Cost-effectiveness of dual antimicrobial therapy for gonococcal infections among men who have sex with men in the Netherlands

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SUPPLEMENT

For simplicity of the notation and terminology, in the supplement we refer to the primary antibiotic (ceftriaxone) as antibiotic A, to the secondary antibiotic (azithromycin) as antibiotic B, and to the alternative antibiotic (third antibiotic option) as antibiotic C.

THE TRANSMISSION MODEL FOR THE CURRENT TREATMENT GUIDELINES WITH MONOTHERAPY

Infected individuals are distinguished according to the NG strain they are infected with. Symptomatic gonorrhea cases may return to their health practitioners, if symptoms persist after treatment, and receive an alternative antibiotic. To account for the extra costs of a second or third visit and of multiple prescriptions of antibiotics, symptomatic gonorrhea cases are further distinguished according to their treatment history, namely, whether they have already received the first-line treatment or not and whether they seek care at GPs or STI clinics. Therefore, the following variables are used in the model (see Figure S1 for a schema of the transmission model):

- $X_k$ is the number of uninfected individuals in risk group $k$;
- $Y_{i0k}$ is the number of asymptomatic gonorrhea cases in sexual risk group $k$, infected with NG strain $i$, who have not yet been treated;
\[ S_{a0k} \text{ and } S_{d0k} \text{ are the numbers of asymptomatic cases with NG strain a or d,} \]
respectively, in sexual risk group \( k \), visiting STI clinics, who have received antibiotic A, but were not cured.

\[ Y_{iik} \text{ is the number of symptomatic gonorrhea cases in sexual risk group } k \text{ who were infected with NG strain } i, \text{ who have not yet been treated;} \]

\[ G_{dk} \text{ is the number of symptomatic cases with NG strain d, in sexual risk group } k, \text{ who have already been to their GP, have received the first-line therapy, but have not yet been cured.} \]

\[ S_{d1k}, S_{d2k} \text{ are the numbers of symptomatic cases with NG strain d, visiting STI clinics, who have received first-line therapy, but are not yet cured (for } S_{d1k} \text{ first a culture is performed to determine antibiotic sensitivity and, based on that, antibiotic C is prescribed; for } S_{d2k} \text{ antibiotic C can be prescribed based on previous culture test).} \]

The subscripts denote: sexual risk group \( k = 1,2,3,4; \) symptomatic or asymptomatic gonorrhea (1 or 0, respectively); NG strain \( i = s, a, b, d \), where \( s \) is the strain sensitive to antibiotics A and B, \( a \) is the strain resistant only to antibiotic A, \( b \) is the strain resistant only to B, and \( d \) is the strain with dual resistance to both A and B. The total size of risk group \( k \) is \( N_k \).

**Model equations.** The model is described by the following equations:

\[
\frac{dX_k}{dt} = \mu(N_k - X_k) - \lambda_k X_k + \tau_d [(1 - q)Y_{iik} + (1 - p)(Y_{aik} + Y_{bik})] + c_2 G_{dk} + c_2 S_{d1k} + c_1 S_{d2k}
\]

\[
+ \gamma(Y_{s0k} + Y_{a0k} + Y_{b0k} + Y_{d0k}) + (1 - p)\varphi_k (Y_{a0k} + Y_{b0k}) + [uc_4 + (1 - u)\gamma](S_{a0k} + S_{d0k}),
\]

\[
\frac{dY_{iik}}{dt} = w\lambda_k X_k - (\mu + \tau_d)Y_{iik},
\]

\[
\frac{dY_{aik}}{dt} = w\lambda_k X_k - (\mu + \tau_d)Y_{aik}, \quad \text{(A1a)}
\]

\[
\frac{dY_{bik}}{dt} = w\lambda_k X_k - (\mu + \tau_d)Y_{bik}.
\]
The rate of entering and departing the sexually active population is $\mu$, the rate of natural recovery is $\gamma$. MSM who want to be tested for gonorrhea (with or without symptoms) or who seek care due to symptoms visit STI clinics (proportion $\theta$) or GPs (proportion $1-\theta$). The fraction of hosts becoming resistant is $p$ when treated with one antibiotic and $q = p^2$ when treated with two antibiotics [1]. Fitness levels for the resistant strains may be different from those for the sensitive strain: if $\beta_i$ is the probability of transmission of NG strain $i$, then $\beta_i = c_i \beta_s$, for $i \neq s$, where $c_i$ denotes the fitness cost of resistance, compared to the sensitive strain $s$. An individual infected from a partner with NG strain resistant to antibiotic(s) acquires the same NG strain and is resistant to the same antibiotic(s).

**Treatment of MSM with symptomatic gonorrhea.** These patients are treated with the first-line antibiotic A, as well as B (to treat presumed chlamydia co-infection) and...
samples are taken for NAAT testing and culture tests. Prescription of A and B has the following results (see decision tree in Figure S3):

- For patients infected with a strain sensitive to A and B ($Y_{a1k}$), a proportion $1-q$ is cured (and becomes susceptible to infection), while a proportion $q$ develops resistance to A and B and 'moves' to class $S_{d1k}$ (if they had visited an STI clinic) or to class $G_{d}$ (if they had visited a GP). Those who developed resistance return with persisting symptoms, a culture is performed and based on the results they are treated with an alternative antibiotic C to which the NG strain is sensitive and they are cured.

- Patients infected with a strain resistant only to A or only to B ($Y_{a1k}, Y_{b1k}$): a fraction $1-p$ of these patients is cured, while a fraction $p$ develops resistance to the other antibiotic and 'moves' to class $S_{d1k}$ (if they had visited an STI clinic) or to class $G_{d}$ (if they had visited a GP). Those who developed resistance return with persisting symptoms, a culture is performed, and they are treated with an alternative antibiotic C to which their strain is sensitive.

- Patients infected with a strain resistant to A and B ($Y_{d1k}$) cannot be cured with these two antibiotics. After prescription of A and B: (i) those visiting STI clinics 'move' to the class $S_{d2k}$, the culture at the initial consultation shows resistance to A and B, therefore they are asked to return to the STI clinic (or they return with persisting symptoms) to receive an alternative antibiotic C to which their strain is sensitive; (ii) those visiting GPs 'move' to the class $G_{d}$, a culture is performed and, based on the results, antibiotic C is prescribed and they are cured.

The average interval from infection until prescription of first-line treatment with A and B is $1/\tau_d$. If they return to their health provider with persisting symptoms and antibiotic sensitivity testing has not been carried out, then cultivation will be carried
out, and based on the results, antibiotics will be prescribed. If they return to their health provider with persisting symptoms and antibiotic sensitivity testing has already been carried out, then (i) if the culture results show resistance to A and B, but sensitivity to an alternative antibiotic C, then they are treated with C after $1/c_1$ days; (ii) if the culture results show sensitivity to A and/or B, then another culture is performed and based on the new culture results they are treated with an alternative antibiotic C, after $1/c_2$ days.

Testing and treatment of MSM with asymptomatic gonorrhea. Individuals without symptoms are tested with a NAAT; if that is positive, they are asked to return to their healthcare provider to receive the first-line antibiotic A. With administration of antibiotic A: (a) those infected with a sensitive strain are cured or develop resistance to A; (b) those infected with a strain resistant to A are not cured with A; a fraction $u$ of those who had been tested at STI clinics, returns for cultivation and receives an alternative antibiotic C and is cured, while the rest remain infectious until natural recovery. The average interval between opportunistic tests plus the time until the patient returns to receive the first-line treatment is $1/\phi_L$ for low-risk MSM (who have no casual partners) and $1/\phi_H$ for high-risk MSM (who have steady and casual partners – see section below for explanation of the sexual risk groups).

Transmission rate of NG. The rate at which men in activity group $k = 1,2,3,4$ get infected with NG is $\lambda_k = \sum_{i=a,d,a,b} \lambda_{ik}$, where $\lambda_{ik}$ is the rate at which men in activity group $k$ get infected with NG strain $i$ as defined from the equations:

$$\lambda_{ik} = \alpha_k \sum_j m_{ij} (1 - (1 - \beta_i)^{\nu}) \frac{Y_j}{N_j} + \alpha_k' \sum_j m_{ij} \beta_i \frac{Y_j}{N_j} + \alpha_k'' \sum_j m_{ij} (1 - (1 - \beta_i)^{\nu}) \frac{Y_j}{N_j}.$$
The probability of transmission of NG strain $i$ per act of UAI is $\beta_i$, with $\beta_i = c_i \beta_s$, for $i \neq s$, where $c_i$ denotes the fitness cost of resistance, compared to the sensitive strain $s$. Also, $a_i$, $a'_i$, $a''_i$ are the numbers of steady, single-act, multiple-acts casual partners; $u_s$ and $u_c$ denote the number of acts of UAI per year per partner, for steady and multiple-acts casual partnerships. Based on data from Rutgers WPF Group, $u_s$ was taken in the range 15-35 acts per year and $u_c$ in the range 2-10 acts per year (see also [2]). Mixing between risk groups $i, j = 1, 2, 3, 4$ is defined by $m_{ij}$ for steady partners:

$$m_{ij} = \alpha \delta_{ij} + (1\alpha - \epsilon) \frac{a_j N_j}{\sum_k a_k N_k},$$

by $m'_{ij}$ for single-act casual partners and $m''_{ij}$ for multiple-acts casual partners:

$$m'_{ij} = \epsilon' \delta_{ij} + (1\epsilon' - \epsilon') \frac{a'_j N_j}{\sum_k a'_k N_k}$$

and

$$m''_{ij} = \epsilon'' \delta_{ij} + (1\epsilon'' - \epsilon'') \frac{a''_j N_j}{\sum_k a''_k N_k},$$

where $\delta_{ij}$ is the Kronecker delta, being equal to 1, if $i = j$, and equal to 0, if $i \neq j$. The parameter $\epsilon$ determines the level of assortativeness in mixing: if $\epsilon = 1$, then mixing is purely assortative; if $\epsilon = 0$, then mixing is purely proportionate. Similarly, $\epsilon'$ and $\epsilon''$ determine the levels of assortativeness in mixing with single-act and multiple-acts casual partners. We found no data to inform the mixing parameters, but earlier studies have indicated that sexual mixing is mostly assortative with steady long-lasting partnerships, but less assortative with casual partners [3,4]. Therefore, for steady partners, we assumed that $\epsilon$ is between 60% and 80%, while for casual partners, $\epsilon'$ and $\epsilon''$ are in the range 40-60%.
**The four sexual risk groups.** In the model, MSM may have steady partners, single-act casual partners (with whom they have only one UAI act), and multiple-acts casual partners (with whom they have multiple sexual contacts). The population is divided into four risk groups according to the number of partners. MSM in risk group 1 have no casual partners. MSM in groups 2, 3, and 4 have steady and casual partners, with increasing total number of partners from group 2 to group 4. Parameters relating to sexual behaviour were mostly obtained from data from the Amsterdam Cohort Study among MSM (see [2] and references therein). The fraction of the population in risk group 1, 2, 3, 4 is 70%, 20%, 7%, 3%, respectively. The annual rates of partner change for MSM in risk group 1, 2, 3, and 4 are:

- For steady partners: 0.27, 0.26, 0.32, and 0.54, respectively;
- For single-act casual partners: 0, 1.36, 4.52, and 20.6, respectively;
- For multiple-act casual partners: 0, 1.36, 3.48, and 13, respectively.

**THE MODEL FOR DUAL THERAPY**

A schematic diagram of the transmission model for dual therapy is shown in Figure S1, S2, while the decision tree for dual therapy is shown in Figure S4. For the transmission model, the equations for \( Y_{stk}, Y_{alk}, Y_{blk}, Y_{dtk}, G_{dk}, S_{d1k}, S_{d2k} \) are the same as in Equations (A1), and the equations for the other variables are:

\[
\frac{dX_k}{dt} = \mu(N_k - X_k) - \lambda_k X_k + \tau_d[(1-q)Y_{stk} + (1-p)(Y_{alk} + Y_{blk})] + c_2G_{dk} + c_2S_{d1k} + c_1S_{d2k}
\]

\[
+ \gamma(Y_{otk} + Y_{otk} + Y_{otk} + Y_{otk}) + \phi_k[(1-q)Y_{otk} + (1-p)(Y_{otk} + Y_{otk})] + [uc_4 + (1-u)\gamma](S_{otk} + S_{otk}),
\]

\[
\frac{dY_{otk}}{dt} = (1-w)\lambda_{otk} X_k - (\mu + \gamma + \phi_k)Y_{otk},
\]

\[
\frac{dY_{otk}}{dt} = (1-w)\lambda_{otk} X_k - (\mu + \gamma + \phi_k)Y_{otk},
\]

\[
\frac{dY_{otk}}{dt} = (1-w)\lambda_{otk} X_k + (1-\theta)\phi_k(qY_{otk} + pY_{otk} + pY_{otk}) - (\mu + \gamma + \theta\phi_k)Y_{otk},
\]

\[
\frac{dS_{otk}}{dt} = [\mu + uc_4 + (1-u)\gamma]S_{otk} + \theta\phi_k(qY_{otk} + pY_{otk} + pY_{otk} + Y_{otk}).
\]
The notation is the same as for Equations (A1). Asymptomatic gonorrhea cases can be detected with opportunistic testing. They are tested with a NAAT and if that is positive, they are asked to return to their health provider to receive antibiotics A and B. With dual therapy, patients infected with a strain resistant to A and B cannot be cured and remain infectious until natural recovery; patients with a strain sensitive to at least one of the two antibiotics can be cured or develop resistance to A and/or B.

**HEALTH OUTCOMES AND COSTS**

From the transmission model, the level of healthcare use in year \( y \) with monotherapy was measured by the numbers of: (1) visits at STI clinics; (2) visits at GPs; (3) NAAT tests; (4) culture tests; (5) doses of ceftriaxone; (6) doses of azithromycin; (7) doses of an alternative antibiotic, denoted by \( H_{m1y}, H_{m2y}, \ldots, H_{m7y} \), respectively. The respective numbers with dual therapy are denoted \( H_{d1y}, H_{d2y}, \ldots, H_{d7y} \). The respective costs, \( s_i \), of visits, tests, and antibiotic doses are shown in Table 1. Medicine prescribed by a GP is obtained at a pharmacy, not by the GP; pharmacies charge a handling fee for all medicine they provide. Medicine prescribed by STI clinics are provided by the clinics; pharmacies charge a handling fee to the STI clinics for all medicine they provide them. These handling fees are reported in Table 1. When patients return to the GP or to the STI clinic for test results or for administration of treatment, a second visit is charged; therefore, the numbers of visits at STI clinics and GPs are in some cases twice those indicated by the rates of testing (\( \tau_d \) or \( \phi_l \)).

The total costs \( C_{my} \) of monotherapy and \( C_{dy} \) of dual therapy in year \( y \) were calculated as:

\[
C_{my} = \sum_{i=1}^{5} s_i H_{miy} + s_7 H_{m7y} \quad \text{and} \quad C_{dy} = \sum_{i=1}^{7} s_i H_{diy}.
\]
Notice, that for monotherapy, the costs of azithromycin were excluded. We calculated for each year $y$, the incremental costs, $\Delta\text{costs}(y) = C_{dy} - C_{my}$, expressing the extra costs of dual therapy compared to monotherapy.

The quality-adjusted life-years (QALY) lost in year $y$ with monotherapy are

$$Q_{my} = [(1 - p_c)w_u d_u + p_c w_c d_c]I_{my} + [(1 - p_c)w_u d_u' + p_c w_c d_c']R_{my},$$

where, $I_{my}$ is the number of new symptomatic infections in year $y$ with monotherapy; $p_c$ is the fraction of gonorrhea infections with complications; $w_c$ and $w_u$ are the weights for quality of life loss for symptomatic gonorrhea with and without complications, respectively (we assumed that asymptomatic cases have no loss of quality of life); $d_c$ and $d_u$ are the durations of symptomatic gonorrhea with complications and without complications, respectively, from infection until receipt of first-line treatment; for those who receive first-line treatment but are not cured, $d_u'$ is the time from receipt of first-line treatment until cure (with alternative treatment) for those with complications and $d_u'$ for those without complications; $R_{my}$ is the number of symptomatic gonorrhea cases who have received first-line treatment but are not cured ($S_{d1}, S_{d2}, G_u, G_d$), in year $y$, with monotherapy. The QALYs lost in year $y$ with dual therapy are similarly defined as

$$Q_{dy} = [(1 - p_c)w_u d_u + p_c w_c d_c]I_{dy} + [(1 - p_c)w_u d_u' + p_c w_c d_c']R_{dy},$$

where $I_{dy}$ is the number of new symptomatic infections and $R_{dy}$ the number of symptomatic gonorrhea cases who have received first-line treatment but are not yet cured, in year $y$, with dual therapy. For each year $y$, the incremental QALYs, $\Delta\text{QALY}(y) = -(Q_{dy} - Q_{my})$, were calculated, representing QALYs gained by switching from monotherapy to dual therapy.
The incremental cost-effectiveness ratio (ICER) in year $y$ was calculated as the ratio of incremental costs divided by incremental QALYs, \( ICER(y) = \Delta \text{costs}(y)/\Delta \text{QALY}(y) \), expressing extra costs per QALY gained, by switching from monotherapy to dual therapy. Costs were discounted by 4% per year and QALYs by 1.5% per year, according to Dutch guidelines [5].

By adding the annual costs over the first $K$ years (for $K=2, 3, ..., 50$), we calculated the cumulative costs over the $K$-year time frame: $\sum_{y=1}^{K} \Delta \text{costs}(y)$. Similarly, the cumulative QALYs were calculated as $\sum_{y=1}^{K} \Delta \text{QALY}(y)$ and cumulative ICER for the $K$-year time frame as $\sum_{y=1}^{K} \text{costs}(y)/\sum_{y=1}^{K} \text{QALY}(y)$.

**Scenarios for improving gonorrhea management**

The following scenarios with improved gonorrhea management are examined:

**Shorter interval until treatment symptomatic gonorrhea**: The average interval until prescription of first-line therapy ($1/\tau_d$) is reduced to 3-8 days (compared to 6-16 days in the baseline scenario) and the average interval between successive prescriptions of antibiotics ($1/c_1$) is reduced to 3-5 days (compared to 5-9 days in baseline scenario).

**More frequent opportunistic screening in high-risk MSM**: It is assumed that high-risk MSM (those who have both steady and casual partners) are more frequently tested for STI’s, such that the average interval between opportunistic screenings was 8-12 months, as opposed to 12-16 months in the baseline scenario.

The results are shown in Figures S9, S10. Compared to the baseline scenario, in the scenario with shorter interval until treatment of symptomatic gonorrhea cases, the
gain in QALYs increases slower and remains lower compared to the baseline scenario, probably because the time that symptomatic gonorrhea cases remain untreated is very short with both monotherapy and dual therapy. Consequently, the ICER declines later and remains much higher than that in the baseline scenario; dual therapy is not cost-effective compared to monotherapy in this scenario (Figures S9, S10).

With more frequent opportunistic screening among high-risk MSM, resistance to the first-line treatment spreads earlier, compared to the baseline scenario (Figure S9); this holds for both monotherapy and dual therapy. When resistance is prevalent with monotherapy and not yet with dual therapy (between the 10th and 20th year), the additional costs decline and the additional QALYs increase, as observed in the baseline scenario. The decline in annual additional costs of dual therapy is higher compared to that in the baseline scenario, because more individuals are treated appropriately with dual therapy than with monotherapy (especially in this period that resistance is prevalent with monotherapy but not with dual therapy) and this difference is higher with more opportunistic screening. Therefore, the cumulative additional costs decline dramatically, the QALYs gained increase radically, and dual therapy becomes cost-saving and cost-effective. However, around the 20th year, the spread of resistance with dual therapy results in an increase in additional costs and in the ICER and dual therapy is not cost-effective after the 25th year.
Figure S1: Flow diagram of the transmission model for gonorrhea infection, with monotherapy. Individuals may be infected with a strain sensitive to antibiotics A, B \((Y_{s0}, Y_{s1})\); resistant to antibiotic A only \((Y_{a0}, Y_{a1}, S_{a0})\); resistant to antibiotic B only \((Y_{b0}, Y_{b1})\); or resistant to antibiotics A and B \((Y_{d0}, Y_{d1}, G_d, S_{d1}, S_{d2}, S_{d0})\). The subscript 0 denotes asymptomatic gonorrhea, while the subscript 1 denotes symptomatic gonorrhea (see Methods for more details).
Figure S2: Flow diagram of the transmission model for gonorrhea infection with dual therapy. Only the submodel for asymptomatic gonorrhea cases is shown here, since the submodel for symptomatic cases is the same as with monotherapy shown in Figure S1. Notation is the same as in Figure S1; see also Methods for more details.
Figure S3: Decision tree for the current treatment guidelines with monotherapy. STI, sexually transmitted infection; GP, general practitioner; NAAT, nucleic acid amplification test; "cult", culture tests; "ant", antibiotic; "opp scr", opportunistic screening.
**Figure S4:** Decision tree for the model with dual therapy. STI, sexually transmitted infection; GP, general practitioner; NAAT, nucleic acid amplification test; "cult", culture tests; "ant", antibiotic; "opp scr", opportunistic screening.
Figure S5: The level of use of healthcare services: annual number of (a) consultations at general practitioners (GPs); (b) consultations at STI clinics; (c) culture tests; (d) nucleic acid amplification (NAAT) tests. The black line and the grey shaded area show the median and the interquartile range from the uncertainty analysis for monotherapy; the grey dots and grey line segments show the median and the interquartile range for dual therapy.
Figure S6: Antibiotic prescriptions under monotherapy and dual therapy: annual numbers of prescriptions of (a) ceftriaxone; (b) azithromycin; (c) alternative antibiotic. The black line and the grey shaded area show the median and the interquartile range from the uncertainty analysis for monotherapy; the grey dots and grey line segments show the median and the interquartile range for dual therapy.
**Figure S7:** The cost-effectiveness plane of dual therapy versus monotherapy for gonorrhea infection for the baseline scenario. The vertical axis shows the cumulative discounted additional costs and the horizontal axis shows the gain in the cumulative discounted QALYs over the 60-year period. The ICER threshold of €20,000 per QALY gained is shown with the red line. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.
Figure S8: Cost-effectiveness of dual therapy compared to monotherapy. Left panels: with discounting according to Dutch guidelines (4% for costs and 1.5% for QALYs); right panels: without discounting. (a), (b) Annual discounted additional costs, in €; negative values denote that the costs of dual therapy are lower than those of monotherapy. (c), (d) Annual discounted QALYs gained; negative values denote QALY loss with dual therapy compared to monotherapy. (e), (f) Annual discounted ICER of dual therapy compared to monotherapy, in € per QALY gained. The solid lines show the medians and the shaded areas the interquartile ranges from the uncertainty analysis. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.
Figure S9. Cost-effectiveness of dual therapy compared to monotherapy. (a) Baseline scenario; (b) scenario where treatment is introduced when 5% of gonorrhea cases has resistance to azithromycin; (c) scenario with earlier treatment initiation for symptomatic gonorrhea; (d) scenario with more frequent opportunistic screening among high-risk men who have sex with men. Results shown for the cumulative discounted additional costs in €10,000 (dark gray shaded area); cumulative discounted additional QALYs (light gray shaded area); cumulative discounted ICER in €1,000 per QALY gained (dash-dotted line); the ICER threshold of €20,000 per QALY gained, scaled in €1,000/per QALY (dotted line); the % of gonorrhea cases with resistance to first-line treatment with monotherapy (dashed line) or dual therapy (solid line).
**Figure S10.** Cost-effectiveness acceptability curves of dual therapy versus monotherapy for the treatment of gonorrhea infections, (a) with discounting, as explained in main text and (b) without discounting. Results are cumulative over a 60-year period. The vertical axis shows the fraction of parameter sets where dual therapy is cost-effective compared to monotherapy, for the respective ICER threshold shown on the horizontal axis. Scenarios shown: the baseline scenario (solid line); treatment strategies are introduced when 5% of gonorrhea cases has resistance to azithromycin (dashed line); earlier treatment initiation for symptomatic gonorrhea cases (dotted line); more frequent opportunistic screening among high-risk men who have sex with men (dashed-dotted line). ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.
Figure S11. Sensitivity of economic results to variations in the probability of development of resistance. Each black dot corresponds to one of the results of the uncertainty analysis. (a) Cumulative discounted ICER and the threshold of €20,000 per QALY gained denoted with red line; (b) cumulative discounted additional costs, in €; (c) cumulative discounted QALY gained. Results shown are cumulative over the 60 years. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.
Table S1. Results from the cost-effectiveness analyses with different discounting rates*

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<td>Cumulative ICER</td>
<td>1.19*10^9</td>
<td>9,372,503</td>
<td>246,194</td>
<td>136,368</td>
<td>93,918</td>
<td>49,295</td>
</tr>
</tbody>
</table>

* Annual results are for the costs, QALYs, and ICER at the 10th, 20th, 30th, 40th, 50th, 60th year; cumulative results for costs, QALYs, and ICER over the first 10, 20, 30, 40, 50, or 60 years. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.
References


Additional references for the main text


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