OFFERING A CHOICE OF DAILY AND EVENT-DRIVEN PRE-EXPOSURE PROPHYLAXIS FOR MSM IN THE NETHERLANDS: A COST-EFFECTIVENESS ANALYSIS

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SUPPLEMENT

We used a stochastic agent-based transmission model and an economic model that we have earlier developed to study the impact and cost-effectiveness of measures for HIV prevention [1-3]. The transmission model describes the formation of sexual relationships between MSM and the transmission of HIV or *N. gonorrhoeae* (NG) via condomless anal intercourse. From the transmission model, we calculated numbers of new HIV and NG infections, HIV and NG tests, MSM receiving antiretroviral treatment, and MSM on PrEP. These numbers were used as input in the economic model to calculate the costs of HIV care, as well as the costs of PrEP monitoring and medication. The structure of the models, model parameters, and data sources have been documented in detail in our earlier publications [1-3]. In this supplement, we provide a copy of the tables with the model parameters, as documented in [1-3].

Table S1. Parameters of the transmission model with distributions.

Model parameter	Distribution[#]	Source[§]
Steady partnerships		
Length (days)	Weibull (0.60888, 920)	ACS
Number sex acts per day[$]		
Days 0-90	Beta (1.11, 2.27)	NWS
Scalar a1 for days 91-180	0.7063611	NWS
Scalar a2 for days 181-360	0.9438086	NWS
Scalar a3 for days 361-720	0.8701950	NWS
Scalar a4 after 720th day	0.7172977	NWS
Casual partnerships		
Length (days)	Gamma (shape = 0.025758, rate = 0.000168)	NWS
Number sex acts per day	Beta (α = 0.4805, β = 3.9098)	NWS
Number of casual partners		
Single, 15-24 years old	Nbinom (size = 0.8480, mean = 6.8892)	ACS
Single, 25-34 years old	Nbinom (size = 1.1508, mean = 9.6369)	ACS
Single, 35-44 years old	Nbinom (size = 1.1508, mean = 9.6369*w1[†])	ACS
Single, 45-54 years old	Nbinom (size = 1.1508, mean = 9.6369*w2[†])	ACS
Single, 55-64 years old	Nbinom (size = 1.1508, mean = 9.6369*w3[†])	ACS
With steady partner, 15-24 years old	Nbinom (size = 0.9934, mean = 2.2943)	ACS
With steady partner, 25-34 years old	Nbinom (size = 0.3034, mean = 3.9506)	ACS
With steady partner, 35-44 years old	Nbinom (size = 0.3034, mean = 3.9506*w1[†])	ACS
With steady partner, 45-54 years old	Nbinom (size = 0.3034, mean = 3.9506*w2[†])	ACS
With steady partner, 55-64 years old	Nbinom (size = 0.3034, mean = 3.9506*w3[†])	ACS
HIV RNA viral load (log_{10} copies/mL)		
Acute HIV	7.0	[4]
Untreated chronic HIV	Normal (mean = 4.5, sd = 0.7)	SHM
Treated chronic HIV unsuppressed	Mixed Normal (mean = 2.5, sd = 0.57) and Normal (mean = 5, sd = 1)	SHM
Treated chronic HIV in rebound	Mixed Normal (mean = 2.1, sd = 0.7) and Normal (mean = 4.4, sd=0.8)	SHM
Time periods in HIV progression (days)		
Before 2012:		
From diagnosis to ART initiation	Nbinom (size = 0.5646, mean = 482.1323)	SHM
From ART initiation to suppression	Nbinom (size = 2.3047, mean =281.6784)[† †]	SHM
From suppression to rebound	Nbinom (size = 1.2012, mean = 579.7795)	SHM
From rebound to suppression	Nbinom (size = 1.6670, mean = 397.8432) [††]	SHM
From 2012 and onwards:		
From diagnosis to ART initiation	Nbinom (size = 0.2952485 , mean = 71.8186)	SHM
From ART initiation to suppression	Nbinom (size = 3.43464, mean = 231.3) [††]	SHM
From suppression to rebound	Nbinom (size = 2.119987, mean = 258.75)	SHM
From rebound to suppression	Nbinom (size = 2.8674, mean = 257.9335) [††]	SHM
Age at sexual debut (years)	Normal (mean = 17.5, sd = 3.4)	ACS

[#]Nbinom, Negative binomial distribution with parameters size and mean; Normal, normal distributions with parameters mean and standard deviation (sd); Beta distribution with parameters alpha and beta; Weibull distribution with parameters alpha and beta.

[§]Distributions obtained from data from the following studies: ACS, Amsterdam Cohort Study among MSM; NWS, Network Study among MSM in Amsterdam; SHM, Stichting HIV Monitoring.

[$] The number of sex acts per day for steady partnerships was a number S drawn from the Beta (1.11, 2.27) distribution for the first 90 days. If the relationship continued, the act rate was S multiplied by scalar a1 for the days 91-180 of the partnership; S multiplied by a1*a2 for days 181-360; S multiplied by a1*a2*a3 for days 361-720; and S multiplied by a1*a2*a3*a4 after the 720th day of the partnership.

† w1, w2 and w3 are scalers determined in the calibration process.

†† For suppression a relatively strict definition was used when analysing SHM data: 2 consecutive RNA measurements of less than 100 copies / ml.

ART, antiretroviral therapy.

Table S2: Parameters of the transmission model relating to sexual behaviour and partner notification.

Parameter	Value	Source
Serosorting with steady partners:		
HIV-positive diagnosed	53.5%	NWS
Negative HIV test in preceding 12 months or no sexual activity in preceding 12 months	63.9%	NWS
Serosorting with casual partners:		
HIV-positive diagnosed	26.1%	NWS
Negative HIV test in preceding 12 months	14.2%	NWS
Factor *a* that makes some MSM more likely to start steady partnerships than other MSM	*a* = 0.5, for 40% of MSM; *a* = 1, for 50% of MSM; *a* = 2, for 10% of MSM	*
Number of MSM in the Netherlands	200,000	[5]
Number of MSM in the model	20,000	*
Age of MSM accounted for in model	15-64 years	*
Percentage of MSM having a steady partner in the preceding 6 months	50-60%	ACS
% of high-risk** MSM choosing a high-risk man as casual partner	75%	*
% of low-risk** MSM choosing a low-risk man as casual partner	75%	*
Partner notification after HIV/STI diagnosis:		
% of casual partners getting tested	14.3%	[6]
% of steady partners getting tested	29.8%	[6]
When an MSM is diagnosed with HIV or gonorrhoea, partners are notified if the relationship is still active, or if the relationship ended within this period:		*
Asymptomatic gonorrhoea	6 months	[7]
Symptomatic gonorrhoea	6 weeks	[7]
HIV	2 years	[6]
Time between partner notification and test of the notified partner	2 weeks	*

*Model assumption.

** High-risk MSM are those with more than 20 partners per six months; low-risk MSM are those with up to 20 partners per six months.

MSM, men who have sex with men; NWS, data from the Network Study among MSM in Amsterdam; ACS, data from the Amsterdam Cohort Study among MSM.

Table S3. Model parameters relating to HIV and gonorrhoea.

Parameter	Value	Source
Duration acute HIV infection	1 month	[4]
Time from HIV infection until HIV can be detected	3 months	[8]
Duration untreated HIV infection, until AIDS development	10 years	[8]
Viral load during acute HIV	7 log10 copies/mL	[4]
ART initiation:		
Old guidelines: when CD4 count falls <350 cells/μL	Until 2011	
Transition from old to new guidelines	2012-2014	
New guidelines: immediate initiation	2015 and thereafter	
Max number rebounds	2	
Probability of having a rebound when on ART:		SHM*
First rebound	18%	
Second rebound (after first rebound)	23%	
Multiplicative factor increasing the probability of HIV transmission when the HIV-positive man has also gonorrhoea	1.17	[9]
Duration untreated gonorrhoea	180 days	Assumption
Duration symptomatic gonorrhoea:		
Until symptoms develop	8 days	[7]
Between symptoms onset and seeking test	7 days	Assumption
Between test and cure	2 days	[7]
% symptomatic gonorrhoea getting treated	100%	Assumption
Duration asymptomatic gonorrhoea		
From infection until becoming infectious	8 days	[7]
From opportunistic test till cure	21 days	Assumption

*Estimated from data from Stichting HIV Monitoring (SHM).

Table S4. Duration of health states.

Health state	Duration	Source
Acute HIV *	30 days	[4, 10]
Chronic HIV asymptomatic	4.4 years	[10], assumption
Chronic HIV symptomatic	4.5 years	[10], assumption
Late stage HIV	1 year	[11], assumption
AIDS	Until death**	Assumption
Epididymitits outpatient visit	10 days	[12]
Epididymitits inpatient visit	6 days	[12]
Epididymitits recovery after inpatient visit	26 days	[12]

* Among individuals with acute HIV infection, we assumed that a percentage p has symptoms for x days and no symptoms for 30-x days. The remaining 100 – p percent of acute infections have no symptoms throughout the 30 days. The percentage p was modelled uniformly distributed in the range 70% to 88% [4, 13]. The duration of symptoms, x, was modelled using a Pert-distribution, with minimum 4 days, most likely 7 days, and maximum 30 days.

** Modelled using a separate Markov-type model (see details in [1,3]).

Table S5. Utilities for each health state

Health state	Utility	Source
HIV-negative and without gonorrhoea	Pert(0.94;1;1)[a]	[14]
HIV and AIDS health states[b]		
Acute HIV symptomatic[c]	Pert(0.6;0.89;0.95)	[14,15]
Acute HIV asymptomatic	As for HIV-negative[d]	
Chronic HIV asymptomatic	As for HIV-negative[d]	
Chronic HIV symptomatic	Pert(0.45;0.82;1)	[14,16]
Late stage HIV	Pert(0.24;0.7;0.8)	[14,16]
AIDS	Pert(0.24;0.7;0.8)	[14,16]
HIV-positive on cART	Pert(0.45;0.94;1)	[14]
Gonorrhoea infections and epididymitis health states		
Asymptomatic gonorrhoea	As without gonorrhoea[d]	
Symptomatic gonorrhoea	0.84	[17]
Epididymitis outpatient	0.46	[17]
Epididymitis inpatient	0.30	[17]
Epididymitis outpatient after inpatient	0.78	[17]

[a] Estimated utility of the general population without HIV and without gonorrhoea. The parameters of Pert distributions are (minimum value; most likely value; maximum value).

[b] HIV/AIDS health state utilities were modelled assuming a correlation of 1.

[c] Only 70%-88% will develop symptoms; see, also, footnote for Table B2.

[d] We assumed that asymptomatic HIV and asymptomatic gonorrhoea have no impact on health-related quality of life.

Table S6. Costs of HIV testing, HIV care and treatment (in 2016 Euros) [1].

	Average (95% uncertainty interval)
Costs HIV testing[a] (€/test)	
HIV-negative individuals[b]	46.6 (44.7-48.4)
HIV-positive individuals:	
test in first three months (false-negative result)[c]	46.4 (44.6-48.3)
test after first three months (true-positive result)	170.7 (167.8-173.7)
Costs of monitoring HIV-positive individuals in care (€/person)[d]	
For the first six months in care	644.0 (639.7-648.2)
After the first six months in care, per year	
Routine control visits	403.1 (386.4-439.5)
Additional visits during viral rebound[e]	272.7 (270.8-274.7)
cART costs (€/person)[f]	
For the first six months in care	4,441.1 (3,567.7-5,155.4)
After the first six months in care, per year	10,605.0 (8,508.9-12,319.4)
Costs of treatment of opportunistic infections[g]	
Hospitalisation (€/person/year)	7,103.5 (1,543.4-13,697.6)

[a] Costs for HIV testing include laboratory test costs and either reference prices for standard consultations (general practitioner and outpatient visit) or estimated staff costs (based on staff time and overhead).

[b] Including potential additional costs for a confirmation test in case of a false positive ELISA test (based on the specificity of the ELISA test).

[c] Individuals tested for HIV during the first three months after infection, were assumed to have always a negative test result.

[d] The monitoring costs include costs for staff including overhead and laboratory tests.

[e] Viral rebound is here defined as a measurement of HIV viral load above 150 copies/ml.

[f] Costs for combination antiretroviral therapy (cART) were based on the most frequently used cART regimes in the Netherlands in 2015 [1,3] and included medication costs and dispensing fees for pharmacies.

[g] Treatment costs for opportunistic infections (excluding cART costs) were calculated by multiplying hospitalizations days with the Dutch weighted mean reference price for hospitalisation days of adults [1,3].

Table S7. Costs related to PrEP programme [3].

Parameter	Estimate	Source
Before start PREP		
Discussion (Assess PrEP eligibility; Check for contraindications)	20-30 minute consult GGD; €1,24/min	[a]
HIV test (negative)	4th Generation ELISA €10,86 + reporting results €2,83	[18] Tariff number 071118
STI test Chlamydia/ gonorrhoea, oral, rectal, urine; syphilis	Routine NZa tariff (€29,54*3) + €8.83	[18] Tariff number 070003 + 070626
Hepatitis C test	€ 13,79	[18] Tariff number 071126
Serum creatinin test	€ 1,54	[18] Tariff number 070419
Start PrEP		
Discussion	20-30 minute consult GGD; €1,24/min	[a]
HIV test (negative)	4th Generation ELISA €10,86 + reporting results € 2,83	[18] Tariff number 071118
1st check after first month		
Routine discussion (Assess PrEP eligibility, check contraindications, start PrEP if clinical indicated)	5-15 minute consult GGD; €1,24/min	[a]
HIV test (negative)	4th Generation ELISA €10,86 + reporting results € 2,83	[18] Tariff number 071118
Serum creatinin test	€ 1,54	[18] Tariff number 070419
Costs of PrEP routine consults.		
Routine discussion (Assess PrEP eligibility, CHeck contraindications, Start prEP if clinical indicated)	20-30 minute consult GGD; €1,24/min	[a]
HIV test (negative)	4th Generation ELISA €10,86 + reporting results € 2,83	[18] Tariff number 071118
STI test Chlamydia/gonorrhoea, oral, rectal, urine; syphilis	Routine NZa tariff (€29,54*3) + €8.83	[18] Tariff number 070003 + 070626
Hepatitis C test	€ 13,79	[18] Tariff number 071126
Serum creatinin test	€ 1,54	[18] Tariff number 070419
PrEP medication		
Daily regime 30 pills/month	€ 30-50 / month	[a]

[a] Data from Public Health Service Amsterdam.

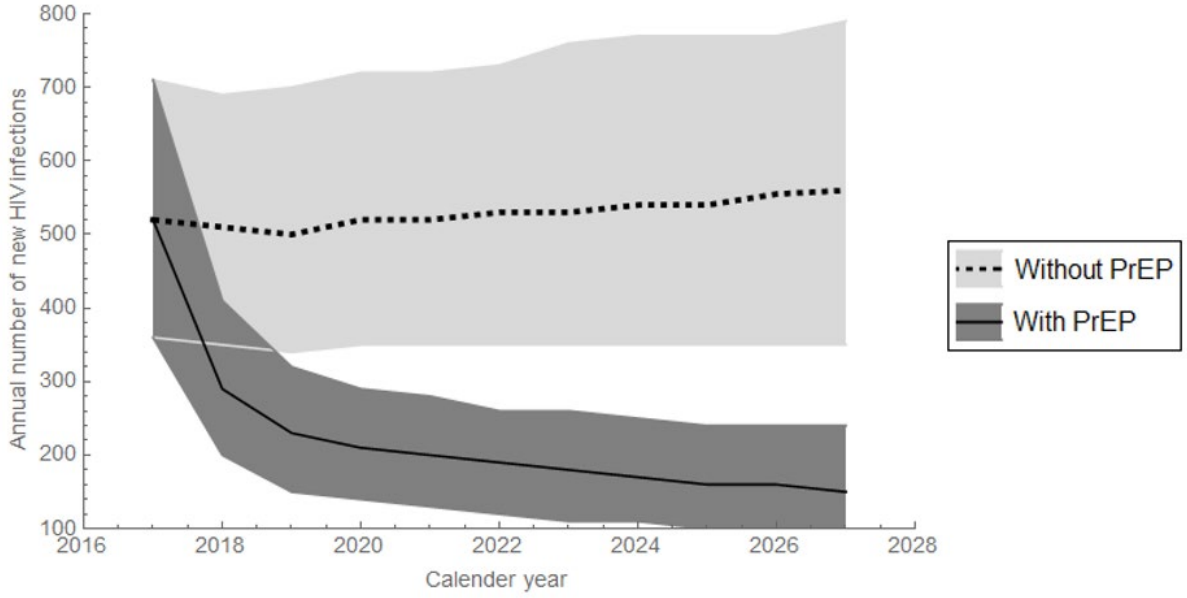

Figure S1: The annual number of new HIV infections in a population of 200,000 MSM, in 2018-2027. The black dotted and solid lines show the medians without and with PrEP, respectively. The grey areas around the black lines show the the interquartile range.

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