

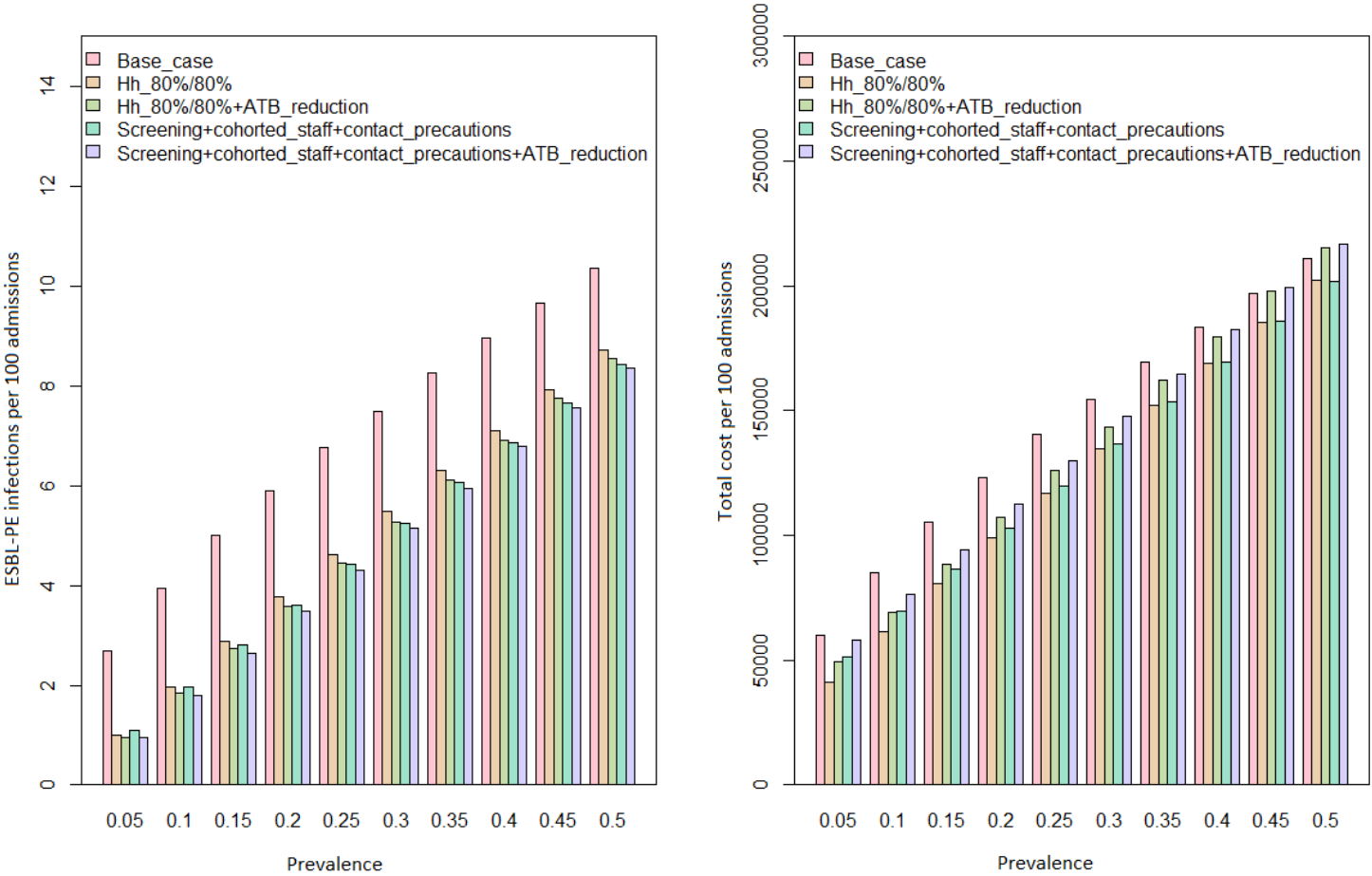
Supplementary material

Supplementary Text S2- Sensitivity analyses

1. Impact of prevalence on admission on health outcomes and costs

The prevalence of ESBL-PE carriage on ICU admission highly influenced health outcomes and costs (**Supplementary Figure S1**) as well as the ranking of the strategies (**Supplementary Table S1**). However, improvement of HH to 80%/80% (Strategy 2) remained the most cost saving strategy, if the prevalence on admission was from 5% to 50%. If 50% of patients carried ESBL-PE on ICU admission, Strategy 2 was dominated by screening + cohorting (Strategy 6).

Figure S1 Impact of prevalence on admission on the number of ESBL-PE infections and total cost of strategies for: (1) Base Case (reference strategy with no control intervention and hand hygiene compliance of 55%/60% before/after patient contact); (2) Hand hygiene improvement to 80%/80%; (6) Screening of all admissions and cohorting of identified carriers; (7) Hand hygiene improvement to 80%/80% and Antibiotic reduction; (10) Screening of all admissions, cohorting of identified carriers and Antibiotic reduction.



When the prevalence on admission was less than 15% the improvement of hand hygiene to 80%/80% (Strategy 2) was the most cost-saving strategy. The second strategy on the efficiency frontier was the combination of hand hygiene 80%/80% with antibiotic reduction (Strategy 7). When the prevalence was 15% the Strategy 10 (Screening + cohorting + ATB reduction) joined the efficiency frontier too. When the prevalence varied from 20% to 45%. Hand hygiene 80%/80% was always on the top of the ranking. followed by Screening + cohorting (Strategy 6) and Screening + cohorting + ATB reduction (Strategy 10). Finally, when 50% of patients carried ESBL-PE on ICU admission. hand hygiene was dominated by screening + cohorting (Strategy6).

Supplementary Table S1. Results of sensitivity analysis. Cost-effectiveness of strategies under **different levels of ESBL-PE carriage on admission**. The prevalence on admission varied from 0.05 to 0.5.

Strategy	Prevalence on admission	Total cost/ 100 admissions (€)	Infections/ 100 admissions	Incremental cost/100 admissions (ΔC) (€)	Incremental effect (ΔE) (infections avoided/100 admissions)	ICER (ΔC/ΔE) (€ / infection avoided)
2: Hh 80%/80%	0.05	41 225	1.01			
7: Hh 80%/80% + ATB reduction		49 639	0.94	8 414	0.07	120 200
6: Screening + cohorting		51 542	1.09			Dominated
10: Screening + cohorting + ATB reduction		58 218	0.94			Dominated by extended dominance
1: Base case		60 031	2.68			Dominated
2: Hh 80%/80%	0.15	80 556	2.89			
7: Hh 80%/80% + ATB reduction		88 498	2.73	7 942	0.16	49 638
10: Screening + cohorting + ATB reduction		94 313	2.63	5 815	0.09	64 611
6: Screening + cohorting		86 713	2.80			Dominated by extended dominance
1: Base case		105 344	4.99			Dominated

2: Hh 80%/80%	0.2	98 843	3.77			
6: Screening + cohorting		103 075	3.61	4 232	0.16	26 450
10: Screening + cohorting + ATB reduction		112 565	3.49	9 490	0.12	79 083
7: Hh 80%/80% + ATB reduction		107 275	3.59			Dominated by extended dominance
1: Base case		123 231	5.90			Dominated
6: Screening + cohorting	0.5	201 668	8.43			
10: Screening + cohorting + ATB reduction		216 470	8.36	14 802	0.07	211 457
2: Hh 80%/80%		202 288	8.72			Dominated
1: Base case		210 957	10.35			Dominated
7: Hh 80%/80% + ATB reduction		215 102	8.54			Dominated

2. Impact of **probability of infection** in patients colonized with ESBL-PE.

Results of sensitivity analysis for a lower and higher probability of infection in colonized ESBL-PE patients versus the basecase analysis are presented in **Supplementary Table S2 A and B**. Overall main results of our analysis were robust to variation in the probability of infection of colonized patients (8% or 30% vs. 16% in our central analysis).

Supplementary Table S2A Results of sensitivity analysis. Cost-effectiveness of strategies when **the probability of infection was set at 0.08**.

Strategy	Total cost/ 100 admissions (€)	Infections/ 100 admissions	Incremental cost/100 admissions (ΔC) (€)	Incremental effect (ΔE) (infections avoided/100 admissions)	ICER (ΔC/ΔE) (€ / infection avoided)
3: Hh 55%/80%	50 550	1.71			
2: Hh 80%/80%	52 428	1.41	1 878	0.304	6 178
7: Hh 80%/80% + ATB reduction	61 945	1.33	9 517	0.079	120 468
10: Screening + cohorting + ATB reduction	68 673	1.29	6 728	0.046	146 261
5: Screening + contact precautions	54 930	2.10			Dominated
1: Base case	56 792	2.43			Dominated
8: Hh 55%/80% + ATB reduction	58 173	1.53			Dominated by extended dominance
6: Screening + cohorting	59 424	1.37			Dominated by extended dominance
9: Screening + contact precautions + ATB reduction	59 706	1.74			Dominated
4: ATB reduction	60 360	1.99			Dominated

Supplementary Table S2B Results of sensitivity analysis. Cost-effectiveness of strategies when **the probability of infection was set at 0.30**.

Strategy	Total cost/ 100 admissions (€)	Infections/ 100 admissions	Incremental cost/100 admissions (ΔC) (€)	Incremental effect (ΔE) (infections avoided/100 admissions)	ICER ($\Delta C/\Delta E$) (€ / infection avoided)
2: Hh 80%/80%	126 096	5.29			
7: Hh 80%/80% + ATB reduction	131 487	4.99	5 391	0.300	17 970
10: Screening + cohorting + ATB reduction	135 825	4.82	4 338	0.170	25 518
6: Screening + cohorting	130 896	5.13			Dominated by extended dominance
8: Hh 55%/80% + ATB reduction	137 917	5.72			Dominated
3: Hh 55%/80%	140 124	6.43			Dominated
9: Screening + contact precautions + ATB reduction	150 335	6.50			Dominated
5: Screening + contact precautions	164 370	7.85			Dominated
4: ATB reduction	164 513	7.48			Dominated
1: Base case	183 951	9.13			Dominated

3. Impact of **lower compliance with HH** than in the base case scenario.

If the baseline compliance with HH was lower than in our core analysis. e.g. 20% before and 40% after patient contact. HH improvement. e.g. to 50%/60% was confirmed to be cost-saving. Screening + cohorting was the second strategy with an ICER of €3 236/infection avoided vs. HH improvement (**Supplementary Table S3A**).

Supplementary Table S3A Results of sensitivity analysis. Cost-effectiveness of strategies when the baseline compliance with **Hand hygiene was set to 20%/40% (instead of 55%/60%)**.

Strategy	Total cost/ 100 admissions (€)	Infections/ 100 admissions	Incremental cost/100 admissions (ΔC) (€)	Incremental effect (ΔE) (infections avoided/100 admissions)	ICER (ΔC/ΔE) (€ / infection avoided)
2: Hh 50%/60%	81 676	3.14			
6: Screening + cohorting	82 867	2.772	1 191	0.368	3 236
10: Screening + cohorting + ATB reduction	91 134	2.632	8 267	0.14	59 050
3: Hh 20%/60%	85 059	3.758			Dominated
8: Hh 20%/60% + ATB reduction	87 440	3.284			Dominated
7: Hh 50%/60% + ATB reduction	88 144	2.891			Dominated by extended dominance
9: Screening + contact precautions + ATB reduction	93 552	3.741			Dominated
4: ATB reduction	95 195	4.075			Dominated
5: Screening + contact precautions	97 350	4.571			Dominated
1: Base case Hh 20% 40%	100 905	5.02			Dominated

If the baseline compliance with HH was 40% before and 50% after patient contact. HH improvement. e.g. to 60%/70% was confirmed to be cost-saving. Screening + cohorting was the second strategy with an ICER of €546/infection avoided vs. HH improvement (**Supplementary Table S3B**).

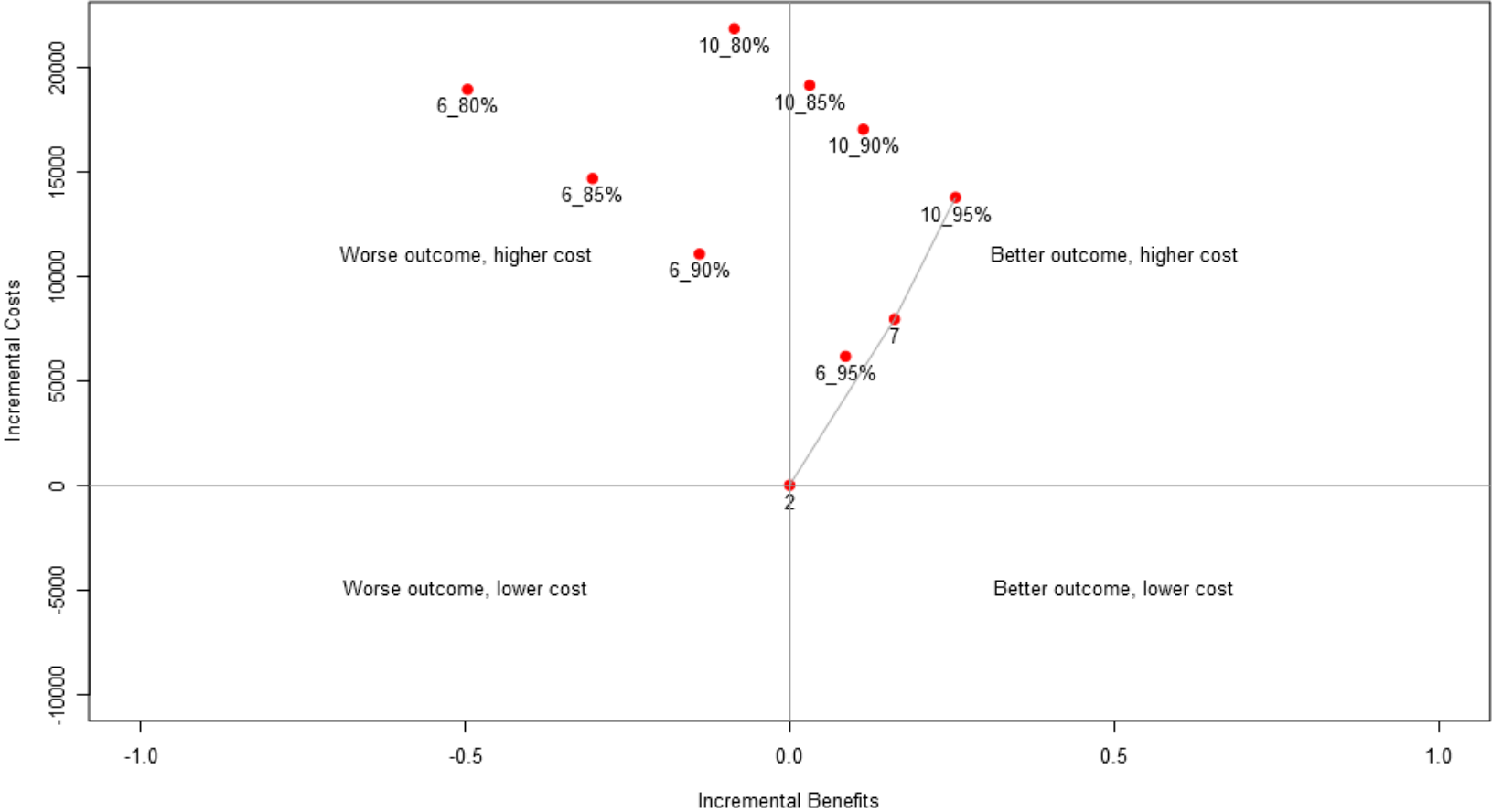
Supplementary Table S3B Results of sensitivity analysis. Cost-effectiveness of strategies when the baseline compliance with **Hand hygiene was set to 40%/50% (instead of 55%/60%)**.

Strategy	Total cost/ 100 admissions (€)	Infections/ 100 admissions	Incremental cost/100 admissions (ΔC) (€)	Incremental effect (ΔE) (infections avoided/100 admissions)	ICER (ΔC/ΔE) (€ / infection avoided)
2: Hh 60%/70%	84 331	3.191			
6: Screening + cohorted staff + contact precautions	84 561	2.77	230	0.421	546
10: Screening + cohorted staff + contact precautions + ATB reduction	92 803	2.629	8 242	0.141	58 454
3: Hh 40%/70%	86 359	3.698	0	0	Dominated
8: Hh 40%/70% + ATB reduction	89 451	3.26	0	0	Dominated
7: Hh 60%/70% + ATB reduction	91 171	2.96	0	0	Dominated by extended dominance
9: Screening + contact precautions + ATB reduction	96 676	3.78	0	0	Dominated
4: ATB reduction	98 264	4.099	0	0	Dominated
5: Screening + contact precautions	98 308	4.495	0	0	Dominated
1: Base case Hh 40%/50%	102 292	4.949	0	0	Dominated

4. Impact of lower **sensitivity to detect ESBL-PE carriage** in screening strategies.

If the sensitivity to detect ESBL-PE on ICU admission was lower than in our core analysis and varied from 80% to 95%. HH 80%/80% (Strategy 2) and HH 80%/80% and antibiotic reduction (Strategy 7) always dominated the screening strategies (Strategy 6 and 10) (**Supplementary Figure S2**).

Figure S2 Cost-effectiveness plane showing the incremental health benefits (infections avoided) and costs of screening and cohorting strategies relative to the Strategy 2. The sensitivity of detection of ESBL carriers at ICU admission in screening and isolation strategies varied from 80% to 95%. Strategies are: (2) Hand hygiene improvement to 80%/80%; (6) Screening of all admissions and cohorting of identified carriers; (7) Hand hygiene improvement to 80%/80% and Antibiotic reduction; (10) Screening of all admissions. cohorting of identified carriers and Antibiotic reduction.



Supplementary Table S4 Impact of a lower, 30% reduction in antibiotic prescribing.

Strategy	Total cost/ 100 admissions (€)	Infections/ 100 admissions	Incremental cost/100 admissions (ΔC) (€)	Incremental effect (ΔE) (infections avoided/100 admissions)	ICER (ΔC/ΔE) (€ / infection avoided)
2: Hh 80%/80%	80 556	2.890	0		
7: Hh 80%/80% + ATB reduction 30%	89 254	2.761	8 698	0.129	67 426
10: Screening + cohorted staff + contact precautions + ATB reduction 30%	95 343	2.680	6 089	0.081	75 173
3: Hh 55%/80%	84 751	3.514	0		
6: Screening + cohorted staff + contact precautions	86 713	2.804	0		
8: Hh 55%/80% + ATB reduction 30%	91 059	3.242	0		
5: Screening + contact precautions	96 716	4.294	0		
9: Screening + contact precautions + ATB reduction 30%	97 620	3.720	0		
4: ATB reduction 30%	104 271	4.285	0		
1: Base case	105 344	4.989	0		

Supplementary Table S5A Impact of infection control nurse’s time working on the hand hygiene program and the level of hand hygiene achieved on model predictions compared to the Base case strategy. The cost-effective ratio (CER) was calculated when the hand hygiene strategy was more expensive but more effective than the base case.

Level of hand hygiene before contact with patient (%)	Level of hand hygiene after contact with patient (%)	Mean increase in hand hygiene from baseline (%)	Number of infections /100 admissions	Total cost /100 admissions (€)	CER (vs base case)
Base case					
55	60	-	4.99	105 344	-
ICN working on Hh program at 1/4 time					
55	60	0.0	4.99	112 783	Hh strategy dominated by the Base case
60	60	2.5	4.65	106 497	3 433
55	65	2.5	4.64	106 366	2 965
60	65	5.0	4.29	99 722	Base case dominated by the Hh strategy
⋮	⋮	⋮	⋮	⋮	Base case dominated by the Hh strategy
80	80	22.5	2.89	74 103	Base case dominated by the Hh strategy
ICN working on Hh strategy at 1/2 time					
55	60	0.0	4.99	120 222	Hh strategy dominated by the Base case
60	60	2.5	4.65	113 789	25 146
55	65	2.5	4.64	113 675	24 160
60	65	5.0	4.29	106 861	2 182
65	65	7.5	4.02	101 484	Base case dominated by the Hh strategy
⋮	⋮	⋮	⋮	⋮	Base case dominated by the Hh strategy
80	80	22.5	2.89	80 556	Base case dominated by the Hh strategy
ICN working on Hh strategy at full time					
55	60	0.0	4.99	135 100	Hh strategy dominated by the Base case
60	60	2.5	4.65	128 375	68 573
55	65	2.5	4.64	128 292	66 551
60	65	5.0	4.29	121 137	22 712
65	65	7.5	4.02	115 442	10 397

55	70	5.0	4.22	119 423	18 278
60	70	7.5	3.98	114 488	9 029
65	70	10.0	3.75	110 092	3 823
70	70	12.5	3.53	105 942	411
55	75	7.5	3.85	111 932	5 806
60	75	10.0	3.68	108 574	2 468
65	75	12.5	3.51	105 357	9
70	75	15.0	3.32	101 754	Base case dominated by the Hh strategy
⋮	⋮	⋮	⋮	⋮	Base case dominated by the Hh strategy
80	80	22.5	2.89	93 462	Base case dominated by the Hh strategy

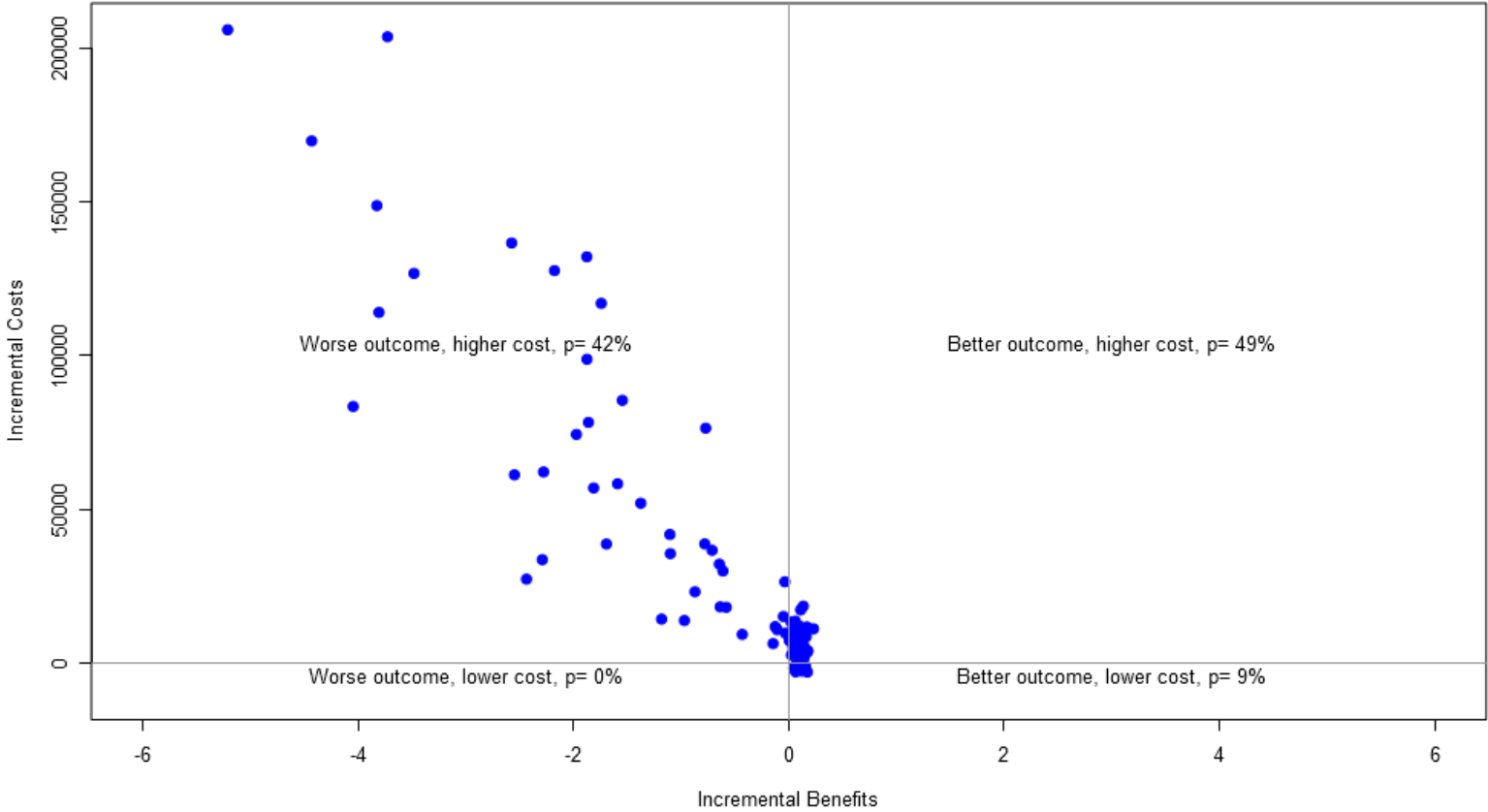
Supplementary Table S5B Impact of infection control nurse's time working on the hand hygiene strategy and the level of hand hygiene achieved on model predictions compared to the Screening and cohorting strategy. The cost-effective ratio (CER) was calculated when the screening and cohorting strategy was more expensive but more effective than the hand hygiene.

Level of hand hygiene before contact with patient (%)	Level of hand hygiene after contact with patient (%)	Mean increase in hand hygiene from baseline (%)	Number of infections/100 admissions	Total cost/100 admissions (€)	CER (vs Hand hygiene strategy)
Screening and cohorting					
55 (with non cohorted patients)	60 (with non cohorted patients)		2.80	86 713	
ICN working on Hh strategy at 1/4 time					
55	60	0.0	4.99	112 783	Hh strategy dominated by Screening and cohorting
⋮	⋮	⋮	⋮	⋮	Hh strategy dominated by Screening and cohorting
70	70	12.5	3.53	85 621	1 496
55	75	7.5	3.85	91 212	Hh strategy dominated by Screening and cohorting
60	75	10.0	3.68	88 104	Hh strategy dominated by Screening and cohorting
65	75	12.5	3.51	85 102	2 283
70	75	15.0	3.32	81 748	9 554
75	75	17.5	3.15	78 568	23 561
55	80	10.0	3.51	84 751	2 763
60	80	12.5	3.38	82 408	7 507
65	80	15.0	3.24	79 993	15 442
70	80	17.5	3.12	77 946	28 012
75	80	20.0	2.99	75 742	58 203
80	80	22.5	2.89	74 103	146 278
ICN working on Hh strategy at 1/2 time					
55	60	0.0	4.99	120 222	Hh strategy dominated by Screening and cohorting
⋮	⋮	⋮	⋮	⋮	Hh strategy dominated by Screening and cohorting
75	75	17.5	3.15	85 136	4 561 €

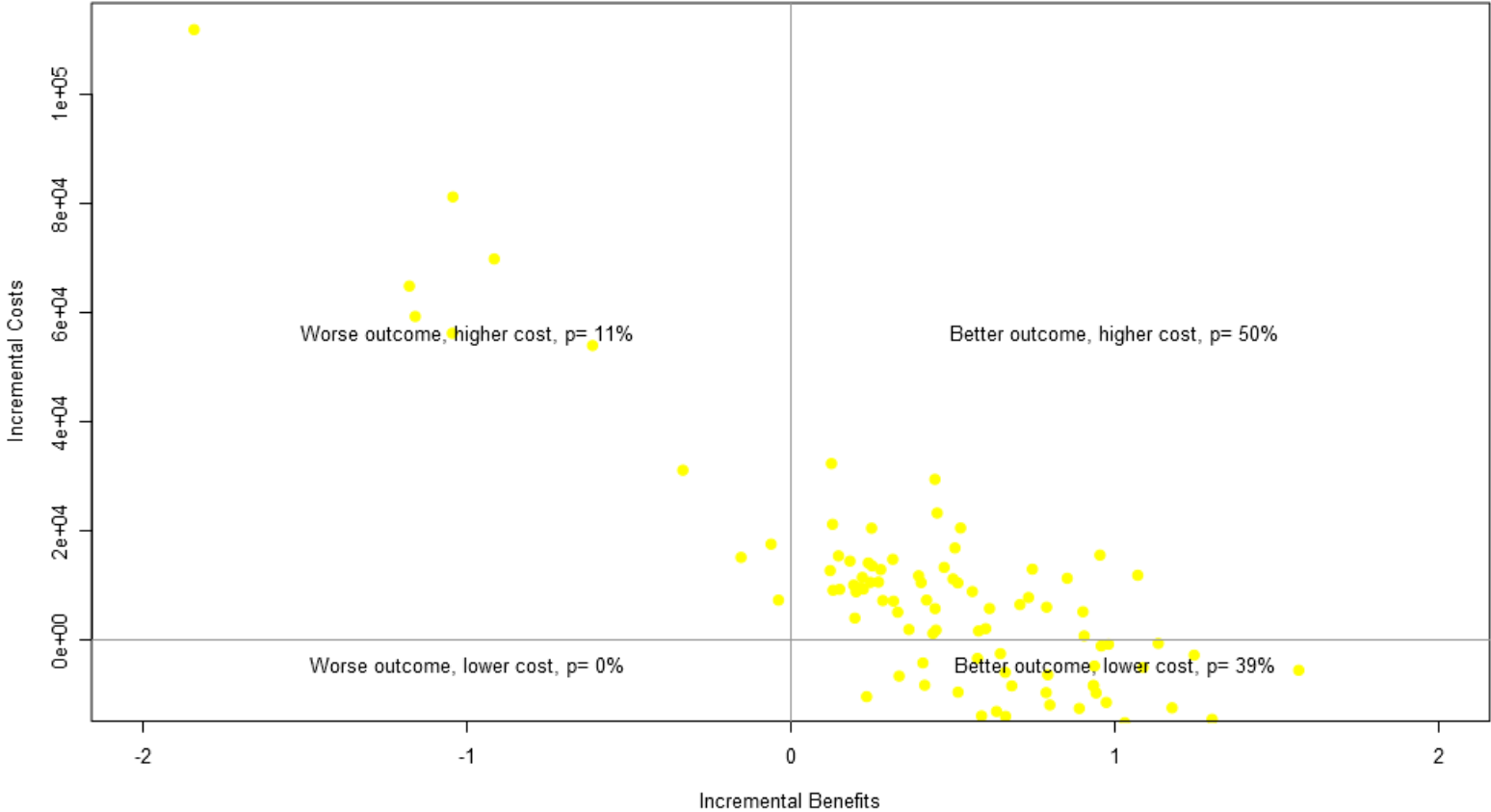
55	80	10.0	3.51	91 498	Hh strategy dominated by Screening and cohorting
60	80	12.5	3.38	89 094	Hh strategy dominated by Screening and cohorting
65	80	15.0	3.24	86 608	Hh strategy dominated by Screening and cohorting
70	80	17.5	3.12	84 516	7 023 €
75	80	20.0	2.99	82 227	23 801 €
80	80	22.5	2.89	80 556	71 424 €
ICN working on Hh strategy at full time					
55	60	0.0	4.99	135 100	Hh strategy dominated by Screening and cohorting
⋮	⋮	⋮	⋮	⋮	Hh strategy dominated by Screening and cohorting
80	80	22.5	2.89	93 462	Hh strategy dominated by Screening and cohorting

Supplementary Figure S3 Results of probabilistic sensitivity analysis. Cost-effectiveness plane shows the incremental health benefits (infections avoided) and costs for Screening and cohorting (Strategy 6). relative to horizontal strategies: A) Hand hygiene improvement to 80%/80% (Strategy 2); B) Hand hygiene improvement to 55%/80% (Strategy3); C) Antibiotic reduction (Strategy 4). The frequency that the Strategy 6 was in one of four quadrant of CE plane is represented by “p”.

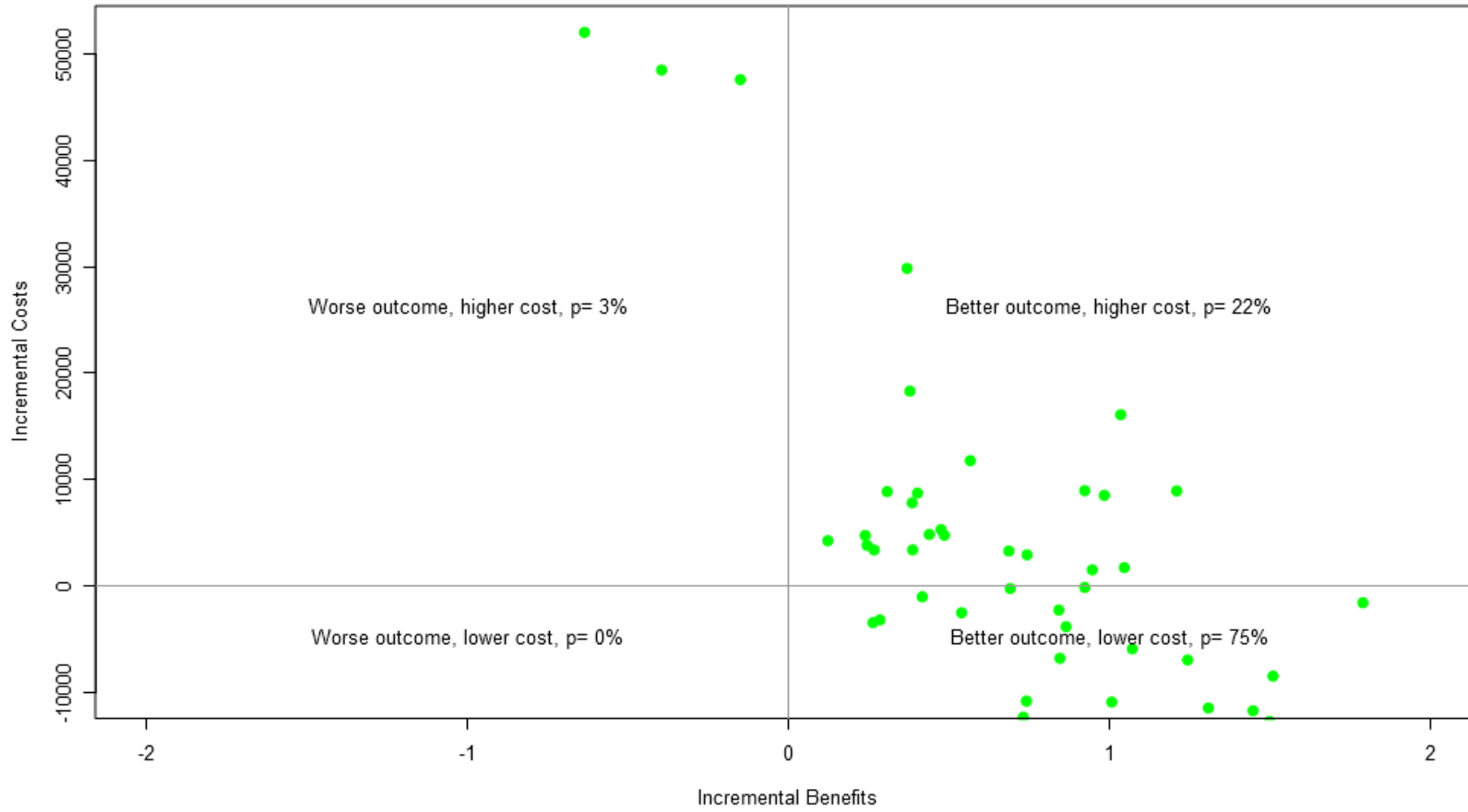
A)



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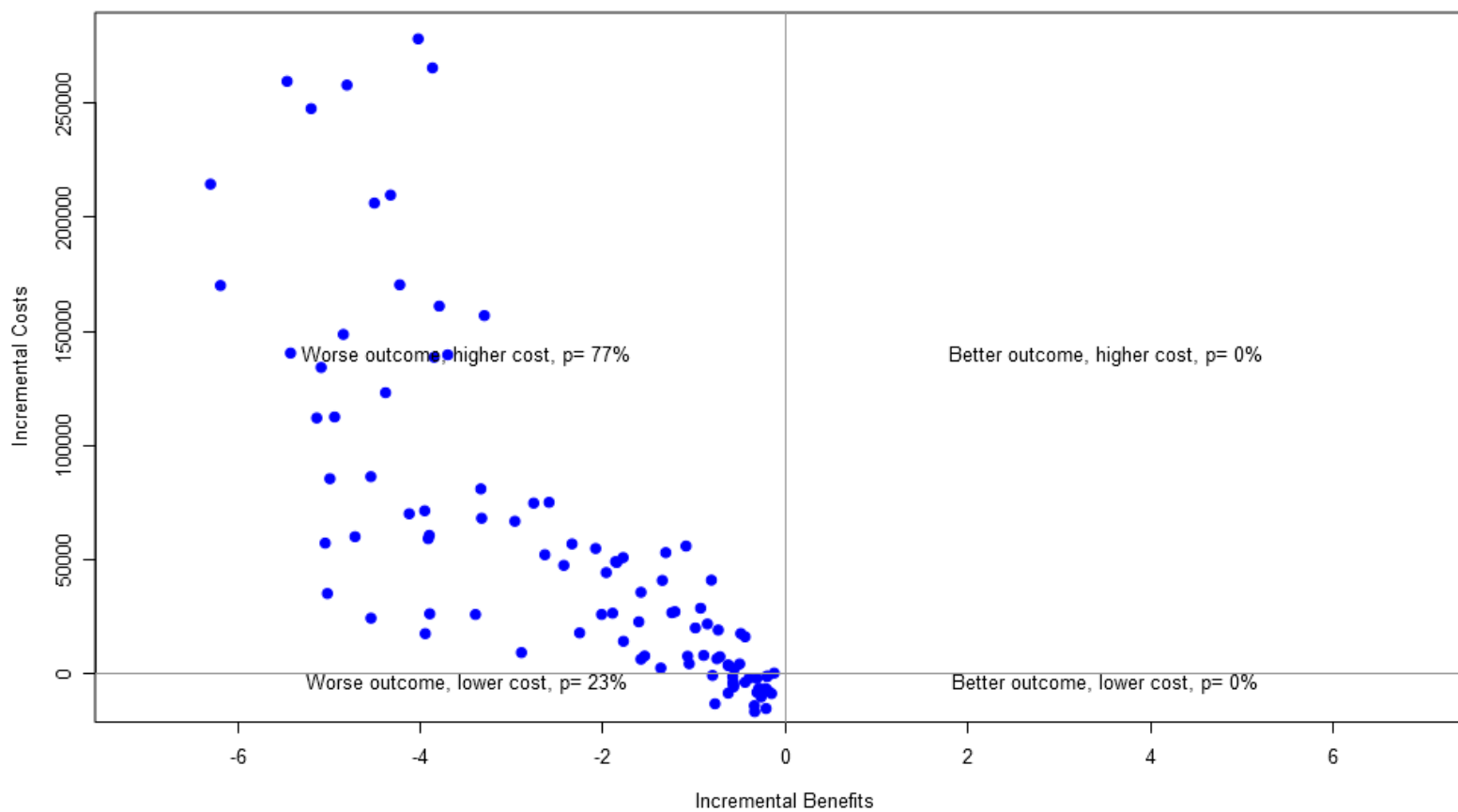


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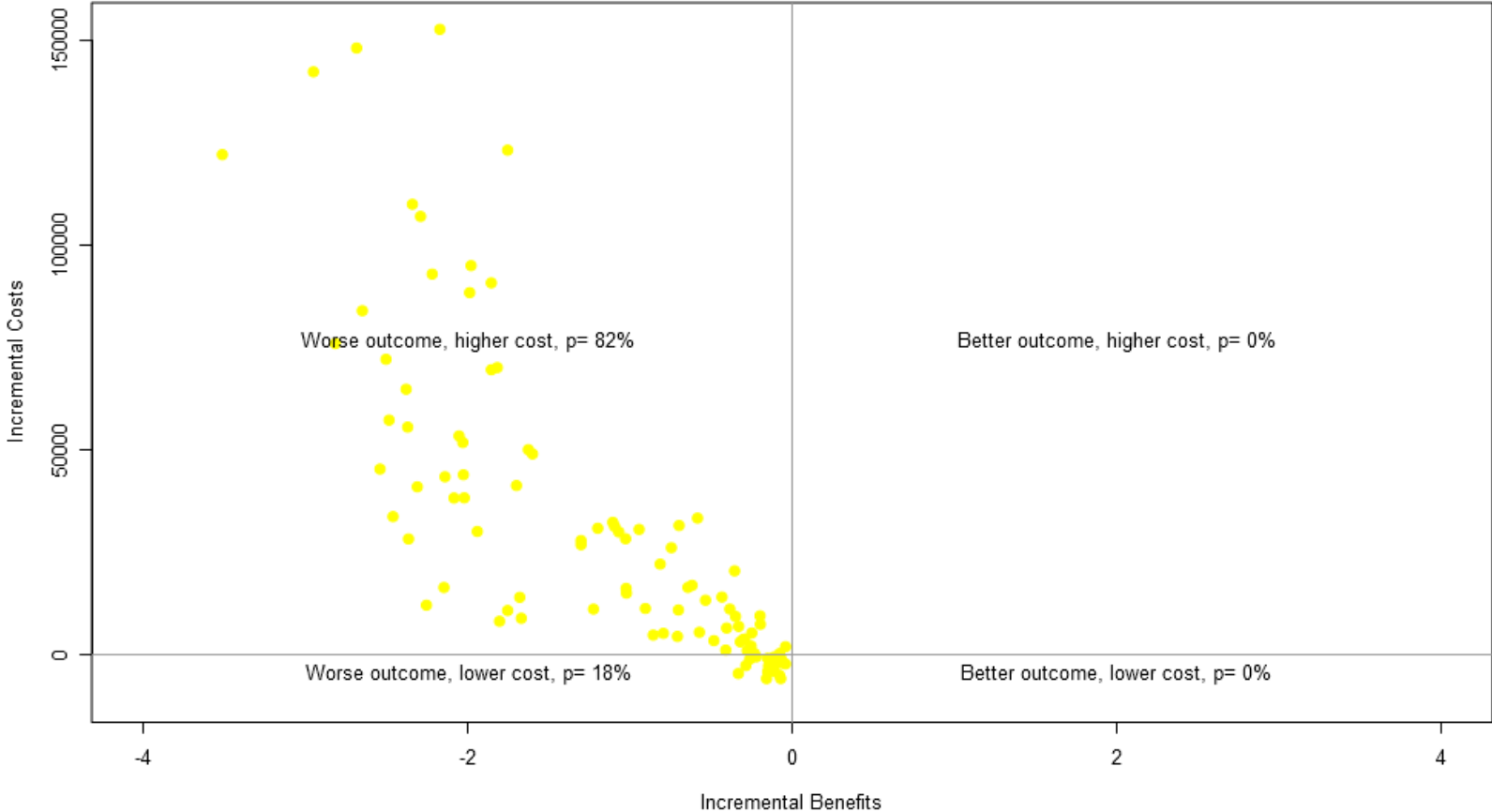


Supplementary Figure S4 Results of probabilistic sensitivity analysis. Cost-effectiveness plane shows the incremental health benefits (infections avoided) and costs for Screening and contact precautions (Strategy 5). relative to horizontal strategies: A) Hand hygiene improvement to 80%/80% (Strategy 2); B) Hand hygiene improvement to 55%/80% (Strategy3); C) Antibiotic reduction (Strategy 4). The frequency that the Strategy 6 was in one of four quadrant of CE plane is represented by “p”.

A)



B)



c)

