology, transmission patterns and management of sexually transmitted diseases is evolving rapidly. The SHCS aims to study these changes in detail.
- iv) Broadly neutralizing antibodies – a prerequisite for an HIV-vaccine: the huge sample repository of historically untreated patients allows longitudinal studies of the evolution of bNab induction of unmet precedence and the identification of unique viral envelopes that were able to induce bNabs in different individuals.
- v) Host genomic and precision medicine: Human genomic studies contribute to a better understanding of HIV pathogenesis and are currently paving the way toward more individualized treatment strategies. The SHCS performs translational research in this field and evaluates the clinical utility of precision approaches in HIV care.

- vi)* HIV transmission: The SHCS is continuously monitoring the Swiss HIV epidemic in particular also using and developing molecular epidemiology methods.
- vii)* HIV cure: The SHCS is investigating relevant factors for the decay of the viral reservoir using a systems biology approach.
- viii)* Health economic assessments and cost-effectiveness analyses: In collaboration with health care providers, the SHCS aims to assess economic aspects of the HIV disease.

The organization of the SHCS is highly dynamic and encompasses a rapid decision-making process. The collected data can be adapted quickly, when an urgent new scientific question arises.

Who is in the cohort?

Since 1988, the SHCS is continuously enrolling HIV-infected individuals. By the end of 2019, 20 845 were registered in one of the seven study centers (5 university hospitals, 2 large cantonal hospitals), its affiliated 14 regional hospitals or with its affiliated 48 private physicians (Table 1). Overall, 5 697 (27.3%) women were included, of whom 2 726 under follow-up in 2019.

Homosexual contact was reported as the presumed mode of HIV transmission in 8 169 (39.2%) of all included patients (46.8% of patients seen in 2019) and 6 881 (33.0%) persons were infected heterosexually (37.9% of patients seen in 2019). Only 966 (9.9%) of patients seen in 2019, were infected through intravenous drug use, while in all patients the percentage was 23.2% (n=4 834).

Overall 15 076 (72.3%) patients have received combined antiretroviral treatment (cART, ≥ 3 drugs from at least drug classes) starting at a median [IQR] age of 37.0 [31.0-45.0] years. Overall, median number of 1.8 [0.1-6.9] years passed between HIV-diagnosis and the beginning of cART. This time span decreased over time and reached minimum in 2019 (<1 month). By the end of 2019, 9

462 (96.8%) of patients seen, have been on treatment and in 9 501 (97.2%) individuals viral load (VL) has been below 400 cps/ml.

The SHCS covers 71% of all patients on ART in Switzerland. This estimate is based on a comparison of the Swiss ART sales data from 2017 to 2019 (IMS Health GmbH, Hergiswil, Switzerland) and the prescription data (type of drug, start and stop date) among patients registered in the SHCS. Between 2009 and 2018, the Swiss Federal Office for Public Health (FOPH) reported 5476 new infections, the SHCS registered in this time period 4 868 (89%)¹³. In 2019, the SHCS included 59% of the estimated number of HIV-infected people in Switzerland. The number of new registrations is slightly decreasing since 2010 (Figure 2 A), which is in line with the numbers published by the FOPH¹³. A median number of 576 patients is recruited per year. The number of actively followed patients is steadily increasing (Figure 2 B).

Since the start of the cohort, the characteristics of the participants changed (Table 2). Going along with constantly increasing numbers of patients on treatment and with suppressed VLs, an increase in median age from 45 [33-57] years in 2009 to 52 [37-67] years in 2019 can be observed among the patients under active follow-up. Simultaneously median BMI of participants rose from 23.4 [21.1-25.9] in 2009 to 24.8 [22.3-27.8] in 2019. In recent years, also the frequency of the mode of transmission of patients seen per year has changed: Number of patients who most likely acquired the HIV-infection through homosexual contacts increased from 3 216 (40.9%) in 2009 to 4 572 (46.8%) in 2019. At the same time, the number of active patients who named IDU as most likely source of infection decreased from 1 248 (15.9%) in 2009 to 966 (9.9%) in 2019. The percentage of patients under follow-up who have experienced a CDC stage C condition decreased over the years, reaching its lowest level in 2019 (21.3%). The probability of death was stable at a low level (0.9%) between 2009 and 2019 (Figure 2 C). In this time

period, 8% of the deaths were AIDS-related. The proportion of AIDS-related death decreased and ranged from 12.8% in 2010 to 0% in 2019. Overall 5 166 (24.8%) of the patients died and 5863 (28.1%) patients were loss to follow-up. The main reasons for loss to follow-up were that patients did not respond to several invitations (39.8% of patients loss-to follow-up) or patients moved abroad (22.7%).

What has been measured?

The SHCS measures consist of a standard dataset, a subset of additional datasets for specific sub-studies and the information about samples stored in biobanks. The datasets can be expanded with new measures whenever indicated.

Standard questionnaire

The SHCS participants are followed-up semi-annually. The assessment covers demographic variables, questions on health behavior, hospitalizations, anthropometric data, co-morbidities, vaccinations, antiretroviral therapy, co-medications and different laboratory measurements. Women are additionally asked to answer a questionnaire about gynecological examinations and obstetric events.

In 2015, the SHCS introduced a new tool to collect detailed information about medications, antiretroviral therapies as well as co-medication. The tool includes an Application Programming Interface (API) to a database with all approved drugs in Switzerland (<https://www.hcisolutions.ch>). The tool allows rapid data entry without typing errors.

Starting from 2017, more detailed information on sexually transmitted diseases and serious non-opportunistic infections is collected. The later are defined as infections, which are treated at least for five days with antibiotics or have led to a hospitalization (e.g. endocarditis, pneumonia,

sepsis).. In 2020, new questions about the emerging corona virus disease 19 (COVID-19) were introduced.

SHCS sub-studies

The SHCS runs numerous sub-studies for which additional systematic data collection is performed.

- i) Host genetics: Since 2016, the SHCS runs an additional biobank as a basis for genome-wide association studies (GWAS) and exome sequencing. By the end of 2019, over 8500 patients had a sample stored for genetic analysis and for over 6100 samples genome wide data is available.
- ii) Metabolics and ageing (M+A) and Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO): The M+A project includes storing of fasting plasma and urine samples, measuring bone mineral density and coronary CT. Neurocognitive assessments are performed to assess the prevalence of neurocognitive impairment (NCI) in the SHCS among patients aged ≥ 45 years ^{14,15}.
- iii) Neutralizing antibodies: The SHCS studied broadly neutralizing antibodies among around 4500 participants and did a large scale screening for binding affinities of patient plasmas to 13 specific HIV- antigens ¹⁶.
- iv) SHCS drug resistance database: The SHCS drug resistance database includes >24,800 viral sequences from genotypic drug resistance tests from over 13,700 patients ^{17,18}.
- v) MoCHiV: The Swiss Mother and Child HIV Cohort Study (MoCHiV) is a section of the SHCS where information about pregnancy, delivery and newborns from HIV-infected mothers is collected. Details will be described elsewhere.

SHCS biobank

The SHCS stores plasma and PBMC samples in a biobank on a regular basis. Since the beginning of the cohort over 270'000 plasma samples (>1.2 million aliquots) and over 160'000 PBMCs (>490'000 aliquots) were stored in the SHCS biobanks.

What has it found? Key findings and publications

The SHCS covers a broad scope of research findings. Since the publication of the original cohort profile in 2009, the SHCS gave new insights in the following topics:

- i) Contribution to the better understanding of the HIV epidemic in Switzerland, which includes the characterization of transmission clusters, the clinical and psychological situation of patients, the prevalence of sexual transmitted diseases, behavioral changes and the impact of new prevention strategies such as the availability of pre-exposure prophylaxis ^{4, 7, 19-23}.
- ii) Documentation and evaluation of different antiretroviral treatment strategies, in particular studies focusing on monitoring, side effects and simplified treatment options ²⁴⁻²⁹.
- iii) Description of the prevalence of HIV drug resistance and its impact on the long-term success of antiretroviral treatment ^{18, 30-34}.
- iv) Identification and characterization of broadly neutralizing antibodies in a trial including about 4500 patients and identification of imprinting HIV-envelopes ^{16, 35, 36}.

- v) Aging and metabolic complications, including neurocognitive disorders, are an important focus of the SHCS. Major efforts were made to increase knowledge on metabolic, cardiovascular, renal, bone and neurocognitive disorders ^{15, 37-39}.
- vi) Description of the hepatitis C epidemiology among HIV infected individuals in Switzerland and the impact of the introduction of direct-acting antivirals (DAAs) ^{6, 40-45}.

For hepatitis B co-infections, the SHCS has studied disease outcomes and led a large investigation on hepatocellular carcinoma ^{46, 47}.
- vii) Successful projects using genetic approaches, such as genome-wide and phylogenetic approaches, gave new insights in the host and viral genetic influences on HIV pathogenesis⁴⁸⁻⁵¹.
- viii) Pharmacokinetics, model-based simulations and clinical validation of drug-drug interactions contributed important new knowledge for optimized treatment strategies ⁵²⁻⁵⁴.
- ix) Studies about host and viral factors during HIV transmission were performed ^{55, 56}.
- x) Characterization of the HIV reservoir among acutely and chronically infected patients helped to identify potential treatment strategies for HIV cure ^{57, 58}.
- xi) A pilot study paved the way for health economic assessments and cost-effectiveness analyses ⁵⁹.
- xii) Projects on pregnancy and childhood were performed including patients from the Swiss Mother and Child HIV Cohort Study (MoCHiV) ^{60, 61}.

- xiii) A pilot study comparing machine learning (ML) techniques to standard statistical methods to predict declining kidney function showed the power of ML when used in high quality rich datasets as the one from the SHCS database ¹¹.

Since the start of the SHCS, 618 original studies were published. In addition, the SHCS provided data for many international collaborations, 396 and 138 studies were published with an active participation or a board participation of an SHCS member. Since 2009, the SHCS published a total of 676 publications.

What are the main strengths and weaknesses?

The main strength of the SHCS is the high quality data collected over 30 years. It has a unique longitudinal data set including a biobank consisting of 1.7 million aliquots. The study has a very high coverage. A high percentage of HIV-infected individuals in Switzerland are included in the SHCS. Between 2009 and 2018, the SHCS covered 89% of all new infections in Switzerland. 71% of all patients on ART are included. In 2019, the SHCS included 59% of the estimated number of HIV-infected people in Switzerland. Over the whole study period, >50% of HIV-infected people in Switzerland were included ^{1 62}. The drop-out rate is low due to the network of specialized private physicians and clinics, which allows the patients to change the study center easily when moving within Switzerland.

Weaknesses of the study include the lack of a control population of HIV-negatives and a slight underrepresentation from ethnic minority groups ⁶³, which may limit generalizability of findings to migrants to some extent. Furthermore, the Swiss law does not allow to update the SHCS data based on links to official registries, such as the death registry ^{2, 64}.

Can I get hold of the data? Where can I find out more?

Additional information about the SHCS is available on the website (<http://shcs.ch/>). The SHCS has a data sharing process. Interested researchers can access data if a study proposal is approved by the SHCS scientific board. The Standard Operating Procedures (SOPs) to submit research proposals for interested research groups are publicly available on the website (<http://www.shcs.ch/132-who-can-submit>).

Appendix

Members of the Swiss HIV Cohort Study: Aebi-Popp K, Anagnostopoulos A, Battegay M, Bernasconi E, Böni J, Braun DL, Bucher HC, Calmy A, Cavassini M, Ciuffi A, Dollenmaier G, Egger M, Elzi L, Fehr J, Fellay J, Furrer H, Fux CA, Günthard HF (President of the SHCS), Haerry D (deputy of "Positive Council"), Hasse B, Hirsch HH, Hoffmann M, Hösli I, Huber M, Kahlert CR (Chairman of the Mother & Child Substudy), Kaiser L, Keiser O, Klimkait T, Kouyos RD, Kovari H, Ledergerber B, Martinetti G, Martinez de Tejada B, Marzolini C, Metzner KJ, Müller N, Nicca D, Paioni P, Pantaleo G, Perreau M, Rauch A (Chairman of the Scientific Board), Rudin C, Scherrer AU (Head of Data Centre), Schmid P, Speck R, Stöckle M (Chairman of the Clinical and Laboratory Committee), Tarr P, Trkola A, Vernazza P, Wandeler G, Weber R, Yerly S.

Ethics approval

The SHCS was approved by the local ethical committees of all participating institutions.

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Conflict of interest

The institution of HF received educational grants from Gilead Sciences, ViiV, MSD, Abbvie and Sandoz. M.C. has received research and travel grants for his institution from ViiV and Gilead. E.B. has received fees for his institution for participation to advisory board from MSD, Gilead Sciences, ViiV Healthcare, Abbvie and Janssen. M.B. has received research or educational grants by Abbvie AG, Gilead Sciences Switzerland Sàrl, Janssen-Cilag AG, MSD Merck Sharp & Dohme AG and ViiV Healthcare GmbH. A.R. has received honoraria for advisory boards and/or travel grants: Janssen-Cilag, MSD, Gilead Sciences, Abbvie, and Pfizer. Unrestricted research grant: Gilead Sciences. All remuneration went to his home institution and not to AR personally. R.D.K. has received grants from the Swiss National Science Foundation and personal fees from Gilead Sciences, outside the submitted work. H.F.G. has received unrestricted research grants from Gilead Sciences and Roche; fees for data and safety monitoring board membership from Merck; consulting/advisory board membership fees from Gilead Sciences, Sandoz and Mepha. A.C. has received unrestricted educational and research grants from MSD, Gilead and

ViiV. P.V. has received fees for his institution for temporary advisory board meetings with pharmaceutical companies including Viiv-Healthcare and MSD. C.M. received a research grant from Gilead and speaker honoraria for her institution from MSD. M.S. has received fees for advisory board participation from Gilead, ViiV, MSD, Sandoz, and Mepha, as well as grants for conferences from Gilead and MSD, unrelated to the present study. GW reports support to his home institution for advisory boards and/or travel grants from MSD, Gilead Sciences and Abbvie, and an unrestricted research grant from Gilead Sciences. All remuneration was provided outside the submitted work. The institution of P.E.T. received research grants and advisory fees from Gilead Sciences and ViiV Healthcare. D. L. B. has received consulting/advisory board membership fees from Gilead Sciences, ViiV and MSD. Remaining authors declare no competing interests.

Figure captions

Figure 1: Age (A) and weight (B) distribution in the Swiss HIV Cohort Study (SHCS) between 1999 and 2019.

Figure 2: No. of newly registered (A), number of active patients (B) in Swiss HIV Cohort Study (SHCS) by most likely route of infection and probability of drop-out and death (C)

References

1. Swiss HIVCS, Schoeni-Affolter F, Ledergerber B, et al. Cohort profile: the Swiss HIV Cohort study. *Int J Epidemiol* 2010; **39**: 1179-89.
2. Gueler A, Moser A, Calmy A, et al. Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population. *AIDS* 2017; **31**: 427-36.
3. Hasse B, Ledergerber B, Furrer H, et al. Morbidity and aging in HIV-infected persons: the Swiss HIV cohort study. *Clin Infect Dis* 2011; **53**: 1130-9.
4. Hasse B, Iff M, Ledergerber B, et al. Obesity Trends and Body Mass Index Changes After Starting Antiretroviral Treatment: The Swiss HIV Cohort Study. *Open Forum Infect Dis* 2014; **1**: ofu040.
5. Hampel B, Kusejko K, Kouyos RD, et al. Chemsex drugs on the rise: a longitudinal analysis of the Swiss HIV Cohort Study from 2007 to 2017. *HIV Med* 2020; **21**: 228-39.
6. Wandeler G, Gsponer T, Bregenzler A, et al. Hepatitis C virus infections in the Swiss HIV Cohort Study: a rapidly evolving epidemic. *Clin Infect Dis* 2012; **55**: 1408-16.
7. Shilaih M, Marzel A, Braun DL, et al. Factors associated with syphilis incidence in the HIV-infected in the era of highly active antiretrovirals. *Medicine (Baltimore)* 2017; **96**: e5849.
8. Kouyos RD, Hasse B, Calmy A, et al. Increases in Condomless Sex in the Swiss HIV Cohort Study. *Open Forum Infect Dis* 2015; **2**: ofv077.
9. Hasse B, Ledergerber B, Hirschel B, et al. Frequency and determinants of unprotected sex among HIV-infected persons: the Swiss HIV cohort study. *Clin Infect Dis* 2010; **51**: 1314-22.

10. Hampel B, Kusejko K, Braun DL, Harrison-Quintana J, Kouyos R, Fehr J. Assessing the need for a pre-exposure prophylaxis programme using the social media app Grindr(R). *HIV Med* 2017; **18**: 772-6.
11. Roth JA, Radevski G, Marzolini C, et al. Cohort-derived machine learning models for individual prediction of chronic kidney disease in people living with HIV: a prospective multicentre cohort study. *J Infect Dis* 2020.
12. Carlisle LA, Turk T, Kusejko K, et al. Viral Diversity Based on Next-Generation Sequencing of HIV-1 Provides Precise Estimates of Infection Recency and Time Since Infection. *J Infect Dis* 2019; **220**: 254-65.
13. HIV, Syphilis, Gonorrhoe und Chlamydiose in der Schweiz im Jahr 2018: eine epidemiologische Übersicht. *BAG-Bulletin* 2019; **41**: 10-36.
14. Metral M, Darling K, Locatelli I, et al. The Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) study: baseline participant profile. *HIV Med* 2020; **21**: 30-42.
15. Tarr PE, Ledergerber B, Calmy A, et al. Subclinical coronary artery disease in Swiss HIV-positive and HIV-negative persons. *Eur Heart J* 2018; **39**: 2147-54.
16. Rusert P, Kouyos RD, Kadelka C, et al. Determinants of HIV-1 broadly neutralizing antibody induction. *Nat Med* 2016; **22**: 1260-7.
17. von Wyl V, Yerly S, Boni J, et al. Emergence of HIV-1 drug resistance in previously untreated patients initiating combination antiretroviral treatment: a comparison of different regimen types. *Arch Intern Med* 2007; **167**: 1782-90.
18. Scherrer AU, von Wyl V, Yang WL, et al. Emergence of Acquired HIV-1 Drug Resistance Almost Stopped in Switzerland: A 15-Year Prospective Cohort Analysis. *Clin Infect Dis* 2016; **62**: 1310-7.

19. Braun DL, Marzel A, Steffens D, et al. High Rates of Subsequent Asymptomatic Sexually Transmitted Infections and Risky Sexual Behavior in Patients Initially Presenting With Primary Human Immunodeficiency Virus-1 Infection. *Clin Infect Dis* 2018; **66**: 735-42.
20. Marzel A, Kusejko K, Weber R, et al. The Cumulative Impact of Harm Reduction on the Swiss HIV Epidemic: Cohort Study, Mathematical Model, and Phylogenetic Analysis. *Open Forum Infect Dis* 2018; **5**: ofy078.
21. Kusejko K, Marzel A, Nguyen H, et al. Differences in social and mental well-being of long-term survivors among people who inject drugs and other participants in the Swiss HIV Cohort Study: 1980-2018. *Antivir Ther* 2020.
22. Anagnostopoulos A, Ledergerber B, Jaccard R, et al. Frequency of and Risk Factors for Depression among Participants in the Swiss HIV Cohort Study (SHCS). *PLoS One* 2015; **10**: e0140943.
23. Gueler A, Schoeni-Affolter F, Moser A, et al. Neighbourhood socio-economic position, late presentation and outcomes in people living with HIV in Switzerland. *AIDS* 2015; **29**: 231-8.
24. Kovari H, Calmy A, Doco-Lecompte T, et al. Antiretroviral Drugs Associated With Subclinical Coronary Artery Disease in the Swiss Human Immunodeficiency Virus Cohort Study. *Clin Infect Dis* 2020; **70**: 884-9.
25. Courlet P, Decosterd LA, Brown JA, et al. Emtricitabine and lamivudine concentrations in saliva: a simple suitable test for treatment adherence. *J Antimicrob Chemother* 2019; **74**: 2468-70.
26. Surial B, Ledergerber B, Calmy A, et al. Changes in renal function after switching from TDF to TAF in HIV-infected individuals: a prospective cohort study. *J Infect Dis* 2020.

27. Young J, Schafer J, Fux CA, et al. Renal function in patients with HIV starting therapy with tenofovir and either efavirenz, lopinavir or atazanavir. *AIDS* 2012; **26**: 567-75.
28. Kovari H, Ledergerber B, Peter U, et al. Association of noncirrhotic portal hypertension in HIV-infected persons and antiretroviral therapy with didanosine: a nested case-control study. *Clin Infect Dis* 2009; **49**: 626-35.
29. Glass TR, Rotger M, Telenti A, et al. Determinants of sustained viral suppression in HIV-infected patients with self-reported poor adherence to antiretroviral therapy. *PLoS One* 2012; **7**: e29186.
30. Scherrer AU, Yang WL, Kouyos RD, et al. Successful Prevention of Transmission of Integrase Resistance in the Swiss HIV Cohort Study. *J Infect Dis* 2016; **214**: 399-402.
31. Abela IA, Scherrer AU, Boni J, et al. Emergence of Drug Resistance in the Swiss HIV Cohort Study Under Potent Antiretroviral Therapy Is Observed in Socially Disadvantaged Patients. *Clin Infect Dis* 2020; **70**: 297-303.
32. Yang WL, Kouyos RD, Boni J, et al. Persistence of transmitted HIV-1 drug resistance mutations associated with fitness costs and viral genetic backgrounds. *PLoS Pathog* 2015; **11**: e1004722.
33. Drescher SM, von Wyl V, Yang WL, et al. Treatment-naive individuals are the major source of transmitted HIV-1 drug resistance in men who have sex with men in the Swiss HIV Cohort Study. *Clin Infect Dis* 2014; **58**: 285-94.
34. von Wyl V, Yerly S, Boni J, et al. Incidence of HIV-1 drug resistance among antiretroviral treatment-naive individuals starting modern therapy combinations. *Clin Infect Dis* 2012; **54**: 131-40.

35. Kouyos RD, Rusert P, Kadelka C, et al. Tracing HIV-1 strains that imprint broadly neutralizing antibody responses. *Nature* 2018; **561**: 406-10.
36. Kadelka C, Liechti T, Ebner H, et al. Distinct, IgG1-driven antibody response landscapes demarcate individuals with broadly HIV-1 neutralizing activity. *J Exp Med* 2018; **215**: 1589-608.
37. Marzel A, Kouyos RD, Reinschmidt S, et al. Dietary Patterns and Physical Activity Correlate With Total Cholesterol Independently of Lipid-Lowering Drugs and Antiretroviral Therapy in Aging People Living With Human Immunodeficiency Virus. *Open Forum Infect Dis* 2018; **5**: ofy067.
38. Beguelin C, Suter A, Bernasconi E, et al. Trends in HCV treatment uptake, efficacy and impact on liver fibrosis in the Swiss HIV Cohort Study. *Liver Int* 2018; **38**: 424-31.
39. Aebi-Popp K, Wandeler G, Salazar-Vizcaya L, et al. Rapid decline of anti-hepatitis C virus (HCV) antibodies following early treatment of incident HCV infections in HIV-infected men who have sex with men. *HIV Med* 2018; **19**: 420-5.
40. Salazar-Vizcaya L, Wandeler G, Fehr J, et al. Impact of Direct-Acting Antivirals on the Burden of HCV Infection Among Persons Who Inject Drugs and Men Who Have Sex With Men in the Swiss HIV Cohort Study. *Open Forum Infect Dis* 2018; **5**: ofy154.
41. Braun DL, Hampel B, Martin E, et al. High Number of Potential Transmitters Revealed in a Population-based Systematic Hepatitis C Virus RNA Screening Among Human Immunodeficiency Virus-infected Men Who Have Sex With Men. *Clin Infect Dis* 2019; **68**: 561-8.
42. Braun DL, Hampel B, Kouyos R, et al. High Cure Rates With Grazoprevir-Elbasvir With or Without Ribavirin Guided by Genotypic Resistance Testing Among Human

Immunodeficiency Virus/Hepatitis C Virus-coinfected Men Who Have Sex With Men. *Clin Infect Dis* 2019; **68**: 569-76.

43. Kovari H, Rauch A, Kouyos R, et al. Hepatitis C Infection and the Risk of Non-Liver-Related Morbidity and Mortality in HIV-Infected Persons in the Swiss HIV Cohort Study. *Clin Infect Dis* 2017; **64**: 490-7.

44. Salazar-Vizcaya L, Kouyos RD, Metzner KJ, et al. Changing Trends in International Versus Domestic HCV Transmission in HIV-Positive Men Who Have Sex With Men: A Perspective for the Direct-Acting Antiviral Scale-Up Era. *J Infect Dis* 2019; **220**: 91-9.

45. Kouyos RD, Rauch A, Boni J, et al. Clustering of HCV coinfections on HIV phylogeny indicates domestic and sexual transmission of HCV. *Int J Epidemiol* 2014; **43**: 887-96.

46. Wandeler G, Gsponer T, Bihl F, et al. Hepatitis B virus infection is associated with impaired immunological recovery during antiretroviral therapy in the Swiss HIV cohort study. *J Infect Dis* 2013; **208**: 1454-8.

47. Beguelin C, Moradpour D, Sahli R, et al. Hepatitis delta-associated mortality in HIV/HBV-coinfected patients. *J Hepatol* 2017; **66**: 297-303.

48. Regoes RR, McLaren PJ, Battegay M, et al. Disentangling human tolerance and resistance against HIV. *PLoS Biol* 2014; **12**: e1001951.

49. Perkins MR, Bartha I, Timmer JK, et al. The Interplay Between Host Genetic Variation, Viral Replication, and Microbial Translocation in Untreated HIV-Infected Individuals. *J Infect Dis* 2015; **212**: 578-84.

50. Guidi M, Foletti G, McLaren P, et al. Vitamin D time profile based on the contribution of non-genetic and genetic factors in HIV-infected individuals of European ancestry. *Antivir Ther* 2015; **20**: 261-9.

51. Barcelo C, Guidi M, Thorball CW, et al. Impact of Genetic and Nongenetic Factors on Body Mass Index and Waist-Hip Ratio Change in HIV-Infected Individuals Initiating Antiretroviral Therapy. *Open Forum Infect Dis* 2020; **7**: ofz464.
52. Barcelo C, Aouri M, Courlet P, et al. Population pharmacokinetics of dolutegravir: influence of drug-drug interactions in a real-life setting. *J Antimicrob Chemother* 2019; **74**: 2690-7.
53. Courlet P, Livio F, Guidi M, et al. Polypharmacy, Drug-Drug Interactions, and Inappropriate Drugs: New Challenges in the Aging Population With HIV. *Open Forum Infect Dis* 2019; **6**: ofz531.
54. Courlet P, Livio F, Alves Saldanha S, et al. Real-life management of drug-drug interactions between antiretrovirals and statins. *J Antimicrob Chemother* 2020.
55. Oberle CS, Joos B, Rusert P, et al. Tracing HIV-1 transmission: envelope traits of HIV-1 transmitter and recipient pairs. *Retrovirology* 2016; **13**: 62.
56. Pillai SK, Abdel-Mohsen M, Guatelli J, et al. Role of retroviral restriction factors in the interferon-alpha-mediated suppression of HIV-1 in vivo. *Proc Natl Acad Sci U S A* 2012; **109**: 3035-40.
57. Bachmann N, von Siebenthal C, Vongrad V, et al. Determinants of HIV-1 reservoir size and long-term dynamics during suppressive ART. *Nat Commun* 2019; **10**: 3193.
58. Strouvelle VP, Braun DL, Vongrad V, et al. No Effect of Pegylated Interferon-alpha on Total HIV-1 DNA Load in HIV-1/HCV Coinfected Patients. *J Infect Dis* 2018; **217**: 1883-8.
59. Leon-Reyes S, Schafer J, Fruh M, et al. Cost Estimates for Human Immunodeficiency Virus (HIV) Care and Patient Characteristics for Health Resource Use From Linkage of Claims Data With the Swiss HIV Cohort Study. *Clin Infect Dis* 2019; **68**: 827-33.

60. Aebi-Popp K, Mercanti V, Voide C, et al. Neglect of attention to reproductive health in women with HIV infection: contraceptive use and unintended pregnancies in the Swiss HIV Cohort Study. *HIV Med* 2018; **19**: 339-46.
61. Aebi-Popp K, Kouyos R, Bertisch B, et al. Postnatal retention in HIV care: insight from the Swiss HIV Cohort Study over a 15-year observational period. *HIV Med* 2016; **17**: 280-8.
62. Yang WL, Kouyos R, Scherrer AU, et al. Assessing the Paradox Between Transmitted and Acquired HIV Type 1 Drug Resistance Mutations in the Swiss HIV Cohort Study From 1998 to 2012. *J Infect Dis* 2015; **212**: 28-38.
63. Staehelin C, Egloff N, Rickenbach M, Kopp C, Furrer H, Swiss HIVCS. Migrants from sub-Saharan Africa in the Swiss HIV Cohort Study: a single center study of epidemiologic migration-specific and clinical features. *AIDS Patient Care STDS* 2004; **18**: 665-75.
64. Ruffieux Y, Lemsalu L, Aebi-Popp K, et al. Mortality from suicide among people living with HIV and the general Swiss population: 1988-2017. *J Int AIDS Soc* 2019; **22**: e25339.