EUnetHTA Covid-19 Response and collaborative initiatives

HTA Network – 27th October 2020

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Collaborative effort

17th of April 2020

RAPID COLLABORATIVE REVIEW ON THE CURRENT ROLE OF ANTIBODY TESTS FOR NOVEL CORONAVIRUS SARS-COV-2 IN THE MANAGEMENT OF THE PANDEMIC

Project ID: RCR OT 01

Published 22nd of June

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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

EUnetHTA Task Force on SARS-COV-2 diagnostics

Work Plan

What is the diagnostic accuracy of molecular methods that detect the presence of the SARS-CoV-2 virus in people with suspected COVID-19

Project ID: ***RCROT02***

Expected early November

Regione Emilia-Romagna

IQWiG

Technoleg Iechyd Cymru
Health Technology Wales

Healthcare Improvement Scotland

Health Information and Quality Authority
An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

SV

ANTIBODY TESTS - Objectives and Scope

To provide a synthesis of the available evidence on several intended clinical uses of antibody tests, addressing the following questions:

Informed by liaison with DG SANTE, ECDC, JRC, Joint WHO Europe/ECDC Laboratory Network - EC Covid-19 Testing WG

European Commission
DG Research & Innovation

Joint Research Centre (JRC)
EU Science Hub

Diagnostic use
Evidence available

Whether and with which testing strategies, antibody tests can be reliably used for:

1 surveillance for early detection of new asymptomatic cases of SARS-CoV-2 acute infection in the general population and/or specific subpopulations;

2 diagnosis of SARS-CoV-2 acute infection in patients presenting symptoms suggestive of SARS-CoV-2 infection:

Other indications for use
Evidence NOT available

How antibody tests can be used for:

3 measuring seroprevalence in communities;

4 ruling out risk of transmission in patients who recovered from SARS-CoV-2 infection;

5 assessing protective immunity in subjects with past and resolved SARS-CoV-2 infection.

Diagnostic Use

Table 4 - 2: Sensitivity and Specificity estimates for IgM+IgG tests

RAPID DIAGNOSTIC TESTS					
Time since symptoms onset Pooled estimate	Overall (9 studies)	Week 1 (12 studies)	Week 2 (13 studies)	Week 3 (13 studies)	Week 4 (10 studies)
Sensitivity overall	68.8 (46.3 - 85)	33.8 (27 - 41.4)	71.5 (65.7 - 76.6)	81.6 (71.9-88.5)	87.8 (78.4-93.4)
Heterogeneity τ^2	1.39	0.08	0.10	0.51	0.0
Specificity	93.2 (71.8 – 98).7	92 (84.7 – 96)	90.2 (75.9 - 96.4)	89.7 (72.8 - 96.6)	92.1 (83.2 - 96.5)
Heterogeneity τ^2	4.14	0.87	2.54	3.23	0.95
CLIA (chemiluminescent immunoassay) 4 studies					
Time since symptoms onset Pooled estimate	Overall (2 studies)	Week 1 (1study)	Week 2 (1study)	Week 3 (1 study)	Week 4 No studies
Sensitivity overall	91.8 (9.4-99.9)	83.3 (50.9-97.1)	87.9 (70.9-96)	97.1 (82.9-99.8)	-
Heterogeneity τ^2	0.0				-
Specificity	76.5 (14.3-98.4)	80 (69.3-87.8)	80 (69.3 - 87.8)	80 (69.3-87.8)	-
Heterogeneity τ^2	0.0				-
ELISA (enzyme-linked immunosorbent assay)- 2 studies					
Time since symptoms onset Pooled estimate	Overall (2 studies)	Week 1 (3 studies)	Week 2 (3 studies)	Week 3 (3 studies)	Week 4 (3 studies)
Sensitivity overall	84.5 (21.8 - 99.1)	37.8 (27 - 49.9)	84.8 (70.3 - 92.9)	88.1 (56.4 - 97.7)	90.7 56. 5-98.7
Heterogeneity τ^2	0.06	0.0	0.0	0.16	0.0
Specificity	98.5 (0 - 100)	95.4 (8.6 - 100)	95.4 (8.6 – 100)	95.4 (8.6 - 100)	95.4 (8.6 - 100)
Heterogeneity τ^2	19.0	3.48	3.48	3.48	3.48

Impact on Decisions

BENEFITS	RISKS
Symptomatic subjects are diagnosed with COVID-19 at an early stage of disease, are promptly isolated and receive necessary healthcare. Contact tracing is activated (True Positive)	Symptomatic subjects are incorrectly diagnosed with SARS-CoV-2 infection, might receive inappropriate health interventions and are unnecessarily put in isolation. Their contacts are unnecessarily traced (False Positive)
Symptomatic subjects are correctly classified as not infected with SARS-CoV-2 and might be diagnosed and receive healthcare for other condition; no contact tracing for SARS-CoV-2 infection is activated (True Negative)	Symptomatic subjects are incorrectly diagnosed for a condition other than SARS-CoV-2 infection, might not receive appropriate care, are not placed in isolation and their contacts are not traced, representing a risk of transmission to others (False Negative)

Table 4 - 6: Natural frequencies - Week 1 from symptom onset

WEEK 1		N of patients out 1,000* submitted to test			
		Rapid IgM + IgG	CLIA IgM + IgG	ELISA IgM + IgG	RT-PCR
Subjects with SARS-CoV-2 infection (N. 570)	Testing positive	193	475	215	507
	Testing negative	377	95	355	63
Subjects with-out SARS-CoV-2 infection (N. 430)	Testing negative	396	344	410	421
	Testing positive	34	86	20	9
	Total	1,000	1,000	1,000	1,000

*Pre-test probability 57%

“Serving” different contexts

Population size	Pre-test probability	Number of false-positive results			Number of false-negative results		
		RDT	CLIA	ELISA	RDT	CLIA	ELISA
100	1%	5	20	8	1	1	1
	10%	4	18	7	6	2	7
	25%	3	15	6	16	4	17
	50%	2	10	4	31	8	33
50.000	1%	2,277	9,900	3,960	311	83	331
	10%	2,070	9,000	3,600	3,110	835	3,310
	25%	1,725	7,500	3,000	7,775	2087	8,275
	50%	1,150	5,000	2,000	15,550	4,175	16,550
8.000.000	1%	364,320	1,58,4000	633,600	49,760	13,360	5,2960
	10%	331,200	1,440,000	576,000	497,600	133,600	529,600
	25%	276,000	1,200,000	480,000	1,244,000	334,000	1,324,000
	50%	184,000	800,000	320,000	2,488,000	668,000	2648,000

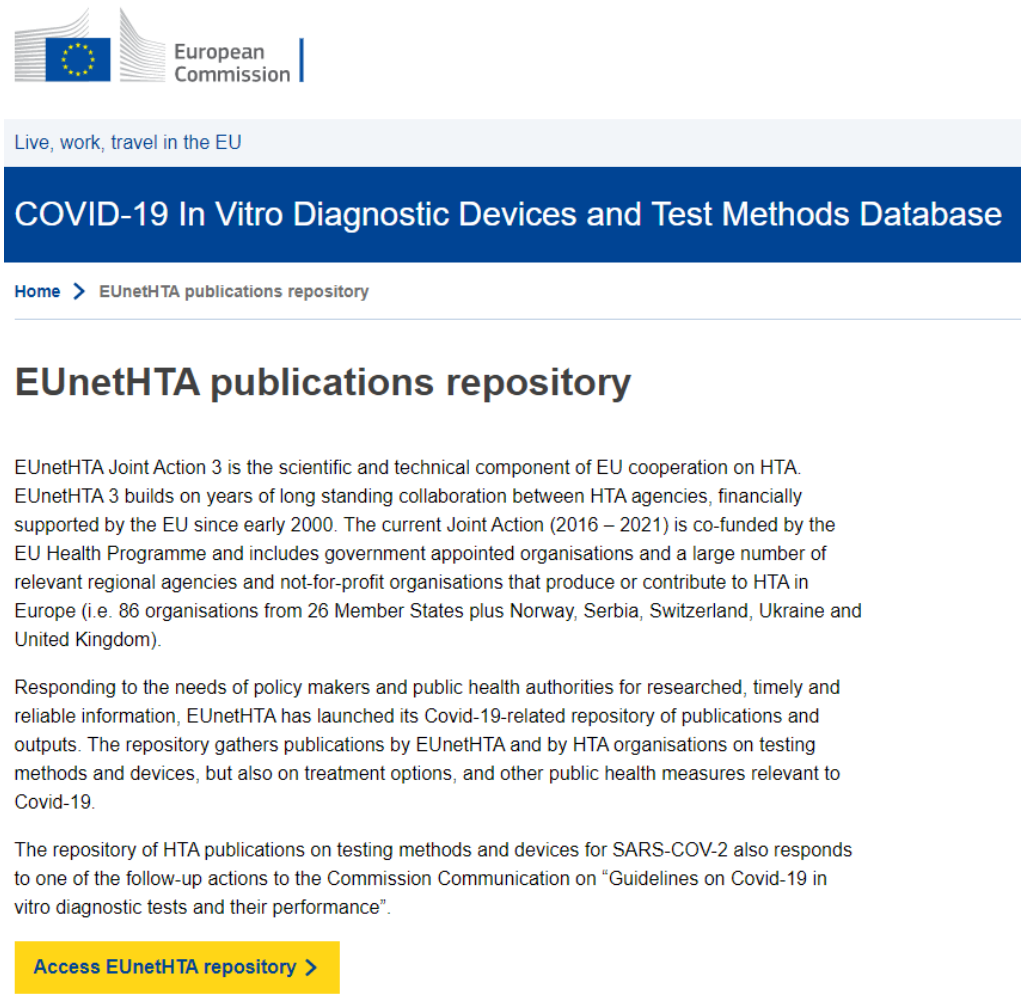
* Test performance: RDT: sensitivity: 33.8 %, specificity: 92%, CLIA: sensitivity: 83.3 %, specificity: 80%, ELISA: sensitivity: 37.8 %, specificity: 95.4%

Dissemination

Report published on the 22nd of June

Results presented at:

- **EC Testing Working Group on June 23rd**
- **EC IVD Competent Authorities meeting on July the 9th**
- **Joint WHO Europe/ECDC Laboratory Network on July the 15th**



https://covid-19-diagnostics.jrc.ec.europa.eu/

Thank you