

Hepatitis C antibody test frequencies and positive rates in Switzerland from 2007 to 2017: a retrospective longitudinal study

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Summary

BACKGROUND AND AIM S: The prevalence of chronic hepatitis C in Switzerland is currently estimated at approximately 32,000 affected individuals (0.37% of the permanent resident population). An estimated 40% of affected individuals in Switzerland is undiagnosed. The Swiss Federal Office of Public Health requires laboratories to report all positive hepatitis C virus (HCV) test results. Approximately 900 newly diagnosed cases are reported annually. The number of HCV tests performed, however, is not collected by the Federal Office of Public Health and positive rates are therefore unknown. The aim of this study was to describe the longitudinal course of the numbers of hepatitis C antibody tests and of positive rates in Switzerland for the years 2007 to 2017.

METHODS: Twenty laboratories were asked to provide the number of HCV antibody tests performed and the number of positive antibody tests per year. Using data from the Federal Office of Public Health reporting system for the years 2012 to 2017, we calculated a factor to correct our values for multiple tests of the same person.

RESULTS: The annual number of HCV antibody tests performed tripled linearly from 2007 to 2017 (from 42,105 to 121,266) while the number of positive HCV antibody test results increased by only 75% over the same period (from 1360 to 2379). The HCV antibody test positive rate steadily decreased from 3.2% in 2007 to 2.0% in 2017. After correction for multiple tests per person, the person-level HCV antibody tested positive rate decreased from 2.2% to 1.7% from 2012 to 2017.

CONCLUSION: In the Swiss laboratories considered, more HCV antibody tests were performed each year in the period (2007–2017) before and during the approval of the new hepatitis C drugs. At the same time, the HCV antibody positive rates decreased, both on a per-test as well as a per-person level. This study is the first to describe the evolution of tests performed and of positive rates for HCV antibody in Switzerland at the national level over several years. In order to more accurately guide future measures to achieve the goal of eliminating hepatitis C by 2030, we recommend annual collection and publication of positive

rates by health authorities, along with mandatory reporting of numbers of tests and people treated.

Introduction

Worldwide, 58 million people are living with hepatitis C. The World Health Organization estimated that in 2019 approximately 290,000 people died from hepatitis C [1]. The prevalence of chronic hepatitis C virus (HCV) infection in Switzerland is estimated at approximately 32,000 (0.37%) affected individuals [2]. An estimated 40% of those affected in Switzerland are undiagnosed [2]. The estimates are based on subpopulation studies and epidemiological modelling, as well as on data from the Federal Office of Public Health reporting system [3]. It must be emphasised though that no systematic prevalence studies in the general population are available for Switzerland.

The Federal Office of Public Health reporting system requires laboratories to report all positive HCV test results: an anti-HCV antibody reaction confirmed by another test – usually an immunoblot test, HCV core antigen detection or HCV ribonucleic acid (RNA) detection. There are even fewer reliable data on incidence than on prevalence in Switzerland. The incidence rate in 2016 was estimated in one study to be 32–39 cases per 100,000 inhabitants [4]. According to the Federal Office of Public Health, the incidence of acute hepatitis C in 2020 was 0.2 per 100,000 inhabitants [5]. At the same time, hepatitis C notification rates have been declining in Switzerland for 20 years [5].

According to information from the Federal Office of Public Health bulletin, approximately 900 newly diagnosed cases are reported annually [6]. This number has been decreasing slightly for several years. The underlying HCV antibody or HCV RNA positive rates are not known. “HCV positive rate” is defined as the proportion of positive HCV tests in either the total number of tests performed in a defined time period or the corresponding number of tested individuals. Positive rates are most likely to be informative about the effectiveness of the testing strategy. Efficient testing aims to achieve the highest possible positive rates, while a low positive rate indicates that testing is being done broadly [7].

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The epidemiological situation regarding hepatitis C in Switzerland is unclear, as many figures are based on estimates. In order to better classify the existing data, additional parameters such as the number of tests performed and the positive rates may be helpful. Therefore the evolution of testing practices in our country over the last few years is of interest for the assessment of the epidemiological situation. Currently, there are no data for Switzerland for either the number of HCV tests performed annually or positive rates.

The aim of this retrospective study was to determine the number of HCV antibody tests performed and the HCV antibody positive rates at all large medical laboratories in Switzerland and to describe antibody testing practices from 2007 to 2017.

Materials and methods

Upon request, the Federal Office of Public Health provided a list of the 20 medical laboratories with the highest numbers of hepatitis C reports. All 20 laboratories were asked to provide the following information for the years 2007–2017: the number of HCV antibody tests performed per year throughout Switzerland (one laboratory also reported data from Lichtenstein), the number of positive antibody tests per year and the number of positive HCV RNA tests following positive antibody tests. While the numbers of antibody tests performed and positive antibody tests were easily available from most laboratories, none of the contacted laboratories could provide the HCV RNA data associated with the positive antibody tests because data preparation or linkage was perceived as too time-consuming. Therefore, the calculation of the annual HCV test positive rates had to be based solely on the numbers of HCV antibody tests performed and positive HCV antibody tests, as available from the primary data collection.

The laboratories provided aggregated totals of the numbers of performed tests and of positive tests. No patient-related individual data were provided, so anonymisation was not necessary. For reasons of data protection, the names of the laboratories are not disclosed. The project was approved by the Ethics Committee of the Canton of Zurich (Basec No.: Req-2018-00789).

HCV antibody test positive rates

The annual HCV antibody test positive rate was calculated by dividing the total number (over all laboratories) of positive HCV antibody tests per year by the total number of HCV antibody tests performed in the same year.

HCV antibody tested positive rates

For the years 2012 to 2017, the Federal Office of Public Health provided yearly numbers of confirmed HCV antibody tests reported and the yearly numbers corrected for multiple reports for one person. No person-related data were provided by the Federal Office of Public Health. Using the provided data, we corrected the HCV antibody *test* positive rates for multiple testing of the same person as follows: For every year from 2012 to 2017, a correction factor (multiple testing factor) was calculated as the ratio of the number of confirmed positive antibody tests per year and the number of individuals with at least one confirmed

positive antibody test in that same year, or – equivalently – as the average number of confirmed positive antibody tests per patient in a specific year. By dividing the HCV antibody *test* positive rates from our laboratory data by these correction factors, we extrapolated Swiss-wide person-level HCV antibody *tested* positive rates, i.e. average proportions of positively tested individuals per antibody test. Correction for multiple positive tests in different years was neither possible nor sought, given our aim of calculating yearly positive rates. Supplementary table S1 summarises all variables and calculations.

We used non-parametric Mann-Kendall tests to search for monotonic trends in the antibody test numbers and positive rates. The significance threshold was set at $p < 0.05$. The use of modified Mann-Kendall tests accounting for serial correlations resulted in identical decisions with equal or smaller p values, and for the sake of brevity we chose not to report these.

Finally, we explored the between-laboratory variability of the antibody positive rates both graphically and by means of non-robust (relative standard deviation [rsd]) and robust (quartile coefficient of dispersion [qcd]) variability measures and assessed the representativeness of our study sample by estimating the analysed proportion of the total HCV antibody test volume in Switzerland. Full details on between-laboratory variability and the representativeness of our data are provided in the Appendix.

Results

Of the 20 laboratories contacted, 13 provided the annual numbers of HCV antibody tests performed as well as the proportions with positive results, but not all 13 laboratories did so for every year between 2007 and 2017 (supplementary table S2). For the years 2007–2008, only 10 laboratories contributed their data. For the years 2009–2010, 11 laboratories provided their data; for the years 2011–2017, data were available from 13 laboratories, which, as the comparison with nationwide the Federal Office of Public Health data shows, account for an estimated 80% of the total HCV antibody test volume in Switzerland (supplementary methods 2).

The annual number of HCV antibody tests performed between 2011 and 2017 showed a linear increase of about 55% from 78,141 to 121,266 ($p = 0.003$; figure 1). Note that only the figures from 2011 to 2017 cover all 13 laboratories, and thus the figures from previous years are not directly comparable. The absolute number of positive HCV antibody test results showed a slight but significant increase by 14% over the same period, from 2090 tests in 2011 to 2379 tests in 2017 ($p = 0.007$).

The HCV antibody *test* positive rate (i.e. without correction) was 3.2% in 2007 and continuously decreased to 2.0% in 2017 ($p < 0.001$; figure 2). After correcting our laboratory data for multiple testing, the HCV antibody *tested* positive rate (i.e. after correction) decreased from 2.2% in 2012 to 1.7% in 2017 ($p = 0.02$; figure 2).

All data underlying figures 1 and 2 are presented in supplementary table S2.

Discussion

In our study, the annual numbers of HCV antibody tests performed in 13 large Swiss laboratories between 2011 and 2017 showed a linear increase of about 55%, while the number of positive HCV antibody test results over the same time increased by about 14%. The HCV antibody test positive rate decreased by 22% between 2012 and 2017. To our knowledge, these are the first published historical data on national hepatitis C test counts and positive rates.

The reasons for the increase in the number of antibody tests performed per year may be seen in the growing evidence on the disease burden and the gaps in the hepatitis C cascade of care in recent years [8, 9], as well as in the introduction of new hepatitis C drugs in 2014 and the increased awareness of hepatitis C in the preceding years following the breakthrough results from pivotal studies [10, 11]. Another possible cause might be the Swiss Hepatitis Strategy, which was launched in 2014 and has conducted annual awareness campaigns since then [12].

The absolute number of positive HCV antibody test results showed a slight increase. Our results thus show a trend similar to the numbers of positive antibody tests reported to the Federal Office of Public Health, which remained ap-

proximately stable over the same period (supplementary table S2).

In contrast to the number of tests performed, antibody positive rates have been decreasing over time, possibly due to changes in testing strategies over the years. Given the increased attention to hepatitis C, the various potential HCV transmission routes and the Swiss Hepatitis Strategy's goal of eliminating viral hepatitis by 2030, it is conceivable that the focus of HCV testing shifted from utmost efficiency to broader testing. Thus, increasingly frequent antibody testing may have taken place in populations with lower prevalence than among the commonly known HCV high-risk groups, namely intravenous substance users and recipients of blood transfusions before 1990 [13]. Broader testing in such populations would explain a decrease in positive rates.

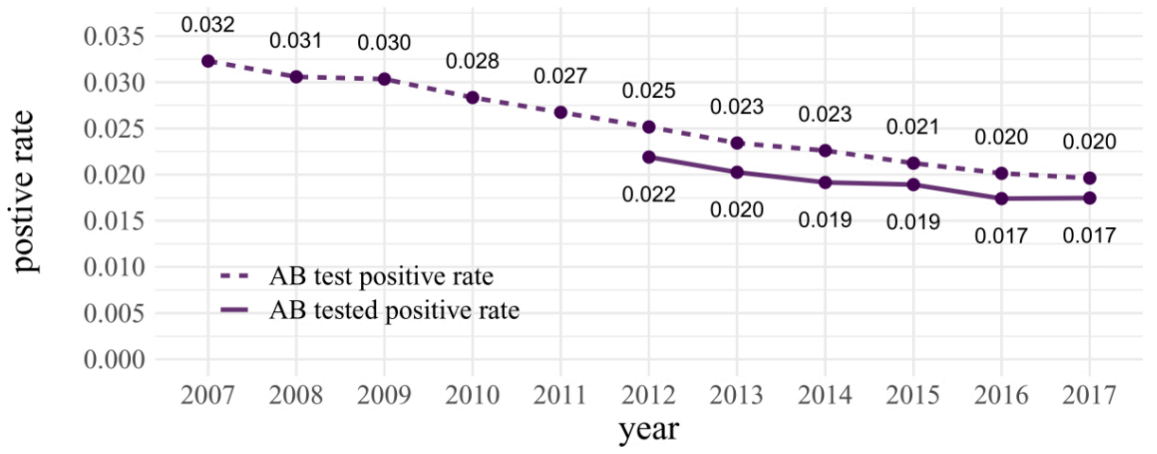
Moreover, the decreasing antibody positive rates could also be due to a decreasing number of untested HCV antibody-positive people in the population. To verify this hypothesis, it would be necessary to know in which populations testing rates have increased.

This retrospective study has several limitations. The 13 laboratories involved in the study are distributed in all parts of the country and all language regions and are

Figure 1: Total numbers of HCV antibody tests and of positive HCV antibody tests in the years 2007–2017 as reported by 13 large laboratories in Switzerland. Years with fewer laboratories are shaded (see main body text). Column heights indicate numbers of tests (left vertical axis) and positive tests (right vertical axis), and area ratios between dark and light columns represent antibody test positive rates. AB: antibody.



Figure 2: HCV antibody test positive rate and the HCV antibody tested positive rate (with correction for multiple testing of individuals). The correction factor was not available before 2012. AB: antibody.



among the 20 (out of a total of 43) laboratories that report most cases to the Federal Office of Public Health. They include the largest providers of medical laboratory tests in the country. Even though the catchment area of many of these laboratories covers the entire country, it may differ from their locations. Although we expect our data to cover about 80% of the Switzerland-wide HCV antibody testing volume, it is not possible to specify exactly how representative our study sample is.

In addition, due to the unfeasible efforts needed for data preparation, none of the respondent laboratories could provide the HCV RNA data. It is therefore not possible to relate our positive antibody tests to actual cases of hepatitis C or to extrapolate from our positive rates to actual hepatitis C prevalence. However, all laboratories involved in the study used 3rd-generation enzyme immune assays (EIA) for HCV antibody detection which, in general, have very high sensitivities and specificities [14]. Lastly, the correction factor for multiple testing of the same individual was determined from the total number of reports to the Federal Office of Public Health, whereas the antibody test positive rates were based on data from selected laboratories only.

One particular strength of this study is that it is the first to comprehensively describe nationwide HCV antibody test frequencies and positive rates over several years, thus providing new information on the epidemiological situation of hepatitis C in Switzerland. We are not aware of any such published data internationally either, so these results may also be of interest to countries with comparable hepatitis C epidemiology.

Conclusion

The yearly number of reported positive HCV antibody tests in the Federal Office of Public Health reporting system, which remained relatively stable during the study period, was accompanied by an increasing number of HCV antibody tests performed over the years and corresponding decreases in both the antibody *test* and *tested* positive rates. To achieve the goal of eliminating hepatitis C in Switzerland, the number of HCV antibody-positive people who have not yet been tested must be significantly reduced. In general, a high *tested* positive rate can be seen as a marker for an efficient testing strategy. This is especially true for infectious diseases with very clearly defined risk populations. However, as the transmission route is unknown in a substantial proportion of hepatitis C patients in Switzerland [13], a broader testing strategy has to be discussed, which inevitably coincides with a reduction of the HCV tested positive rate.

For monitoring of hepatitis C elimination targets by 2030, we recommend annual collection and publication of testing and positive rates along with mandatory reporting and treatment counts by public health authorities. Decreasing numbers of newly reported cases accompanied by rapidly declining positive and treatment rates at stable testing rates

would then indicate successful implementation of the hepatitis C elimination roadmap.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. The employer of PB (Arud) has received project and research grants from Abbvie and Gilead. These two biopharmaceutical companies have hepatitis C related drugs/research. No other potential conflict of interest related to the content of this manuscript was disclosed.

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Appendix

The appendix is available for download as a separate file at <https://doi.org/10.57187/smw.2023.40085>.