

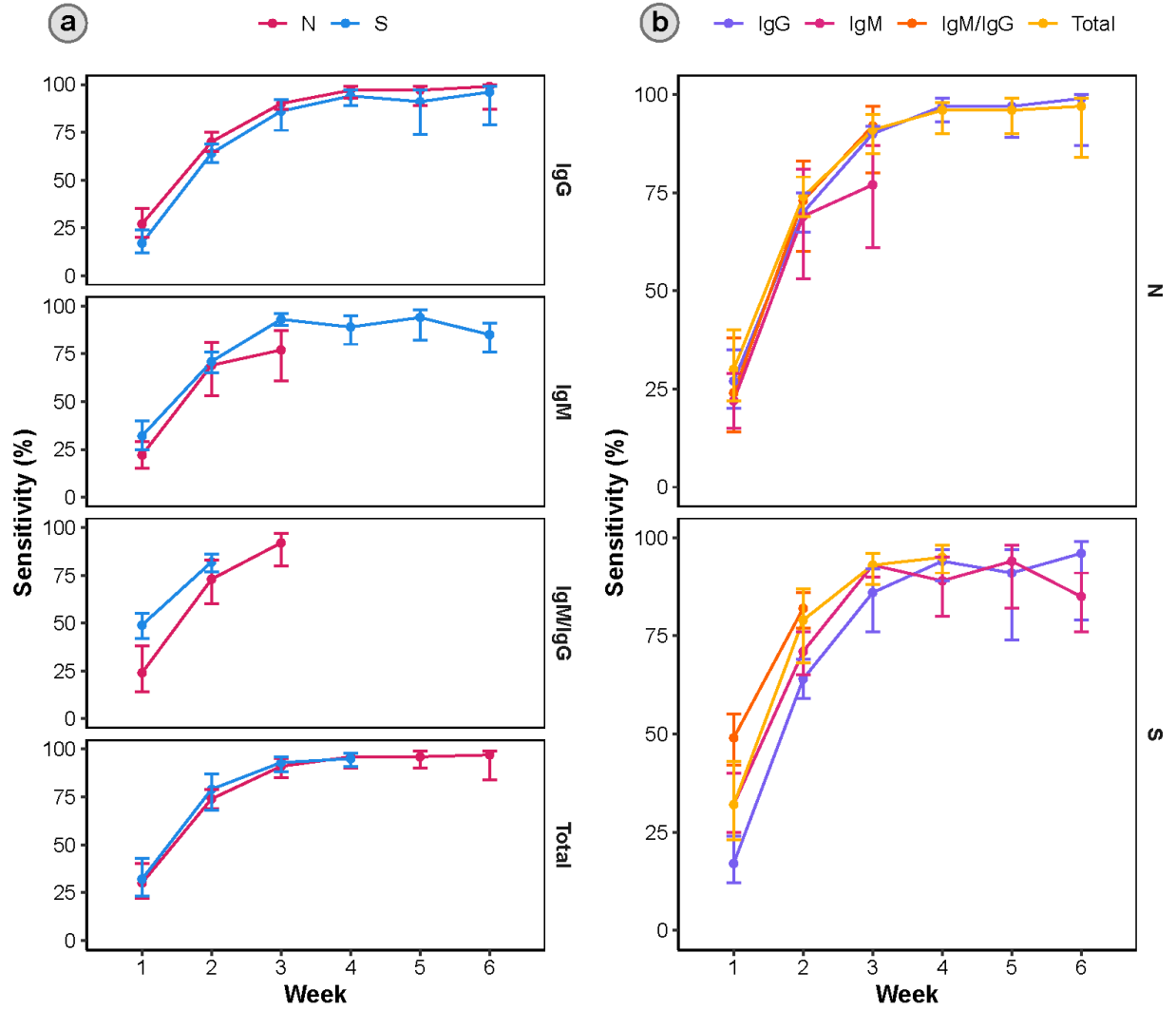
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Executive Summary

- Detection of SARS-CoV-2 antibodies after symptom onset in patients with COVID-19

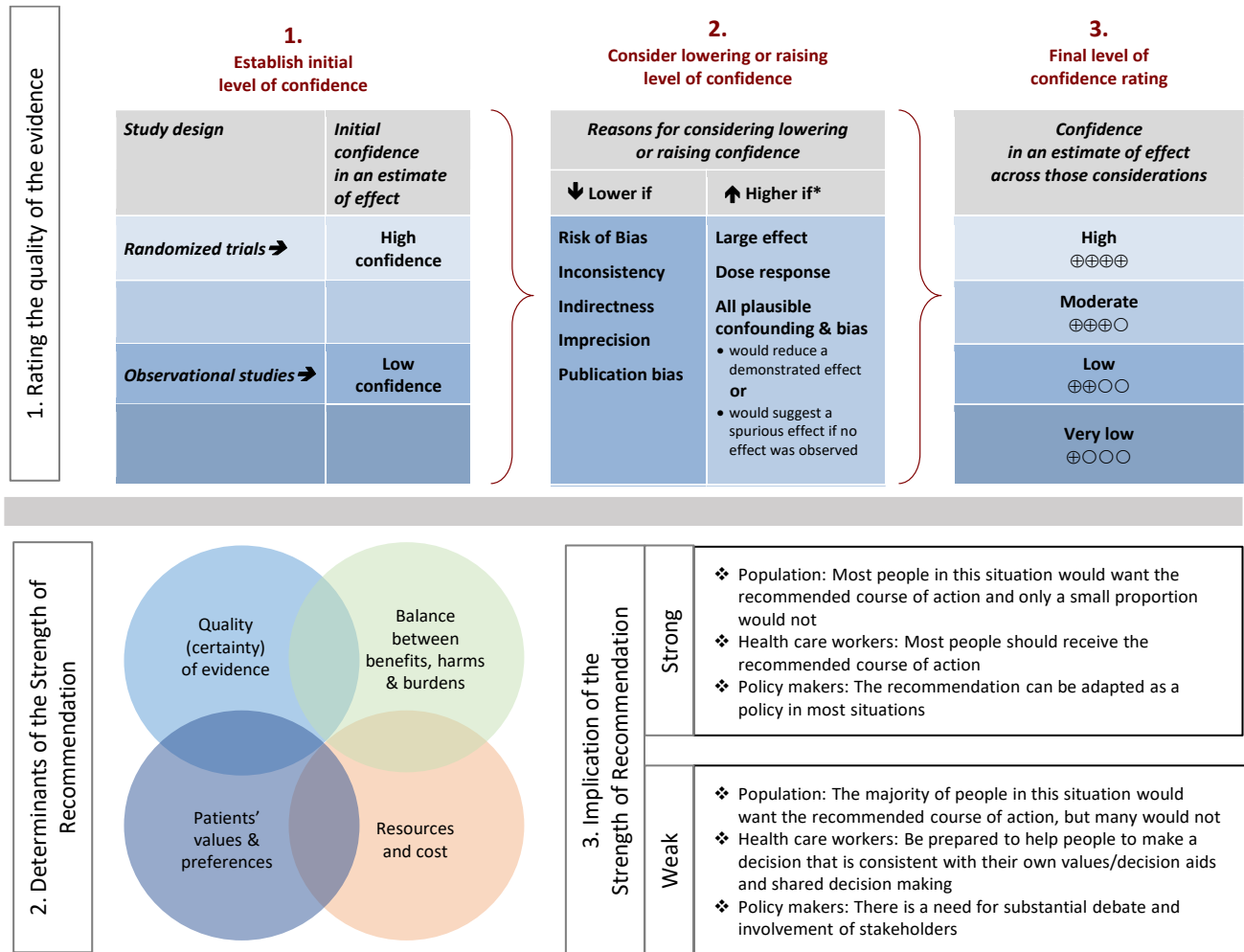
Figure 1. Detection of SARS-CoV-2 antibodies after symptom onset in patients with COVID-19. Panel a: Sensitivity of detection of anti-nucleocapsid (N) and anti-spike (S) antibodies over time, stratified by antibody class. Panel b: Sensitivity of assays that detect SARS-CoV-2 IgG, IgM, IgM/IgG, and total antibody over time, stratified by antibody target.



Methods

- Approach and implications to rating the quality of evidence and strength of recommendations using the GRADE methodology

Figure 2. Approach and implications to rating the quality of evidence and strength of recommendations using the GRADE methodology (unrestricted use of the figure granted by the U.S. GRADE Network)



Recommendations

Serology testing in the first two weeks after symptom onset

- Performance of IgM Serology testing 1 and 2 weeks after onset of COVID-19 symptoms
- Performance of IgG Serologic testing 1 and 2 weeks after onset of COVID-19 symptoms
- Performance of IgM or IgG Serologic testing 1 and 2 weeks after onset of COVID-19 symptoms

Table 1a. Performance of IgM Serology testing 1 and 2 weeks after onset of COVID-19 symptoms

IgM	Week 1			Week 2		
Sensitivity	27% (95% CI: 22 to 34)			64% (95% CI: 58 to 70)		
Specificity	99% (95% CI: 98 to 99)			99% (95% CI: 98 to 100)		
Outcome	Effect per 1,000 patients tested					
	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a
True positives (patients with COVID-19)	14 (11 to 17)	54 (44 to 68)	135 (110 to 170)	32 (29 to 35)	128 (116 to 140)	320 (290 to 350)
False negatives (patients incorrectly classified as not having COVID-19)	36 (33 to 39)	146 (132 to 156)	365 (330 to 390)	18 (15 to 21)	72 (60 to 84)	180 (150 to 210)
Quality of the evidence	50 studies, 2464 patients ⊕⊕○○ Low ^{b,c}			52 studies, 3481 patients ⊕⊕○○ Low ^{b,c}		
	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a
True negatives (patients without COVID-19)	941 (931 to 941)	792 (784 to 792)	495 (490 to 495)	941 (931 to 950)	792 (784 to 800)	495 (490 to 500)
False positives (patients incorrectly classified as having COVID-19)	9 (9 to 19)	8 (8 to 16)	5 (5 to 10)	9 (0 to 19)	8 (0 to 16)	5 (0 to 10)
Quality of Evidence	50 studies, 10077 patients ⊕⊕⊕○ Moderate ^c			52 studies, 9956 patients ⊕⊕⊕○ Moderate ^c		

Explanations

- 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- Unexplained inconsistency in the sensitivity results.
- The population from the studies was mainly unvaccinated individuals and those without a prior known history of COVID-19, which may overestimate test accuracy within vaccinated or previously infected populations.

Table 1b. Performance of IgG Serologic testing 1 and 2 weeks after onset of COVID-19 symptoms

IgG	Week 1			Week 2		
Sensitivity	24% (95% CI: 19 to 30)			66% (95% CI: 62 to 69)		
Specificity	99% (95% CI: 99 to 99)			99% (95% CI: 99 to 99)		
Outcome	Effect per 1,000 patients tested					
	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a
True positives (patients with COVID-19)	12 (10 to 15)	48 (38 to 60)	120 (95 to 150)	33 (31 to 34)	132 (124 to 138)	330 (310 to 345)
False negatives (patients incorrectly classified as not having COVID-19)	38 (35 to 40)	152 (140 to 162)	380 (350 to 405)	17 (16 to 19)	68 (62 to 76)	170 (155 to 190)
Quality of the evidence	88 studies, 4250 patients ⊕⊕○○ Low ^{b,c}			90 studies, 5161 patients ⊕⊕○○ Low ^{b,c}		
	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a
True negatives (patients without COVID-19)	941 (941 to 941)	792 (792 to 792)	495 (495 to 495)	941 (941 to 941)	792 (792 to 792)	495 (495 to 495)
False positives (patients incorrectly classified as having COVID-19)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)
Quality of Evidence	88 studies, 22321 patients ⊕⊕⊕○ Moderate ^c			90 studies, 19982 patients ⊕⊕⊕○ Moderate ^c		

Explanations

- 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- Unexplained inconsistency in the sensitivity results.
- The population from the studies was mainly unvaccinated individuals and those without a prior known history of COVID-19, which may overestimate test accuracy within vaccinated or previously infected populations.

Table 1c. Performance of IgM or IgG Serologic testing 1 and 2 weeks after onset of COVID-19 symptoms

IgM or IgG	Week 1			Week 2		
Sensitivity	35% (95% CI: 27 to 44)			74% (95% CI: 69 to 79)		
Specificity	98% (95% CI: 96 to 99)			98% (95% CI: 96 to 99)		
Outcome	Effect per 1,000 patients tested					
	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a
True positives (patients with COVID-19)	17 (14 to 22)	70 (54 to 88)	175 (135 to 220)	37 (34 to 40)	148 (138 to 158)	370 (345 to 395)
False negatives (patients incorrectly classified as not having COVID-19)	33 (28 to 36)	130 (112 to 146)	325 (280 to 365)	13 (10 to 16)	52 (42 to 62)	130 (105 to 155)
Quality of the evidence	28 studies, 1137 patients ⊕⊕○○ Low ^{b,c}			28 studies, 1685 patients ⊕⊕○○ Low ^{b,c}		
	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a	pre-test probability of 5% ^a	pre-test probability of 20% ^a	pre-test probability of 50% ^a
True negatives (patients without COVID-19)	931 (912 to 941)	784 (768 to 792)	490 (480 to 495)	931 (912 to 941)	784 (768 to 792)	490 (480 to 495)
False positives (patients incorrectly classified as having COVID-19)	19 (9 to 38)	16 (8 to 32)	10 (5 to 20)	19 (9 to 38)	16 (8 to 32)	10 (5 to 20)
Quality of Evidence	28 studies, 4466 patients ⊕⊕⊕○ Moderate ^c			28 studies, 4388 patients ⊕⊕⊕○ Moderate ^c		

Explanations

- 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- Unexplained inconsistency in the sensitivity results.
- The population from the studies was mainly unvaccinated individuals and those without a prior known history of COVID-19, which may overestimate test accuracy within vaccinated or previously infected populations.

Serology testing to assess previous SARS-CoV-2 infection – antibody class

- Performance of IgM Serologic testing in weeks 3 to 8 after onset of COVID-19 symptoms
- Performance of IgG Serologic tests weeks 3 to 8 after onset of COVID-19 symptoms
- Performance of IgM or IgG Serologic tests 3 to 8 weeks after onset of COVID-19 symptoms
- Performance of total antibodies Serologic tests weeks 3 to 8 after onset of COVID-19 symptoms

Table 2a. Performance of IgM Serologic testing in weeks 3 to 8 after onset of COVID-19 symptoms

IgM	Week 3			Week 4			Week 5			Week 6			Week 7			Week 8		
Outcome	Effect per 1,000 patients tested																	
	5% ^a	20% ^a	50% ^a	5% ^a	20% ^a	50% ^a	5% ^a	20% ^a	50% ^a	5% ^a	20% ^a	50% ^a	5% ^a	20% ^a	50% ^a	5% ^a	20% ^a	50% ^a
Sensitivity	83% (95% CI: 74 to 90)			86% (95% CI: 75 to 93)			89% (95% CI: 75 to 96)			85% (95% CI: 75 to 91)			73% (95% CI: 60 to 83)			73% (95% CI: 62 to 82)		
Specificity	99% (95% CI: 98 to 100)			99% (95% CI: 97 to 100)			99% (95% CI: 97 to 100)			99% (95% CI: 94 to 100)			100% (95% CI: 31 to 100)			99% (95% CI: 57 to 100)		
True positives (patients with COVID-19)	42 (37 to 45)	16 (14 to 18)	415 (370 to 450)	43 (38 to 47)	172 (150 to 186)	430 (375 to 465)	45 (38 to 48)	178 (150 to 192)	445 (375 to 480)	43 (38 to 46)	170 (150 to 182)	425 (375 to 455)	37 (30 to 42)	146 (120 to 166)	365 (300 to 415)	37 (31 to 41)	146 (124 to 164)	365 (310 to 410)
False negatives (patients incorrectly classified as not having COVID-19)	8 (5 to 13)	34 (20 to 52)	85 (50 to 130)	7 (3 to 12)	28 (14 to 50)	70 (35 to 125)	5 (4 to 12)	22 (8 to 50)	55 (25 to 100)	7 (4 to 12)	30 (18 to 50)	75 (45 to 125)	13 (8 to 20)	54 (34 to 80)	135 (85 to 200)	13 (9 to 19)	54 (36 to 76)	135 (90 to 190)
Quality of the evidence	33 studies, 2054 patients ⊕⊕○○ Low ^{b,c}			17 studies, 1211 patients ⊕⊕○○ Low ^{b,c}			10 studies, 890 patients ⊕⊕○○ Low ^{b,c}			10 studies, 693 patients ⊕⊕○○ Low ^{b,c}			4 studies, 337 patients ⊕⊕○○ Low ^{b,c}			4 studies, 328 patients ⊕⊕○○ Low ^{b,c}		
True negatives (patients without COVID-19)	94 (93 to 95)	792 (784 to 800)	495 (490 to 500)	941 (922 to 950)	792 (776 to 800)	495 (485 to 500)	941 (922 to 950)	792 (776 to 800)	495 (485 to 500)	941 (922 to 950)	792 (776 to 800)	495 (485 to 500)	941 (922 to 950)	792 (776 to 800)	495 (485 to 500)	941 (922 to 950)	792 (776 to 800)	495 (485 to 500)
False positives (patients incorrectly classified as having COVID-19)	9 (9 to 9)	8 (0 to 16)	5 (0 to 10)	9 (0 to 28)	8 (0 to 24)	5 (0 to 15)	9 (0 to 28)	8 (0 to 24)	5 (0 to 15)	9 (0 to 28)	8 (0 to 24)	5 (0 to 15)	9 (0 to 28)	8 (0 to 24)	5 (0 to 15)	9 (0 to 28)	8 (0 to 24)	5 (0 to 15)
Quality of Evidence	33 studies, 7640 patients ⊕⊕⊕○ Moderate ^c			17 studies, 5095 patients ⊕⊕⊕○ Moderate ^c			10 studies, 2457 patients ⊕⊕⊕○ Moderate ^c			10 studies, 3687 patients ⊕⊕⊕○ Moderate ^c			4 studies, 552 patients ⊕⊕⊕○ Moderate ^c			4 studies, 1919 patients ⊕⊕⊕○ Moderate ^c		

Explanations

- a. 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- b. Unexplained inconsistency in the sensitivity results

- c. These studies were conducted mainly with populations who had not been vaccinated and before emergence of currently circulating viral variants. Therefore, the estimates presented above may overestimate test accuracy in contemporary populations with high seroprevalence to SARS-CoV-2.

Table 2b. Performance of IgG Serologic tests weeks 3 to 8 after onset of COVID-19 symptoms

IgG	Week 3			Week 4			Week 5			Week 6			Week 7			Week 8		
Sensitivity	89% (95% CI: 85 to 92)			95% (95% CI: 90 to 98)			95% (95% CI: 90 to 98)			97% (95% CI: 91 to 99)			92% (95% CI: 88 to 95)			94% (95% CI: 85 to 98)		
Specificity	99% (95% CI: 99 to 99)			99% (95% CI: 98 to 0.99)			99% (95% CI: 98 to 0.99)			99% (95% CI: 98 to 100)			99% (95% CI: 98 to 100)			99% (95% CI: 97 to 100)		
Outcome	Effect per 1,000 patients tested																	
	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a
True positives (patients with COVID-19)	45 (43 to 46)	178 (170 to 184)	445 (425 to 460)	48 (45 to 49)	190 (180 to 196)	475 (450 to 490)	48 (45 to 49)	190 (180 to 196)	475 (450 to 490)	49 (46 to 50)	194 (182 to 198)	485 (455 to 495)	46 (44 to 48)	184 (176 to 190)	460 (440 to 475)	47 (43 to 49)	188 (170 to 196)	470 (425 to 490)
False negatives (patients incorrectly classified as not having COVID-19)	5 (4 to 7)	22 (16 to 30)	55 (40 to 75)	2 (1 to 5)	10 (4 to 20)	25 (10 to 50)	2 (1 to 5)	10 (4 to 20)	25 (10 to 50)	1 (0 to 4)	6 (2 to 18)	15 (5 to 45)	4 (2 to 6)	16 (10 to 25)	40 (25 to 60)	3 (1 to 7)	12 (4 to 30)	30 (10 to 75)
Quality of the evidence	47 studies, 2591 patients ⊕⊕○○ Low ^{b,c}			27 studies, 1545 patients ⊕⊕○○ Low ^{b,c}			16 studies, 918 patients ⊕⊕○○ Low ^{b,c}			14 studies, 832 patients ⊕⊕○○ Low ^{b,c}			5 studies, 246 patients ⊕⊕○○ Low ^{b,c}			3 studies, 251 patients ⊕⊕○○ Low ^{b,c}		
	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a
True negatives (patients without COVID-19)	94 (91 to 94)	792 (792 to 792)	495 (495 to 495)	94 (91 to 94)	792 (792 to 792)	495 (495 to 495)	94 (91 to 94)	792 (792 to 792)	495 (495 to 495)	94 (91 to 94)	792 (792 to 792)	495 (495 to 495)	94 (91 to 94)	792 (792 to 792)	495 (495 to 495)	94 (91 to 94)	792 (792 to 792)	495 (495 to 495)
False positives (patients incorrectly classified as having COVID-19)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)	9 (9 to 9)	8 (8 to 8)	5 (5 to 5)
Quality of Evidence	47 studies, 1053 patients ⊕⊕⊕○ Moderate ^c			27 studies, 6323 patients ⊕⊕⊕○ Moderate ^c			16 studies, 3240 patients ⊕⊕⊕○ Moderate ^c			14 studies, 3944 patients ⊕⊕⊕○ Moderate ^c			5 studies, 696 patients ⊕⊕⊕○ Moderate ^c			3 studies, 1082 patients ⊕⊕⊕○ Moderate ^c		

Explanations

- 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- Unexplained inconsistency in the sensitivity results
- These studies were conducted mainly with populations who had not been vaccinated and before emergence of currently circulating viral variants. Therefore, the estimates presented above may overestimate test accuracy in contemporary populations with high seroprevalence to SARS-CoV-2.

Table 2c. Performance of IgM or IgG Serologic tests 3 to 8 weeks after onset of COVID-19 symptoms

IgM or IgG	Week 3			Week 4			Week 5			Week 6			Week 7			Week 8			
Sensitivity	93% (95% CI: 88 to 96)			93% (95% CI: 83 to 98)			94% (95% CI: 88 to 97)			96% (95% CI: 80 to 99)			NR			NR			
Specificity	98% (95% CI: 96 to 99)			99% (95% CI: 94 to 100)			99% (95% CI: 95 to 100)			99% (95% CI: 89 to 100)			NR			NR			
Outcome	Effect per 1,000 patients tested																		
	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	
True positives (patients with COVID-19)	47 (44 to 48)	18 (6 to 17)	46 (44 to 48)	47 (42 to 49)	186 (66 to 96)	465 (115 to 90)	47 (44 to 49)	188 (176 to 194)	470 (440 to 485)	48 (40 to 50)	192 (160 to 198)	480 (400 to 495)	NR	NR	NR	NR	NR	NR	NR
False negatives (patients incorrectly classified as not having COVID-19)	3 (2 to 6)	14 (8 to 24)	35 (20 to 60)	3 (1 to 8)	14 (4 to 34)	14 (4 to 34)	3 (1 to 6)	12 (6 to 24)	30 (15 to 60)	2 (0 to 10)	8 (2 to 40)	20 (5 to 100)	NR	NR	NR	NR	NR	NR	NR
Quality of the evidence	17 studies, 646 patients ⊕⊕○○ Low ^{b,c}			6 studies, 363 patients ⊕⊕○○ Low ^{b,c}			6 studies, 442 patients ⊕⊕○○ Low ^{b,c}			3 studies, 91 patients ⊕⊕○○ Low ^{b,c}			NR			NR			
	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a
True negatives (patients without COVID-19)	93 (91 to 94)	784 (68 to 792)	490 (480 to 495)	941 (893 to 950)	792 (52 to 870)	495 (70 to 500)	941 (903 to 950)	792 (760 to 800)	495 (475 to 500)	941 (845 to 950)	792 (712 to 800)	495 (445 to 500)	NR	NR	NR	NR	NR	NR	NR
False positives (patients incorrectly classified as having COVID-19)	19 (9 to 38)	16 (8 to 32)	10 (5 to 20)	9 (0 to 57)	8 (0 to 48)	5 (0 to 30)	9 (0 to 47)	8 (0 to 40)	5 (0 to 25)	9 (0 to 10)	8 (0 to 88)	5 (0 to 55)	NR	NR	NR	NR	NR	NR	NR
Quality of Evidence	17 studies, 3075 patients ⊕⊕⊕○ Moderate ^c			6 studies, 1344 patients ⊕⊕⊕○ Moderate ^c			6 studies, 950 patients ⊕⊕⊕○ Moderate ^c			3 studies, 450 patients ⊕⊕⊕○ Moderate ^c			NR			NR			

Explanations

- 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- Unexplained inconsistency in the sensitivity results
- These studies were conducted mainly with populations who had not been vaccinated and before emergence of currently circulating viral variants. Therefore, the estimates presented above may overestimate test accuracy in contemporary populations with high seroprevalence to SARS-CoV-2.

Table 2d. Performance of total antibodies Serologic tests weeks 3 to 8 after onset of COVID-19 symptoms

Total Antibodies	Week 3			Week 4			Week 5			Week 6			Week 7			Week 8		
Sensitivity	92% (95% CI: 88 to 94)			95% (95% CI: 92 to 97)			95% (95% CI: 91 to 97)			96% (95% CI: 90 to 99)			88% (95% CI: 71 to 95)			NR		
Specificity	100% (95% CI: 99 to 100)			99% (95% CI: 99 to 100)			99% (95% CI: 98 to 100)			99% (95% CI: 98 to 100)			100% (95% CI: 87 to 100)			NR		
Outcome	Effect per 1,000 patients tested																	
	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a
True positives (patients with COVID-19)	46 (44 to 47)	18 (4 to 17 to 6 to 188)	460 (440 to 470)	48 (46 to 49)	190 (184 to 194)	475 (460 to 485)	48 (46 to 49)	190 (182 to 194)	475 (455 to 485)	48 (45 to 50)	192 (180 to 198)	480 (450 to 495)	44 (36 to 48)	176 (142 to 190)	440 (355 to 475)	NR	NR	NR
False negatives (patients incorrectly classified as not having COVID-19)	4 (3 to 6)	16 (12 to 24)	40 (30 to 60)	2 (1 to 4)	10 (6 to 16)	25 (15 to 40)	2 (1 to 4)	10 (6 to 18)	25 (15 to 45)	2 (0 to 5)	8 (2 to 20)	20 (5 to 50)	6 (2 to 14)	24 (10 to 58)	60 (25 to 145)	NR	NR	NR
Quality of the evidence	23 studies, 1177 patients ⊕⊕○○ Low ^{b,c}			14 studies, 706 patients ⊕⊕⊕○ Moderate ^c			11 studies, 479 patients ⊕⊕⊕○ Moderate ^c			8 studies, 239 patients ⊕⊕⊕○ Moderate ^c			3 studies, 44 patients ⊕⊕⊕○ Moderate ^c			NR		
	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a	5%^a	20%^a	50%^a
True negatives (patients without COVID-19)	95 (90 to 94 to 1 to 950)	800 (700 to 800)	500 (495 to 500)	941 (941 to 950)	792 (792 to 800)	495 (495 to 500)	941 (931 to 950)	792 (784 to 800)	495 (490 to 500)	941 (931 to 950)	792 (784 to 800)	495 (490 to 500)	950 (950 to 950)	800 (800 to 800)	500 (435 to 500)	NR	NR	NR
False positives (patients incorrectly classified as having COVID-19)	0 (0 to 9)	0 (0 to 8)	0 (0 to 5)	9 (0 to 9)	8 (0 to 8)	5 (0 to 5)	9 (0 to 19)	8 (0 to 16)	5 (0 to 10)	9 (0 to 19)	8 (0 to 16)	5 (0 to 10)	0 (0 to 123)	0 (0 to 104)	0 (0 to 65)	NR	NR	NR

Quality of Evidence	23 studies, 4991 patients	14 studies, 2949 patients	11 studies, 2109 patients	8 studies, 1558 patients	3 studies, 386 patients	NR
	⊕⊕⊕○	⊕⊕⊕○	⊕⊕⊕○	⊕⊕⊕○	⊕⊕⊕○	
	Moderate ^c	Moderate ^c	Moderate ^c	Moderate ^c	Moderate ^c	

Explanations

- a. 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission rates, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- b. Unexplained inconsistency in the sensitivity results
- c. These studies were conducted mainly with populations who had not been vaccinated and before emergence of currently circulating viral variants. Therefore, the estimates presented above may overestimate test accuracy in contemporary populations with high seroprevalence to SARS-CoV-2.

Serologic testing to assess previous SARS-CoV-2 Infection – antibody target

- Performance of IgM Serologic tests that target the spike versus nucleocapsid antigens
- Performance of IgG Serologic tests that target the spike versus nucleocapsid antigens

Table 3a. Performance of IgM Serologic tests that target the spike versus nucleocapsid antigens

	IgM Spike							IgM Nucleocapsid						
Sensitivity	69% (95% CI: 65 to 73)							63% (95% CI: 58 to 69)						
Specificity	100% (95% CI: 100 to 100)							100% (95% CI: 100 to 100)						
Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 5% ^a		pre-test probability of 20% ^a		pre-test probability of 50% ^a		
True positives (patients with COVID-19)	1 studies 909 patients ^b	case-control type studies	Not serious	serious ^c	not serious	serious ^d	none	34 (33 to 37)	32 (29 to 34)	13 (13 to 14)	126 (116 to 138)	34 (32 to 36)	315 (290 to 345)	⊕⊕ ○○ Low
False negatives (patients incorrectly classified as not having COVID-19)								2 more TP in IgM Spike	12 more TP in IgM Spike	30 more TP in IgM Spike				
								16 (13 to 17)	18 (16 to 21)	62 (54 to 70)	74 (62 to 84)	15 (13 to 17)	185 (155 to 210)	
								2 fewer FN in IgM Spike	12 fewer FN in IgM Spike	30 fewer FN in IgM Spike				
True negatives (patients without COVID-19)	1 studies 1478 patients ^e	case-control type studies	Not serious	serious ^c	not serious	serious ^d	none	950 (950 to 950)	950 (950 to 950)	800 (800 to 800)	800 (800 to 800)	500 (500 to 500)	500 (500 to 500)	⊕⊕ ○○ Low

COVID-19)								0 fewer TN in IgM Spike	0 fewer TN in IgM Spike	0 fewer TN in IgM Spike	
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	
								0 fewer FP in IgM Spike	0 fewer FP in IgM Spike	0 fewer FP in IgM Spike	

Explanations

- 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission levels, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- Out of the 909 patients, 606 samples were tested for IgM Spike and 303 were tested for IgM nucleocapsid
- There is no indirectness of comparison since these studies compared the two targets within the same population and assay. However, the population from the studies is mainly individuals with pre-vaccination, and pre-currently circulating variants infection, which may overestimate the test accuracy in contemporary populations.
- Serious imprecision due to low number of studies and events.
- Out of the 14,778 patients, 9852 samples were tested for IgM anti-spike antibodies and 4926 were tested for IgM anti-nucleocapsid antibodies.

Table 3b. Performance of IgG Serologic tests that target the spike versus nucleocapsid antigens

	IgG Spike							IgG Nucleocapsid						
Sensitivity	69% (95% CI: 49 to 84)							75% (95% CI: 58 to 87)						
Specificity	99% (95% CI: 99 to 100)							99% (95% CI: 98 to 99)						
Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 5% ^a		pre-test probability of 20% ^a		pre-test probability of 50% ^a		
							IgG Spike	IgG Nucleocapsid	IgG Spike	IgG Nucleocapsid	IgG Spike	IgG Nucleocapsid		
True positives (patients with COVID-19)	6 studies (2379 patients) ^b	case-control type accuracy study	not serious	serious ^c	serious ^d	not serious	none	34 (25 to 42)	38 (29 to 44)	13 (8 to 16)	150 (116 to 174)	34 (24 to 42)	375 (290 to 435)	⊕⊕ ○○ Low
								4 fewer TP in IgG Spike		12 fewer TP in IgG Spike		30 fewer TP in IgG Spike		
								16 (8 to 25)	12 (6 to 21)	62 (32 to 102)	50 (26 to 84)	15 (8 to 25)	125 (65 to 210)	
False negatives (patients incorrectly classified as not having COVID-19)								4 more FN in IgG Spike		12 more FN in IgG Spike		30 more FN in IgG Spike		
True negatives (patients without COVID-19)	6 studies (21495 patients) ^e	cohort & case-control type studies	not serious	serious ^c	not serious	not serious	none	94 (94 to 95)	941 (931 to 941)	79 (79 to 80)	792 (784 to 792)	49 (49 to 50)	495 (490 to 495)	⊕⊕ ⊕○ Moderate
								0 fewer TN in IgG Spike		0 fewer TN in IgG Spike		0 fewer TN in IgG Spike		

False positives (patients incorrectly classified as having COVID-19)								9 (0 to 9)	9 (9 to 19)	8 (0 to 8)	8 (8 to 16)	5 (0 to 5)	5 (5 to 10)	
								0 fewer FP in IgG Spike	0 fewer FP in IgG Spike	0 fewer FP in IgG Spike				

Explanations

- a. 5%, 20% and 50% pre-test probabilities were used to account for low and moderate community transmission levels, for cases of known close contact (e.g., household contacts), and for outbreaks or surges of highly transmissible variants (e.g., first Omicron surge).
- b. Out of the 2379 patient samples, 1339 samples were tested for IgM anti-spike antibodies and 1040 were tested for IgM anti-nucleocapsid antibodies
- f. There is no indirectness of comparison since these studies compared the two targets within the same population and assay. However, the population from the studies is mainly individuals pre-vaccination, and pre-infection with currently circulating variants, which may overestimate the test accuracy in contemporary populations.
- c. Unexplained inconsistency in the sensitivity results
- d. Out of the 21,495 patient samples, 13,194 samples were tested for IgM anti-spike antibodies and 8301 were tested for IgM anti-nucleocapsid antibodies.