Cost-Effectiveness of Meningococcal Vaccination among Men who Have Sex with Men in New York City

Appendix

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Estimation of the size of the target population

The size of the target population was estimated using data from the New York City (NYC) Community Health Survey and the NYC HIV/AIDS surveillance registry. The NYC Community Health Survey is an annual, cross-sectional, telephone survey designed to collect information on self-reported health status and risk behaviors among NYC residents.[1] Based on 2011 data, there were an estimated 2.06 million men in NYC reporting at least 1 sexual partner and 4.8%, or 105,000, (95% confidence interval 74,000-134,000) of these men self-reported sex with at least one male partner in the prior12 months. The NYC HIV/AIDS surveillance registry, a population-based registry of all diagnoses of AIDS since 1981 and HIV infection since 2000 reported to the NYC Department of Health and Mental Hygiene (DOHMH).[2] The registry contains demographic, HIV transmission risk and clinical information including viral load and CD4 count on persons diagnosed with HIV in NYC. Using data from this registry the HIV-infected MSM population in NYC was estimated at 39,000 (all of whom were assumed to be sexually active), indicating that there were 66,000 (105,000 minus 39,000) sexually active HIV-uninfected MSM. The percentage of HIV-infected MSM with CD4 cell count<200 was estimated to be 13% based on surveillance registry data from the general population of NYC HIV-infected persons with any transmission risk factor.

To determine the proportion of the HIV-uninfected MSM population targeted by the DOHMH recommendations to vaccinate HIV-uninfected men "who had intimate contact with any man met online, through a smartphone application, or at a bar or party," we used National HIV Behavioral Surveillance (NHBS) data in which 31.4% of NYC sexually active MSM with unknown HIV status at the time of the interview reported having at least one sex partner in the past 12 months whom they met on the internet (unpublished data). The target population was,

therefore, assumed to consist of 39,000 HIV-infected MSM and 21,000 (66,000 multiplied by 31.4%) HIV-uninfected MSM, for a total of 60,000 MSM.

Estimation of Vaccine coverage and effectiveness

Vaccine coverage was based on provider reporting to DOHMH. Reporting sites included DOHMH sexually transmitted disease and immunization clinics, NYC Health and Hospitals Corporation sites, academic medical centers in NYC, private physician groups with large MSM populations and community-based partners who conducted special vaccination outreach events. Supplementary figure 2 illustrates the vaccine coverage rate for receipt of at least 1 dose of MCV-4 vaccine expressed as a percentage of the target population of 60,000 MSM over 1 year. Vaccination counts as reported to DOHMH were adjusted by 10% to account for under-reporting. From October 2012 to September 2013, 17,750 MSM were reported to have received at least 1 dose of MCV4. The base case vaccine coverage rate (17%) is the weighted average vaccine coverage over 1 year.

Among HIV-uninfected MSM, we estimated meningococcal quadrivalent conjugate vaccine (MCV4) effectiveness to be 90% over 1 year.[3] To determine MCV-4 effectiveness in the HIV-infected population with CD4>200 after 1 dose, we compared the reported percentage of HIV-infected patients with a four-fold rise in serum bactericidal antibody (SBA) titer at week 4 (60.5%),[4] with this percentage in immunocompetent adults (88.5%).[5] To calculate 2nd dose effectiveness in the HIV-infected population, we compared the proportion of HIV-infected adolescents with SBA titers >8 at approximately 72 weeks (49%),[4] with this proportion in the immunocompetent population (60%).[6] The reductions in efficacy derived from this method were comparable to the results of a meningococcal serogroup C conjugate vaccine immunogenicity study comparing antibody response in HIV-infected and HIV-uninfected adolescents and young

adults (72% HIV-infected with a 4-fold SBA response versus 100% in HIV-uninfected).[7] Vaccine immunogencity was stratified by CD4 cell count above and below 200 due to a demonstrated a significantly lower immunogenicity in HIV-infected adolescents with CD4 % less than 15.[4] Specifically, the immune response of HIV-infected adults with CD4 cell counts less than 200 was assumed to be consistent with the response reported for adolescents with <15% CD4 (only 13% with 4-fold rise in SBA at week 4).[8] The ratios for HIV-infected antibody responders to HIV-uninfected antibody responders, stratified by number of doses and CD4 cell count, were multiplied by the vaccine effectiveness in the HIV-negative population (90%) to estimate vaccine effectiveness in the HIV-positive population.

Critical vaccination threshold and herd immunity function

The critical vaccination threshold is defined as the proportion of immune individuals in the population required to eliminate transmission of the outbreak strain and was calculated using the following equation.[9]

$$\text{Critical vaccination threshold} = \frac{1-(1/R_0)}{\text{Vaccine effectiveness}}$$

R_0 is the basic reproductive rate defined as the average number of secondary infections generated by a primary case. Using R_0=1.36 [10] and the weighted average of the vaccine effectiveness in HIV-infected and HIV-uninfected MSM (71%), a critical vaccination threshold of 37% was derived. The relationship between the risk of IMD in unvaccinated MSM and vaccination coverage was adopted from published functions of herd immunity described by a basic Susceptible-Infected-Recovered (SIR) model of infectious disease transmission in a

homogenous, randomly vaccinated population (Supplementary Figure 3).[9,11] This relationship assumes the risk of IMD in unvaccinated MSM declines exponentially as a function of vaccine coverage until the critical vaccination threshold is achieved. The curve was fit using the weighted average NYC outbreak IMD incidence in HIV-infected and HIV-uninfected MSM (16 IMD cases per 100,000 person) prior to vaccination and the baseline incidence of IMD in the United States (0.3 IMD cases per 100,000 persons) at a vaccine coverage equal to the critical vaccination threshold (37%).[12] Herd immunity reaches its maximum effect at the critical vaccination threshold (37%). Since vaccine coverage was assumed to be 17% over the 1 year time period, the point estimate of herd immunity impact in the model is a 20% reduction in the unvaccinated IMD incidence (Supplementary Figure 3). We derived the maximum herd immunity impact used in sensitivity analysis based on vaccination coverage of at least 30% occurring 1 year after DOHMH vaccination recommendations. Applying the herd immunity assumption in Supplementary Figure 3 with vaccine coverage=30%, corresponded to a 63% reduction in IMD risk in unvaccinated MSM.

Health state utilities and quality-adjusted life expectancy

Quality-adjusted life-years (QALYs) were calculated by multiplying health state utility values by the time spent in each health state. The age-adjusted baseline quality of life for non-HIV infected MSM was derived from utility scores from a nationally representative sample of healthy adults.[13] Life expectancy for HIV-uninfected MSM was from standard life table mortality data.[14] Health related quality of life for HIV-infected MSM was the mean utility value from a community health preference survey and was stratified by CD4 cell count.[15] HIV-infected MSM with a CD4 count above 200 had life expectancy of 28.3 years and HIV-infected MSM

with CD4 cell count below 200 had a life expectancy of 19.4 years.[16] Hypothetical patients who recovered from IMD experienced a short-term temporary disutility for 30 days based on the quality of life impact of pneumococcal meningitis.[17] Hypothetical patients who suffered IMD-related disability experienced utility reductions for their remaining life expectancies. Utility values for epilepsy and hearing loss were mean EQ-5D index scores from a nationally representative community-based preference survey.[13] The utility value for amputation was the mean of multiple studies evaluating the quality of life of amputees following critical limb ischemia.[18] Severe neurologic disability resulted in both utility loss and lower life expectancy, resulting in a quality-adjusted life-expectancy loss of 11.2 QALYs derived from published data on stroke.[19]

Labor costs for outbreak response

Thirty-nine percent (26/66) of NYC DOHMH employees responded to a staff survey to quantify weekly hours devoted to the IMD outbreak response. Civil service job titles were used to derive hourly wages and calculate labor costs. The average number of hours spent per person per week on work related to the IMD outbreak response was 6-8 (range 0-20 hours) with total labor costs estimated to be $196,000 (September 2012-December 2012), $157,000 (January 2013-April 2013) and $62,000 (May 2013-August 2013).

Probabilistic sensitivity analyses (PSA)

PSAs were conducted using 1,000 random draws from probability distributions for each variable and recalculating the cost-effectiveness for each of the 1,000 iterations. Supplementary table 1 reports the variables, ranges and distributions applied in PSA. Probability and utility parameters were assigned as uniform distributions for inputs for which there was greatest uncertainty, or were assigned triangular distributions with the base case value defined as the mode. Uncertainty ranges in Supplementary Table 1 reflect upper and lower limits based on

plausible ranges. We assigned a beta distribution for IMD case fatality ratio based on data from the NYC outbreak. Costs were assigned gamma distributions which is conventional in cost-effectiveness analysis.[20] Separate PSAs were conducted for the herd immunity and no herd immunity scenarios. In the herd immunity scenario, the vaccine coverage was assumed to vary between (8% and 30%) with a uniform distribution to account for uncertainty around the estimated size of the target population and vaccine reporting. For each coverage proportion, estimated the impact of herd immunity (reduction in IMD risk in unvaccinated MSM) was assigned based on the modeled herd immunity relationship (Supplementary Figure 3). Supplementary figure 4 illustrates results from PSA.

~~Supplementary~~ Table S1: Model inputs, ranges and distributions applied in probabilistic sensitivity analysis.

Inputs	Base case	Range	Distribution
Probability values			
IMD incidence in NYC MSM (per 100,000 persons)			
HIV-uninfected	7.6	4.0-24.0	Uniform
HIV-infected	20.1	13.0-25.0	Uniform
Vaccine effectiveness			
HIV-uninfected	90%	75-95%	Triangular
HIV-infected CD4≥200			
1 dose	61%	30-90%	Triangular
2 doses	76%	35-95%	Triangular
HIV-infected CD4 < 200			
1 dose	17%	5-35%	Triangular
2 doses	20%	10-40%	Triangular
Vaccine coverage			
HIV-uninfected	17%	9-30%	Uniform
HIV-infected			
1 dose	17%	9-30%	Uniform
2 doses	54%	3-13%	Uniform
Proportion of at risk MSM	65%	30%-	Uniform

Inputs	Base case	Range	Distribution
with HIV		90%	
Proportion of HIV+ MSM with CD4<200	13%	5-25%	Triangular
Proportion of vaccine administered at public sector price	42%	0-100%	Triangular
Reduction in IMD risk attributable to herd immunity	20%	0-63%	Supplementary figure 3
IMD clinical outcomes			
Death			
HIV-uninfected[a]	20%	5-40%	Beta
HIV-infected[a]	41%	10-60%	Beta
Neurologic disability	18%	5-40%	Triangular
Hearing loss	9.3%	1-20%	Triangular
Epilepsy	5.8%	1-10%	Triangular
Amputation	1.7%	0-5%	Triangular
Utility values			
Baseline HIV-uninfected (by age)			
35-44	0.922	0.89-0.95	Uniform
45-54	0.871	0.84-0.90	Uniform
55-64	0.842	0.81-0.87	Uniform

Inputs	Base case	Range	Distribution
65-74	0.823	0.79-0.85	Uniform
75-84	0.790	0.76-0.82	Uniform
Baseline HIV-infected			
CD4 ≥ 200	0.866	0.85-0.88	Uniform
CD4<200	0.846	0.83-0.86	Uniform
Acute IMD	0.200	0.1-0.4	Uniform
IMD sequelae			
Hearing loss	0.776	0.70-0.86	Uniform
Epilepsy	0.766	0.70-0.86	Uniform
Neurologic disability	0.704	0.60-0.80	Uniform
Amputation	0.540	0.25-0.75	Uniform
Cost (2012 US dollars)[b]			
Acute IMD			
Hospitalization	$51,627	+/- 50%	Gamma
Ancillary/Outpatient services	$9,904	+/- 50%	Gamma
Prophylaxis of contacts[1]	$300	+/- 50%	Gamma
Lifetime costs of IMD sequelae			

Inputs	Base case	Range	Distribution
Epilepsy	$6,188	+/- 50%	Gamma
Hearing loss	$72,189	+/- 50%	Gamma
Amputation	$77,960	+/- 50%	Gamma
Neurologic disability	$183,740	+/- 50%	Gamma

[a] Case fatality in HIV-infected and HIV-uninfected MSM was based on the mortality rates during the New York City outbreak. From 2010-2013, 5 of 12 HIV-infected MSM with IMD died and 7 recovered. Among HIV-uninfected MSM, 2 of 10 with IMD died and 8 recovered. For HIV-infected the numbers 5 and 7 define the shape of the beta distribution and similarly the numbers 2 and 8 defined the shape of the beta distribution for HIV-uninfected.

[b] Gamma distributions were parameterized by inputting the mean (base case value) and standard deviation (assumed to be 25% of base case value) in TreeAge Pro. .

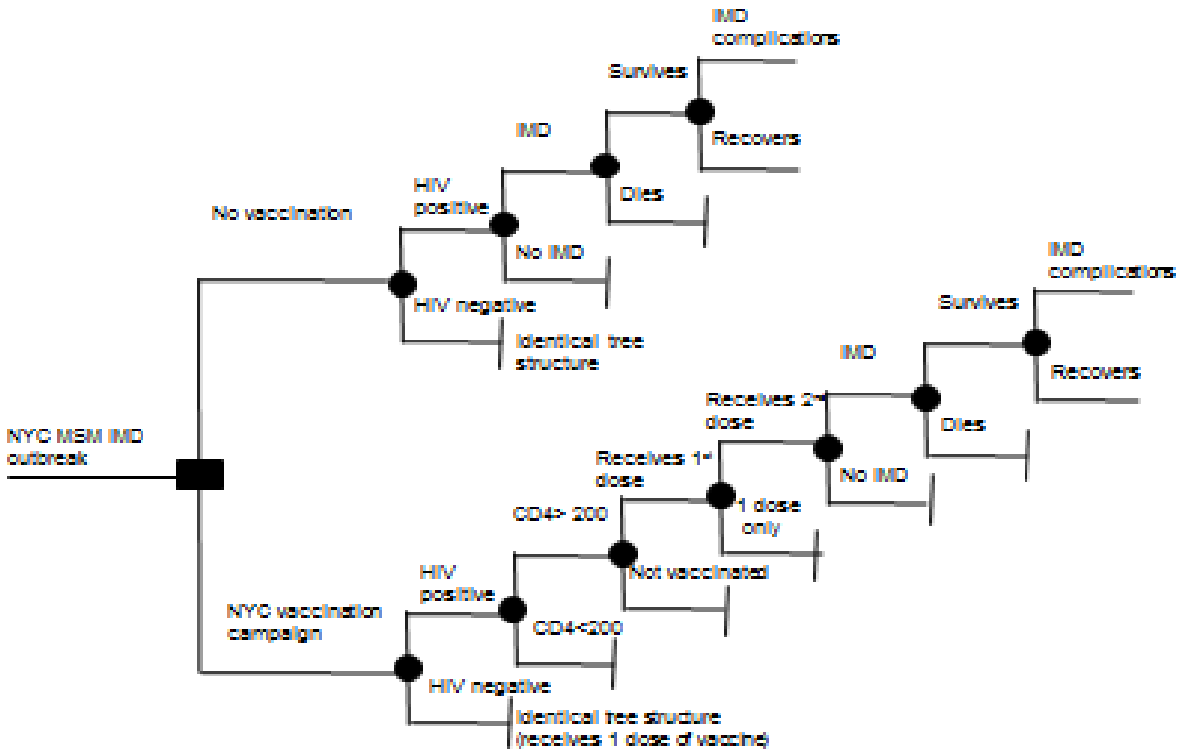
~~Supplementary~~ Table S2: Projected effectiveness of meningococcal vaccination in 60,000 New York City men who have sex with men over 1 year time frame.

	No vaccination	Vaccination	Difference[a]	Difference Range[b]
IMD cases				
Herd immunity	9.6	6.9	2.7	0.9-6.0
No herd immunity	9.6	8.5	1.1	0.5-2.1
IMD deaths				
Herd immunity	3.7	2.7	1.0	0.2-2.5
No herd immunity	3.7	3.3	0.4	0.1-0.9
Life years (undiscounted)				
Herd immunity	1,989,305	1,989,339	33.4	8.6-86.6
No herd immunity	1,989,305	1,989,319	13.6	4.2-31.5

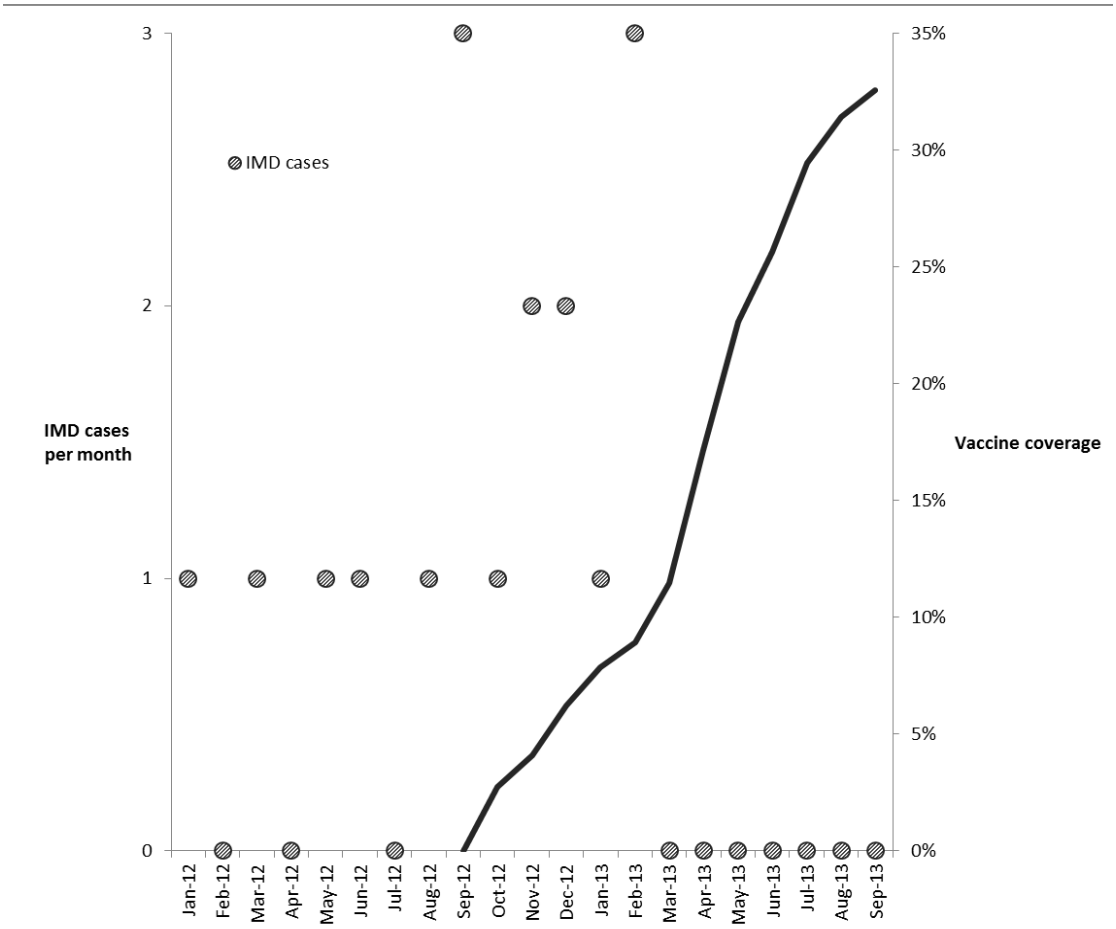
[a]Differences may not match previous columns exactly due to rounding

[b]Ranges represent 2.5 and 97.5 percentiles from probabilistic sensitivity analysis.

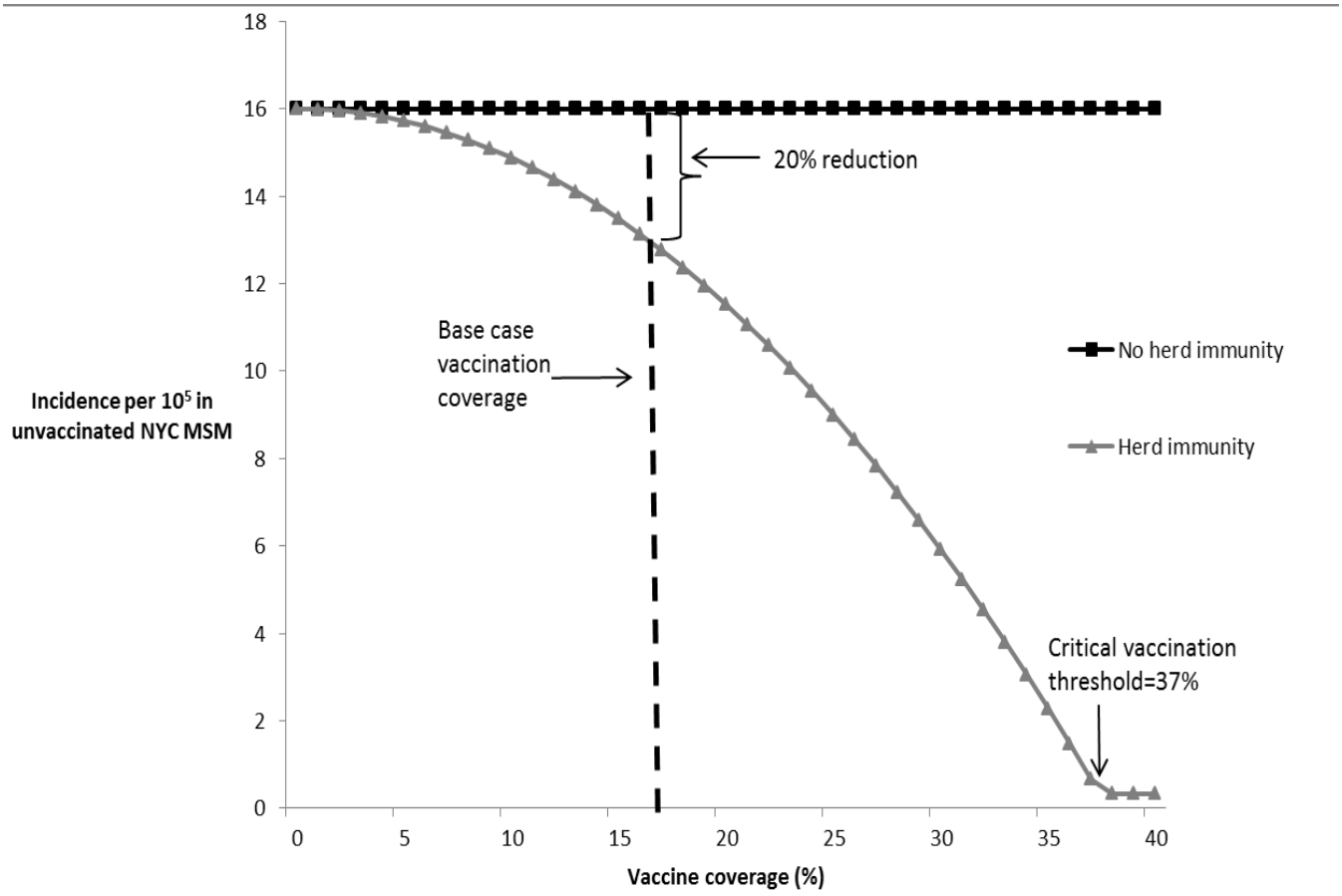
~~Supplementary~~ **Figure S1**: Decision tree structure for New York City outbreak of invasive meningococcal disease (IMD) in men who have sex with men (MSM). Circles represent chance events and are assigned probabilities. The model is used to calculate expected costs, IMD cases, IMD deaths, life-years and quality-adjusted life-years gained for each strategy for a a target population of approximately 60,000 HIV-infected MSM and at-risk HIV-uninfected MSM.



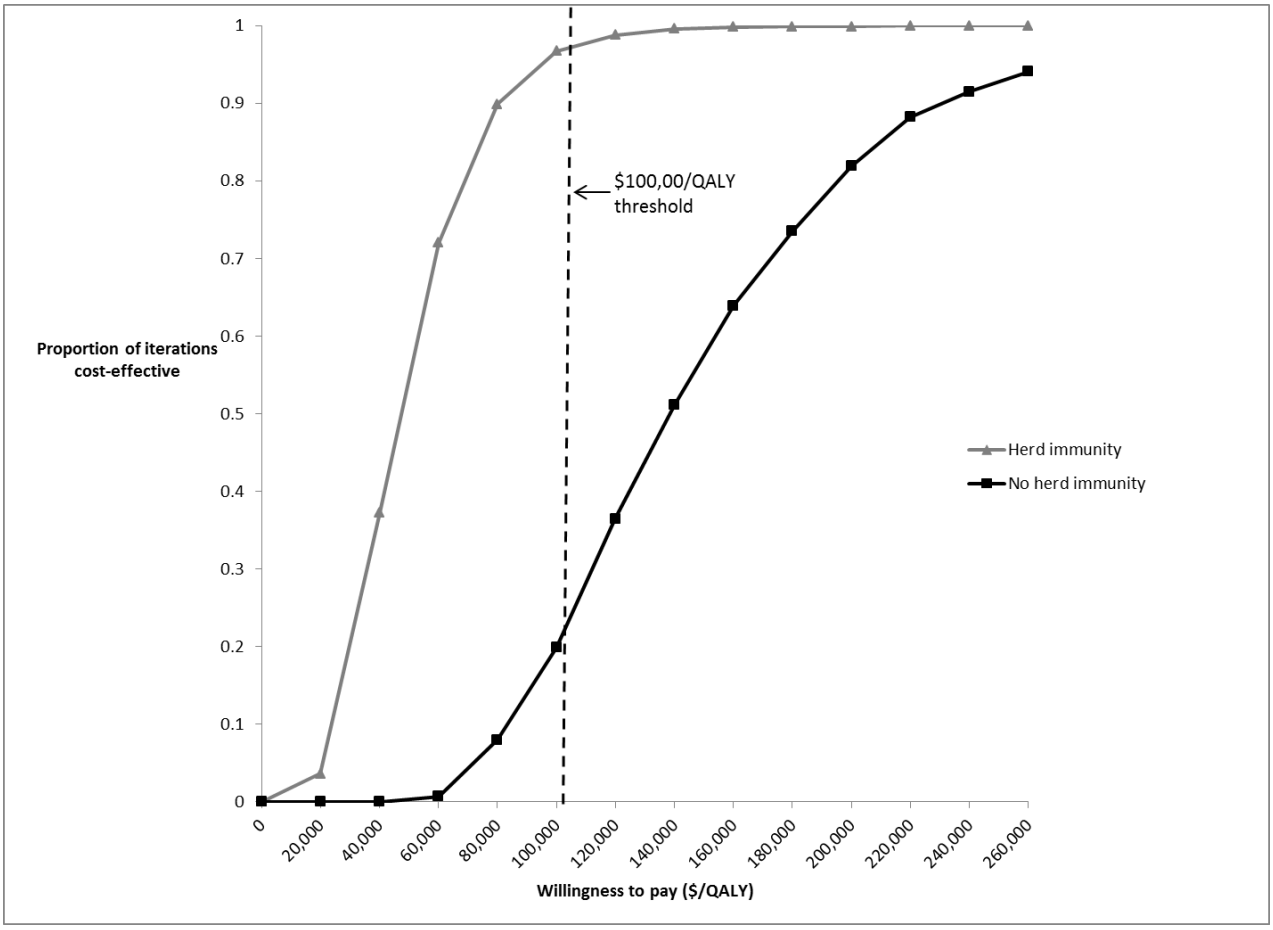
~~**Supplementary**~~ **Figure S2**: The figure illustrates the monthly count of invasive meningococcal disease (IMD) cases among NYC MSM and cumulative vaccine coverage based on reporting of first dose of meningococcal vaccine to DOHMH from January 2012-September 2013. Vaccine coverage assumes a target population of 60,000. The figure shows a sustained reduction in IMD cases after February 2013 corresponding with a rapid increase in vaccine uptake during this time period.



~~**Supplementary**~~ **Figure S3:** The graph plots the incidence of IMD in unvaccinated MSM as a function of vaccine coverage. In the absence of herd immunity, incidence remains constant. When herd immunity is present, incidence declines exponentially until the critical vaccination threshold is achieved and plateaus at pre-outbreak IMD incidence.



~~**Supplementary**~~ **Figure S4:** Cost-effectivness acceptability curve showing the probability that meningococcal vaccination is cost-effective for a given willingness to pay value. Separate PSAs were conducted for scenarios with and without herd immunity.



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