Thieme

Cost-effectiveness analysis of SARS-CoV-2 infection prevention strategies including pre-endoscopic virus testing and use of high risk personal protective equipment

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submitted 8.7.2020
accepted after revision 20.10.2020
published online 20.10.2020

Bibliography
Endoscopy 2021; 53: 156–161
DOI 10.1055/a-1294-0427
ISSN 0013-726X

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Figs. 1s – 4s, Tables 1s – 4s
Supplementary material is available under https://doi.org/10.1055/a-1294-0427

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ABSTRACT

Background Infection prevention strategies to protect healthcare workers in endoscopy units during the post-peak phase of the COVID-19 pandemic are currently under intense discussion. In this paper, the cost-effectiveness of routine pre-endoscopy testing and high risk personal protective equipment (PPE) is addressed.

Method A model based on theoretical assumptions of 10 000 asymptomatic patients presenting to a high volume center was created. Incremental cost-effectiveness ratios (ICERs) and absolute costs per endoscopy were calculated using a Monte Carlo simulation.

Results ICER values for universal testing decreased with increasing prevalence rates. For higher prevalence rates (≥ 1 %), ICER values were lowest for routine pre-endoscopy testing coupled with use of high risk PPE, while cost per endoscopy was lowest for routine use of high risk PPE without universal testing.

Conclusion In general, routine pre-endoscopy testing combined with high risk PPE becomes more cost-effective with rising prevalence rates of COVID-19.

Introduction

In the post-peak phase of the COVID-19 pandemic, various strategies for a return to normal have been under discussion, with the aim of protecting healthcare workers (HCWs) and patients from infection [1]. Return strategies could be complicated by the fact that up to 40 % of patients may remain asymptomatic [2 – 4].

One option for a return to normalcy would be routine pre-endoscopy virus testing, especially if it is quickly available, e. g. as a point-of-care (POC) test with sufficient sensitivity [5]. Test-

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ing could be coupled with the use of high risk personal protective equipment (PPE) including FFP-2 masks, as well as a pre-endoscopy risk-assessment questionnaire [6, 7]. However, there is a discrepancy among the recommendations published by international societies, especially with regards to the indication for pre-endoscopic virus testing and its consequences on the extent of PPE [7, 8]. Also, some institutions may not have the capacity to ensure the consequential virus testing of all patients prior to an endoscopic intervention.

The cost-effectiveness of using pre-endoscopic testing and extensive PPE use for all patients is at least questionable. In this paper, we present a cost-effectiveness analysis of pre-endoscopy testing strategies for asymptomatic patients in a large volume tertiary care endoscopy unit.

Methods

We analyzed and compared costs, effects, and incremental cost-effectiveness ratios (ICERs) for eight pre-endoscopy virus testing and infection protection strategies (▶ **Table 1**). We assumed that all patients presenting for endoscopy would undergo a pre-screening questionnaire for clinical signs of COVID-19, after which symptomatic patients were excluded (**Fig. 1s**, see online-only Supplementary Material).

Costs

Costs comprised of PPE, laboratory costs, personnel costs, economic costs, quarantine costs, and loss of labor costs associated with infection of HCW (**Tables 1s – 3s**).

Effect

Effect was the number of patients who tested positive in pre-endoscopy virus testing. This is as an indirect marker for the quality of infection prevention and control because test-positive patients were either postponed or treated with high risk PPE. The sensitivity and specificity of the testing strategies are shown in ▶ **Table 2** [9 – 11].

Incremental cost-effectiveness ratio (ICER)

The ICER was calculated by comparing the costs and effect with a control strategy that involved neither pre-endoscopic virus testing nor routine use of FFP-2 masks (Strategy 1).

ICER = (C1 – C2)/(E1 – E2), where C = cost and E = effect.

Data analysis

A Monte Carlo simulation for four different prevalence rates (0.01 %, 0.1 %, 1 %, and 5 %) and based on 10 000 asymptomatic patients, 20 full-time HCWs with two FFP-2 masks per day, and 250 working days was performed (**Fig. 2s**). Results were reported using the Laplace, minimin, and minimax rules.

▶ **Table 1** Infection prevention and control strategies used for the cost-effectiveness analysis. High risk PPE included FFP-2 masks, goggles, and water-resistant gowns, while low risk PPE included surgical/medical face masks, apron, and gloves.

Strategy 1	**No routine pre-endoscopy virus test; use of surgical masks, goggles, gloves, and apron for all procedures**
Strategy 2	No routine pre-endoscopy virus test; additional use of FFP-2 and water-resistant gowns for all procedures
Strategy 3	Decentralized POC antigen test; use of surgical masks, goggles, gloves, and apron for all procedures
Strategy 4	Decentralized POC antigen test; additional use of FFP-2 and water-resistant gowns for all procedures irrespective of test result
Strategy 5	Centralized laboratory-based rapid PCR test[1]; use of surgical masks, goggles, gloves, and apron for all procedures
Strategy 6	Centralized laboratory-based rapid PCR test[1]; additional use of FFP-2 and water-resistant gowns for all procedures irrespective of test result
Strategy 7	Centralized laboratory-based standard PCR test[2]; use of surgical masks, goggles, gloves, and apron for all procedures
Strategy 8	Centralized laboratory-based standard PCR test[2]; additional use of FFP-2 and water-resistant gowns for all procedures irrespective of test result

PPE, personal protective equipment; POC, point of care.
[1] e. g. Xpert Xpress SARS-CoV-2; Cepheid, USA.
[2] e. g. cobas SARS-CoV-2; Roche diagnostics, Switzerland.

▶ **Table 2** Diagnostic accuracy and 95 % confidence interval (CI) of the tests used in the model [9 – 11].

	Standard PCR: Cobas Assay	Rapid PCR: Xpert Cepheid	Rapid antigen test
Sensitivity (95 %CI)	97 % (92.5 % – 97.5 %)	95 % (92.5 % – 97.5 %)	57.60 % (48.3 % – 60 %)
Specificity (95 %CI)	100 % (96.1 % – 99.9 %)	100 % (96.1 % – 99.9 %)	100 % (97.85 %-99.9 %)

PCR, polymerase chain reaction.

▶ **Table 3** Calculation of total costs for each strategy (in euros).

	1 No diagnostic test, no high risk PPE	2 No diagnostic test, high risk PPE	3 Antigen test, no high risk PPE	4 Antigen test, high risk PPE	5 Rapid PCR, no high risk PPE	6 Rapid PCR, high risk PPE	7 PCR, no high risk PPE	8 PCR, high risk PPE
Laboratory, personnel, economic costs, €	0	0	173 000	173 000	1 678 500	1 678 500	2 733 500	2 733 500
Costs of PPE, €	0	107 200	0	107 200	0	107 200	0	107 200
Test-positive cases, n[1]	0	0	5.76	5.76	9.5	9.5	9.7	9.7
False-negative cases, n[1]	10	10	4.24	4.24	0.5	0.5	0.3	0.3
Costs of quarantine and PCR testing of exposed HCWs for 14 days, €[2]	136 092	0	57 764	0€	6 905	0€	4 186	0
Costs of infected HCWs and PCR testing for up to 28 days sick leave, €[2]	21 927	2 730	9 297	1 158	1 096	137	658	82
Total costs, €	158 019[3]	109 930	240 061[3]	281 358	1 686 502[3]	1 785 837	2 738 343[3]	2 840 782

PPE, personal protective equipment; PCR, polymerase chain reaction; HCW, healthcare worker.
[1] Dependent on diagnostic yield of test.
[2] Quarantine costs, dependent on both diagnostic yield of tests and prevalence, were simulated for a total of 14 days, while labor costs associated with sick leave after infection of a HCW were simulated for a maximum time frame of 28 days, with costs including PCR tests during quarantine or sick leave.
[3] Dependent on both diagnostic yield of tests and prevalence.

Results

For 10 000 patients per year, 20 HCWs will use 10 000 FFP-2 masks (assuming a year has 250 working days and two masks are used per day). Exemplary for a prevalence rate of 0.1 %, ▶ **Table 3** shows the absolute total costs for 10 000 patients. Also included are the number of test-positive patients (effect), as well as the number of false-negative patients according to the sensitivities provided in ▶ **Table 2**. In order to consider stochastic effects and the range of diagnostic yields, further results for varying prevalence rates are shown after the Monte Carlo simulation (▶ **Table 4**).

ICER according to the Laplace rule

At a prevalence of 0.01 % and 0.1 %, the lowest ICER value was seen for strategy 3 (POC antigen test without routine high risk PPE use). When the prevalence rate increased to 1 % and 5 %, the lowest ICER value was seen for strategy 4 (POC antigen test with high risk PPE use).

ICER according to the minimin rule or the best-case scenario

The minimin rule uses the most favorable possible values in the simulation and produces results correlating to a low risk situation for a given set of values. For a prevalence rate of 0.01 %, the lowest ICER produced for the minimin rule was observed when strategy 3 (POC antigen test without routine high risk PPE use) was implemented. At higher prevalence rates of 0.1 %, 1 %, and 5 %, the lowest ICER value for the minimin rule was produced in strategy 4 (POC antigen test with high risk PPE use).

ICER according to the minimax rule or the worst-case scenario

The minimax rule uses the worst possible values and produces results correlating to a high risk situation for a given set of values. For a prevalence rate of 0.01 %, the lowest ICER was observed for strategy 3 (POC antigen test without routine FFP-2 use). At higher prevalence rates, the lowest ICER value was produced in strategy 4 (POC antigen test with high risk PPE use).

Costs per endoscopy according to the Laplace rule

At a prevalence of 0.01 %, the lowest cost per endoscopy was seen for strategy 1 (no routine pre-endoscopy test, no routine high risk PPE use). At a higher prevalence rate, the lowest cost per endoscopy was produced in strategy 2 (no routine pre-endoscopy test, high risk PPE use for all procedures) (▶ **Table 4**).

Costs per endoscopy according to the minimin rule or the best-case scenario

For a prevalence rate of 0.01 %, the lowest costs per endoscopy was observed for strategy 1 (no routine pre-endoscopy test, no routine high risk PPE use). At higher prevalence rates of 1 % and 5 %, the lowest costs per endoscopy were in strategy 2 (no routine pre-endoscopy test, high risk PPE use for all procedures).

▶ **Table 4** Results of the Monte Carlo simulation after 1000 iterations per prevalence setting showing the incremental cost – effectiveness ratios (ICERs) and costs per endoscopy (in euros) for four different prevalence rates of asymptomatic infections. The numbers in bold for the Laplace, Minimin and Minimax columns indicate the optimal strategy for each simulation setting. The confidence interval (CI) width marked in bold represents the strategy with the lowest variability across the iterations.

	Costs per endoscopy, €				**ICER**			
	Prevalence				**Prevalence**			
	0.01 %	**0.1 %**	**1 %**	**5 %**	**0.01 %**	**0.10 %**	**1 %**	**5 %**
Strategy 1								
▪ Laplace	**1.87**	18.57	185.56	927.76				
▪ Minimin	**0.85**	**8.41**	83.98	419.86				
▪ Minimax	**3.15**	31.39	313.79	1 568.89				
▪ CI width	1.65	16.53	165.29	826.45				
Strategy 2								
▪ Laplace	10.75	**11.04**	**13.93**	**26.76**				
▪ Minimin	10.73	10.87	**12.17**	**17.98**				
▪ Minimax	10.77	**11.26**	**16.15**	**37.85**				
▪ CI width	**0.03**	**0.29**	**2.86**	**14.29**				
Strategy 3								
▪ Laplace	18.11	25.16	95.84	409.97	**259 866**	**11 774**	−13 035	−15 240
▪ Minimin	17.67	20.86	52.85	195.01	**135 164**	−696	−14 282	−15 489
▪ Minimax	18.67	30.59	150.11	681.32	**548 296**	**40 617**	−10 150	−14 663
▪ CI width	0.72	7.00	69.96	349.78	**259 804**	**25 980**	**2 598**	**520**
Strategy 4								
▪ Laplace	28.03	28.16	29.38	34.81	419 121	17 451	**−22 716**	**−26 286**
▪ Minimin	28.03	28.08	28.63	31.09	217 224	**−2 739**	**−24 735**	**−26 690**
▪ Minimax	28.04	28.25	30.32	39.50	886 101	64 149	**−18 046**	**−25 352**
▪ CI width	**0.01**	**0.12**	**1.21**	**6.05**	420 634	42 063	4 206	841
Strategy 5								
▪ Laplace	167.95	168.68	176.03	208.71	1 597 820	145 570	345	−12 564
▪ Minimin	167.90	168.23	171.56	186.35	867 854	72 573	−6 955	−14 024
▪ Minimax	168.01	169.24	181.68	236.94	3 286 202	314 408	17 229	−9 187
▪ CI width	0.08	0.73	7.28	36.39	1 520 814	152 081	15 208	3 042
Strategy 6								
▪ Laplace	178.57	178.58	178.71	179.28	1 700,059	155 150	659	−13 073
▪ Minimin	178.57	178.58	178.63	178.89	923 519	77 496	−7 106	−14 626
▪ Minimax	178.57	178.59	178.81	179.76	3 496 165	334 761	18 621	−9 481
▪ CI width	**0.00**	**0.01**	**0.13**	**0.63**	1 617 847	161 785	16 178	3 236
Strategy 7								
▪ Laplace	273.47	274.31	282.89	321.02	2 632 347	249 022	10 690	−10 495
▪ Minimin	273.41	273.79	277.67	294.93	1 434,382	129 226	−1 290	−12 891
▪ Minimax	273.55	274.97	289.48	353.95	5 403 194	526 107	38 398	−4 953
▪ CI width	0.10	0.85	8.49	42.45	2 495 847	249 585	24 958	4 992

▶ **Table 4** (Continuation)

	Costs per endoscopy, €				ICER			
	Prevalence				Prevalence			
	0.01 %	0.1 %	1 %	5 %	0.01 %	0.10 %	1 %	5 %
Strategy 8								
▪ Laplace	284.07	284.09	284.23	284.89	2 735 256	258 557	10 887	−11 128
▪ Minimin	284.07	284.08	284.14	284.44	1 490 357	134 067	−1 562	−13 618
▪ Minimax	284.07	284.10	284.35	285.46	5 614 660	546 498	39 681	−5 369
▪ CI width	**0.00**	**0.01**	**0.15**	**0.73**	2 593 630	259 363	25 936	5 187

Costs per endoscopy according to the minimax rule or the worst-case scenario

For a prevalence rate of 0.01 %, the lowest cost per endoscopy was seen when strategy 1 (no routine pre-endoscopy test, no routine high risk PPE use) was implemented. At higher prevalence rates of 0.1 %, 1 %, and 5 %, the lowest cost per endoscopy was for strategy 2 (no routine pre-endoscopy test, high risk PPE use for all procedures).

Discussion

The data suggest that the lowest costs are accrued when no virus testing is done prior to endoscopy provided symptomatic patients or patients at higher risk of having COVID-19 are excluded.

In terms of the ICER, for low prevalence situations (0.01 % and 0.1 %), the ICER values were lowest when a strategy of POC antigen testing without the routine use of high risk PPE for all patients was implemented. However, for higher prevalence rates of 1 % and 5 %, the lowest ICER values were achieved with rapid POC antigen testing coupled with high risk PPE use for all patients. The high cost of PCR tests and their longer turnaround times seem to reduce their cost-effectiveness when compared with POC antigen tests. In general, however, it is obvious that, the higher the prevalence rate, the more cost-effective a pre-endoscopy virus testing strategy and the use of high risk PPE become (**Fig. 3s**).

For costs per endoscopy, at a very low prevalence of 0.01 %, no routine pre-endoscopy test coupled with standard PPE use produced the lowest costs per endoscopy. However, for prevalence rates between 0.1 % and 5 %, strategy 2, in which no pre-endoscopy test is done but FFP-2 masks are used with all patients, produced the lowest costs per endoscopy. This means that in terms of absolute numerical costs per endoscopy procedure, it does not seem to be effective to perform routine pre-endoscopy tests in all patients without taking clinical symptoms or risk-stratification history into consideration (**Fig. 4s**).

This study has a number of limitations. Even though we calculated the cost of labor lost during sick leave after exposure to COVID-19 based on infection probabilities provided by Chu et al [12], it remains a limitation that the costs of treating HCWs who may have contracted the virus cannot be exactly quantified. Furthermore, it is impossible to differentiate between the infection risks for the various endoscopy personnel who are present in the room but with different tasks, such as nurses and endoscopists.

Further limitations include the approximate values used to determine the costs, as well as the theoretical assumptions that had to be made in order to perform the cost-effectiveness analysis. The wide range of PPE costs seen across various regions was not taken into consideration. Also, we did not include the cost of surgical masks, goggles, and shields as we assumed that these were items that, in daily practice, are either reusable after disinfection or not particularly resource-sensitive. The cost of disinfection of rooms and the additional cost for the use of PPE for patients in the endoscopy unit were not taken into consideration either. In some countries, costs may not be a consideration and our study may apply especially to countries that have the economic power and possibilities of dynamic acquisition of PPE. However, in many other countries, the costs of testing may outweigh the reimbursement received for the procedure and this should also be taken into consideration.

Finally, published clinical data on the true sensitivity and specificity of the various test methods are lacking. Also, the positive or negative predictive values of the different tests were not used in the simulation, even though these values may influence the false-negative or false-positive results, depending on the prevalence rate.

In conclusion, in a theoretical model, routine pre-endoscopy virus testing and the concurrent use of high risk PPE, irrespective of patient risk, test results, and prevalence rate, is not generally cost-effective. In terms of ICER values, universal pre-endoscopy virus testing combined with the use of high risk PPE in all patients irrespective of test results becomes cost-effective when the prevalence rate among asymptomatic individuals rises to 1 % or more.

Competing interests

The authors declare that they have no conflict of interest.

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