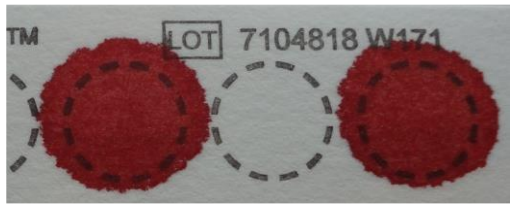
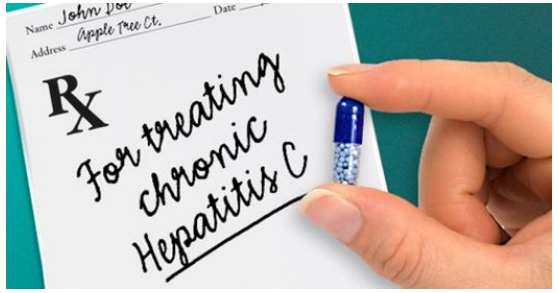




Simplifying testing and treatment

Experiences from Swiss OAT programmes including pharmacies

Andrea Bregenzer

Swiss Hepatitis Symposium, Bern, 27.11.2023

Barriers to diagnosis/treatment

Possible solutions

- **Hard to reach population** (people who use drugs (PWUD) / OAT patients, migrants, prisoners, …)

➢ «Go to where the patients are», «think outside the clinic» Bajis, 2020

- **Lack of awareness** and **knowledge** among patients and health-care providers

➢ Patient and provider **education** Cunningham, 2022

Cunningham, 2022

- **Stigma**, including self-stigma

➢ **On-site** testing + treatment, **opt-out** screening

- **Difficult venous access** after long-term intravenous drug use

➢ Diagnostic tests using **saliva** or **capillary blood** (rapid POCT, DBS, PSC)

- In case of referral to a specialist, PWUD often have difficulties keeping appointments (repeated **no show** → no new appointment → no treatment)

➢ On-site testing + treatment, **telemedicine** (HepCare), **integrated care**, patient navigation or care coordination Cunningham, 2022

- Long **waiting times** for a specialist appointment + long turn-around times for laboratory tests (e.g. 1-2 weeks for HCV-RNA) → «test-and-treat/vaccinate» approach not possible → high risk of loss-to follow-up

➢ On-site testing + treatment, telemedicine (HepCare), integrated care

➢ **Rapid POCTs**, reflex RNA or HCV core antigen testing if HCV-antibody-positive EASL, 2020

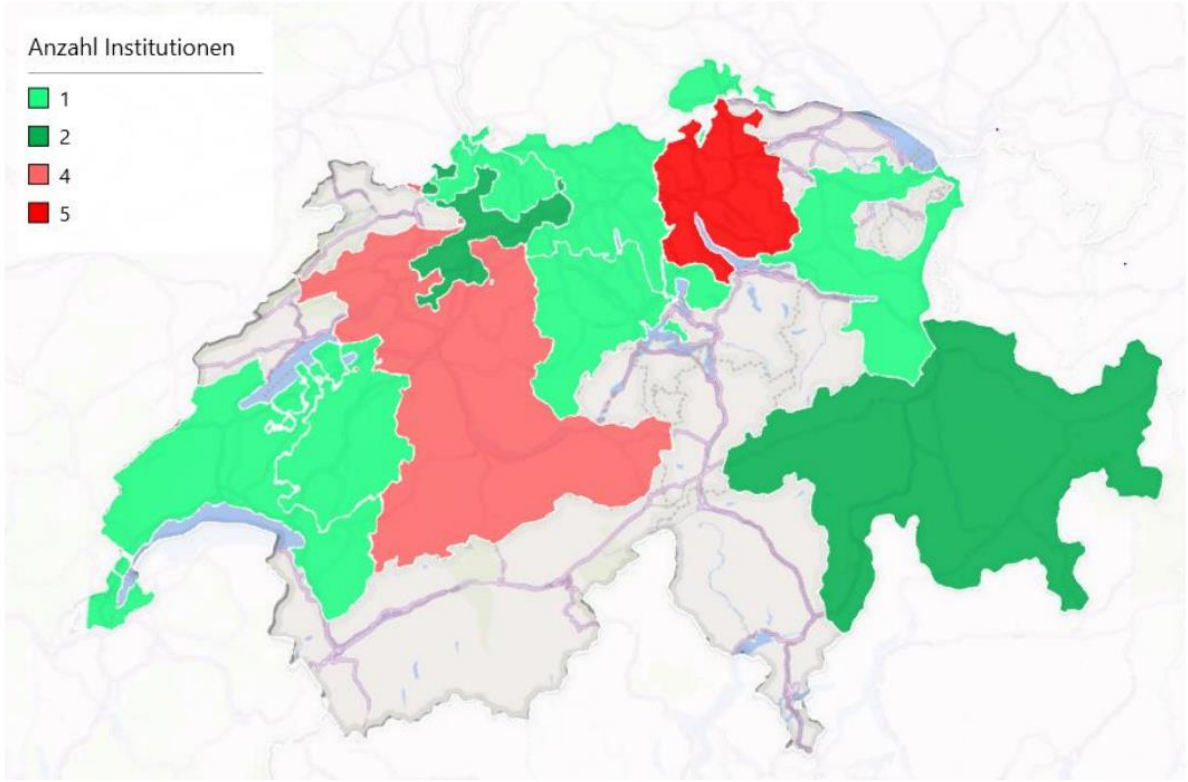
- In case of a positive screening test, another venous blood draw must be performed for RNA/DNA

➢ **Single visit diagnosis** with either capillary rapid POCTs or **reflex testing** (venous blood, DBS, PSC)

Opioid agonist therapy (OAT) in Switzerland (8.7 million inhabitants)

- **22,000-27,000 persons with opioid dependency** in Switzerland (BAG) → **~80%** in an **OAT program**:
  - 16,000 in a methadone, buprenorphine, slow release morphine or levomethadone program (canton)
  - 1,700 in a heroin program (FOPH = Federal Office of Public Health)

- Prescription of **heroin** (diacetylmorphine) restricted to 23 institutions in 14 cantons (Annual report 2022):



- In 60%, **OAT** is **prescribed** by the GP (BAG)

- **OAT provider** :

CH (n=15,800, 2022) (www.substitution.ch)**:**
- Pharmacy: 51% (8,090)
- Treating physician: 14% (2,204)
- Institution: 33% (5,285)

AG (n=734, 2022) (www.substitution.ch)**:**
- Pharmacy: 79% (579)
- Treating physician: 1% (9)
- Institution: 20% (145)

- **Frequency of appearance:** 54% 1x/wk, 21% 2-3x/wk, 7% 4-5x/wk, 17% every or nearly every day (Annual report 2021)

- Proportion of OAT patients with **ongoing intravenous drug use**: ~27% (Bruggmann, 2017)

2013-2015 Start of the Argovian OAT cohort / SAMMSU cohort

Bregenzer, 2017

Setting:

- **Since 2011**, **telaprevir** and **boceprevir** (1st generation DAAs, which had to be given with Peg-IFN and RBV) available **for genotype 1** (SASL, 2012); less toxic **IFN-free DAA treatments on the horizon**
- *Decentralised setting*: 631 OAT patients cared for by 161 OAT prescribers (Ø 4 OAT patients / physician) → **low case-load** (<10 HCV patients) → low knowledge (Wade, 2017) → for GPs, HCV is an «orphan disease» compared to upper respiratory tract infections + hypertension («daily business») (Finley, 2018)

Tools used:

- Free **HIV/HCV rapid POCTs** with **capillary blood** (OAT prescriber) and non-invasive liver fibrosis assessment with mobile **Fibroscan®** (study team)

Results:

- Proportion **never HIV-screened**↓: **26%** (53/205) → **2%** (5/205)
- No new HIV diagnoses (last first HIV diagnosis 2008)
- Proportion **never HCV-screened**↓: **24%** (49/205) → **2%** (4/205)
- **14 new HCV diagnoses**, **10 false-negative results** (all HCV-RNA negative)
- Proportion of chronic hepatitis C patients **lacking liver fibrosis assessment**↓: **52%** (32/61) → **2%** (1/65)

Persisting gaps: **19%** (18/95) of the **HCV-antibody-positive patients not HCV-RNA-tested**; **54%** (33/61) of the patients developing **chronic HCV infection never treated**

2018-2021 HCV elimination in a Swiss OAT program Bregenzer, 2022

Setting:

• **Since 2017**, **pangenotypic DAAs** were **reimbursed** in Switzerland **irrespective** of liver **fibrosis stage**, but they **had to be prescribed by** an infectious disease specialist, a gastroenterologist/hepatologist or an addiction specialist with experience in HCV treatment

• *Centralised setting*: heroin program of the canton Aargau (Brugg)

Tools used:

• **Infectious disease specialist** + **study nurse** → **4-weekly visits** offering HIV/HCV antibody rapid testing (20 min) and rapid POC HCV RNA quantification (**GeneXpert®**, 60 min) from capillary blood, non-invasive liver fibrosis assessment (Fibroscan®, 5–10 min) and **HCV treatment prescription on-site**

Results:

• Proportion **ever HCV-ab-tested**↑: **83%** (106/128) → **93%** (120/129)

• Proportion of HCV-ab-positive patients **ever HCV-RNA-tested**↑: **89%** (47/53) → **98%** (56/57)

• Proportion of HCV-ab-neg. patients with a **recent HCV-ab-test** (≤1y ago)↑: **28%** (15/53) → **87%** (55/63)

• Prop. of HCV-ab-pos.-RNA-neg. patients with a **recent HCV-RNA-test**↑: **50%** (15/30) → **92%** (48/52)

• Proportion of chronic hepatitis C patients **ever treated**↑: **60%** (21/35) → **92%** (55/60)

• **HCV-RNA-pos.**, if HCV-ab-pos. and HCV-RNA-tested↓: **38%** (18/47) → **7%** (6/84)

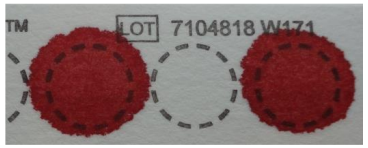
Persisting gaps: **Rapid POC HCV RNA quantification** with capillary blood requires a mobile, but expensive analyzer **restricting** its use **to centralized settings** (Bregenzer, 2019).

2023 HCV elimination program in pharmacies (canton AG)

Setting: *Decentralised setting*

- **FOPH guidelines 2019**: HIV/HCV/HAV/HBV screening of all PWUDs; HCV treatment, if CHC; yearly HIV/HCV-ab-/HCV-RNA screening, if negative; HAV/HBV vaccination, if not immune
- **Since 2022, no DAA prescriber restriction** anymore + DAAs reimbursed for **inpatients**
- **HCV RNA quantification from capillary DBS** with the **Xpert® HCV Viral Load test** was established in the microbiology laboratory of the Cantonal Hospital Aarau (Bregenzer, 2021)
- Cantonal physician: **HAV/HBV vaccination in pharmacies**, if **individual prescription**

Tools used:



- Pharmacists offer to their OAT patients: **capillary HIV/HCV** and **HAV antibody rapid testing, HCV RNA** quantification from **capillary DBS** as well as **HCV treatment** + **HAV/HBV vaccination on-site**.

Preliminary results (First pharmacy (44 OAT patients) started in 10/2023.)**:**

- **9** patients with **adequate HCV management** (either HCV-ab-neg. + last HCV-ab-test ≤1y ago or HCV-ab-pos.-RNA-neg. + last HCV-RNA-test ≤1y ago); among them a couple only recently treated for HCV in close collaboration with the pharmacy due to repeated no-show at the infectious diseases outpatient clinic
- **5** patients **already** left the pharmacy (one death)
- **30 remaining** patients → **19 approached** so far → **13 (68%) agreed to be tested**: 13 HIV-ab-tests, 10 HCV-ab-tests, 3 HCV-RNA-tests in DBS → so far no positive results; 12 HAV-ab-tests (2 positive)

Preliminary conclusion: Rapid POCTs with capillary blood + DBS-sampling feasible in Swiss pharmacies

Summary 1: Solved problems

(Lee, 2011; Smookler, 2021; Muñoz-Chimeno, 2023)

- **HCV antibody testing** *(yearly screening)***:** rapid POCT with saliva or capillary blood (5-20 min)
- **HCV RNA testing** *(yearly screening)***:** rapid POCT (GeneXpert®) (60 min) or DBS (GeneXpert®)
- **Early chronic HCV infection:** HCV RNA decrease <2 log U/ml within 4 weeks (Martinello, 2018)
- **Genotyping:** dispensible with the use of pangenotypic DAAs (EASL, 2020)
- **DAA reimbursement:** since 2017, DAAs reimbursed in Switzerland without liver fibrosis restriction; since 2022, no prescriber restriction and DAAs separately reimbursed for inpatients
- **Liver fibrosis staging:** transient elastography (Fibroscan®) or APRI-score instead of liver biopsy
- **Treatment options** (no or compensated cirrhosis)**:** 1) Sofosbuvir/Velpatasvir (Epclusa®) (once daily 1 tablet for 12 weeks) or 2) Glecaprevir/Pibrentasvir (Maviret®) (once daily 3 tablets for 8 weeks, with food)
- **Monitoring on treatment:** HCV RNA at baseline, week 2-4 (adherence?, optional), week 8 or 12 (EOT, optional), 12 weeks after the end of treatment (SVR12); SVR4 as a proxy for SVR12 (Yoshida, 2015)
- **Adherence:** improved due to better tolerable all-oral treatments and shorter treatment duration; pangenotypic DAA treatments more forgiving than initially thought (Cunningham, 2020)
- **Treatment success**: >95% irrespective of genotype, HIV co-infection, cirrhosis and prior treatment failure with pegylated inferferon and ribavirin; low reinfection rate (<2/100 PY)

Summary 2: Persistent problems and unmet needs (1/2)

- **Hepatitis rapid tests**, **HCV core antigen** and **HDV RNA** currently **not reimbursed** in Switzerland
- **Reflex testing** for **HCV RNA** (or **HCV core antigen**) currently **not established** in Switzerland
- **DBS- or PSC-testing** currently **not established** in Switzerland on the **national level** (2 labs interested)

… although the EASL guidelines on hepatitis C 2020 recommend: 1) rapid point-of-care tests with fingerstick whole blood or crevicular fluid (saliva) for facilitating HCV antibody screening, 2) whole blood sampled on DBSs as an alternative to serum or plasma obtained by venipuncture for HCV antibody screening and RNA testing, 3) reflex testing for HCV RNA or HCV core antigen in patients found to be HCV antibody positive and 4) HCV core antigen as an alternative to HCV RNA to document treatment success or diagnose reinfection EASL, 2020.

- **Risk-based screening** is **not fully implemented** (e.g. not all patients with intoxication or injection abscesses receive HIV/HCV testing)
- Although less stigmatizing, **opt-out screening** (e.g. emergency department, psychiatry) **not** established
- **No HCV registry** in Switzerland and no possibility to document the HIV/HCV/HAV/HBV-status of OAT patients within the platform www.substitution-online.ch (helpful for the recommended yearly screening)
- Although, since 2022, Swiss **GPs and psychiatrists** are allowed to prescribe DAAs themselves, they **continue referring** their patients **to a specialist** and rarely use the telemedical option HepCare

Summary 2: Persistent problems and unmet needs (2/2)

• **Since 2020**, combined HAV/HBV vaccination with **Twinrix®** is **not reimbursed** in Switzerland anymore → one has to apply for cost approval at the health insurance (2-4 weeks) or vaccinate separately against hepatitis A + B (more expensive + more injections)

(BAG Bulletin 16/2021)

• **HBV vaccination in Switzerland**: babies only since 2019, 11-15 year-old adolescents since 1998 → people **born before 1983** (currently ≥40 years old) **not systematically vaccinated** and thus not immune against HBV unless naturally infected (anti-HBs and anti-HBc positive)

• So far **no reliable rapid POCTs for anti-HBs and anti-HBc** → desirable for a «test-and-vaccinate» approach; however, they are in development (https://www.magia-diagnostics.com/diagnostics/)

• **Pharmacists** currently **not reimbursed** for performing **rapid POCTs** concerning hepatitis and HIV, for **sampling** fingerstick whole blood on **DBSs or PSCs** and for **vaccinating against hepatitis A/B**

• **Cantonal differences** regarding the **vaccinations pharmacists** are **allowed to perform** (https://pharmasuisse.org/system/files/media/documents/2023-08/Erlaubte-Impfungen-in-der-Apotheke-nach-Kantonen-Stand-25-07-2023.pdf)

JVA Lenzburg