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

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Appendix: Online Supplementary Material

Supplementary table 1: Overview of variables and calculations

Variables		
- Data source: Laboratories:		
$a_{l,j}$	Number of AB tests in laboratory *l* and year *j*	
$a^{+}_{l,j}$	Number of positive AB tests in laboratory *l* and year *j*	
- Data source: FOPH (figures for all of Switzerland):		
$a^{+}_{f,j}$	Number of confirmed positive AB tests in year *j*	
$p^{a^{+}}_{f,j}$	Number of individuals with at least one confirmed positive AB test in year *j*	
Derived quantities		
Formula:	Term used in text:	Explanation:
$\frac{\sum_l a^{+}_{l,j}}{\sum_l a_{l,j}}$	AB *test* positive rate in year *j*	Fraction of positive AB tests among all AB tests in year *j*
$c = \frac{a^{+}_{f,j}}{p^{a^{+}}_{f,j}}$	Correction factor for year *j*	Average number of positive AB tests per positively tested individual in year *j*
$\frac{1}{c} \cdot \frac{\sum_l a^{+}_{l,j}}{\sum_l a_{l,j}}$	AB *tested* positive rate in year *j*	Average proportion of positively tested individuals per AB test in year *j*

Abbreviation: AB: antibody

Supplementary table 2: Raw data and calculated AB positive rates by year, with between- and within laboratory variability

Description	Data source	Year											rsd	qcd
		2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	(calculated)	
# AB tests	laboratory D1	6081	6619	6851	8921	10157	11680	13589	14064	14932	17427	17726	36%	30%
	laboratory D2	3778	3993	3884	3862	3832	4057	4784	5296	5441	4618	4755	14%	10%
	laboratory D3	2878	3929	4286	5373	6240	7631	8926	9481	10936	13049	14796	49%	36%
	laboratory D4	6669	7319	7481	8230	8205	8459	8485	9680	8514	9896	9906	13%	7%
	laboratory D5	10449	11121	11186	11663	13125	13656	15138	17109	19059	20664	21442	27%	23%
	laboratory D6					1272	3528	3535	4136	8521	9777	9514	60%	44%
	laboratory D11			1714	1809	2057	2397	2923	3151	3409	3605	3902	29%	25%
	laboratory D12	234	2442	2623	2825	3326	3425	3547	3665	4236	5555	5631	44%	18%
	laboratory D20	982	1108	1358	921	1114	1106	1092	1157	1368	1649	1633	20%	11%
	laboratory F7	6345	6921	11199	12949	13129	11463	11960	10100	10633	11158	12557	21%	8%
	laboratory F10			9892	9760	9822	10101	10168	10506	10847	11912	11808	8%	5%
	laboratory I8	2417	2620	2938	2965	3152	3090	2777	3132	3353	3504	3332	11%	6%
	laboratory I9	2272	2598	2522	2647	2710	2227	3080	3208	3577	4151	4264	23%	14%
total	(calculated)	42105	48670	65934	71925	78141	82820	90004	94685	104826	116965	121266	31%	18%
rsd	(calculated)	74%	63%	67%	69%	73%	67%	68%	67%	64%	65%	66%		
qcd	(calculated)	46%	45%	51%	53%	57%	53%	54%	52%	50%	48%	49%		
# positive AB tests	laboratory D1	172	217	176	195	217	236	260	256	268	305	313	20%	12%
	laboratory D2	170	149	142	130	113	134	135	139	108	128	138	12%	4%
	laboratory D3	117	129	168	186	183	213	256	233	217	265	278	26%	16%
	laboratory D4	436	381	336	366	331	290	293	315	303	331	308	13%	7%
	laboratory D5	98	57	60	43	46	44	44	47	55	50	58	29%	12%
	laboratory D6					45	94	102	135	215	226	242	51%	38%
	laboratory D11			153	116	168	211	183	182	175	145	127	18%	11%
	laboratory D12	0	207	214	277	233	197	152	180	202	220	194	37%	7%
	laboratory D20	44	40	33	30	31	34	45	43	54	62	59	26%	19%
	laboratory F7	67	65	125	183	154	139	125	104	106	113	99	30%	13%
	laboratory F10			311	258	294	267	273	253	299	282	300	7%	6%
	laboratory I8	117	94	134	106	130	93	94	107	77	80	82	19%	12%
	laboratory I9	139	150	149	149	145	132	146	146	147	148	181	8%	1%
total	(calculated)	1360	1489	2001	2039	2090	2084	2108	2140	2226	2355	2379	16%	4%
rsd	(calculated)	87%	68%	53%	57%	58%	51%	52%	50%	51%	53%	53%		
qcd	(calculated)	37%	45%	17%	30%	32%	39%	43%	37%	34%	40%	47%		

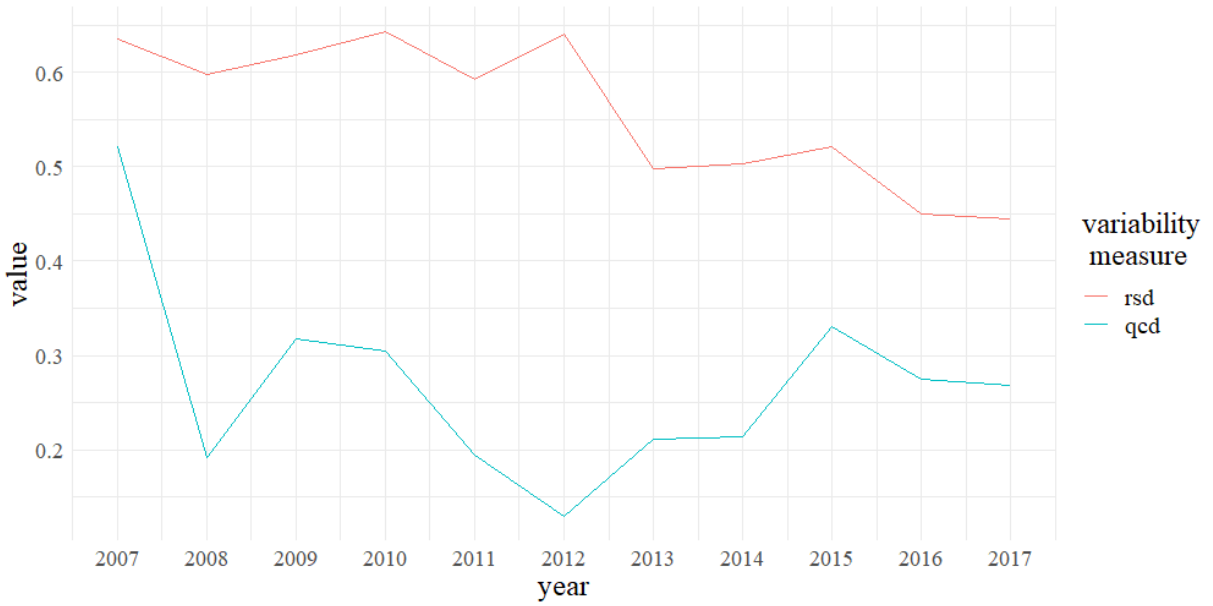
AB *test* positive rate	(calculated D1)	0.028	0.033	0.026	0.022	0.021	0.020	0.019	0.018	0.018	0.018	0.018	23%	14%
	(calculated D2)	0.045	0.037	0.037	0.034	0.029	0.033	0.028	0.026	0.020	0.028	0.029	21%	11%
	(calculated D3)	0.041	0.033	0.039	0.035	0.029	0.028	0.029	0.025	0.020	0.020	0.019	26%	20%
	(calculated D4)	0.065	0.052	0.045	0.044	0.040	0.034	0.035	0.033	0.036	0.033	0.031	26%	14%
	(calculated D5)	0.009	0.005	0.005	0.004	0.004	0.003	0.003	0.003	0.003	0.002	0.003	51%	22%
	(calculated D6)					0.035	0.027	0.029	0.033	0.025	0.023	0.025	16%	10%
	(calculated D11)			0.089	0.064	0.082	0.088	0.063	0.058	0.051	0.040	0.033	32%	23%
	(calculated D12)	0.000	0.085	0.082	0.098	0.070	0.058	0.043	0.049	0.048	0.040	0.034	50%	30%
	(calculated D20)	0.045	0.036	0.024	0.033	0.028	0.031	0.041	0.037	0.039	0.038	0.036	17%	10%
	(calculated F7)	0.011	0.009	0.011	0.014	0.012	0.012	0.010	0.010	0.010	0.010	0.008	15%	7%
	(calculated F10)			0.031	0.026	0.030	0.026	0.027	0.024	0.028	0.024	0.025	9%	4%
	(calculated I8)	0.048	0.036	0.046	0.036	0.041	0.030	0.034	0.034	0.023	0.023	0.025	25%	17%
	(calculated I9)	0.061	0.058	0.059	0.056	0.054	0.059	0.047	0.046	0.041	0.036	0.042	17%	14%
overall	(calculated)	0.032	0.031	0.030	0.028	0.027	0.025	0.023	0.023	0.021	0.020	0.020	18%	14%
rsd	(calculated)	63%	60%	62%	64%	59%	64%	50%	50%	52%	45%	44%		
qcd	(calculated)	52%	19%	32%	30%	19%	13%	21%	21%	33%	27%	27%		
# positive (conf.) AB tests	FOPH						2065	1959	2057	1959	2129	2002	3%	2%
# individuals with ≥ 1 (conf.) positive AB test	FOPH						1797	1694	1743	1745	1840	1782	3%	1%
Correction factor	(calculated)						1.149	1.156	1.180	1.123	1.157	1.123	2%	1%
AB *tested* positive rate	(calculated D1)						0.018	0.017	0.015	0.016	0.015	0.016	6%	3%
	(calculated D2)						0.029	0.024	0.022	0.018	0.024	0.026	16%	6%
	(calculated D3)						0.024	0.025	0.021	0.018	0.018	0.017	18%	14%
	(calculated D4)						0.030	0.030	0.028	0.032	0.029	0.028	5%	3%
	(calculated D5)						0.003	0.003	0.002	0.003	0.002	0.002	10%	4%
	(calculated D6)						0.023	0.025	0.028	0.022	0.020	0.023	11%	4%
	(calculated D11)						0.077	0.054	0.049	0.046	0.035	0.029	35%	17%
	(calculated D12)						0.050	0.037	0.042	0.042	0.034	0.031	17%	9%
	(calculated D20)						0.027	0.036	0.031	0.035	0.032	0.032	10%	4%
	(calculated F7)						0.011	0.009	0.009	0.009	0.009	0.007	13%	2%
	(calculated F10)						0.023	0.023	0.020	0.025	0.020	0.023	7%	5%
	(calculated I8)						0.026	0.029	0.029	0.020	0.020	0.022	17%	15%
	(calculated I9)						0.052	0.041	0.039	0.037	0.031	0.038	17%	5%
overall	(calculated)						0.022	0.020	0.019	0.019	0.017	0.017	9%	6%
rsd	(calculated)						64%	50%	50%	52%	45%	44%		
qcd	(calculated)						13%	21%	21%	33%	27%	27%		

Abbreviations: AB: antibody; rsd: relative standard deviation (= coefficient of variance); qcd: quartile coefficient of dispersion

Supplementary methods 1: Exploration of the between-laboratory variability

As mentioned above, we assume that our data covers approximately 80% of all HCV AB tests in Switzerland. Since the data stem from different-sized laboratories in different parts of the country, the variability in numbers and rates between laboratories (and - for comparison - within the same laboratory over time) may be of interest. In order to explore this variability, we present individual values per laboratory and year of the number of AB tests (A.), the number of positive AB tests (B.), the AB *test* positive rate (C.) and the AB *tested* positive rate (D.) and, additionally, calculated their between-laboratory variabilities (E.) using both a non-robust and a robust measure (Supplementary table 2). For better illustration, counts and rates and the variability of the AB *test* positive rate over time are shown graphically in the following Supplementary figure x, facets A.-D. and E..

E.



Supplementary figure 1: A. Number of HCV AB tests, B. number of positive HCV AB tests, C. AB *test* positive rate, D. AB *tested* positive rate, by laboratory and year, and E. between-laboratory variability the AB *test* positive rate per year. (Between-laboratory variability measures of the AB *tested* positive rates are not shown, since they coincide, where defined, with the corresponding variability measures of the AB *test* positive rates.) **Abbreviations**: AB: antibody; rsd: relative standard deviation (= coefficient of variance); qcd: quartile coefficient of dispersion.

The relative standard deviation (rsd) as the less robust measure of the between-laboratory lies within a range from 44% to 63%, and the more robust quartile coefficient of dispersion (qcd) ranges from 13% to 52%. The rsd shows a tendency to decrease in the more recent years which can be explained mainly by the rates in laboratories D11 and D12 converging towards the mean rates. The relatively stable qcd confirms that overall, AB *test* positive rates (and thus AB *tested* positive rates) remain on a moderate level, and that the decrease in between-laboratory variability can be attributed to few outliers who contributed few tests before 2012. Overall, the between-laboratory variabilities are about twice as large as the within-laboratory variabilities over time (rsd: min 9% - max 51%; qcd: min 4% - max 30%).

Supplementary methods 2: Representativeness of the study sample

We assume that the data from our sample of 13 laboratories is reasonably representative for all HCV antibody testing in Switzerland for the following reasons:

- First, according to the FAMH (the medical laboratories of Switzerland), there are only 43 laboratories that potentially determine HCV antibodies, and our sample contains 13 of the 20 largest of these. Notably, all three major language regions of Switzerland are represented among them.

- Secondly, and even more importantly, if the total numbers of positive HCV AB tests provided by the laboratories in our sample is tentatively multiplied with a positive predictive value (PPV) of 72% (as suggested by Cadieux et al. 2016; see below) then this yields estimated numbers of confirmed tests close to the numbers provided by the Federal Office of Public Health (FOPH) for *all* Switzerland. With the numbers already provided in Supplementary table 2:

Year	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**
# positive AB tests (13 laboratories):	2084	2108	2140	2226	2355	2379
estimated # confirmed positive AB tests (13 laboratories) = # positive AB tests (13 laboratories) * 0.72	1500	1518	1541	1603	1696	1713
# positive confirmed AB tests (all Switzerland, according to FOPH):	2065	1959	2057	1959	2129	2002
estimated fraction of confirmed tests covered by study sample, by year	73%	77%	75%	82%	80%	86%
estimated fraction of confirmed tests covered by study sample, mean over all years	**79%**					

Abbreviations: AB: antibody; FOPH: Federal Office of Public Health

Thus, our study includes roughly 73%-86% of all positive HCV AB tests from all of Switzerland in 2012-2017, suggesting a reasonable degree of representativeness of our laboratories and our data.

Reference: Cadieux G, Campbell J, Dendukuri N. Systematic review of the accuracy of antibody tests used to screen asymptomatic adults for hepatitis C infection. CMAJ Open. 2016;4(4):E737-E745. doi:10.9778/cmajo.20160084