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Cohort Profile Update

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Cohort Profile Update: The Swiss HIV Cohort Study (SHCS)

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Key Features

- The Swiss HIV cohort study (SHCS), a national, multicentre cohort, has been continuously enrolling HIV-infected adults since 1988 to monitor the HIV epidemic in Switzerland.
- After 30 years of follow-up, changing characteristics and behaviour 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, 9816 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: comedication and comorbidities, 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].

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, multicentre, clinic-based, prospective, longitudinal, observational study including HIV-infected adults in Switzerland. The study design provides continuous enrolment and semi-annual study visits, where sociodemographic and clinical and laboratory information is collected. Patients are recruited by all university hospitals in Switzerland, by numerous regional hospitals and by 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 past 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, comedications and comorbidities, 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 9816 patients were still under follow-up .

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

What is the reason for the new focus?

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

In the past 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 past 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 ageing 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 comorbidities and number of comedications (Figure 1).

In recent years, the SHCS also observed behavioural 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

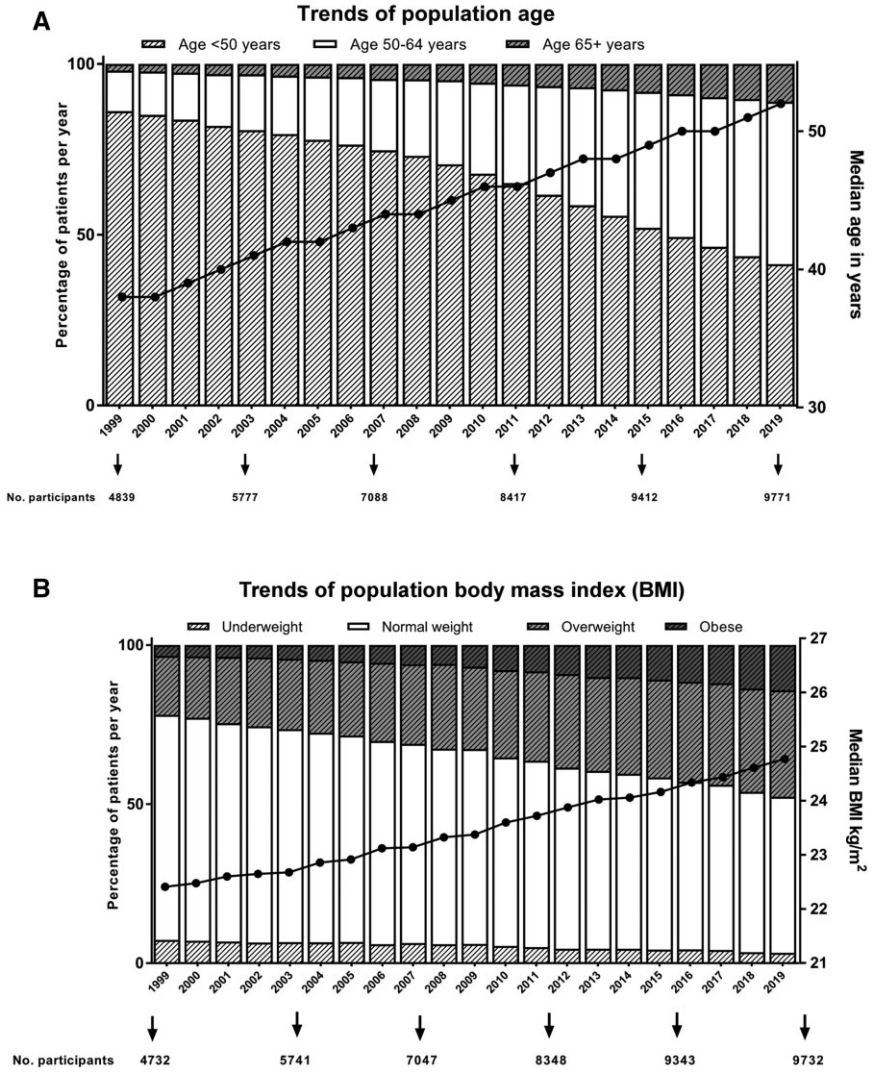

Figure 1 Age (A) and weight (B) distribution in the Swiss HIV Cohort Study (SHCS) between 1999 and 2019.

and chlamydia.[6–9] The availability of HIV pre-exposure prophylaxis among non-infected individuals might lead to additional behavioural 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 ageing 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 are evolving rapidly. The SHCS aims to study these changes in detail.

iv. Broadly neutralizing antibodies (bNabs), 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 (five university hospitals, two large cantonal hospitals), its affiliated 14 regional hospitals or with its affiliated 48 private physicians (Table 1). Overall, 5697 (27.3%) women were included, including 2726 under follow-up in 2019.

Homosexual contact was reported as the presumed mode of HIV transmission in 8169 (39.2%) of all included patients (46.8% of patients seen in 2019) and 6881 (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; in all patients the percentage was 23.2% ($n = 4\,834$).

Overall 15 076 (72.3%) patients have received combined antiretroviral treatment (cART, three or more drugs from at least two drug classes) starting at a median [interquartile range (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 a minimum in 2019 (<1 month). By the end of 2019, 9462 (96.8%) of patients seen have been on treatment, and in 9501 (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 dates) among patients registered in the SHCS. Between 2009 and 2018, the Swiss Federal Office for Public Health (FOPH) reported 5476 new infections, whereas the SHCS registered in this time period 4868 (89%).[13] In 2019, the SHCS included 59% of the estimated number of HIV-infected people in Switzerland.

The numbers of new registrations have been slightly decreasing since 2010 (Figure 2A), which is in line with the numbers published by the FOPH.[13] A median number of 576 patients is recruited per year. The number of actively followed patients is steadily increasing (Figure 2B).

Since the start of the cohort, the characteristics of the participants have changed (Table 2). 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 body mass index (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: numbers of patients who most likely acquired the HIV infection through homosexual contacts increased from 3216 (40.9%) in 2009 to 4572 (46.8%) in 2019. At the same time, the number of active patients who named intravenous drug use (IDU) as most likely source of infection decreased from 1248 (15.9%) in 2009 to 966 (9.9%) in 2019. The percentage of patients under follow-up who have experienced a Centers for Disease Control and Prevention (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 2C). 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 5166 (24.8%) of the patients died and 5863 (28.1%) patients were lost to follow-up. The main reasons for loss to follow-up were that patients did not respond to several invitations (39.8% of patients lost 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.

Table 1 Demographic and selected baseline characteristics of all Swiss HIV Cohort Study (SHCS) participants in the seven centres (data collection until 31 December 2019)

SHCS	Total	Basel	Bern	Geneva	Lausanne	St Gallen	Ticino	Zurich
Patients ever registered (%)	20 845 (100)	2214 (10.6)	2696 (12.9)	3079 (14.8)	3307 (15.9)	1243 (6.0)	636 (3.1)	7670 (36.8)
Female patients (%)	5697 (27.3)	683 (30.3)	834 (30.3)	915 (29.6)	1081 (32.8)	362 (29.5)	210 (31.0)	1612 (21.3)
Ethnicity: number of patients (%)								
White	14 127 (67.8)	1402 (62.2)	1628 (59.2)	1413 (45.8)	1732 (52.5)	796 (64.9)	519 (76.6)	6637 (87.9)
Black	2274 (10.9)	270 (12.0)	388 (14.1)	500 (16.2)	571 (17.3)	116 (9.5)	13 (1.9)	416 (5.5)
Latin-American	564 (2.7)	51 (2.3)	50 (1.8)	104 (3.4)	85 (2.6)	21 (1.7)	18 (2.7)	564 (2.71)
Asian	595 (2.9)	94 (4.2)	93 (3.38)	58 (1.9)	56 (1.7)	31 (2.5)	9 (1.3)	254 (3.4)
Unknown	3251 (15.6)	434 (19.3)	585 (21.3)	1006 (32.6)	849 (25.7)	262 (21.4)	113 (16.7)	2 (0.0)
Other	34 (0.2)	3 (0.1)	5 (0.2)	6 (0.2)	5 (0.2)	0 (0.0)	6 (0.9)	9 (0.1)
Number of patients under active follow-up								
Total (% of active patients)	9816 (100)	1179 (12.0)	1357 (13.8)	1248 (12.7)	1556 (15.9)	208 (7.6)	330 (3.4)	3501 (35.7)
Female patients (% of active patients)	2726 (27.8)	371 (31.5)	428 (31.5)	417 (33.4)	541 (34.8)	208 (32.3)	98 (29.7)	663 (18.9)
Loss to follow-up								
Total (% of all patients)	11 029 (52.9)	1075 (47.7)	1392 (50.6)	1839 (59.6)	1742 (52.8)	581 (47.4)	348 (51.3)	4052 (53.7)
Died (% of loss to follow-up)	5166 (46.8)	437 (40.7)	663 (47.6)	865 (47.0)	752 (43.2)	346 (59.0)	153 (44.0)	1950 (48.1)
Did not respond to invitation (% of loss to follow-up)	2337 (21.2)	279 (26.0)	243 (17.5)	282 (15.3)	302 (17.3)	70 (12.1)	56 (16.1)	1105 (27.3)
Moved abroad (% of loss to follow-up)	1332 (12.1)	139 (12.9)	135 (9.7)	372 (20.2)	213 (12.2)	70 (12.1)	47 (13.5)	356 (8.8)
Other reason (% of loss to follow-up)	2194 (19.9)	220 (20.5)	351 (25.2)	320 (17.4)	475 (27.3)	95 (16.4)	92 (26.4)	641 (15.8)
Most likely route of infection: number of patients (% of all patients)								
Homosexual contacts	8169 (39.2)	802 (35.6)	867 (31.5)	1147 (37.2)	1085 (32.9)	311 (25.4)	197 (29.1)	3760 (49.8)
Heterosexual contacts	6881 (33.0)	862 (38.2)	1040 (37.8)	1126 (36.5)	1374 (41.7)	476 (38.8)	249 (36.7)	1754 (23.2)
Intravenous drug use	4834 (23.2)	443 (19.7)	680 (24.7)	643 (20.8)	693 (21.0)	358 (29.2)	208 (30.7)	1818 (24.1)
Contaminated blood	205 (1.0)	14 (0.6)	26 (1.0)	51 (1.7)	34 (1.0)	15 (1.2)	5 (0.7)	60 (0.8)
Perinatally contaminated	118 (0.6)	17 (0.8)	16 (0.6)	26 (0.8)	26 (0 .8)	9 (0.7)	2 (0.3)	22 (0.3)
Unknown/other	629 (3.02)	116 (5.2)	120 (4.4)	94 (3.1)	86 (2.6)	57 (4.7)	17 (2.5)	139 (1.8)
Age at HIV diagnosis (year)								
Mean (median)	33.9 (32.0)	34.5 (32.0)	34.0 (31.0)	33.4 (31.0)	33.4 (31.0)	33.9 (31.0)	33.5 (30.0)	34.1 (32.0)
IQR	[26-40]	[26-41]	[26-40]	[26-39]	[26-39]	[25-40]	[25-39]	[26-40]
Treatment: number of patients (% of all patients)	17 677 (84.8)	1972 (87.5)	2348 (85.4)	2549 (82.6)	2779 (84.3)	1048 (85.5)	572 (84.4)	6409 (84.9)
Naïve	3168 (15.2)	282 (12.5)	401 (14.6)	538 (17.4)	519 (15.7)	178 (14.5)	106 (15.6)	1144 (15.1)
ART	2601 (12.5)	226 (10.0)	269 (9.8)	481 (15.6)	464 (14.1)	127 (10.4)	41 (6.1)	993 (13.2)
cART	15 076 (72.3)	1746 (77.5)	2079 (75.6)	2068 (67.0)	2315 (70.2)	921 (75.1)	531 (78.3)	5416 (71.7)

(Continued)

Table 1 Continued

SHCS	Total	Basel	Bern	Geneva	Lausanne	St Gallen	Ticino	Zurich
Age when cART started: years								
Mean (median)	38.7 (37.0)	39.4 (38.0)	38.8 (37.0)	38.5 (37.0)	38.1 (37.0)	39.0 (38.0)	39.0 (37.0)	38.6 (37.0)
IQR	[31.0-45.0]	[32.0-46.0]	[31.0-45.0]	[31.0-44.0]	[31.0-44.0]	[31.0-45.0]	[32.0-44.0]	[31.0-44.0]
Time between HIV diagnosis and cART: years								
Mean (median)	4.1 (1.8)	4.3 (1.5)	4.0 (1.7)	4.9 (2.9)	4.1 (1.6)	3.8 (1.3)	4.7 (2.5)	3.9 (1.7)
IQR	[0.1-6.9]	[0.1-7.1]	[0.1-6.3]	[0.2-8.4]	[0.1-6.7]	[0.1-6.0]	[0.2-8.7]	[0.1-6.5]
CD4 cell count at start of ART (cell count/μl)								
Mean (median)	269.3 (234.0)	290.6 (251.0)	258.0 (219.0)	275.3 (236.0)	291.9 (258.0)	273.0 (230.0)	293.1 (270.0)	252.8 (220.0)
IQR	[109.0-367.0]	[117.0-397.0]	[101.0-347.0]	[117.0-375.0]	[127.0-393.0]	[100.0-380.0]	[130.0-396.0]	[100.0-350.0]
HIV-related diseases (% of all patients)								
Patients with B-events	4221 (20.3)	544 (24.1)	575 (20.9)	543 (17.6)	694 (21.0)	496 (40.5)	179 (26.4)	1420 (18.8)
Patients with C-events	7086 (34.0)	775 (34.4)	902 (32.8)	1150 (37.3)	1074 (32.6)	266 (21.7)	214 (31.6)	2507 (33.2)
Type of health care provider at registration (% of all patients)								
Cohort centre	9438 (45.3)	1088 (48.3)	1368 (49.8)	1159 (37.5)	1438 (43.6)	670 (54.7)	345 (50.9)	3370 (44.6)
Other outpatient clinic or hospital	1271 (6.1)	416 (18.5)	387 (14.1)	20 (0.7)	52 (1.6)	93 (7.6)	116 (17.1)	187 (2.5)
Private physician	2779 (13.3)	143 (6.3)	148 (5.4)	513 (16.6)	627 (19.0)	19 (1.6)	19 (2.8)	1310 (17.3)
Unknown/missing	7357 (35.3)	607 (26.9)	846 (30.8)	1395 (45.2)	1181 (35.8)	444 (36.2)	198 (29.2)	2686 (35.6)

Naïve, individuals never treated with antiretroviral therapy (ART); cART, combined antiretroviral treatment; B-event and C-event, HIV disease progression classified as category B and C based on the classification system of the Centers for Disease Control and Prevention (CDC).

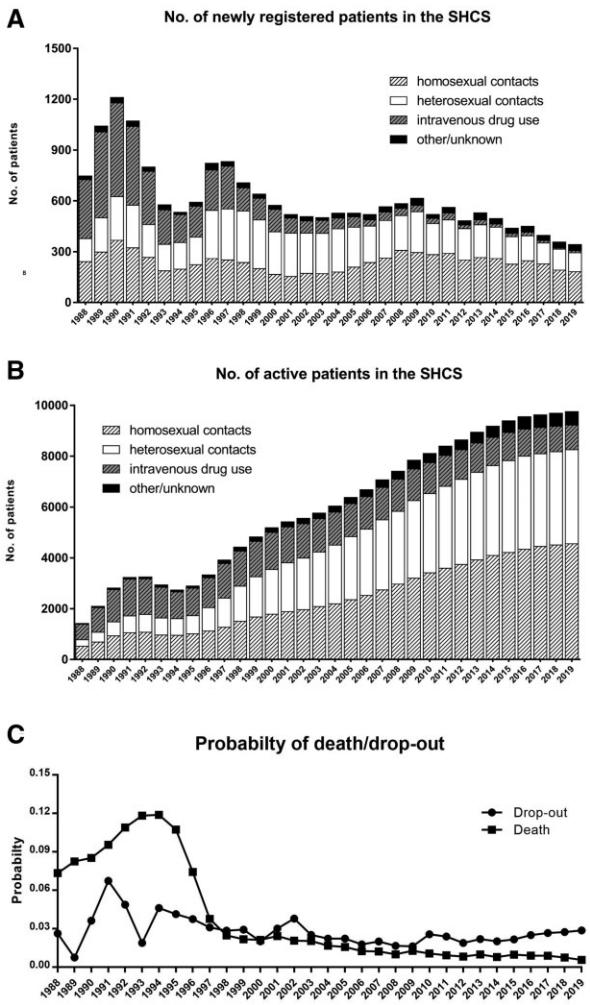

Figure 2 Number of newly registered (A), and number of active patients (B) in Swiss HIV Cohort Study (SHCS) by most likely route of infection, and probability of drop-out and death (C).

Standard questionnaire

The SHCS participants are followed up biannually. The assessment covers demographic variables, questions on health behaviour, hospitalizations, anthropometric data, comorbidities, vaccinations, antiretroviral therapy, comedications and different laboratory measurements. Women are additionally asked to answer a questionnaire about gynaecological examinations and obstetric events.

In 2015, the SHCS introduced a new tool to collect detailed information about medications, antiretroviral therapies as well as comedication. The tool includes an Application Programming Interface (API) to a database with all approved drugs in Switzerland [https://www.hciso lutions.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 latter are defined as infections which are treated at least for 5 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 are available.
ii. Metabolics and Ageing (M+A) and Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO): the M+A project includes storing 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. The Swiss Mother and Child HIV Cohort Study (MoCHiV): 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) have been 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 has given new insights in the following topics:

Table 2 Number of active patients in the Swiss HIV Cohort Study (SHCS) seen in the respective calendar year

	1989	1999	2009	2019
All (%)	2108 (100)	4844 (100)	7860 (100)	9771 (100)
Male	1552 (73.6)	3380 (69.8)	5497 (69.9)	7072 (71.2)
Female	556 (26.4)	1464 (30.2)	2363 (30.1)	2699 (27.6)
Ethnicity (%)				
White	1125 (53.4)	4091 (84.5)	6315 (80.3)	7497 (76.7)
Black	5 (0.2)	359 (7.4)	1022 (13.0)	1434 (14.7)
Latin-American	4 (0.2)	72 (1.5)	204 (2.6)	384 (3.9)
Asian	7 (0.3)	104 (2.2)	297 (3.8)	423 (4.3)
Other	1 (0.1)	14 (0.3)	20 (0.3)	18 (0.2)
Unknown	966 (45.8)	204 (4.2)	2 (0.0)	15 (0.2)
Most likely route of infection: (%)				
Homosexual contacts	703 (33.4)	1685 (34.8)	3216 (40.9)	4572 (46.8)
Heterosexual contacts	385 (18.3)	1590 (32.8)	3054 (38.9)	3702 (37.9)
Intravenous drug use	966 (45.8)	1395 (28.9)	1248 (15.9)	966 (9.9)
Unknown/others	54 (2.6)	174 (3.6)	342 (4.4)	531 (5.4)
Age in years median [IQR]	31 [27-0]36	38 [33-44]	45 [39-51]	52 [43-58]
On ART treatment (%)	283 (13.4)	3596 (74.2)	6559 (83.5)	9462 (96.8)
VL <400 cps/ml (%)	Not available	2762 (57.0)	6538 (83.2)	9501 (97.2)
VL <50 cps/ml (%)	Not available	Not available	6008 (76.4)	9214 (94.3%)
Median CD4 cell count at baseline; CD4 nadir [IQR]	180 [80-305.5]	237 [117-359]	250 [130-365]	276 [151-421.5]
Patients with AIDS (CDC stage C)	361 (24.3)	1148 (24.5)	1838 (23.7)	2045 (21.1)
BMI kg/m^2 median [IQR]	Not available	22.4 [20.5-24.6]	23.4 [21.1-25.9]	24.8 [22.3-27.8]

ART, antiretroviral treatment; VL, HIV-1 RNA viral load; BMI, body mass index.

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 sexually transmitted diseases, behavioural 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. ageing 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, giving new insights into the host and viral genetic influences on HIV pathogenesis[48–51];

viii. pharmacokinetics, model-based simulations and clinical validation of drug-drug interactions contributing important new knowledge for optimized treatment strategies[52–54];

ix. studies about host and viral factors during HIV transmission performed[55,56];

x. characterization of the HIV reservoir among acutely and chronically infected patients, helping to identify potential treatment strategies for HIV cure[57,58];

xi. a pilot study paving the way for health economic assessments and cost-effectiveness analyses[59];

xii. projects on pregnancy and childhood performed, including patients from the Swiss Mother and Child HIV Cohort Study (MoCHiV)[60,61];

xiii. a pilot study comparing machine learning (ML) techniques with standard statistical methods to predict declining kidney function and showing the power of ML when used in high-quality rich datasets such 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 the active participation or 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 dataset 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 and 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 centre easily when moving within Switzerland.

Weaknesses of the study include the lack of a control population of HIV-negatives and a slight under-representation from ethnic minority groups,[63] which may limit generalizability of findings to migrants to some extent. Furthermore, Swiss law does not allow updating 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].

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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.

Conflict of Interest

The institution of H,F, received educational grants form 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 in advisory boards 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 from Janssen-Cilag, MSD, Gilead Sciences, Abbvie and Pfizer and an unrestricted research grant from Gilead Sciences; all reamuneration went to his home institution and not to A.R. 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 and consulting/advisory board membership fees from Gilead Sciences, ViiV, 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 in return 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. G.W. reports support to his home institution for advisory boards and/or travel grants from MSD, Gilead Sciences and

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