World Health Organization

GUIDELINES FOR THE MANAGEMENT OF SYMPTOMATIC SEXUALLY TRANSMITTED INFECTIONS

WEB ANNEX H. DETAILED METHODS FOR THE MODELLING OF THE COST AND EFFECTIVENESS OF APPROACHES FOR MANAGING WOMEN WITH VAGINAL DISCHARGE

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CONTENTS

Introduction

This report provides a summary of the methods used in the model to simulate a range of patient management flow charts based on syndromic management plus existing diagnostic procedures/ tests (e.g. speculum exam, Gram stain) and hypothetical point-of-care tests (POCT) for vaginal discharge in different prevalence, country or clinic settings. The model builds on previous work of WHO to provide a comprehensive, flexible model. We consider the impact of testing symptomatic women.

In the cost analysis we incorporate the direct costs of management of women with vaginal discharge: test cost, treatment cost, according to by infection (chlamydia, gonorrhoea and combined bacterial vaginitis/trichomonas vaginalis treatment), plus optionally the costs of long term consequence (pelvic inflammatory disease, ectopic pregnancy and infertility) and / or partner management. Lastly, we apply an "AMR tax" to antibiotic prescriptions to simulate future costs associated with drug resistant infections or other unintended consequences from antibiotic use.

Management Scenario Pathway:

We consider several flowcharts. Patients with symptoms of vaginal discharge presenting to clinics are treated based on different flowcharts. Treatment is a combination of ceftriaxone and azithromycin dual treatment plus treatment for TV/BV.

We demonstrate the model outputs for 2 baseline scenarios representing different populations:

1. General population of women attending a sexually transmitted infection clinic, low prevalence 5% gonorrhoea/chlamydia (symptomatic only)
2. General population of women attending a sexually transmitted infection clinic, high prevalence 20% gonorrhoea/chlamydia (symptomatic only)

Model parameters

A full list of the input parameters for the model used for making decisions for this guideline is listed below. Parameters are context-specific and reflect an average patient population and care setting. The model can be fully specified with tailored population and cost parameters to inform local or national decisions in future.

Table 1. Input parameters used for this guideline

Demographic and infection prevalence	
Coinfection (gonorrhoea & chlamydia) in symptomatic women	28%
Proportion completing treatment when indicated	100%
Long term consequence	
Proportion of women with untreated gonorrhoea/chlamydia developing pelvic inflammatory disease (PID)	0.3
Proportion of women with PID requiring and accessing outpatient services	0.15
Proportion of women with PID requiring and accessing hospital services	0.02
Proportion of women with untreated PID becoming infertile or having an ectopic pregnancy	0.25
Costs	
Cost of dual treatment (chlamydia/gonorrhoea)	$1.66
Cost of treatment for *Trichomonas vaginalis*/bacterial vaginitis	$0.10
Cost of partner treatment	$0.12
Average outpatient costs per case of PID	$4.00
Average cost of hospitalization	$45.00
Average costs to woman to access health services	$1.00
Social costs of infertility / ectopic pregnancy	$500.00
Partner management & reinfection	
Proportion of treated women receiving partner treatment	0.8
Number of partners receiving treatment per index woman	0.2
Proportion of women re-infected, among those whose partner is treated	0.3
Proportion of women re-infected, among those whose partner is not treated	0.6

Flowcharts

Table 2. Different flowcharts modelled for this guideline

No treatment	
Treat all	
1a:	Risk assessment then treat high risk women for *Neisseria gonorrhoeae* (NG) & *Chlamydia tra-chomatis* (CT)
2a:	Speculum exam then treat for NG&CT if positive (presence of signs of cervicitis – mucupus)
3a:	Speculum exam, treat for NG&CT if positive, and if negative perform microscopy (gram stain) and if positive for presence of gram-negative diplococci or pus cell > 20 /hpf) treat for NG&CT
4:	Speculum exam, treat for NG&CT if positive, and if negative perform POCT and if positive test, treat for NG and/or CT
5:	Microscopy (gram stain) then treat for NG&CT if positive
6:	Risk assessment and/or genital exam then treat for NG&CT if risk assessment positive (context specific e.g. age) and /or genital exam positive (presence of vaginal discharge)
7:	Risk assessment and/or genital exam, if positive then perform speculum exam then treat for NG&CT if speculum positive
8:	Risk assessment and/or genital exam, if positive perform speculum exam then treat for NG&CT if speculum positive, if negative speculum perform microscopy then treat for NG&CT if positive
9:	Risk assessment and/or genital exam, if positive then perform low cost POCT then treat for NG and/or CT if positive POCT
10a:	Risk assessment then perform low cost POCT in women at high risk, then treat for NG and/or CT if positive POCT
11a:	Perform low cost POST then treat for NG and/or CT if positive POCT
12:	Risk assessment and/or genital exam, if positive then perform high cost POCT then treat for NG and/or CT if positive POCT
13a:	Risk assessment then perform high cost POCT in women at high risk, then treat for NG and/or CT if positive POCT
14a:	Perform high cost POCT then treat for NG and/or CT if positive POCT
15:	WHO risk: LOW prevalence: risk assessment and/or speculum exam then treat for NG & CT if positive risk assessment and/or speculum; HIGH prevalence: treat all for NG &CT
16:	WHO spec: LOW prevalence: genital examination, if positive for discharge then risk assess-ment, if high risk then treat for NG & CT; HIGH prevalence: genital examination, if positive then treat for NG &CT
Number of partners receiving treatment per index woman	
Proportion of women re-infected, among those whose partner is treated	
Proportion of women re-infected, among those whose partner is not treated	

NG= *Neisseria gonorrhoeae;* CT = *Chlamydia trachomatis;* POCT = point-of-care test

The sensitivity and specificity of different steps in the flowcharts were synthesized when appropriate, and calculated by adding sensitivity and specificity together for some algorithms (e.g., WHO algorithms):

Table 3. Sensitivity and Specificity for different steps in the flowcharts

To identify NG and/or CT		
	Sensitivity	Specificity
Treat all	100%	0%
Risk assessment [Cornier 2010]	63	60
Risk assessment or genital exam [Tolosa 2012]	92	12
Genital exam [Tolosa 2012?]	78	20
Speculum [Haberland 1995]	73	56
Gram stain/microscopy [Sloan 2000]	52	73
Speculum or microscopy	87	41
WHO algorithm by risk (low prevalence)	90	34
WHO algorithm by risk (high preva-lence)	100	0
WHO algorithm by speculum (low prev-alence)	49	68
WHO algorithm by speculum (high prevalence)	78	20

Table 4. Hypothetical sensitivity and specificity of point of care tests (POCT) for NG

Parameter	POCT a*	POCT c
Sensitivity	0.80	0.95
Specificity	0.90	0.98

*low cost POCT

Economic Analysis

The model was used to carry out cost-effectiveness analyses of different management strategies. Net costs combine the cost of testing, the cost of treatment, the cost of partner treatments, the cost of treating AMR infections, the health and social costs of sequalae from untreated infections, and the "AMR tax" (if applied). Equations for key outcomes and costs are outlined in Table 5.

Table 5. Overview Management Strategy Equations

Eq. 1	Total cost of testing	Number presenting x cost of test
Eq. 2	Cost of treatment	Sum of treatment cost x number treated
Eq. 3	Cost of partner treatments	Number partners receiving treatment x cost of part-ner treatment
Eq. 4	Cost of treating AMR infections	Number correctly diagnosed with ng resistant ng x cost of treating resistant ng
Eq. 5	AMR Tax (Unnecessary treatments)	Number without ng incorrectly treated with ceftri-axone x hypothetical AMR tax
Eq. 6	AMR Tax (Necessary treatments)	Number total single antibiotic treatments x hypo-thetical AMR tax on all treatments
Eq. 7	Health sector cost of sequalae	
Eq. 8	Other social cost of sequalae	
Eq. 9	Net Cost	Sum of testing, treatment, partner treatments, AMR treatments, AMR tax, health sector cost, other social cost
Eq. 10	Net Cost per client	Net cost ÷ number presenting

1. Testing and Treating

The costs of testing and treating are calculated for specific management pathways or flowcharts and inputted into the overall analysis. Testing is calculated as the product of the number tested and the cost of testing (eq. 1), with costs compounded for multiple testing methods (i.e. risk assessment + POCT). The cost of treatment is calculated as the product of the number treated and the cost of treatment (eq.2). For syndromic management pathways, we assume dual treatment for women testing positive. Flowcharts including a POCT assume the differential diagnosis and treatment of NG and CT infections, and costs reflect single treatment therapies. Treatment costs for all symptomatic pathways also include the costs associated with treating all women for TV/BV. We calculate the number of partner treatments by multiplying the number of women treated by the probability that partners receive and comply with treatment. We calculate the cost of partner treatments by multiplying the number of partner treatments by the cost of the treatment (typically lower than primary treatments) (eq.3) *(27)*.

2. Health and Social Costs

Health and social costs are estimated to be the total cost of PID sequalae, resulting from untreated NG/CT infections (Eq. 7 & 8). Health and social costs are calculated according to previous cost analyses for symptomatic pathways *(27)*. In a departure from the previous work, the health and social costs of asymptomatic infections are factored into the new model. In cases where the number of asymptomatic women presenting is not set at zero, the number of untreated asymptomatic infections contribute to the health and social costs of sequalae. In cases where asymptomatic patients aren't managed (NT), the model assumes all asymptomatic infections are untreated. The number of PIDs, ectopic pregnancies, and infertility cases are calculated based on respective costs, relative to the number untreated NG/CT infections.

3. AMR Tax cost

We incorporate the cost of AMR in the form of an AMR tax, which can be applied to either all antibiotic treatments or to only those which are unnecessary. The AMR tax represents the current and future burden of AMR, including costs associated with treating resistant infections, increased morbidity and mortality, as well as the cost of developing new drug therapies. For our results in this paper, we calculate this hypothetical AMR tax to be a tax associated with each single treatment of ceftriaxone and azithromycin whether appropriate (patient has NG/CT) or inappropriate (treatment due to false negative).

Model outputs

We present the following model outcomes for all the different scenarios

Logistic outcomes: number of women correctly treated, number of unnecessary treatments

Health outcomes: number of onward infections, number of long-term consequences (pelvic inflammatory disease, ectopic pregnancy and infertility)

Cost outcomes: Total cost of pathway including treatment and test costs, costs of managing long term consequences.

We use these outputs to define three key outcomes that measure the success of a given diagnostic pathway. These are net cost per client seen, percent correctly treated (or not treated), and number of unnecessary antibiotic treatments. We consider a pathway successful if the net cost per client seen and number of unnecessary treatments are minimized, and the percent treated correctly is maximized.

We use a static model in different settings and a single step of onward transmission rather than a full dynamic model. This is suitable for calculating current costs and comparing scenarios, however in the longer-term interventions which reduce the prevalence of infection at a population level may have additional indirect benefits over time on long term consequences which are not captured in this analysis.

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