Note: this document is a confidential and unofficial English translation of the performance evaluation report of the COVID-19 antigenic rapid diagnosis orientation tests from the AP-HP

Assessment of the diagnostic performance of COVID-19 antigenic rapid diagnosis orientation tests

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The reference technique to diagnose the virus infection "Severe Acute Respiratory Coronavirus 2" (SARS-CoV-2), responsible for the "Coronavirus Disease 2019" (COVID-19), is based on the "polymerase chain reaction (PCR) that allows the detection of viral RNA from a nasopharyngeal sample.

Performing PCR tests requires expensive equipment, trained staff and must be carried out in a certified medical biology laboratories. The results are available only after 4 to 6 hours for the most rapid PCR tests. The performance of PCR tests (very high sensitivity and specificity), however, make them the most adapted tool for diagnosing the infection in symptomatic subjects and contact subjects.

Antigenic tests as PCR tests, are direct tests that detect a component of viral particles, in this case viral proteins expressing antigens. They are by definition less sensitive than PCR tests because they do not involve an amplification step. They are today marketed as individual rapid diagnosis orientation tests (RDOT), the results are available in about 15 to 30 minutes.

The value of antigenic RDOT in the diagnosis or screening of COVID-19 disease is their ability to identify positive subjects (sensitivity) and negative subjects (specificity).

Objective

The objective of this study was to evaluate the diagnostic performances of 6 COVID-19 antigenic RDOT (sensitivity, specificity, positive and negative predictive values from pre-specified hypothesis) carried out on nasopharyngeal samples ; collected from : 1) in none infected subjects with SARS-CoV-2 because they were tested before the start of the epidemic; 2) in subjects with a positive SARS-CoV-2 PCR (presence of RNA), tested while symptomatic at the time of the first epidemic wave (March and April 2020).

Material and Methods

This was a retrospective study carried out using nasopharyngeal samples collected prospectively, of which the infectious status for SARS-CoV-2 was known, from patients who consulted or who were admitted to Henri Mondor de Créteil Hospital: between March and April 2020 for SARS-CoV-2 PCR positive samples; between April and August 2019 for SARS CoV-2 PCR negative samples.

The tested samples included:

- **297 aliquots** of nasopharyngeal samples frozen at -80 ° C in commercial viral transport medium (Cepheid® or Deltalab®) or physiological serum, **tested positive for SARS-CoV-2 PCR** (RT-PCR developed by the NRC for respiratory viruses from Pasteur Institut or RealStar® SARS-CoV-2 RT-PCR, Altona Diagnostics, Germany), tested between March 9 and April 9, 2020**.**

The selection of samples for the study was made in a randomized way for the severity of the infection (mild or severe / critical), after stratification on the Ct values and the date of onset of symptoms.

- **337 aliquots** of nasopharyngeal samples frozen at -80 ° C in commercial viral transport medium (Cepheid®) **negative for SARS-CoV-2** because they were taken before the virus circulating period, i.e. between April and August 2019 .

The assessment focused on 6 COVID-19 antigenic RDOTs, acquired by AP-HP from French distributors:

- **SARS-CoV-2 COVID-19 Respi-Strip (Coris BioConcept, Gembloux, Belgium),** in collaboration with Médecins sans Frontières and Épicenter. **"CORIS"** in the rest of the document.
- **Standard Q COVID-19 Ag (SD BIOSENSOR, Inc., Korea),** in collaboration with Médecins sans Frontières and Épicenter. **"BIOSENSOR"** in the rest of the document.
- **PanBio COVID-19 Antigen Rapid Test (Abbott, Chicago, Illinois, USA).** "ABBOTT"in the rest of the document.
- **Biosynex COVID-19 Ag BSS (Biosynex, Strasbourg, France). "BIOSYNEX"** in the rest of the document.
- **NG Test SARS-CoV-2 Ag (NG Biotech, Guipry, France). "NG BIOTECH"** in the rest of the document.
- **COVID-VIRO Antigen Rapid Test (AAZ, Boulogne-Billancourt, France).** "AAZ"in the rest of the document

The tests were carried out by laboratory staff using a volume of viral transport medium of 100 µL, following an adaptation of the protocol to the use of viral transport medium. Each test was interpreted independently by two different technicians. A third reading was carried out in the event of discrepancy.

Results

The results are presented below for each test. They include :

1) The **sensitivity** (Se, percentage of positive RDOT results among the cases identified as positive by PCR [i.e., true positives / (true positives + false negatives)]), indicated in red in the tables.
2) The **specificity** (Sp, percentage of negative RDOT among the control subjects identified as negative [i.e., true negatives / (true negatives + false positives)]), indicated in blue in the tables.
3) **Positive predictive valu**es (PPV: probability that a positive test is a true positive in PCR, defined by the formula Se * P / (Se * P + (1-P) * (1-Sp)) [with P = prevalence]) and **negative** (NPV: probability that a negative test is a true negative in PCR, defined by the formula Sp * (1-P) / (Sp * (1-P) + P * (1-Se))), calculated for pre-specified prevalence of infection in the tested population of 1% and 5%, compatible with a screening context.
   Positive and negative predictive values are presented at the end of the section "Results" for different prevalence values of infection in the tested population.

1) Test CORIS

CORIS												
	Specificity				Sensitivity				PPVI		NPV	
	Case control num	negative case control	IC 95%		Case num.	% Case positive	IC 95%		Prevalence 1%	Prevalence 5%	Prevalence 1%	Prevalence 5%
Global	337	**100,0%**	98,9%	100,0%	292	**35,3%**	29,8%	41,1%	100,0%	100,0%	99,4%	96,7%
Per sub-groupes	Inset of symptoms											
	Time limit 0-3j				97	**53,6%**	43,2%	63,8%	100,0%	100,0%	99,5%	97,6%
	Time limit 4-7j				102	**37,3%**	27,9%	47,4%	100,0%	100,0%	99,4%	96,8%
	Time limit 8-11j				62	**12,9%**	5,7%	23,9%	100,0%	100,0%	99,1%	95,6%
	Time limit ≥12j				24	**20,8%**	7,1%	42,2%	100,0%	100,0%	99,2%	96,0%
	Time limit ≤7j				199	**45,2%**	38,2%	52,4%	100,0%	100,0%	99,4%	97,2%
	Ct value											
	Ct ≤20				39	**89,7%**	75,8%	97,1%	100,0%	100,0%	99,9%	99,5%
	Ct]20-25]				89	**62,9%**	52,0%	72,9%	100,0%	100,0%	99,6%	98,1%
	Ct]25-30]				72	**15,3%**	7,9%	25,7%	100,0%	100,0%	99,2%	95,7%
	Ct >30				88	**1,1%**	0,0%	6,2%	100,0%	100,0%	99,0%	95,1%
	Ct ≤33				242	**42,6%**	36,3%	49,1%	100,0%	100,0%	99,4%	97,1%
	Ct ≤25				128	**71,1%**	62,4%	78,8%	100,0%	100,0%	99,7%	98,5%
	Ct ≤23				94	**84,0%**	75,0%	90,8%	100,0%	100,0%	99,8%	99,2%
	Severity											
	benign				202	**37,1%**	30,5%	44,2%	100,0%	100,0%	99,4%	96,8%
	Severe				89	**31,5%**	22,0%	42,2%	100,0%	100,0%	99,3%	96,5%

Global sensitivity *versus* PCR: 35,3% - Sensitivity for Ct ≤33: 42,6%

- Specificity: 100% PS :Invalid results: 5 positives by PCR

2) BIOSENSOR Test

SD BIOSENSOR 2												
	Specificity				Sensitivity				PPVI		NPV	
	Case control num	negative case control	IC 95%		Case num.	% Case positive	IC 95%		Prevalence 1%	Prevalence 5%	Prevalence 1%	Prevalence 5%
G lo bal	337	**93,2%**	89,9%	95,6%	291	**60,1%**	54,3%	65,8%	8,2%	31,8%	99,6%	97,8%
Per sub-groupes	Inset of symptoms											
	Time limit 0-3j				97	**80,4%**	71,1%	87,8%	10,7%	38,4%	99,8%	98,9%
	Time limit 4-7j				102	**61,8%**	51,6%	71,2%	8,4%	32,3%	99,6%	97,9%
	Time limit 8-11j				62	**40,3%**	28,1%	53,6%	5,7%	23,8%	99,4%	96,7%
	Time limit ≥12j				23	**30,4%**	13,2%	52,9%	4,3%	19,1%	99,3%	96,2%
	Time limit ≤7j				199	**70,9%**	64,0%	77,1%	9,5%	35,4%	99,7%	98,4%
	Ct value											
	Ct ≤20				39	**100,0%**	91,0%	100,0%	12,9%	43,6%	100,0%	100,0%
	Ct]20-25]				88	**89,8%**	81,5%	95,2%	11,8%	41,0%	99,9%	99,4%
	Ct]25-30]				72	**65,3%**	53,1%	76,1%	8,8%	33,6%	99,6%	98,1%
	Ct >30				88	**11,4%**	5,6%	19,9%	1,7%	8,1%	99,0%	95,2%
	Ct ≤33				241	**71,8%**	65,6%	77,4%	9,6%	35,7%	99,7%	98,4%
	Ct ≤25				127	**92,9%**	87,0%	96,7%	12,1%	41,8%	99,9%	99,6%
	Ct ≤23				93	**97,8%**	92,4%	99,7%	12,7%	43,1%	100,0%	99,9%
	Severity											
	benign				202	**59,9%**	52,8%	66,7%	8,2%	31,7%	99,6%	97,8%
	Severe				88	**61,4%**	50,4%	71,6%	8,4%	32,2%	99,6%	97,9%

Global sensitivity *versus* PCR: 60,1% - Sensitivity for Ct ≤33: 71,8%

- Specificity: 93,2% PS : Invalid results :6 positives by PCR

3) ABBOTT Test

ABBOTT											
	Specificity				Sensitivity				PPVI		NPV	
	Case control num	negative case control	IC 95%		Case num.	% Case positive	IC 95%		Prevalence 1%	Prevalence 5%	Prevalence 1%	Prevalence 5%
Global	337	**100,0%**	98,9%	100,0%	295	**55,3%**	49,4%	61,0%	100,0%	100,0%	99,6%	97,7%
Per sub-groupes	Inset of symptoms											
	Time limit 0-3j				97	**79,4%**	70,0%	86,9%	100,0%	100,0%	99,8%	98,9%
	Time limit 4-7j				103	**52,4%**	42,4%	62,4%	100,0%	100,0%	99,5%	97,6%
	Time limit 8-11j				63	**33,3%**	22,0%	46,3%	100,0%	100,0%	99,3%	96,6%
	Time limit ≥12j				24	**37,5%**	18,8%	59,4%	100,0%	100,0%	99,4%	96,8%
	Time limit ≤7j				200	**65,5%**	58,5%	72,1%	100,0%	100,0%	99,7%	98,2%
	Ct value											
	Ct ≤20				40	**95,0%**	83,1%	99,4%	100,0%	100,0%	99,9%	99,7%
	Ct]20-25]				90	**83,3%**	74,0%	90,4%	100,0%	100,0%	99,8%	99,1%
	Ct]25-30]				73	**57,5%**	45,4%	69,0%	100,0%	100,0%	99,6%	97,8%
	Ct >30				88	**8,0%**	3,3%	15,7%	100,0%	100,0%	99,1%	95,4%
	Ct ≤33				245	**65,7%**	59,4%	71,6%	100,0%	100,0%	99,7%	98,2%
	Ct ≤25				130	**86,9%**	79,9%	92,2%	100,0%	100,0%	99,9%	99,3%
	Ct ≤23				96	**94,8%**	88,3%	98,3%	100,0%	100,0%	99,9%	99,7%
	Severity											
	benign				202	**58,4%**	51,3%	65,3%	100,0%	100,0%	99,6%	97,9%
	Severe				92	**47,8%**	37,3%	58,5%	100,0%	100,0%	99,5%	97,3%

Global sensitivity *versus* PCR: 55,3% - Sensitivity for Ct ≤33: 65,7%

- Specificity: 100% PS: Invalid results: 2 positives by PCR

4) BIOSYNEX Test

BIOSYNEX											
	Specificity				Sensitivity				PPVI		NPV	
	Case control num	negative case control	IC 95%		Case num.	% Case positive	IC 95%		Prevalence 1%	Prevalence 5%	Prevalence 1%	Prevalence 5%
G lo bal	337	**100,0%**	98,9%	100,0%	297	**59,6%**	53,8%	65,2%	100,0%	100,0%	99,6%	97,9%
Par sous-groupes	Inset of symptoms											
	Time limit 0-3j				97	**81,4%**	72,3%	88,6%	100,0%	100,0%	99,8%	99,0%
	Time limit 4-7j				103	**56,3%**	46,2%	66,1%	100,0%	100,0%	99,6%	97,8%
	Time limit 811j				63	**42,9%**	30,5%	56,0%	100,0%	100,0%	99,4%	97,1%
	Time limit ≥12j				26	**42,3%**	23,4%	63,1%	100,0%	100,0%	99,4%	97,1%
	Time limit ≤7j				200	**68,5%**	61,6%	74,9%	100,0%	100,0%	99,7%	98,4%
	Ct value											
	Ct ≤20				40	**97,5%**	86,8%	99,9%	100,0%	100,0%	100,0%	99,9%
	Ct]20-25]				90	**92,2%**	84,6%	96,8%	100,0%	100,0%	99,9%	99,6%
	Ct]25-30]				74	**63,5%**	51,5%	74,4%	100,0%	100,0%	99,6%	98,1%
	Ct >30				89	**9,0%**	4,0%	16,9%	100,0%	100,0%	99,1%	95,4%
	Ct ≤33				247	**71,3%**	65,2%	76,8%	100,0%	100,0%	99,7%	98,5%
	Ct ≤25				130	**93,8%**	88,2%	97,3%	100,0%	100,0%	99,9%	99,7%
	Ct ≤23				96	**96,9%**	91,1%	99,4%	100,0%	100,0%	100,0%	99,8%
	Severity											
	benign				202	**60,4%**	53,3%	67,2%	100,0%	100,0%	99,6%	98,0%
	Severe				94	**58,5%**	47,9%	68,6%	100,0%	100,0%	99,6%	97,9%

Global sensitivity *versus* PCR: 59,6% - Sensitivity for Ct ≤33: 71,3%

- Specificity: 100% PS: Invalid results: NONE

5) NG BIOTECH Test

NG-BIOTECH											
	Specificity				Sensitivity				PPVI		NPV	
	Case control num	negative case control	IC 95%		Case num.	% Case positive	IC 95%		Prevalence 1%	Prevalence 5%	Prevalence 1%	Prevalence 5%
Global	337	**98,5%**	96,6%	99,5%	297	**32,3%**	27,0%	38,0%	17,9%	53,1%	99,3%	96,5%
Per sub-groupes	Inset of symptoms											
	Time limit 0-3j				97	**52,6%**	42,2%	62,8%	26,1%	64,8%	99,5%	97,5%
	Time limit 4-7j				103	**30,1%**	21,5%	39,9%	16,9%	51,4%	99,3%	96,4%
	Time limit 811j				63	**14,3%**	6,7%	25,4%	8,8%	33,4%	99,1%	95,6%
	Time limit ≥12j				26	**15,4%**	4,4%	34,9%	9,4%	35,1%	99,1%	95,7%
	Time limit ≤7j				200	**41,0%**	34,1%	48,2%	21,6%	59,0%	99,4%	96,9%
	Ct value											
	Ct ≤20				40	**80,0%**	64,4%	90,9%	35,0%	73,7%	99,8%	98,9%
	Ct]20-25]				90	**54,4%**	43,6%	65,0%	26,8%	65,6%	99,5%	97,6%
	Ct]25-30]				74	**18,9%**	10,7%	29,7%	11,3%	39,9%	99,2%	95,8%
	Ct >30				89	**1,1%**	0,0%	6,1%	0,8%	3,8%	99,0%	95,0%
	Ct ≤33				247	**38,9%**	32,8%	45,3%	20,7%	57,7%	99,4%	96,8%
	Ct ≤25				130	**62,3%**	53,4%	70,7%	29,6%	68,6%	99,6%	98,0%
	Ct ≤23				96	**72,9%**	62,9%	81,5%	32,9%	71,9%	99,7%	98,6%
	Severity											
	benign				202	**34,7%**	28,1%	41,7%	18,9%	54,9%	99,3%	96,6%
	Severe				94	**27,7%**	18,9%	37,8%	15,7%	49,3%	99,3%	96,3%

Global sensitivity *versus* PCR: 32,3% - Sensitivity for Ct ≤33: 38,9%

- Specificity: 98,5% PS: Invalid results: NONE

6) AAZ Test

AAZ											
	Specificity				Sensitivity				PPVI		NPV	
	Case control num	negative case control	IC 95%		Case num.	% C as positive	IC 95%		Prevalence 1%	Prevalence 5%	Prevalence 1%	Prevalence 5%
Global	337	**100,0%**	98,9%	100,0%	295	**61,7%**	55,9%	67,3%	100,0%	100,0%	99,6%	98,0%
Per sub-groupes	Inset of symptoms											
	Time limit 0-3j				97	**81,4%**	72,3%	88,6%	100,0%	100,0%	99,8%	99,0%
	Time limit 4-7j				103	**61,2%**	51,1%	70,6%	100,0%	100,0%	99,6%	98,0%
	Time limit 8-11j				63	**42,9%**	30,5%	56,0%	100,0%	100,0%	99,4%	97,1%
	Time limit ≥12j				24	**37,5%**	18,8%	59,4%	100,0%	100,0%	99,4%	96,8%
	Time limit ≤7j				200	**71,0%**	64,2%	77,2%	100,0%	100,0%	99,7%	98,5%
	Ct value											
	Ct ≤20				40	**100,0%**	91,2%	100,0%	100,0%	100,0%	100,0%	100,0%
	Ct]20-25]				90	**94,4%**	87,5%	98,2%	100,0%	100,0%	99,9%	99,7%
	Ct]25-30]				73	**65,8%**	53,7%	76,5%	100,0%	100,0%	99,7%	98,2%
	Ct >30				88	**9,1%**	4,0%	17,1%	100,0%	100,0%	99,1%	95,4%
	Ct ≤33				245	**73,5%**	67,5%	78,9%	100,0%	100,0%	99,7%	98,6%
	Ct ≤25				130	**96,2%**	91,3%	98,7%	100,0%	100,0%	100,0%	99,8%
	Ct ≤23				96	**97,9%**	92,7%	99,7%	100,0%	100,0%	100,0%	99,9%
	Severity											
	benign				202	**62,4%**	55,3%	69,1%	100,0%	100,0%	99,6%	98,1%
	Severe				92	**59,8%**	49,0%	69,9%	100,0%	100,0%	99,6%	97,9%

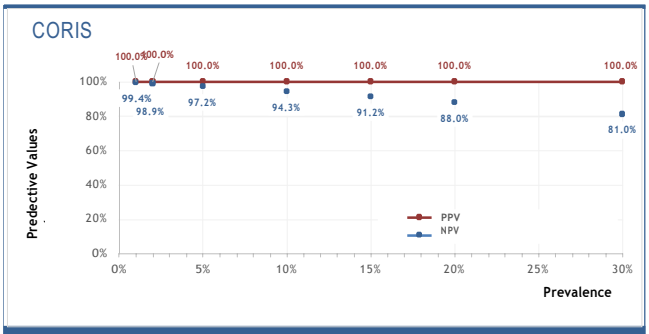
Global sensitivity *versus* PCR: 61,7% - Sensitivity for Ct ≤33: 73,5%

- Specificity: 100% PS: Invalid results: 2 positives by PCR

Cross-reactions with other respiratory viral infections in the event of a "false positive" (samples negative for SARS-CoV-2 because they were taken before the appearance of the virus):

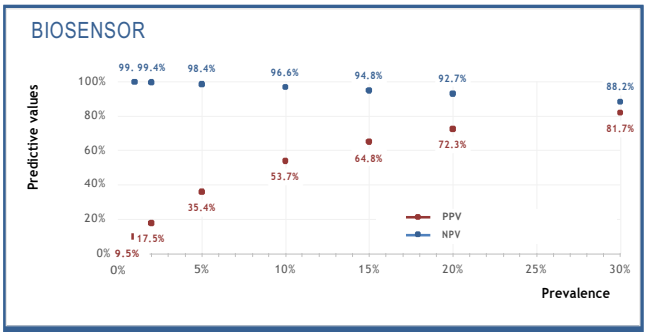
FilmArray Results	N	%	False positives Biosensor	False positives NG Biotech
No viral infection detected	**268**	**79,5%**	**16**	**5**
Other viral infection detected	**69**	**20,5%**	**6**	**0**
Rhinovirus/Enterovirus	21	30,%	**3**	
Parainfluenza 3	11	15,%	**2**	
Influenza A H3	8	11,%		
Coronavirus 229E	6	8,7%		
Coronavirus HKU1	7	9.8%		
Coronavirus NL63	3	4,3%	**1**	
Metapneumovirus	3	4,3%		
Parainfluenza 1	3	4,3%		
Respiratory syncytial virus	3	4,3%		
Coronavirus 229E + Parainfluenza 3	1	1,4%		
Coronavirus OC43	1	1,4%		
Rhinovirus/Enterovirus + Coronavirus HKU1	1	1,4%		
Respiratory syncytial virus+Rhinovirus/Entérovirus	1	1,4%		

Association between positive (in red) and negative (in blue) predictive values of the 6 antigenic RDOT according to the prevalence of infection in the tested population: Simulation based on the sensitivity values observed in symptomatic subjects for less than 7 days.



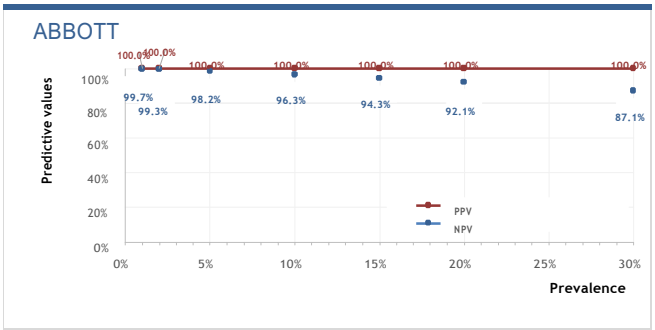
Prevalence (%)	Case (n)	None-case (n)	True positive (n)	False neg. (n)	True neg. (n)	False positive (n)	PPV (%)	NPV (%)
1.0%	10	990	5	5	990	<1	100.0%	99.4%
2.0%	20	980	9	11	980	<1	100.0%	98.9%
5.0%	50	950	23	27	950	<1	100.0%	97.2%
10.0%	100	900	45	55	900	<1	100.0%	94.3%
15.0%	150	850	68	82	850	<1	100.0%	91.2%
20.0%	200	800	90	110	800	<1	100.0%	88.0%
30.0%	300	700	136	164	700	<1	100.0%	81.0%

Simulation on 1000 fictitious patients considering sensitivity if symptoms <7 days = 45.2% and specificity =



Prevalence (%)	Case (n)	None-case (n)	True positive (n)	False Neg. (n)	True neg. (n)	False positive (n)	PPV (%)	NPV (%)
					923			
1.0%	10	990	7	3	913	67	9.5%	99.7%
2.0%	20	980	14	6	885	67	17.5%	99.4%
5.0%	50	950	35	15	839	65	35.4%	98.4%
10.0%	100	900	71	29	792	61	53.7%	96.6%
15.0%	150	850	106	44	746	58	64.8%	94.8%
20.0%	200	800	142	58	652	54	72.3%	92.7%
30.0%	300	700	213	87		48	81.7%	88.2%

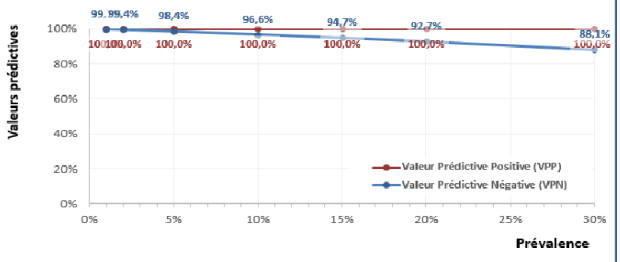
Simulation on 1000 fictitious patients considering sensitivity if symptoms <7 days = 70.9% and specificity



Prevalence (%)	Case (n)	None-cas (n)	True positifs (n)	False neg. (n)	True neg. (n)	False positifs (n)	PPV (%)	NPV (%)
1.0%	10	990	7	3	990	<1	100.0%	99.7%
2.0%	20	980	13	7	980	<1	100.0%	99.3%
5.0%	50	950	33	17	950	<1	100.0%	98.2%
10.0%	100	900	66	35	900	<1	100.0%	96.3%
15.0%	150	850	98	52	850	<1	100.0%	94.3%
20.0%	200	800	131	69	800	<1	100.0%	92.1%
30.0%	300	700	197	104	700	<1	100.0%	87.1%

Simulation on 1000 fictitious patients considering sensitivity if symptoms <7 days = 65.5% and specificity = 100.0%

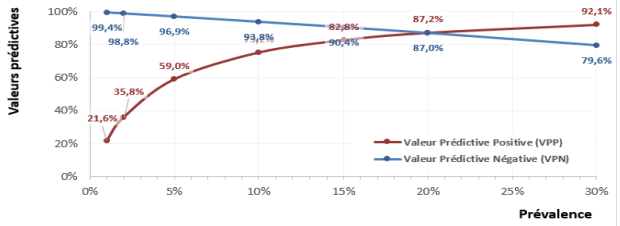
BIOSYNEX



Prévalence (%)	Cas (n)	Non-cas (n)	Vrais positifs (n)	Faux négatifs (n)	Vrais négatifs (n)	Faux positifs (n)	VPP (%)	VPN (%)
1,0%	10	990	7	3	990	<1	100,0%	99,7%
2,0%	20	980	14	6	980	<1	100,0%	99,4%
5,0%	50	950	34	16	950	<1	100,0%	98,4%
10,0%	100	900	69	32	900	<1	100,0%	96,6%
15,0%	150	850	103	47	850	<1	100,0%	94,7%
20,0%	200	800	137	63	800	<1	100,0%	92,7%
30,0%	300	700	206	95	700	<1	100,0%	88,1%

Simulation sur 1000 patients fictifs en considérant une sensibilité si symptômes <7jours = 68.5% et une spécificité = 100.0%

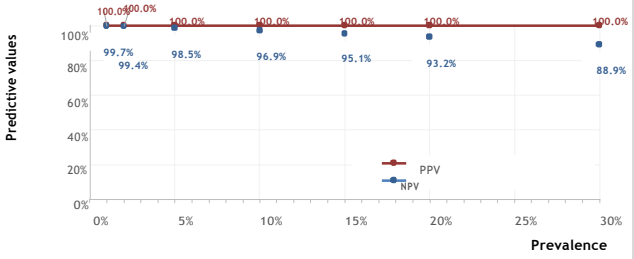
NG-BIOTECH



Prévalence (%)	Cas (n)	Non-cas (n)	Vrais positifs (n)	Faux négatifs (n)	Vrais négatifs (n)	Faux positifs (n)	VPP (%)	VPN (%)
1,0%	10	990	4	6	975	15	21,6%	99,4%
2,0%	20	980	8	12	965	15	35,8%	98,8%
5,0%	50	950	21	30	936	14	59,0%	96,9%
10,0%	100	900	41	59	887	14	75,2%	93,8%
15,0%	150	850	62	89	837	13	82,8%	90,4%
20,0%	200	800	82	118	788	12	87,2%	87,0%
30,0%	300	700	123	177	690	11	92,1%	79,6%

Simulation sur 1000 patients fictifs en considérant une sensibilité si symptômes <7jours = 41.0% et une spécificité = 98.5%

AAZ



Prevalence (%)	Case (n)	None-case (n)	True positive (n)	False negative (n)	True neg. (n)	False positive (n)	PPV (%)	NPV (%)
1.0%	10	990	7	3	990	<1	100.0%	99.7%
2.0%	20	980	14	6	980	<1	100.0%	99.4%
5.0%	50	950	36	15	950	<1	100.0%	98.5%
10.0%	100	900	71	29	900	<1	100.0%	96.9%
15.0%	150	850	107	44	850	<1	100.0%	95.1%
20.0%	200	800	142	58	800	<1	100.0%	93.2%
30.0%	300	700	213	87	700	<1	100.0%	88.9%

Simulation on 1000 fictitious patients considering sensitivity if symptoms <7 days = 71.0% and specificity = 100.0%

Synthesis

- The CORIS and NG BIOTECH tests have shown insufficient sensitivity for use in the context of diagnosis and screening for COVID-19 infection (respective sensitivities for a Ct ≤33 of 42.6% and 38.9%).

- The sensitivity of the BIOSENSOR, ABBOTT, BIOSYNEX and AAZ tests was considered satisfactory for use in a large-scale screening context:
    - Overall sensitivity is 55% -62% compared to PCR.
    - Sensitivity is 66-74% for viral loads of Ct ≤33 in PCR (Opinion of 09/25/2020 of the French Society of Microbiology: "If the value of Ct is ≤33, the presence of virus RNA is consistent with significant viral shedding ").
    - Sensitivity is 87% -96% for viral loads of Ct <25 , ie high viral loads corresponds to the most contagious patients.

- The specificity of the CORIS, ABBOTT, BIOSYNEX and AAZ tests was excellent (100%), while that of the BIOSENSOR and NG BIOTECH tests was only acceptable (93.2% and 98.5% respectively) and associated with a loss of positive predictive value of these tests if they are used in populations with low prevalence in the context of screening. The (regulatory) confirmation of positive RDOT results by performing a PCR overcomes this insufficiency. However, the use of less specific tests exposes the risk of loss of confidence of the tested population in the event of too many false positives. The positive predictive value of the NG BIOTECH test improves markedly when the prevalence in the population tested exceeds 10%.

- None of the antigenic RDOT tested meets the sensitivity conditions expected for diagnostic use as a replacement for PCR in symptomatic subjects (overall sensitivity of around 60% compared to PCR for the most sensitive tests).

- The ABBOTT, BIOSYNEX and AAZ tests demonstrated in this study the best performance in terms of sensitivity, specificity and predictive values, compatible for use in the context of mass screening in low prevalence populations (airports at arrival, universities, companies, communities, etc.).

Limitations of the study

- The study population consisted exclusively of subjects with symptoms of COVID-19 recruited during the first epidemic wave of March-April 2020.

- The antigenic tests were carried out on frozen specimens stored at -80 ° C in viral transport medium and not on fresh nasopharyngeal specimen as recommended by the manufacturer.

- The viral transport media used were various (commercial and artisanal media), some of which may be more sensitive to the freezing-thawing phases.

- The tests were carried out in a university hospital laboratory by qualified and trained personnel. Their realization is however extremely simple after minimal training.

Conclusions

1) **None of the evaluated antigenic RDOT tests meet the diagnostic performance requirements allowing use as an alternative to PCR for the diagnosis of COVID-19 disease in symptomatic subjects or positive contact subjects (overall sensitivity is 60% for the best tests compared to PCR), for which a search for viral RNA by PCR must be carried out in a medical biology laboratory, and the result in less than 48 hours.**

2) **Globally, the satisfactory performance of certain antigenic RDOT tests make them the tool of choice for carrying out mass screening in populations with low prevalence (airports on arrival, universities, companies, communities, etc.), that might be overlooked, or clog medical biology laboratories unnecessarily. Their speed and ease of implementation allow repeatability of tests within given populations, which is crucial in the context of a rapidly evolving pandemic. In this context, the antigenic RDOT make it possible to identify uninfected subjects with excellent predictive value, and to detect in a sensitive manner the infected subjects with a high viral load, that is to say the most contagious subjects, in order to identify contact subjects and break the chains of contamination. It is recalled that, for regulatory reasons, the results of positive RDOT must be confirmed by PCR test.**

3) **In this context of application, among the 6 tested RDOT, the BIOSENSOR test showed an acceptable performance, while the ABBOTT, BIOSYNEX and AAZ tests were the most efficient.**

4) **Several other antigenic RDOT are being evaluated and the results will be subject to updates.**