SUPPLEMENTARY MATERIAL

Manuscript

Microscopic examination of Gram stained smears for anogenital gonorrhea in men who have sex with men is cost-effective: evidence from a modelling study

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1. Uncertainty analysis for the parameters of the transmission model

The transmission model and the uncertainty analysis are described in detail earlier.[1]. Briefly, we defined a range for the expected positivity rate among tested MSM (5.9-7.3%) based on the anogenital gonorrhea positivity rate of 6.6% among MSM at the STI clinic of Amsterdam.[2] Prior parameter distributions (uniform distribution) were defined for uncertain parameters (see Table S1). From these distributions, 10,000 sets of parameter values were randomly sampled using Latin Hypercube Sampling.[3] This is a statistical method for generating a near-random sample of parameter values from a multidimensional distribution. The range of each of the 19 uncertain parameters is divided into 10,000 equally probable intervals. Then 10,000 samples are drawn ensuring that there is only one sample in each 1/10000 part of each parameter. After creating the 10,000 parameter sets, the model equations were solved numerically with these parameter values and with the current testing strategy of the STI clinic of Amsterdam (GSS for symptomatic MSM), until the equations reached a steady endemic state. At that point, parameter sets (posterior distributions) were selected that resulted in positivity rates within the defined positivity range; 145 parameter sets were selected. Subsequently, the equations were solved only with the selected parameter sets and the annual numbers of anogenital gonorrhea infections, tests, and treatment doses at each health state were calculated for the following ten years with each treatment strategy.

Table S1. Parameters for the transmission model included in uncertainty analysis (Source: Bartelsman *et. al.* Sex Transm Infect 2018;94:174–179*).

Parameter	Values	Source
Probability of gonorrhea transmission per UAI act	0.25-0.45	[21,22]
Percentage of symptomatic gonorrhea infections	30-90%	[22]
Level of assortativeness in sexual mixing		
between steady partners	60-80%	[23,24]
between casual partners	40-60%	[23,24]
UAI frequency in the time between test and treatment (when no GSS)		
with steady partners	74-94/year	STI clinic**
with casual partners	20-34/year	STI clinic**
UAI frequency outside the interval between test and treatment		
with steady partners	15-35/year	[10]
with casual partners	1-4/year	[10]
% of MSM with sexual partners who engage in UAI during the period between testing and treatment	8-16%	STI clinic**
Average interval from infection until seeking care at STI clinic, for symptomatic gonorrhea cases	4-20 days	[25,26]
Average interval between testing and treatment for those treated after culture results are positive	7-19 days	STI clinic**
Average interval from infection until natural recovery (for untreated)	5-7 months	[25,27]
Sensitivity of Gram tests for symptomatic gonorrhea	95% (92%-98%)	STI clinic**
Sensitivity of Gram tests for asymptomatic gonorrhea	50% (40%-60%)	STI clinic**
Specificity of Gram tests	99.8% (99.7-99.9%)	***
% lost to follow up, among those with positive NAAT	7% (2-12%)	[7]
% reporting STI symptoms, among those with negative NAAT	44% (34-54%)	[7]
Average interval between opportunistic gonorrhea tests (for those without symptoms)		
Low-risk MSM	12-30 months	[28-30]
High-risk MSM	6-14 months	[28-30]
Sensitivity of NAAT tests	100%	Assumption
Specificity of NAAT tests	100%	Assumption

Abbreviations: MSM, men who have sex with men; UAI, unprotected anal intercourse; STI, sexually transmitted infection.

* The table is based on Table 1 in *Bartelsman et. al. Sex Transm Infect 2018;94:174–179*. The only difference is the sensitivity of Gram tests: in *Bartelsman et. al. 2018* we used for all cases the average of the sensitivity for symptomatic and that for asymptomatic gonorrhea cases.

** Calculated from data from the STI clinic of Amsterdam.

*** The specificity was calculated as the average of urogenital and anal Gram stained smears, from data of the STI clinic of Amsterdam.

2. Data from the transmission model used in the economic model

From the transmission model, the following annual numbers were calculated, where appropriated, and formed the input for the economic model (see also Figures S1-S2):

i) MSM with asymptomatic anogenital gonorrhea and not tested;

ii) MSM with symptomatic anogenital gonorrhea and tested positive with GSS & treated;

iii) MSM with symptomatic anogenital gonorrhea and tested negative with GSS & positive with NAAT & late treated;

iv) MSM with symptomatic anogenital gonorrhea and tested negative with GSS & positive with NAAT & lost-to-follow-up;

v) MSM with symptomatic anogenital gonorrhea and tested only with NAAT & late treated;

vi) MSM with symptomatic anogenital gonorrhea and tested only with NAAT & lost-to-follow-up;

vii) uninfected MSM with symptoms and tested positive with GSS & treated;

viii) uninfected MSM with symptoms and tested negative with GSS and NAAT;

ix) uninfected MSM with symptoms and tested only with negative NAAT;

x) MSM with asymptomatic anogenital gonorrhea and tested positive with GSS & treated;

xi) MSM with asymptomatic anogenital gonorrhea and tested negative with GSS & positive with NAAT & late treated;

xii) MSM with asymptomatic anogenital gonorrhea and tested negative with GSS & positive with NAAT & lost-to-follow-up;

xiii) MSM with asymptomatic anogenital gonorrhea and tested only with NAAT & late treated;

xiv) MSM with asymptomatic anogenital gonorrhea and tested only with NAAT & lost-to-

follow-up;

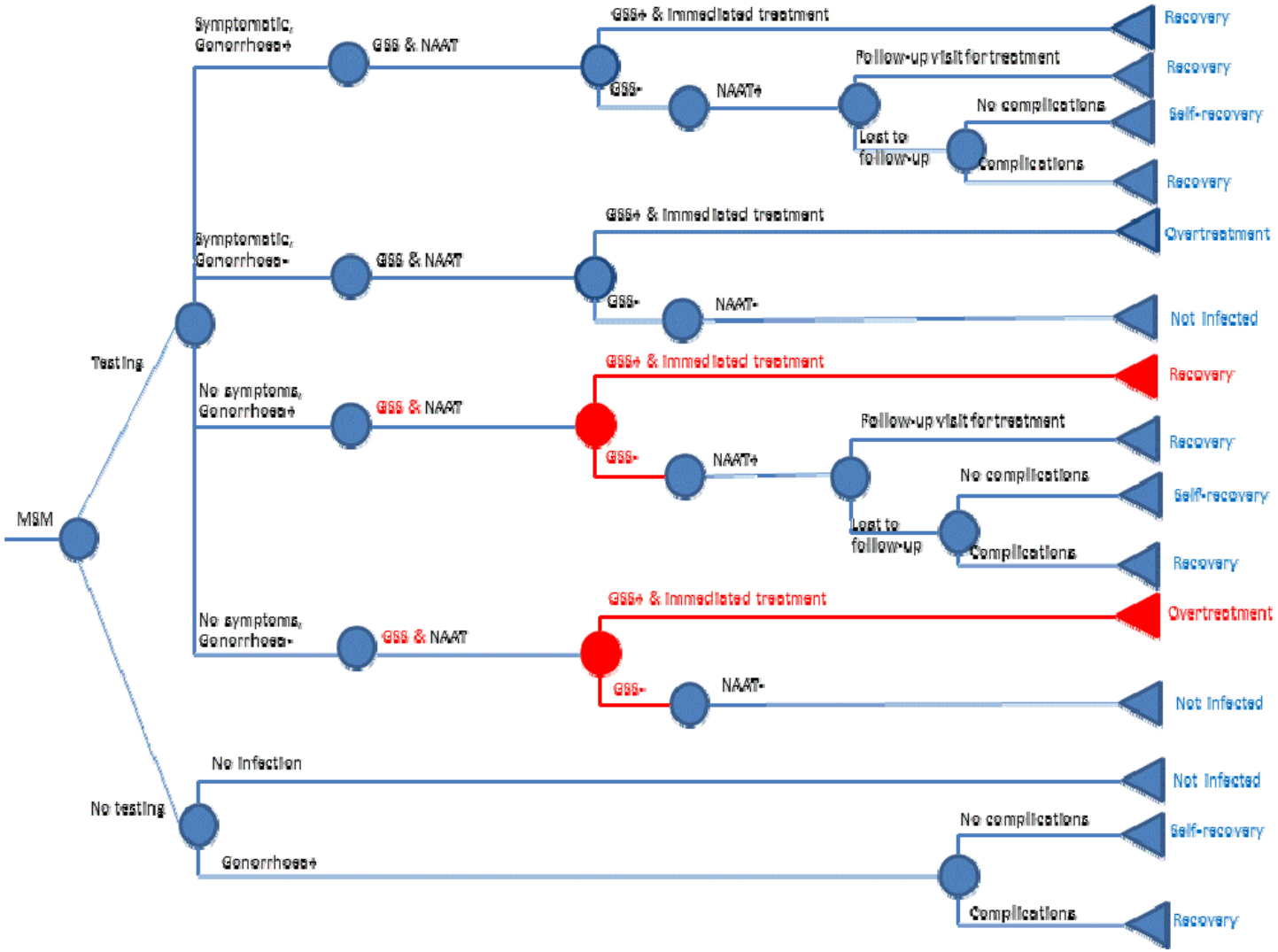
xv) uninfected MSM without symptoms and tested positive with GSS & treated;

xvi) uninfected MSM without symptoms and tested negative with GSS and NAAT;

xvii) uninfected MSM without symptoms and tested only with negative NAAT.

Based on the annual number of untreated anogenital gonorrhea infections (i.e. i, iv, vi, xii, xiv) a natural history model was combined in order to estimate the number of complications of untreated anogenital gonorrhea infections in men. For more details on complications see Figure S.3.

Figure S1. Schematic overview of the economic model for anogenital GSS for all MSM (i.e. extending GSS) versus anogenital GSS only for symptomatic MSM (the current testing strategy at the STI clinic of Amsterdam).

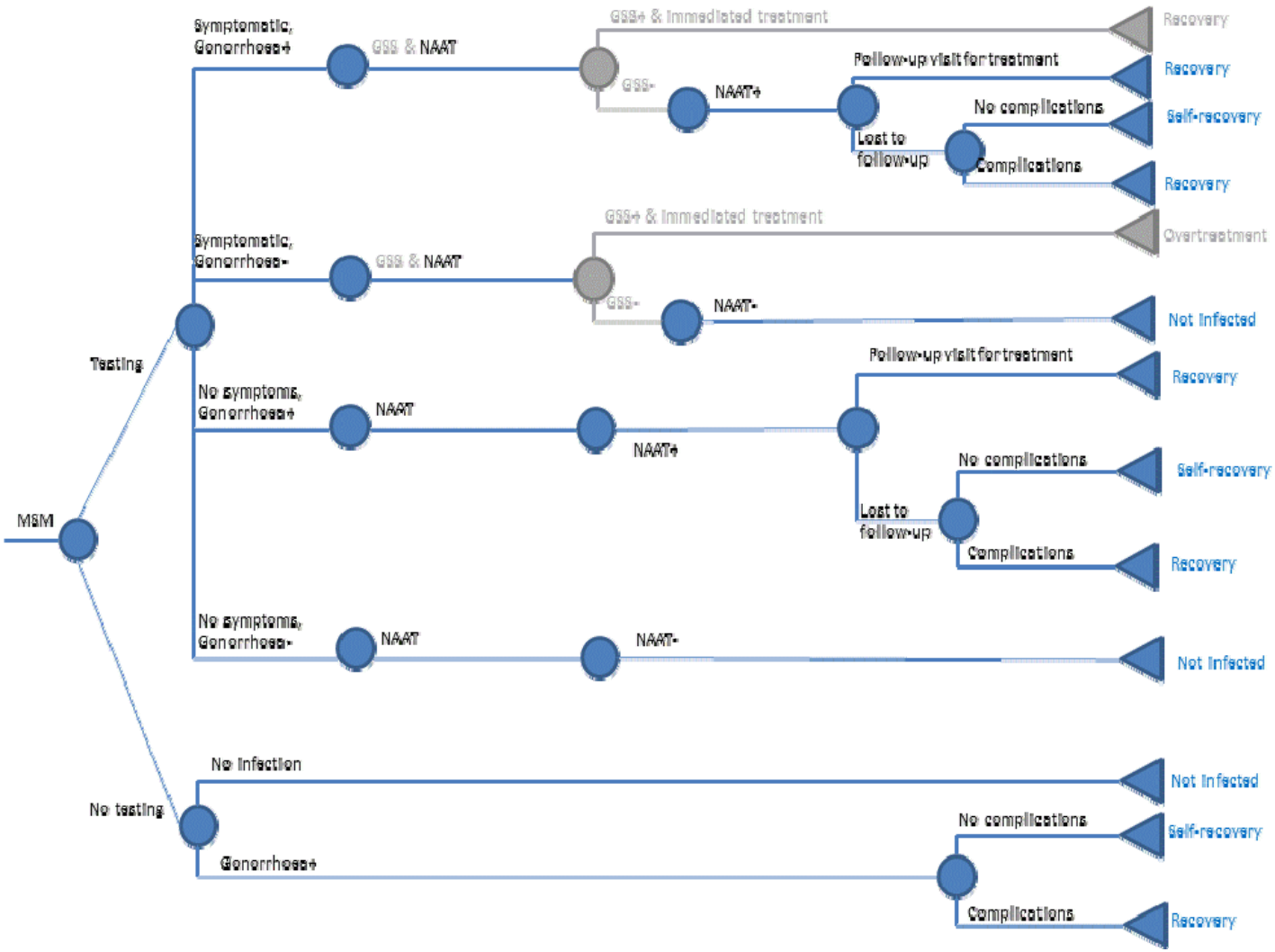


Note 1: Red marks the additional outcomes/tests when extending GSS to all MSM compared to the current practice. The blue outcomes are considered in the current testing strategy, and the blue and the red outcomes are considered when extending GSS.

Note 2: A positive NAAT included a call for treatment if no presumptive therapy was given and an additional culture for testing the antibiotic resistance when treated.

Used abbreviations: GSS: Gram stain smears; NAAT: nucleic acid amplification tests.

Figure S2. Schematic overview of the economic model for no anogenital GSS testing for MSM (i.e. abandoning GSS) versus anogenital GSS only for symptomatic MSM (the current testing strategy.

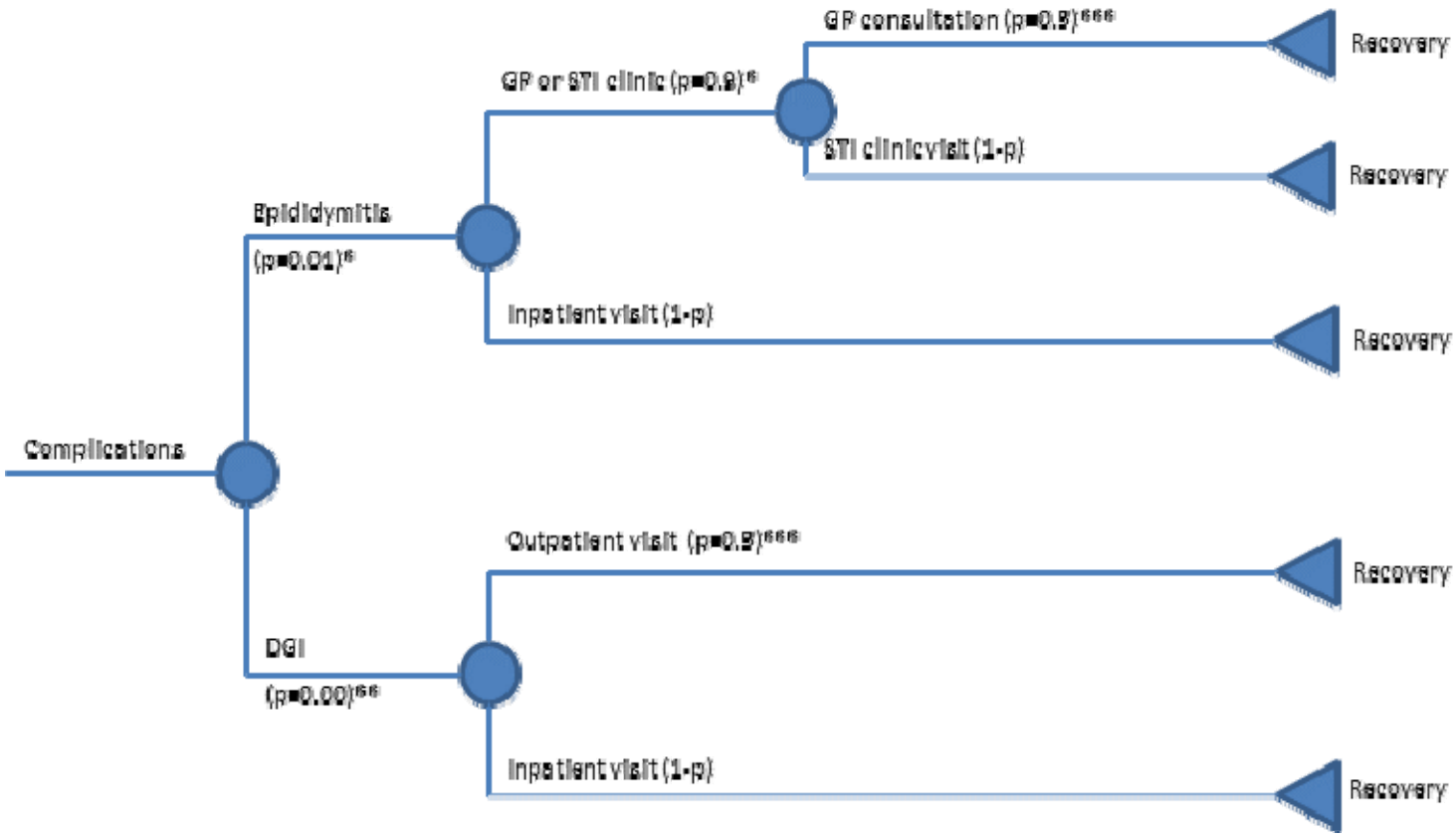


Note 1:Grey marks the waning outcomes/tests when GSS is abandoned (no GSS testing strategy) compared to the current practice. The blue and grey outcomes are considered in the current testing strategy, and ONLY blue outcomes are considered when abandoning GSS.

Note 2: A positive NAAT included a call for treatment if no presumptive therapy was given and an additional culture for testing the antibiotic resistance when treated.

Used abbreviations: GSS: Gram stain smears; NAAT: nucleic acid amplification tests.

Figure S3. Schematic overview of the economic model for untreated anogenital gonorrhea infections developing complications.



* Based on [4].
** According to Rice et al.[5] DGI is a potential sequela of untreated gonorrhea infections. However, DGI is seldom seen in daily practice, therefore DGI was only considered in a scenario analysis as a potential sequela. [4-6].
***No information was available over the distribution between these two health states. We therefore assumed in the basecase that the distribution would be 50%. In sensitivity analyses this was assumed to be 10% and 90%, respectively.
Used abbreviations: GP, general practitioner; DGI, disseminated gonorrhea infection; STI, sexually transmitted infection.

Table S2. Health Utility Indices.

Health states	Health utility [4]
Healthy person	1
Asymptomatic gonorrhea infection	1
Symptomatic gonorrhea infection	0.84
Epididymitis outpatient	0.46
Epididymitis inpatient	0.30
Epididymitis outpatient after inpatient	0.78
DGI outpatient	0.6
DGI inpatient	0.52
DGI outpatient after inpatient	0.78

Used abbreviation: DGI, disseminated gonorrhea infection.

Table S3. Duration of health states

Health states	Duration (days)
Symptomatic gonorrhea; directly treated	Calculated from two intervals
Symptoms till first visit	Discrete distribution using numbers provided in Table S4
Symptoms after treatment	Uniform distribution (min. 2 days; max. 3 days)*
Symptomatic gonorrhea; late treated	Calculated from three intervals
Symptoms till first visit	Discrete distribution using numbers provided in Table S4
Between first visit and treatment	Uniform distribution (min. 7 days; max. 19 days) [1]
Symptoms after treatment	Uniform distribution (min. 2 days; max. 3 days)*
Symptomatic gonorrhea lost to follow-up	Duration as that with natural recovery [1]
Symptomatic gonorrhea infection until self-recovery	Uniform (min. 5 months; max. 7 months)
Epididymitis outpatient	Calculated from two intervals**
Symptoms till first visit	Discrete distribution using numbers provided in Table S4
Symptoms after treatment	Uniform distribution; min. 2 days; max. 3 days*
Epididymitis inpatient	Calculated from three intervals
Symptoms till visit hospital	Uniform distribution; min. 1 day; max. 3 days*
Hospitalization	Uniform distribution; min. 2 days; max. 7 days [4]
Symptoms after treatment	Pert distribution; min. 14 days; most likely 21 days; max. 60 days*
DGI outpatient	8 days [4]
DGI inpatient	Calculated from two intervals
Hospitalization	4 days [4]
Symptoms after treatment	7 days [4]

* Model assumption, based on expert opinion.

** Treated infections do not develop complications.

Used abbreviation: DGI, disseminated gonorrhea infection.

Table S4. Distribution of time with symptoms suggesting gonorrhea or epididymitis until patients visit the STI clinic of Amsterdam[a].

	% of patients with specific duration of symptoms (till visit clinic)			
	<7 days	2 weeks	3 weeks	≥1 month
Urogenital gonorrhea[b,d]				
Urethral discharge (N=1085)	75.6%	17.6%	3.7%	3.1%
Dysuria (N=689)	70%	21.6%	4.8%	3.6%
Anorectal gonorrhea[c, d]				
Anal discharge (N=241)	49.4%	27.8%	15.8%	7.1%
Epididymitis[e]				
Pain in testicles (N=25)	72%	20%	4%	4%

a) All clients from the STI clinic of Amsterdam who reported STI related symptoms were asked whether they had 1) secretion, pus or clear fluid from the urethra or 2) discomfort when urinating, 3) painful testicles, or 4) pus (yellow–green) or clear secretion from the anus. For all types of symptoms, the moment of onset was asked: in the last 7 days, 2 weeks, 3 weeks, 1 month or longer. For the present study we used data from the period from July 2013 until September 2016 to estimate the moment of onset of symptoms until clinic visit in male clients with diagnosis of gonorrhea infection and diagnosis of epididymitis.

b) A total of 1557 men had a urogenital gonorrhea infection, whereof 1131 having symptoms, either urethral discharge or dysuria, or both.

c) A total of 2650 men had an anorectal gonorrhea infection, but only 241 had symptoms.

d) Based on the here presented data we assumed that 82% of all symptomatic gonorrhea infections would have been an urogenital gonorrhea infection (50% having urethral discharge resulting in an STI clinic visit and 50% having dysuria) and 18% would have been an anorectoral gonorrhea infection.

e) There were 26 epididymitis cases. For one of the 26 men with the diagnosis epididymitis, no information on duration and symptoms were available.

Table S5. Costing parameters used for the cost-effectiveness analyses

Activity	Cost prices/unit used (in 2016 euros)						Resources / Remarks
	Consultation[a]/ Hospitalization	Source	Test[b]	Source	Medication	Source	
Standard medical consultation at STI clinic	12.65	[7]					
NAAT test			21.38	[c]			
Culture test			24.04	[c]			
GSS test	3.15	[1]	0.71	[1]			
Treatment	10.44	[1]			0.85	[1] [d]	
GSS negative result	0.84	[1 7]					
Call for treatment (false negative GSS; positive NAAT); per attempt	2.53	[1 7]					Number of attempts modelled as a pert distribution (min. 0; most likely 1; max. 3)
Call for treatment; no show	7.59	[1 7]					3 attempts
Medical consultation STI clinic by epididymitis[e]							
- Per consultation	31.32	[f]			8.38	[c]	2 consultations,[5] 1st for treatment[g], 2nd follow-up;
Medical consultation GP by epididymitis[e]							
- Per consultation	33.32	[8]			30.39	[8 9h]	2 consultations,[5] 1st for treatment[g], 2nd follow-up;
Hospitalization by epididymitis:							
- 1 GP consultation as gatekeeper	33.32	[8]					Length of hospital stay was modelled as uniform distribution (min. 2 days; max. 7 days)
- Hospital admission/day	480.62	[8]					
- 1 outpatient consultation	91.88	[8]					
GP visit in case of DGI:							
- 1 GP consultation for treatment	33.32	[8]			31.39	[8 9] [i]	
Hospitalization by DGI:							
- 1 GP consultation as gatekeeper	33.32	[8]					4 days in hospital [5];
- Hospital admission/day	480.62	[8]					
- 1 outpatient consultation	91.88	[8]					

[a] Costs per consultation at the STI clinic included time costs of the staff (doctor, nurse) for patient contacts and administration, and overhead.[1 7] For GP consultations, outpatient consultations and hospital admission we used Dutch references prices, according to Dutch guidelines.[8]

[b] Test costs at STI clinic visits include test and other non-testing supplies.

[c] Based on data of the STI outpatient clinic of the Public Health Service of Amsterdam.

[d] Medication for gonorrhea infection consisted of Ceftriaxone (1000 mg) and Lidocaine (10 ml). Medication usage was based on protocols of STI outpatient

clinic of the Public Health Service of Amsterdam.
[e] Assuming that 50% of all outpatient visits would consult the STI clinic and 50% would consult their GP.
[f] Based on the unit prices for staff as derived by Bartelmans et al. [17] and assuming per consultation 15-minutes for a nurse and 15-minutes for a medical doctor.
[g] Medication for epididymitis consisted of Doxycycline (100 mg twice a day for 14 days). Medication usage was based on protocols of STI outpatient clinic of the Public Health Service of Amsterdam.
[h] Medication costs included pharmacy delivery fees, according to Dutch guidelines.[8]
[i] Medication for DGI consisted of Levofloxaxin and included the pharmacy delivery fees.[8]
Used abbreviations: GSS, microscopy with Gram stain smears; NAAT, nucleic acid amplification tests; GP, general practitioner; DGI, disseminated gonorrhea infection.

Table S6. Sensitivity analyses conducted and parameters used

Parameter	Value basecase	Value in sensitivity analysis	Rationale/Sources*
Discount rates costs & effects	3% and 3%	2% and 2% 4% and 4% 4% and 1.5%	According to Dutch guidelines [8]
Time horizon**	10 years	5 years 15 years	Shorter and longer time-horizon (as some interventions become more or less cost-effective with longer implementation)
Sensitivity of GSS***	50%	95%	Assuming for asymptomatic gonorrhea infections the same sensitivity as for symptomatic gonorrhoea infections, i.e. 95%.
% developing epididymitis	1%	0.5%, 1.5%	
% visiting GP by epididymitis	50%	10%, 90%	
% developing DGI	0%	1%	
% visiting GP by DGI	50%	10%, 90%	
Lower cost price for tests (i.e. NAAT & culture)	100%	70%,30%	
Maximum duration of interval with complaints due to epididymitis after hospitalization	60 days	180 days	Modelled using a pert distribution with minimum 14 days, most likely 21 days and different maximum, based on expert opinion

*The values examined in sensitivity analysis are hypothetical lower and higher values, unless otherwise mentioned.
**To examine the impact of the time horizon, the calculations with the transmission model were carried out for 15 years. The analyses with the economic model were carried out using only the first five or only the first ten years, to calculate results for each time horizon.
***With different sensitivity, the numbers of tests and numbers of MSM in each health state were also different (while for all other items in the sensitivity analysis, the numbers calculated from the transmission model were the same). This value of sensitivity was used for testing both urethral and anal samples with GSS.
Used abbreviations: GSS, microscopy with Gram stained smears; NAAT, nucleic acid amplification tests; GP, general practitioner; DGI, disseminated gonorrhea infection.

Table S7. No GSS (alternative) strategy versus GSS for symptoms (current) strategy (i.e. abandoning GSS): Full details for scenario analysis

Scenarios	No GSS (alternative) strategy versus GSS for symptoms (current) strategy (i.e. abandoning GSS)			
	Incremental effect (i.e. QALYs gained)[a]	Incremental costs[b] (*1000)	ICER (€/QALY)[c]	ICER to be found in the quadrant[c]
Basecase[d]	-72 (-187 to -21)	7 (-185 to 407)	-101 (-2520 to 7000)	NW (NW – SW)
Changing the time horizon (basecase 10 years)				
Shorter time horizon (i.e. 5 years)	-38 (-98 to -11)	0.1 (-100 to 205)	-3 (-2430 to 7030)	NW (NW – SW)
Longer time horizon (i.e.15 years)	-101 (-265 to -29)	13 (-259 to 582)	-133 (-2550 to 6990)	NW (NW – SW)
Applying different discount rates (basecase 3% for both QALYs and costs)				
Dutch discount rate (1.5% for QALYs and 4% for costs versus 3% for both QALYs and costs)	-77 (-200 to -22)	7 (-178 to 390)	-87 (-2260 to 6300)	
2% for both QALYs and costs	-75 (-195 to -21)	8 (-193 to 426)	-105 (-2510 to 7000)	NW (NW – SW)
4% for both QALYs and costs	-69 (-180 to -20)	7 (-178 to 390)	-97 (-2520 to 7000)	NW (NW – SW)
Dutch discount rate (1.5% for QALYs and 4% for costs)	-77 (-200 to -22)	7 (-178 to 390)	-87 (-2260 to 6300)	NW (NW – SW)
Assuming a higher sensitivity of GSS for urethral samples (basecase 50%)				
Higher sensitivity of GSS for urethral samples (i.e. 95%)	-72 (-187 to -21)	7 (-185 to 407)	-101 (-2520 to 7000)	NW (NW – SW)
Percentage developing epididymitis (basecase 1%) / Percentage being treated by GP (basecase 50% by GP and 50% in an STI-clinic)				
Lower percentage developing epidydimititis (0.5%)[c]	-72 (-187 to -21)	6 (-186 to 404)	-77 (-2500 to 7020)	NW (NW – SW)
Higher percentage developing epidydimititis (1.5%)[d]	-72 (-187 to -21)	9 (-185 to 411)	-125 (-2540 to 6970)	NW (NW – SW)
Lower percentage visiting a GP in case of epidydimititis (10%)	-72 (-187 to -21)	7 (-185 to 407)	-100 (-2520 to 7000)	NW (NW – SW)
Higher percentage visiting a GP in case of epidydimititis (90%)	-72 (-187 to -21)	7 (-185 to 408)	-102 (-2520 to 7000)	NW (NW – SW)
Percentage developing DGI (basecase 0%) and percentage being treated by GP (remaining cases are treated in an STI-clinic)				
Percentage developing DGI (1%), whereof 50% visit a GP	-72 (-187 to -21)	17 (-182 to 429)	-236 (-2650 to 6890)	NW (NW – SW)
Percentage developing DGI (1%(, whereof 10% would visit a GP	-72 (-187 to -21)	24 (-180 to 446)	-338 (-2750 to 6810)	NW (NW – SW)
Percentage developing DGI (1%), whereof 90% would visit a GP	-72 (-187 to -21)	10 (-185 to 413)	-133 (-2550 to 6970)	NW (NW – SW)
Considering different testing costs (basecase 100%)				
Lower cost price for tests (70% of basecase costs)	-72 (-187 to -21)	-1 (-184 to 373)	20 (-2280 to 6960)	SW (NW – SW)

Lower cost price for tests (30% of basecase costs)	-72 (-187 to -21)	-13 (-182 to 327)	181 (-1970 to 6910)	SW (NW – SW)
Percentage developing epidydimitis (basecase 1%))				
Max days of symptoms after treating epididymitis (180 days versus 60 days)	-72 (-187 to -21)	7 (-185 to 407)	-101 (-2520 to 6990)	NW (NW – SW)

a) Abandon GSS would in all scenarios always result in a negative health impact (i.e.negative incremental QALYs gained are actually QALYs lost).

b) Note, negative incremental costs are actually savings. The 95% uncertainty interval ranges from cost saving (i.e. negative costs) to additional costs.

c) The estimated ICER needs to be interpreted with care as all simulations are either in the north-west (NW) quadrant or south-west (SW) quadrant. Results in the north-west quadrant, the alternative strategy is dominated by the current strategy as more costly and a negative health effect (for illustration see Figure S.4). Results in the south-west quadrant indicate that the alternative has a negative health effect, but would be cost-savings.

d) Abandon GSS would result in the basecase in additional epididymitis cases of on average 9 (95% UI: 2 –22) over ten-years. Whereas expanding GSS would avert on average 0.8 (95% UI: 0.2-2.1) epididymitis cases at the cost of € 176,578 (95% UI: €66,592 to €705,405) per averted epididymitis case

Table S8. GSS for all (alternative) strategy versus GSS for symptoms (current) strategy (i.e. expanding GSS): full details for scenario analysis

Scenarios	GSS for all (alternative) strategy versus GSS for symptoms (current) strategy (i.e. abandoning GSS)			
	Incremental effect (i.e. QALYs gained)	Incremental costs (*1000)	ICER (€/QALY)[a]	ICER to be found in quadrant[a]
Basecase[b]	1.1 (0.1 to 3.3)	148 (86 to 217)	135,000 (36,500 to 2,360,000)	NE (NE – NE)
Changing the time horizon (basecase 10 years)				
Shorter time horizon (i.e. 5 years)	0.5 (0 to 1.5)	80.9 (47.7 to 116.5)	158,000 (45,300 to 2,260,000)	NE (NE – NE)
Longer time horizon (i.e.15 years)	1.6 (0.1 to 4.9)	207 (120 to 303)	128,000 (33,200 to 2,400,000)	NE (NE – NE)
Applying different discount rates (basecase 3% for both QALYs and costs)				
2% for both QALYs and costs	1.1 (0.1 to 3.5)	155 (90 to 226)	135,000 (36,300 to 2,360,000)	NE (NE – NE)
4% for both QALYs and costs	1 (0.1 to 3.2)	143 (83 to 208)	136,000 (36,800 to 2,370,000)	NE (NE – NE)
Dutch discount rate (1.5% for QALYs and 4% for costs)	1.2 (0.1 to 3.6)	143 (83 to 208)	121,000 (32,600 to 2,120,000)	NE (NE – NE)
Assuming a higher sensitivity of GSS for urethral samples (basecase 50%)				
Higher sensitivity of GSS for urethral samples (i.e. 95%)	2.2 (0.2 to 6.4)	132 (68 to 214)	60,700 (13,800 to 1,140,000)	NE (NE – NE)
Percentage developing epidydimitis (basecase 1%) / Percentage being treated by GP (basecase 50% by GP and 50% in an STI-clinic)				
Lower percentage developing epidydimititis (0.5%)[c]	1.1 (0.1 to 3.3)	149 (86 to 217)	136,000 (35,000 to 2,020,000)	NE (NE – NE)
Higher percentage developing epidydimititis (1.5%)[d]	1.1 (0.1 to 3.3)	148 (86 to 217)	134,000 (37,100 to 2,480,000)	NE (NE – NE)
Lower percentage visiting a GP in case of epidydimititis (10%)	1.1 (0.1 to 3.3)	148 (86 to 217)	135,000 (36,500 to 2,360,000)	NE (NE – NE)
Higher percentage visiting a GP in case of epidydimititis (90%)	1.1 (0.1 to 3.3)	148 (86 to 217)	135,000 (36,500 to 2,360,000)	NE (NE – NE)
Percentage developing DGI (basecase 0%) and percentage being treated by GP (remaining cases are treated in an STI-clinic)				
Percentage developing DGI (1%), whereof 50% visit a GP	1.1 (0.1 to 3.3)	147 (86 to 216)	134,000 (37,000 to 2,520,000)	NE (NE – NE)
Percentage developing DGI (1%(, whereof 10% would visit a GP	1.1 (0.1 to 3.3)	147 (86 to 216)	133,000 (36,800 to 2,510,000)	NE (NE – NE)
Percentage developing DGI (1%), whereof 90% would visit a GP	1.1 (0.1 to 3.3)	148 (86 to 217)	134,000 (37,300 to 2,530,000)	NE (NE – NE)
Considering different testing costs (basecase 100%)				
Lower cost price for tests (70% of basecase costs)	1.1 (0.1 to 3.3)	149 (87 to 217)	136,000 (37,100 to 2,360,000)	NE (NE – NE)
Lower cost price for tests (30% of basecase costs)	1.1 (0.1 to 3.3)	150 (89 to 216)	137,000 (38,000 to 2,350,000)	NE (NE – NE)
Percentage developing epidydimitis (basecase 1%))				

Max days of symptoms after treating epididymitis (180 days versus 60 days)	1.1 (0.1 to 3.3)	148 (86 to 217)	135,000 (36,600 to 2,410,000)	NE (NE – NE)

a) All estimated ICER results are to be found in the north-east (NE) quadrant (see Figure S4). The alternative results in a higher health effect (i.e. QALYs gained) and additional costs (for illustration see Figure S4). The Dutch threshold is €20,000 per QALYs gained. Alternatives with an ICERs below this threshold are considered to be cost-effective.

Figure S.4 - The incremental cost-effectiveness plane - illustration

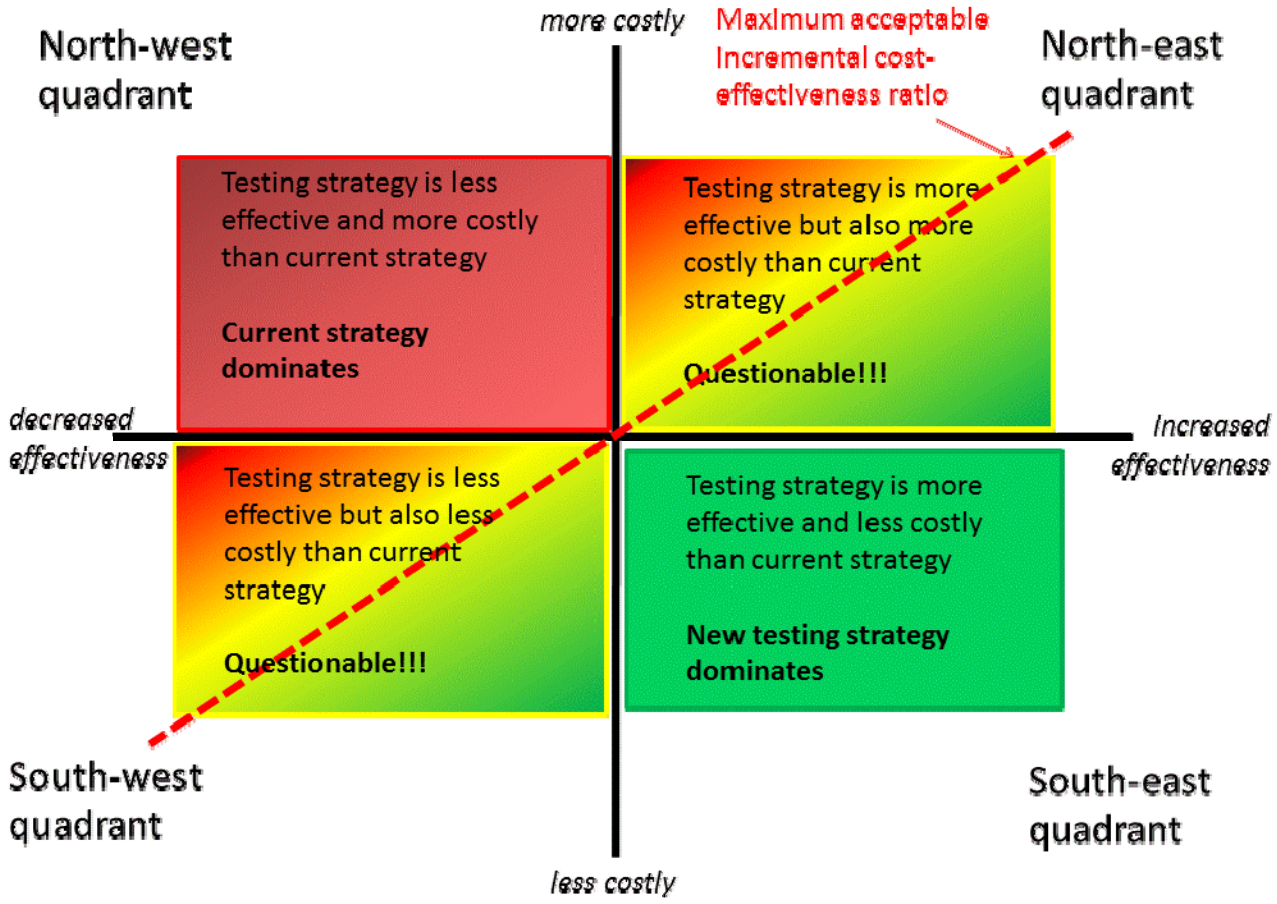
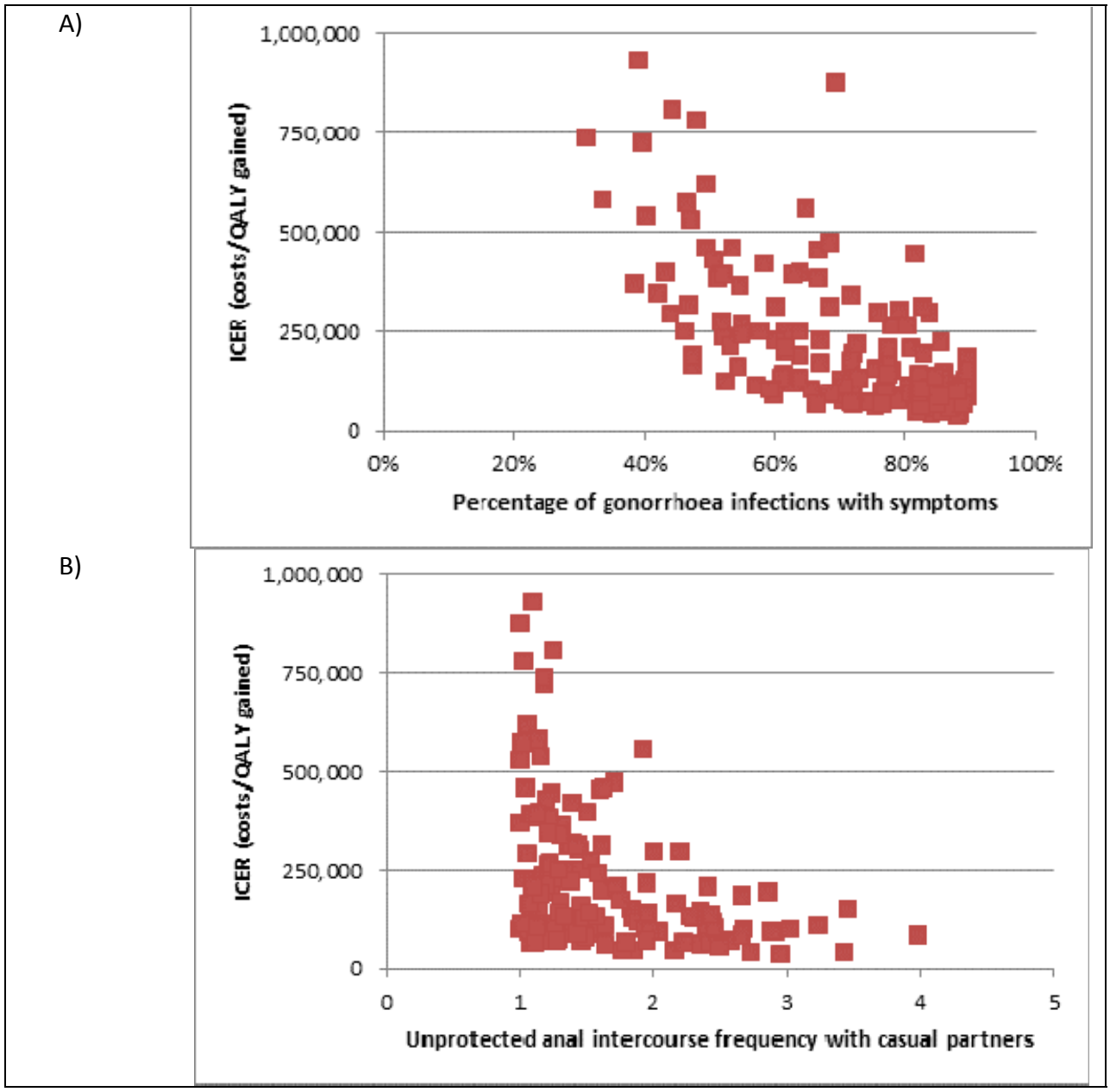


Figure S.5 - The incremental cost-effectiveness ratio (ICER) for expanding GSS (GSS for all MSM versus GSS for symptomatics) in relation with a) the percentage of gonorrhea infections with symptoms; and b) the frequency of acts of unprotected anal intercourse with casual partners.



Note 1: The ICER (vertical axes) is plotted against epidemiological parameters from the transmission model: (a) the percentage of gonorrhea infections with symptoms; and (b) the frequency of acts of unprotected anal intercourse (UAI) with casual partners. The ICER is presented as incremental costs in 2016 euros per quality-adjusted life-years (QALY) gained. Costs and QALYs are cumulative over ten years.

Note 2: For readablity reasons, results were only presented up to the 95th percentile. The remaining 7 ICERs values were €1.1 million; €1.4 million; €2.5 million; €2.7 million; €3.2 million; €6.7 million and €16.9 million/QALY gained.

References

1. Bartelsman M, Vaughan K, Van Rooijen MS, et al. The impact of point-of-care management on the transmission of anogenital gonococcal infections among men who have sex with men in Amsterdam: a mathematical modelling and cost-effectiveness study. *Sex Transm Infect* 2017;Sep 23. pii: sextrans-2017-053159. doi: 10.1136/sextrans-2017-053159. [Epub ahead of print]
2. Van den Broek S, Van Rooijen M, Van Veen M, et al. Jaarverslag SOA polikliniek 2014 (in Dutch). Amsterdam: GGD Amsterdam, 2015.
3. McKay MD, Beckman RJ, Conover WJ. A comparison of three methods for selecting values of input variable in the analysis of output from a computer code. *Technometrics* 1979;21:239-45.
4. Medicine Io. Vaccines for the 21st Century: A Tool for Decisionmaking *Washington, DC: National Academy Press* 2000
5. Rice PA. Gonococcal arthritis (disseminated gonococcal infection). *Infect Dis Clin North Am* 2005;19(4):853-61. doi: 10.1016/j.idc.2005.07.003
6. LCI-richtlijn Gonorroe: Rijksinstituut voor Volksgezondheid en Milieu

2013 [Available from: http://www.rivm.nl/Documenten_en_publicaties/Professioneel_Praktisch/Richtlijnen/Infectieziekten/LCI_richtlijnen/LCI_richtlijn_Gonorroe.
7. Bartelsman M, Straetemans M, Vaughan K, et al. Comparison of two Gram stain point-of-care systems for urogenital gonorrhoea among high-risk patients: diagnostic accuracy and cost-effectiveness before and after changing the screening algorithm at an STI clinic in Amsterdam. *Sex Transm Infect* 2014;90(5):358-62. doi: 10.1136/sextrans-2013-051500. Epub 2014 May 23.
8. Hakkaart-van Roijen LVdL, N. Bouwmans, C. Kanters, T. Swan Tan, S. Kostenhandleiding: Methodologie van kostenondezroek en referentieprijzen voor economische evaluties in de gezondheidszorg, 2015.
9. Nederland Z. Medicijnkosten Diemen: Zorginstituut Nederland 2016 [Available from: http://www.medicijnkosten.nl/ accessed April 20 2016.