**Appendix (as supplied by the authors): Model description, calculation of model parameters, and supplementary information on the results of the sensitivity analyses**

The purpose of this supplementary appendix is to provide detailed descriptions of the design of the model, the steps taken to ensure its validity, construction of model parameters, and to provide supplementary information on the results of sensitivity analyses. Each of these three objectives is executed in turn below.

## A1.0 Model Description

The model was programmed as a cohort model with a Markov structure, modified to incorporate time and patient history in several different ways. The cohort modeling framework was selected due to computational ease of application of one-way and probabilistic sensitivity analysis.

At the heart of the model are five base states in the DAM arm of the model, and four in the MMT arm. In the DAM arm, these states are DAM treatment, MMT-post DAM (MPD), abstinence (ABS), relapse (REL), and death. For the MMT arm, the states are MMT treatment, ABS, REL and death. Patients in the hypothetical cohort enter the model in the DAM or MMT state and transition through the base states until death.

This simple Markov Chain, with five states in the DAM arm and four in the MMT arm, was modified to accommodate three attributes of opioid dependence and its treatment that significantly alter the outcome of the model. First, among patient with multiple attempts at opioid substitution treatment, episodes of treatment, on average, become longer with each successive attempt (1), while episodes of relapse tend to get shorter. Second, HIV status has a significant effect on the probability of mortality (2), costs (3) and health-related quality of life (4). Finally, exponential survival curves are not sufficient to model the percentage of a cohort remaining in a given state from one period to the next in the model, as constructed. As such, the transition probabilities needed to depend on the number of periods a patient has been in a given state.

We employed a methodology making use of R's functionality with multi-dimensional arrays described by Hawkins et al. (5) in order to program time dependence within each of the model states to match the empirical evidence on their time to discontinuation. Markov Chain calculations are a series of weighted averages, usually represented using the notation of matrix multiplication. Essentially, Hawkins represents the transition probabilities in a multi-dimensional array of numbers instead of a two-dimensional matrix. As long as the array is sufficiently sparse, and enough of the transitions are set to zero, Hawkins gives a method of breaking up the arrays, doing certain calculations piecemeal, and achieving the correct weighted averages.

We designed the model as a discrete time Markov Chain, not a continuous time model, so that we could accurately calculate the Markov trace and obtain analysis of the cohort at intermediate time periods. In order to accommodate the above significant features, we expanded the state space, such that each state is indexed by several variables: base state, HIV status, treatment episode number, and number of cycles in base state. For example, a state could be "DAM, HIV positive, $4^{th}$ episode, $6^{th}$ cycle". The resulting state space is large, and the transition matrix is

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very sparse; for example, a patient cannot move from "DAM, HIV positive, 4th episode, 3 periods" to "DAM, HIV positive, 4th episode, 8 periods." In fact, no more than nine states can be reached from any given state. In terms of computation time, R is able to efficiently compile a large, multi-dimensional array of zeros, so it is simply a matter of populating the non-zero cells of the transition array.

*A1.1 Model Validation*

*A1.1.1 Internal Consistency*

Model validation was executed in a sequence of steps to ensure the model produced expected results. First, focusing on the Markov trace, after setting the probability of HIV seroconversion to zero, we (a) set all SMRs equal to 1 to ensure probabilities of mortality from statistical life tables were being entered correctly; (b) with SMRs equal to 1, checked transitions to subsequent cycles of DAM/MMT (cycle j, (j=4,5,6)) by setting the starting distribution in DAM/MMT cycle 3 equal to zero; (c) changed probabilities of transition from DAM/MMT cycle 3 to abstinence, MPD and relapse, setting each probability equal to zero in sequence to ensure appropriate transitions to other health states; (d) set hazard ratios on successive periods of treatment and relapse equal to one, then returned them to their stated values to ensure appropriate differences in time-to-discontinuation in successive cycles; (e) included SMRs into the model one at a time, to determine their impact on survival in specific health states; and (f) re-set probabilities of HIV seroconversion to their derived values and checked the model trace plots on the proportion of patients in HIV-negative and HIV-positive health states. Second, we focused on the calculation and accumulation of costs and QALYs in the model. After setting the discount factor to zero, we (a) set all utilities equal to one to ensure QALY estimates equalled estimated survival; (b) set utilities to zero to ensure QALY estimates equalled zero; (c) set all costs equal to zero to ensure total costs equalled zero; (d) re-inserted each cost component one at a time to ensure appropriate total costs for each component. Finally, we created a simplified version of the model in Microsoft Excel, setting exponential distributions on the times to discontinuation in each health state (thus not accounting for time-dependency in the transition probabilities), to ensure the primary model, coded in R, produced identical outputs with exponential distributions set. Assuming exponential distributions on times to discontinuation of each health states altered the model structure, providing constant transition probabilities in each state. While superior fit with Weibull distributions was confirmed through Likelihood Ratio tests, and the bias in probability estimates favoured MMT, DAM remained a cost-saving strategy in this alternate scenario (see Table 2, primary manuscript). Relaxing another structural feature of the model, that of non-constant times to discontinuation of successive episodes of treatment and relapse, resulted in diminished benefits and higher costs due to proportionately less time spent in treatment and more time in relapse; however the decision rule did not change (Table 2).

*A1.1.2 Comparison with within-trial analysis*

As a secondary step in validating our model, we aimed to determine whether results of the baseline model, estimated at a 1-year time horizon and from a societal perspective, were qualitatively similar to a within-trial analysis of reported trial data over the 12-month horizon of the NAOMI trial. This entailed a direct comparison between the DAM and MMT arms in the trial, completed on an intent-to-treat basis.

Capture of follow-up data was 95.4% for the NAOMI trial. Missing values were imputed using multiple imputation techniques, and executed with SAS v9.2 MI procedure. Subsequently, all self-reported resource utilization data, captured at quarterly intervals and representing the 30-day

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period prior to assessment, were assumed to be representative of the full 90-day periods between assessments and extrapolated accordingly. Data on drug treatment utilization (DAM and MMT) were available for the duration of follow-up, as was information on criminal charges. For each cost component, estimates of resource use for the 12-month period were multiplied by unit costs identified for the primary model and described in section A2.0 below. Results are reported in Table A1 below. Comparing these results to those of the model with treatment-specific costs and QALYs, estimated with a one-year time horizon, we find they are qualitatively similar, with the DAM treatment strategy yielding lower costs (cost savings of $27,977) and higher QALYs (incremental QALY gain of 0.0256). The baseline model underestimated costs and the difference in costs between trial arms for several reasons: first, generalized linear mixed models used to estimate the costs of health resource use, criminal activity and criminal charges (described in section A2.2 below) accounted for baseline measures of each of these items, and the costs of treatment and relapse were pooled by treatment arm. These differences resulted in more conservative estimates of the incremental costs of DAM vs. MMT in the baseline model. Second, the model did not base it's estimates of time to discontinuation of methadone treatment on observed data in the NAOMI trial, as there was a 'lottery effect' observed, where individuals who were randomized to receive MMT did not present for treatment from the outset. As this lottery-effect was clearly an artifact of the trial, we feel that our model estimates are more representative of a 'real-world' methadone treatment experience, and thus more applicable to this study's stated objectives.

*A1.1.3 External Consistency*

Finally, we tested the external consistency of our model by comparing the overall (pooled across health states) age- and gender-adjusted annual mortality rate in the MMT arm to estimates from a study by Bargagli et al. (6). In this study, SMRs were presented for IDUs in six different European cities, with Barcelona reporting the highest SMRs among the cities. Given advanced disease severity in the study population, we chose Barcelona as the comparator for external validation. Age- and gender-specific unadjusted mortality rates in the baseline model formulation for the MMT cohort were within 0.01 of estimates fitted with these alternative parameters.

*A1.2 Specification of Probabilistic Sensitivity Analysis*

Probabilistic sensitivity analysis was implemented via Monte Carlo simulation. Appropriate theoretical distributions were chosen for each applicable parameter. Where possible, the joint distribution between parameter estimates was incorporated. Following the method in Hawkins' paper (particularly, the number of sojourn states), runtime increases polynomially with respect to the number of cycles. The proportion of the hypothetical cohort reaching the mortality state reached 0.9999 prior to the 510th monthly period (42.5 years). Due to the highly discounted outcomes and virtually the entire cohort having reached the terminal state, the effects on QALYs and costs approached zero. As such, for considerations to computation time, we chose to only run the model for 510 periods after each of the simulations during our probabilistic sensitivity analysis. Standard errors on expected QALYs stabilized (within 0.001) at 2000 simulations for the baseline model.

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## A2.0 Calculation of Model Parameters

Parameters on disease progression costs and QALYs were estimated from trial data or external sources. In most cases, these parameters were estimated via regression analysis, controlling for age, gender and HIV status (if available), as included in our model design.

*A2.1 Disease Progression*
*A2.1.1 State Transition*
Time-dependent probabilities of transitioning out of the DAM, MMT, MMT post-DAM (MPD), relapse and abstinence states were estimated using Weibull regression models. Results from each of these models are presented in Table A2. For each model specification, we ran likelihood ratio tests to determine whether a gamma distribution provided a statistically significantly better fit than exponential distribution. As an exponential distribution is simply a gamma distribution with $\alpha = 1$, a likelihood ratio test was appropriate in this instance. Weibull regression models estimated with a gamma distribution provided better fit for all but the abstinence state, in which the fit with gamma or exponential distribution was not statistically significantly different. Weibull regression analysis was thus used to generate time-dependent transition probabilities in the initial cycles for each of the health states.

Estimates on transition out of the DAM state was based on n=115 patients randomized to receive DAM in the NAOMI study. As patients in the NAOMI trial were required to transition out of DAM according to regulatory constraints, a maximum follow-up period of 12 month follow-up data was available. Treatment discontinuation was defined as 30 days without dispensed medication.

Parameter estimates for both MMT and relapse states were derived from BC MMTOS data. Episode durations were based on administrative drug dispensation data from the BC PharmaNet database. Once again, episodes were considered discontinued if no records of dispensation existed over a 30-day period. Detailed descriptions of procedures used to manipulate drug dispensation data and define treatment episodes were presented in Nosyk et al. (1). For this analysis, we selected patients who were (a) alive at the end of study follow-up, (b) had at least 3 treatment episodes, (c) received a maximum dose of at least 60mg/day in their 3$^{rd}$ treatment episode; and (d) did not reach our functional measure of abstinence (treatment episodes lasting at least 12 weeks, with final daily dose $\leq$ 5mg) in any treatment episode. Weibull regression analysis was conducted on individuals' 3$^{rd}$ treatment episodes, according to the specification of our cohort model.

Patient-level data on drug-abstinent patients was unavailable from either the NAOMI or BC MMTOS datasets, the former due to a relatively short recall period and the latter due to the fact that drug use was not observed. We therefore calibrated data points from a published plot describing time to discontinuation of drug abstinence. We generated 1,500 data points from a Kaplan-Meier plot of the probability of remaining drug- abstinent among a cohort of patients enrolled in the observational Amsterdam Cohort Study (7). A Weibull regression model was estimated with these data points to obtain parameters from the gamma distribution to approximate the time to discontinuation of drug abstinence.

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Two key structural assumptions were made in applying the above methodology. First, we assumed the duration of an MMT episode is equivalent in length following relapse and following an episode of DAM, where the transition from DAM to MMT was a clinical decision made during the course of treatment. Second, we assumed relapse episodes following DAM were equivalent in duration to relapse episodes following MMT. To relax the first assumption, we estimated the time to discontinuation of MMT post-DAM from n=26 NAOMI participants who switched, voluntarily (n=8) or involuntarily (n=18), from DAM to MMT during the course of study follow-up. As those switching out of DAM involuntarily could be expected to relapse sooner than those doing so voluntarily, this can be considered a conservative estimate of time to discontinuation from this model state. The implicit assumption of equality in relapse periods following MMT and DAM was also tested explicitly in one-way sensitivity analysis. We used NAOMI trial data on n=37 patients randomized to receive DAM who discontinued treatment (according to the definition of treatment discontinuation stated above) to estimate the expected time to discontinuation of a relapse episode following DAM. Details of these alternative parameter estimates are provided in Table A3 below.

After discontinuing episodes of DAM, MMT, relapse and abstinence, subject to survival, individuals could transition to a limited number of health states, based on observed patient-level data or assumption. Estimates of probabilities of transition to alternate health states and their sources are listed in Table A4. These estimates were independent of time and model cycle. Patients receiving DAM could transition to MMT following treatment according to their own or their physicians' directives, as observed in both the Swiss observational cohort study (8) and the NAOMI trial. From relapse, patients could only transition to a treatment (DAM, MMT) state, while from abstinence, patients could only transition to the relapse state. Transition to death was possible from each model health state.

Based on prior evidence on durations of MMT episodes, there is reason to believe successive episodes of treatment, and potentially also relapse, may differ in duration over the life-course of an opioid-dependent individual. We incorporated this evidence into our simulation model through the use of random effects (random intercept) Cox proportional hazards, or frailty models, which estimated hazard ratios for successive treatment and relapse episodes controlling for age and gender. Proportionality of model effects was assessed through inspection of Schoenfeld residual plots. Application of these techniques was described in Nosyk et al. (1).

Transition probabilities for the $j+1^{th}$ cycle of the model were multiplied by hazard ratios on successive treatment episodes. While data on successive DAM episodes was unavailable, we hypothesized that the results on the durations of successive methadone treatment episodes may extend to other forms of opiate substitution, and potentially also other forms of substance abuse treatment. We therefore used hazard ratios from MMT frailty models as multipliers in later cycles of DAM treatment, as well as methadone treatment post-DAM. Results of these analyses are presented in Table A5.

*A2.1.2 HIV Seroconversion*

The approach we used in calculating the monthly probability of HIV seroconversion from each health state was derived from previous studies by Zaric (9) and Bayoumi and Zaric (10). Formulas and parameters used to calculate the monthly probability of HIV seroconversion were

listed in Table A6. The annual risk of sexual transmission per partner was converted to a monthly risk using the formula: $S_m = [1 - (1 - S_a)^{1/12}]$. Note that the risk of seroconversion in the abstinence state is a function of only sexual transmission, as injection drug use ceases by definition.

Ranges were initially used in a deterministic modeling approach. In order to make the calculations probabilistic, we interpreted the ranges as 99% confidence intervals and assumed normal distributions for each parameter, and zero covariance between parameters. This allowed us to estimate a confidence interval surrounding the probability of HIV seroconversion by health state. Note that we did not model the potential for HIV-positive individuals to spread the virus to other users or sexual partners, as done in Bayoumi and Zaric (10). We focused solely on the health and criminal outcomes of the hypothetical cohort.

*A2.1.3 Transition to Mortality*

Estimates for transition to mortality from each of the states were based on national estimates of death rates for the general population, then multiplied by standardized mortality ratios for the DAM and relapse states, with the MMT/MPD state death risk calculated using the relative risk of mortality in MMT vs. out of treatment. Mortality risk among HIV-negative patients in the abstinence state was assumed to be equivalent to that of the general population. Annual mortality rates obtained from statistical life tables (23), shown in Table A7 below, were converted to monthly transition probabilities using the following formula: $P_m = [1 - (1-P_a)^{1/12}]$.

There were several challenges in incorporating estimated mortality within the different health states of the model, and among HIV-negative and HIV-positive individuals. These challenges stem from a lack of information on state-specific mortality risks for the patient population under study, ie. opioid dependent individuals entering their third treatment attempt. We conducted a review of the literature on estimates of mortality opioid dependent patients, and found few applicable studies that reported state-specific SMRs or relative risks of mortality between states of relapse and abstinence. Many of the studies estimating SMRs for patients in MMT focused on earlier-stage opioid-dependent patients, thus providing SMRs that were likely too low for the chronic, treatment-resistant cohort of individuals eligible for DAM. For example, a recent study of all opioid substitution treatment clients in New South Wales, Australia, estimated SMRs of 4.5 (4.3, 4.8) in treatment, and 8.0 (7.7, 8.3) out of treatment (24).

None of the articles identified in the review provided reasonable SMR estimates for chronic, treatment refractory opioid dependent patients in MMT. As such, we used estimates of relative risk of death during treatment in comparison to untreated use (25).

The baseline estimate of mortality in the relapse state was derived from the Vancouver Injection Drug Users Study (VIDUS), an ongoing observational cohort study of injection drug users conducted in Vancouver, British Columbia (26). Alternatively, Bargagli et al. (6) estimated SMRs for eight separate European cohorts (Amsterdam, Barcelona, Denmark, Dublin, London, Rome, Vienna) of opiate users compiled by the European Monitoring Centre for Drugs and Drug Addiction working group. Cohorts in either study may have spent some time in MMT, making these estimates less than ideal, however estimates from the VIDUS study were chosen based on the fact that data collected on local subjects was presented.

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Finally, using data on Swedish opioid dependent individuals followed-up between 1967-1988, Gronbladh et al. (27) estimated state-dependent risks of mortality (MMT: SMR=8, relapse following MMT: SMR=55, regular use: SMR=63 and abstinence: SMR=4), among a relatively small (N=166) cohort of opiate users entering treatment and a comparator cohort of regular users (N=115). Given the small size of the study and the fact that it pre-dated the HIV epidemic, we chose to use these estimates as in sensitivity analysis only.

Our estimates on the risk of mortality in DAM were derived from Rehm et al. (2005), who estimated an overall SMR of 9.7 (95% CI: 7.3 – 12.8) from the only cohort of DAM users followed prospectively in an observational context. While there are no head-to-head comparisons of mortality risk among patients in DAM vs. MMT, using the above-described sources provided us with similar SMRs for patients in either form of substitution treatment. In sensitivity analysis, we also explored the effect of equalizing the rates of mortality of patients in DAM and MMT, using SMRs reported in Rehm et al. (28) for either form of treatment.

The literature was also reviewed to determine the relative risks of mortality of HIV-positive injection drug users versus HIV-negative users. In many studies, the relative risk of mortality was not statistically significant. One study, conducted using a population-level database for all patients with HIV who had accessed HAART found injection drug use was not associated with decreased survival among HIV-infected patients initiating HAART (29). Another article showed survival of HIV-positive IDUs receiving HAART at high CD4 cell count levels (>350 cells/μL) approximated those of HIV-negative IDUs (30). Kohli et al. (31) reported no incremental independent risk of mortality attributable to illicit drug use or methadone receipt amongst a cohort of HIV-positive injection drug users.

Given the results of the studies cited above, we assumed HIV-negative and HIV-positive individuals (injection drug users) in DAM, MMT and relapse faced the same probability of mortality; in other words there was no elevated risk of mortality among opioid dependent individuals as a result of HIV-positive status.

The SMR for HIV-positive individuals in the abstinence state were derived from an article from the ART cohort collaboration (2). Those reaching the abstinence state in our model were assumed to have SMRs equivalent to a lower risk group in relatively early stages of disease progression: Men who have sex with men (MSM) with HIV at the time of ART initiation (rather than AIDS), CD4-cell counts of 200-349 cells/μL, and 6-month viral load ≤ 500 copies/ml [SMR: 1.47 (1.07-2.01)]. Given the inherent variability in this parameter, we conducted one-way sensitivity analyses to determine the effect of varying this parameter to the extreme SMR values presented for non-IDUs. Estimates of the risk of mortality for each health state were presented in Table A8.

*A2.2 Calculation of Costs*

Within our modeling framework, individuals accumulated costs in three domains: drug treatment (including opioid substitution treatment and treatment for HIV and HCV), health resource utilization, and crime.

*A2.2.1 Treatment Costs*

Costs of substitution treatment (DAM and MMT) were obtained from manufacturer's invoices. Mean daily doses of methadone and DAM were multiplied by drug costs, while the operational costs of the Vancouver treatment facility were included to provide fully-allocated costs of drug treatment. Drug treatment costs also included operating costs of the NAOMI treatment clinic, which included on-staff nurses, pharmacists and counsellors. Protocol-driven costs such as additional urinalyses, research staff and data analysts employed by the NAOMI study were excluded in order to provide an estimate of the costs of treatment delivery in a non-experimental context. Monthly costs of MMT and DAM are provided in Table A9.

Drug treatment costs for HIV patients in Canada are well-documented (32), and though HIV treatment is provided either free of charge or is heavily subsidized in Canada, some patients may not access treatment because of perceived risks of development of treatment-resistant strains as a result of non-compliance by physicians, or difficulties in navigating the health care system (33). We therefore incorporated costs of HIV treatment among prevalent cases for a proportion of patients receiving treatment, estimated from an observational cohort study conducted in Vancouver, British Columbia (34).

HCV is also highly prevalent among injection drug users, with nearly 63% of the NAOMI study sample HCV+, however the probability of treatment is very low (35). Given high prevalence of HCV at baseline, HCV transmission was not modeled explicitly; thus HCV prevalence among trial participants was assumed to be constant throughout the duration of the simulation model.

Finally, while mental health conditions are highly prevalent among opioid dependent patients, sound estimates of prevalence were absent, as were the percentage of prevalent cases receiving treatment. Information on the percentage of MMT patients receiving medications for mood and anxiety disorders was available in the BC MMTOS, it was unclear to what extent this constituted off-label use, including prescription for cocaine dependence and abuse. We therefore excluded costs of pharmacological treatment for mental health conditions. Monthly costs of HIV and HCV treatment are presented in Table A10.

*A2.2.2 Costs of health resource utilization*

Costs of health resource utilization were derived from self-reported and administrative records collected alongside the NAOMI trial. Data on inpatient and outpatient care was collected at each study assessment, and multiplied by unit costs provided in Table A11. Unit costs of inpatient care were derived from the St. Paul's Hospital Cost Model (SPHCM) (43, 44), which provides fully-allocated costs of all hospital activities in a representative tertiary-care teaching hospital in Vancouver, British Columbia. The model was constructed following the methodology described in Drummond et al (45). Unit costs of outpatient care were derived from the British Columbia Medical Association Guide to Fees (37).

We used trial data to construct estimates of mean monthly healthcare costs by identifying periods of DAM, MMT and relapse (not in treatment). We considered patients not receiving a DAM or MMT dispensation from either the trial clinic or an outside setting throughout the duration of the recall period of a single trial assessment (30 days) as being 'not in treatment', and thus in the relapse state.

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Relapse state patients were drawn from both trial arms; there were no statistically significant differences among these patients in terms of health resource use or criminality. It should be noted that this amounts to 'in-treatment' analysis, and thus differs from the intent-to-treat perspective in which the trial was conducted and its results reported.

Summary statistics of health resource utilization among NAOMI participants receiving MMT, DAM, or not in treatment (relapse state) are presented in Table A12. Rates of both inpatient and outpatient care were substantially higher among patients in the relapse state, but similar among patients in DAM and MMT.

Health resource utilization estimates were multiplied by unit costs of inpatient and outpatient care to construct monthly costs of care throughout the duration of the trial. In order to calculate unbiased estimates of costs in each health state, controlling for age, gender and HIV status, we estimated a generalized linear mixed regression model with a gamma distribution and log link. Fitted values of monthly costs by age and gender were estimated for each health state for HIV+ and HIV- individuals. The covariance matrix of the regression model was used to account for correlation in health and criminal outcomes. Cholesky decomposition was used to generate correlated draws from the regression models in probabilistic sensitivity analysis.

Results are presented in Tables A14 and A15. We found that while costs of health resource utilization in MMT were higher than in DAM, this difference was not statistically significant. The baseline model did not differentiate treatment modality (pooled treatment), thus providing a conservative estimate on the total costs of DAM (Table A14). In subsequent analysis, treatment-specific monthly costs of health resource utilization were estimated (Table A15). In either model formulation, costs of health resource utilization during periods of treatment were statistically significantly lower than during periods of relapse. Furthermore, HIV-positive individuals accrued statistically significantly higher costs of health resource utilization independent of age, gender and health state.

*A2.2.3 Costs of crime and criminal charges*

The costs of crime were also derived from NAOMI study participants, and were based on self-reported criminal activity. Further, informed consent was obtained for each participant to obtain data on arrests and charges over a 36-month time period (12 months prior, to 24 months following randomization) through courthouse records.

The methodology for deriving the unit costs of police enforcement, court processing and victimization followed that of Wall et al. (38). We attempted to retrieve unit costs using the same methodology but using updated sources where possible. Costs of police enforcement and criminal victimization were re-calculated using updated sources, while updated sources were not available for the calculation of court costs and the out-of-pocket costs of personal victimization as a result of violent crime (pain and suffering). These were therefore obtained directly from the Wall et al. (38) study and adjusted for inflation.

The cost per criminal code incident was calculated as the total criminal code incidents divided by the total police budget in the 2007 calendar year (40) and adjusted for inflation. The costs of

household victimization were calculated as the total number of criminal incidents of property theft/damage divided by the total estimated out-of-pocket losses in 1999 (42) and adjusted for inflation. As these cost estimates included out-of-pocket costs of criminal victimization, they represented costs borne by society.

One-way sensitivity analysis was performed on the unit costs of criminal activity. In the sensitivity analysis, the costs were uniformly derived from Wall et al. (38) and inflation-adjusted to 2009$CDN (police contact: $3,344.12; household victimization: $849.78). Results were qualitatively similar and therefore not presented.

Summary statistics on self-reported criminal involvement are presented in Table A13. Property theft and violent crime were more prevalent during periods of relapse and similar among patients in either form of treatment.

Generalized linear mixed regression models (gamma distribution, log link) were estimated separately for self-reported criminal activity and administrative records of charges. In each case, mean costs for each health state were estimated controlling for age and gender (HIV status was not statistically significant in univariate analysis). The model on self-reported criminal activity was populated with 5 repeated measures for each patient (one for each study assessment), while 12 monthly intervals were used in the regression model on criminal charges.

Results of the regression models and covariance matrices (used in probabilistic sensitivity analysis) are presented in Table A14. Estimated costs of criminal involvement were roughly twice as high during periods of relapse in comparison to periods in treatment. Costs of criminal charges were also higher during periods of relapse; however the margin of difference was lower. The costs of both criminal activity and criminal charges were not statistically significantly different in MMT and DAM; therefore pooled-treatment models were estimated. Treatment-specific estimates were derived from subsequent analyses and used in sensitivity analysis (Table A15).

The costs of corrections (incarceration, probation and parole) were excluded in our analysis due to the difficulty in attribution of these costs to health states defined in the NAOMI patient-level data. For instance, it was known at baseline assessment that some patients were currently on parole or probation, however the start and duration of these sentences was unknown. Given that the regression models were designed to capture changes in health state (DAM, MMT, relapse) on a monthly basis, we were unable to determine at what point the costs of probation/parole should be discontinued. Further, given the lag in arrest, charge, trial and sentencing, it was not possible for us to attribute the criminal sentence to a health state based on available self-reported information. These costs were therefore omitted, making our estimates of the total costs of crime somewhat conservative. Given the observed differences in criminal activity among health states, it is reasonable to expect the magnitude of corrections costs to follow the same rank order (DAM $\leq$ MMT $<$ relapse), suggesting the cost estimates used favoured the MMT arm.

The costs of criminal activity and charges were also estimated without inclusion of out-of-pocket costs due to property theft and violent crime, for use in sensitivity analyses considering the third party payer perspective. These additional results are presented in Table A16.

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It should be noted that our costing approach for criminal activity was not identical to that used by Wall et al. (38). The former added costs per incidents of illicit drug possession and trafficking. Given the high levels of self-reported criminal activity, and the low-level of policing to stop these activities, we felt it was unrealistic to add police costs for them. Our approach of only costing self-reported property and violent crimes was consistent with that of Dijkgraaf et al. (46).

*A2.3 Calculation of QALYs*

Health utility estimates for the DAM, MMT and relapse state were derived from NAOMI trial data using methodology similar to that used for state costs. Generalized linear mixed regression models on EQ-5D health utility estimates, collected at quarterly intervals throughout trial follow-up, were specified using the same methodology to classify observations as being in DAM/MMT or not in treatment. The regression model also controlled for age and gender. HIV-status was not a statistically significant predictor of Health-related quality of life (HRQoL) and was therefore excluded from the model. Expected values of health utilities in each health state, regression parameter estimates and the variance-covariance matrix are provided in Table A14. Once again, we found HRQoL estimates were not statistically significant during periods of MMT and DAM. We therefore estimated an alternative model differentiating treatment modality (Table A15). These estimates were used in sensitivity analysis.

Little follow-up data exists on the health outcomes of rehabilitated, abstinent opioid dependent patients. Health utility estimates among HIV-negative patients in the abstinence state were therefore assumed to be equivalent to that of the general population. Age-stratified general population EQ-5D health utility estimates were captured from a cross-sectional study from a population-based sample of respondents from Alberta, Canada (Johnson and Pickard, 2000), and are presented in Table A17 below. The effect of this assumption on estimated ICERs was tested in sensitivity analysis, assuming no improvement in HRQoL following treatment.

Standard deviations on HRQoL estimates in this study were large as a result of relatively small sample sizes within age strata. In order to ensure a uniform pattern of HRQoL decline over time within model simulations, differences in HRQoL (and their standard deviations) between age strata were estimated and implemented in probabilistic sensitivity analysis. Simulated parameters for the probabilistic model were drawn from a multivariate normal distribution following mean parameters in Table A17 and variance-covariance matrix in Table A18. In sensitivity analysis, we assumed individuals had no HRQoL improvement following treatment.

EQ-5D health utility estimates for HIV-positive patients in the abstinence state were derived from a study on a general population of patients with advanced HIV/AIDS (4) (EQ-5D index score: mean=0.77; SD=0.19).

## A3.0 Additional Model Sensitivity Analyses

Additional one-way sensitivity analyses were conducted to determine the robustness of the base-case findings and presented in Tables A19 and A20. When DAM was only offered for one continuous treatment episode, the treatment strategy remained cost-saving; however the benefits

in health (0.25 incremental QALYs gained) and cost savings ($24,700) were diminished. A younger cohort of chronic, treatment refractory opioid dependent individuals (age at model entry=30) accumulated greater costs and QALYs, with proportionately larger cost savings ($52,400 in cost savings with access to DAM); conversely, QALY gains and cost savings were diminished for an older cohort (age=50). ICERs for males were substantially more favourable than those for females due to their higher levels of criminal activity during periods of relapse. Using treatment-specific costs and utilities resulted in greater cost savings at the mean ($119,900), but also wider credible intervals. As the duration of relapse episodes in DAM-experienced clients and the duration of methadone episodes following DAM are uncertain, we used limited trial follow-up data for these parameters as an alternative to baseline model assumptions. Due to small sample sizes in the trial-based parameters, credible intervals on ICERs were large, however base-case results were upheld. Changes in mortality rates primarily impacted results at the lifetime horizon. Using exponential distributions on time-to-event parameters, thus eliminating the need for time-dependent transition probabilities, resulted in higher costs and lower QALYs, but similar ICERs compared to the base case. Eliminating the probability of HIV seroconversion lead to decreases in the percentage of costs attributable to health resource utilization over longer time horizons, however results were similar. Results were not sensitive to assumptions on QALY gains among abstinent HIV-negative individuals, as a small proportion of time was estimated to be spent in the abstinence state. Finally, setting discount rates equal to zero lead to higher costs and QALYs, however cost components remained similar in proportion and ICERs were similar to the base case.

While local data sources were used wherever possible to ensure a high level of internal validity, efforts were made to determine the sensitivity of our results to both structural and parameter uncertainty. The results were most sensitive to changes in the duration of DAM retention and in costs of crimes committed; however, threshold analysis showed the results to be robust to wide ranges of values in these parameters. Given that reported 12-month MMT retention rates are similar across many settings across North America,(1,48) as are DAM retention rates across international settings,(49-51) it is likely our results are generalizable to other North American settings.

Appendix to: Nosyk B, Guh DP, Bansback NJ, et al. Cost-effectiveness of diacetylmorphine versus methadone for chronic opioid dependence refractory to treatment. *CMAJ* 2012. DOI:10.1503/cmaj.110669.

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**Table A1. Results of within-trial analysis for the purpose of validation of the baseline simulation model**

| | Bootstrapped Mean (95% CI) | |
|---|---|---|
| | **DAM** | **MMT** |
| Costs of drug treatment | 14,188 (13,228, 15,121) | 2,010 (1,736, 2,287) |
| Costs of resource utilization | 4,586 (2,949, 6,493) | 6,498 (4,393, 8,943) |
| Costs of HIV treatment | 746 (337, 1,212) | 825 (419, 1,326) |
| Costs of Hepatitis C treatment | 218 (189, 248) | 211 (181, 242) |
| Costs of inpatient care | 3,152 (1,679, 4,952) | 4,803 (2,789, 7,146) |
| Costs of outpatient care | 470 (294, 691) | 659 (437, 938) |
| Cost of Crime | 68,042 (39,040, 105,845) | 106,285 (62,460, 157,187) |
| Costs of criminal involvement | 63,149 (33,772, 100,038) | 100,271 (57,429, 150,656) |
| Costs of criminal charges | 4,893 (2,845, 7,323) | 6,014 (3,854, 8,550) |
| Total costs | 86,816 (57,017, 124,308) | 114,794 (71,334, 165,849) |
| | | |
| Unadjusted QALYs | 0.781 (0.755, 0.807) | 0.749 (0.720, 0.777) |
| Adjusted QALYs | 0.778 (0.755, 0.801) | 0.752 (0.728, 0.776) |
| | | |
| *Incremental costs: DAM vs. MMT* | -27977.17 | |
| *Incremental QALYs: DAM vs. MMT* | 0.0256 | |

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**Table A2. Results of Weibull regression models for time to discontinuation in primary model states**

| *DAM state [NAOMI study, N=115]* | | | | | | |
|---|---|---|---|---|---|---|
| | **β** | **SE** | **95% C.I.** | | **$\chi^2$** | **P-value** |
| Intercept | 3.679 | 0.299 | 3.092 | 4.266 | 151.07 | < 0.01 |
| Scale | 1.315 | 0.206 | 0.968 | 1.786 | | |
| **Covariance** | **Intercept** | **Scale** | | **Parameter** | **LR-stat.** | **P-value** |
| Intercept | 0.09 | | λ | 0.061 | 2.86 | 0.07 |
| Scale | 0.043 | 0.042 | γ | 0.761 | | |
| *Relapse state [BC MMTOS, N=1,525]* | | | | | | |
| | **β** | **SE** | **95% C.I.** | | **$\chi^2$** | **P-value** |
| Intercept | 3.572 | 0.053 | 3.468 | 3.675 | 254.11 | < 0.01 |
| Scale | 1.488 | 0.041 | 1.410 | 1.571 | | |
| **Covariance** | **Intercept** | **Scale** | | **Parameter** | **LR-stat.** | **P-value** |
| Intercept | 0.003 | | λ | 0.091 | 377.86 | < 0.01 |
| Scale | 0.0004 | 0.002 | γ | 0.672 | | |
| *MMT state [BC MMTOS, N=2,489]* | | | | | | |
| | **β** | **SE** | **95% C.I.** | | **$\chi^2$** | **P-value** |
| Intercept | 3.373 | 0.038 | 3.300 | 3.447 | 8014.40 | < 0.01 |
| Scale | 1.556 | 0.031 | 1.496 | 1.618 | | |
| **Covariance** | **Intercept** | **Scale** | | **Parameter** | **LR-stat.** | **p-value** |
| Intercept | 0.001 | | λ | 0.114 | 603.56 | < 0.01 |
| Scale | 0.0003 | 0.001 | γ | 0.643 | | |
| *Abstinence state [Termorshuizen et al.(7); N=1,500:derived]* | | | | | | |
| | **β** | **SE** | **95% C.I.** | | **$\chi^2$** | **P-value** |
| Intercept | 3.035 | 0.035 | 2.967 | 3.103 | 7708.08 | < 0.01 |
| Scale | 1.255 | 0.026 | 1.205 | 1.308 | | |
| **Covariance** | **Intercept** | **Scale** | | **Parameter** | **LR-stat.** | **P-value** |
| Intercept | 0.0012 | | λ | 0.089 | 134.40 | < 0.01 |
| Scale | -0.0002 | 0.00068 | γ | 0.797 | | |

λ: Weibull scale parameter; γ: Weibull shape parameter. BC MMTOS: BC Methadone Maintenance Treatment Outcome Study; NAOMI: North American Opiate Medication Initiative study.

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**Table A3. Results of Weibull regression models for time to discontinuation: sensitivity analysis**

| *MMT post-DAM state [NAOMI trial; N=26]* | | | | | | |
|---|---|---|---|---|---|---|
| | **β** | **SE** | **95% C.I.** | | **$\chi^2$** | **P-value** |
| Intercept | 2.642 | 0.272 | 2.109 | 3.175 | 94.23 | < 0.01 |
| Scale | 1.108 | 0.232 | 0.735 | 1.67 | | |
| **Covariance** | **Intercept** | **Scale** | | **Parameter** | **LR-stat.** | **P-value** |
| Intercept | 0.074 | | λ | 0.092 | 0.25 | 0.62 |
| Scale | 0.01 | 0.054 | γ | 0.903 | | |
| *Relapse post-DAM state [NAOMI trial; N=37]* | | | | | | |
| | **β** | **SE** | **95% C.I.** | | **$\chi^2$** | **P-value** |
| Intercept | 1.583 | 0.555 | 0.495 | 2.67 | 8.14 | <0.01 |
| Scale | 2.689 | 0.463 | 1.919 | 3.768 | | |
| **Covariance** | **Intercept** | **Scale** | | **Parameter** | **LR-stat.** | **P-value** |
| Intercept | 0.308 | | λ | 0.555 | 2.98 | 0.06 |
| Scale | 0.038 | 0.214 | γ | 0.372 | | |

λ: Weibull scale parameter; γ: Weibull shape parameter. NAOMI: North American Opiate Medication Initiative study.

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**Table A4: External estimates of transition to alternate health states following discontinuation in Treatment (DAM, MMT, MPD), Relapse, Abstinence[$]**

| Transition | Parameter Estimate | Notes |
|---|---|---|
| *Transition post-DAM [Rehm et al., 2001 [8]; N=1,001*]* | | |
| DAM to MPD | 407 (40.66%) | Includes transition to methadone and 'other' forms of treatment. |
| DAM to Relapse | 370 (36.96%) | Includes transition as a result of violence/illegal trafficking, imprisonment, health reasons, treatment break off/refusal/lack of compliance and 'other'. |
| DAM to Abstinence | 224 (22.38%) | |
| *Transition post-MMT [BC MMTOS; N=3,909**]* | | |
| MMT to Relapse | 3,748 (95.88%) | |
| MMT to Abstinence | 161 (4.12%) | Abstinence assumed if duration of episode > 12 weeks and final daily dose < 5mg. |
| *Transition post-Abstinence* | | |
| Abstinence to Relapse | 100% | By assumption |
| *Transition post-Relapse* | | |
| Relapse to Treatment | 100% | By assumption |

[$] all probabilities of transitioning are conditional on survival. * Results presented in Table 2 [8]; 1031 total patients followed up, 30 deaths, 144 missing values. ** Among BC MMTOS individuals with at least 3 episodes who did not suffer mortality during follow-up.

**Table A5. Results of proportional hazards random intercept regression to estimate duration in successive treatment and relapse episodes from BC MMTOS**

| | HR | SE | 95% CI | |
|---|---|---|---|---|
| *MMT state [N=15,816]* | | | | |
| Duration of 3$^{th}$ episode | Ref | -- | -- | -- |
| Duration of 4$^{th}$ episode | 0.923 | 0.033 | 0.865 | 0.986 |
| Duration of 5$^{th}$ episode | 0.965 | 0.042 | 0.889 | 1.049 |
| Duration of 6$^{th}$ episode | 0.952 | 0.041 | 0.877 | 1.032 |
| *Relapse state [N=9,915]* | | | | |
| Duration of 3$^{th}$ episode | Ref | -- | -- | -- |
| Duration of 4$^{th}$ episode | 1.220 | 0.048 | 1.110 | 1.340 |
| Duration of 5$^{th}$ episode | 1.350 | 0.060 | 1.201 | 1.520 |
| Duration of 6$^{th}$ episode | 1.442 | 0.056 | 1.292 | 1.610 |

Ref: reference group. *Full specification of MMT state model described in Nosyk et al. (1). Relapse state model controlled for age, gender, duration of previous treatment episode.

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**Table A6. Parameters and calculation of monthly probability of HIV seroconversion***

| | Label | Estimate** | Source |
|---|---|---|---|
| *Sexual seroconversion* | | | |
| Monthly risk of sexual transmission, per partner | $R^{sex}$ | 0.00083 (0.00042, 0.0075) | [11] |
| Relative risk with condom use | $RR^{c}$ | 0.13 (0.01, 0.3) | [9] |
| Sex acts in which condoms are used, % | | | |
| HIV-negative IDU (treatment or relapse) | $P_{\bar{A}}^{C}$ | 47 (20, 70) | VIDUS |
| HIV-negative Abstinent | $P_{A}^{C}$ | 19 (16, 22) | [12] |
| No. sex partners per month | | | |
| IDU | $N_{\bar{A}}^{SP}$ | 2 (1, 5) | SEOSI |
| Abstinent | $N_{A}^{SP}$ | 1 (1, 2) | [9] |
| *Seroconversion through needle sharing* | | | |
| Risk of HIV transmission through needle sharing per act | $R^{needle}$ | 0.8 (0.3, 4.0) | [9, 13-15] |
| Relative risk of transmission through needle sharing after bleach sterilization | $RR^{bleach}$ | 0.15 (0.0, 0.3) | [15-17] |
| Injections involving needle sharing, % | $P^{ns}$ | 13 (5, 21) | SEOSI |
| Injections involving sharing of needles sterilized with bleach, % | $P^{ns\text{-}b}$ | 50 (40, 60) | [18, 19] |
| Relative risk of needle sharing among users receiving treatment | $RR^{ns\text{-}tx}$ | 0.30 (0.2, 1.0) | [20] |
| Monthly no. injections per user (Mean (SD)) | $N^{inj}$ | 59.25 (30.4, 121.67) | [21, 22] |
| Relative risk of street injection by users in treatment | $RR^{inj\text{-}tx}$ | 0.17 (0.1, 0.25) | |

| **Probabilities of HIV Seroconversion** | **Probability (SD)#** |
|---|---|
| $P^{abs} = P_{A}^{C} (N_{A}^{SP} * R^{sex} * RR^{c}) + (1- P_{A}^{C})*(N_{A}^{SP} * R^{sex})$ | 0.0007 (0.0001) |
| $P^{tx} = P_{\bar{A}}^{C} (N_{\bar{A}}^{SP} * R^{sex} * RR^{c}) + (1- P_{\bar{A}}^{C})*(N_{\bar{A}}^{SP} * R^{sex}) + N^{inj}(RR^{inj\text{-}tx}* P^{ns}*(1- P^{ns\text{-}b}) *RR^{ns\text{-}tx}* R^{needle}) + N^{inj}(RR^{inj\text{-}tx}* P^{ns}*P^{ns\text{-}b}* RR^{ns\text{-}tx}* R^{needle}* RR^{bleach})$ | 0.0028 (0.0010) |
| $P^{rel} = P_{\bar{A}}^{C} (N_{\bar{A}}^{SP} * R^{sex} * RR^{c}) + (1- P_{\bar{A}}^{C})*(N_{\bar{A}}^{SP} * R^{sex}) + N^{inj}( P^{ns}*(1- P^{ns\text{-}b}) * R^{needle}) + N^{inj}(P^{ns}*P^{ns\text{-}b}* R^{needle}* RR^{bleach})$ | 0.0364 (0.0146) |

NAOMI: North American Opiate Medication Initiative. VIDUS and SEOSI indicate personal communication from the Vancouver Injection Drug Users Study (VIDUS) and the Scientific Evaluation of Supervised Injecting (SEOSI) cohorts, respectively. *As described in Bayoumi and Zaric (10). ** Estimate and range - assumed 99% confidence interval in probabilistic analysis.

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**Table A7. Base annual probability of mortality (Abstinence state, HIV-negative)**

| Age | Male | Female |
|---|---|---|
| <19 | 0.00055888 | 0.0004062 |
| 20 to 29 | 0.00083037 | 0.0003368 |
| 30 to 39 | 0.00110190 | 0.0005974 |
| 40 to 49 | 0.00230268 | 0.0014348 |
| 50 to 59 | 0.00586789 | 0.0036619 |
| 60 to 69 | 0.01576579 | 0.0092491 |
| 70 to 79 | 0.04137332 | 0.0247155 |
| 80 to 89 | 0.11062751 | 0.0761103 |
| 90-99 | 0.25647016 | 0.1997090 |
| 100+ | 0.48111140 | 0.4178473 |

**Table A8. Estimated mortality risks for model health states**

| | Mortality risk | | Source |
|---|---|---|---|
| | Female | Male | |
| *Baseline Estimates* | | | |
| Abstinence state, HIV-negative | | -Table A6 - | [23] |
| Abstinence state, HIV-positive | | 1.47 (1.07, 2.01) | [2] |
| Relapse state [SMR (95% CI)] | 47.3 (36.1, 58.5) | 20.7 (17.2, 24.2) | [26] |
| MMT state [RR (95% CI, vs. relapse] | | 0.35 (0.18, 0.69) | [25] |
| DAM state [SMR (95% CI)] | 17.2 (10.0, 29.6) | 8.4 (6.0, 11.6) | [28] |
| *Sensitivity Analyses* | | | |
| 1. MMT state [SMR (95% CI)] | 17.2 (10.0, 29.6) | 8.4 (6.0, 11.6) | [28] |
| 2. MMT state [SMR]* | | 8.4 | [27] |
| Relapse state [SMR] | | 55.3 | [27] |
| Abstinence state [SMR] | | 3.8 | [27] |

SMR: Standardized mortality ratio; RR: Relative risk. * 95% CIs for SMRs from Gronbladh et al. [27] were not reported; SMR for relapse state: MMT clients following involuntary discharge; SMR for abstinence state: MMT clients following voluntary discharge. ** highest site-specific SMRs: Barcelona, N=1137. # lowest site-specific SMRs: Denmark, N=701.

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**Table A9. Parameters and calculation of study treatment costs**

| | DAM | MMT |
|---|---|---|
| Monthly drug cost | 58.85 | 57.60 |
| Drug cost (mg) | 0.005 | 0.020 |
| Daily dosage (mg) [Mean (SD)] | 392.3 (174.3) | 96.0 (41.5) |
| Monthly overhead cost* | 1356.36 | 271.78 |
| Total costs [Mean (SD)] | 1415.21 (25.68) | 329.38 (24.46) |

*including wages of on-site administrators, nurses, pharmacist, physician, social worker, treatment delivery, security, medical supplies and other operating costs of injection clinic.

**Table A10. Parameters and calculation of drug treatment costs**

| | Estimate | Source |
|---|---|---|
| *HIV* | | |
| Mean monthly drug cost | $645.52 | |
| Baseline Prevalence | 24/251 (9.6%) | [32] |
| % treated | 833/1239 (67.2%) | [35] |
| Monthly drug cost: treated | $960.60 | [33] |
| *HCV* | | |
| Mean monthly drug cost** | $28.30 | |
| Prevalence^ | 158/251 (62.9%) | [32] |
| % treated | 4229/171660 (2.5%) | [36] |
| Monthly drug cost: treated* | $1800 | BC PNET* |

BC PNET: British Columbia PharmaNet database. All costs presented in 2009$CDN. HIV: Human Immunodeficiency Virus; HCV: Hepatitis-C Virus. ^ Assumed constant prevalence of HCV infection among model cohorts. * Assumed combination therapy, regardless of genotype. ** Applied to overall patient cohort, thus incorporating prevalence of HCV among NAOMI participants.

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**Table A11. Unit costs of health resource utilization and crime**

| | 2009$CDN | Source |
|---|---|---|
| *Inpatient Care* | | |
| Hospital Admission | 50.79 | SPHCM |
| ED Admission | 13.55 | SPHCM |
| ED visit | 312.48 | SPHCM |
| Regular Inpatient care (per day) | 531.16 | SPHCM |
| Intensive care unit: per day | 854.67 | SPHCM |
| Surgical Procedure | 2605.09 | SPHCM |
| *Outpatient care* | | |
| GP visit | 31.04 | [37] |
| Specialist visit | 44.22 | [37] |
| HIV counselling (visit) | 86.79 | [38, 39] |
| Addiction counselling (visit) | 86.79 | [38, 39] |
| *Law Enforcement* | | |
| Police | 4,692.83 | [40] |
| Court | | |
| Minor offenses* | 1,694.54 | [38, 41] |
| Income-related property crime | 1,911.39 | [38, 41] |
| Motor-vehicle violations | 3,730.59 | [38, 41] |
| Capital offenses | 5,800.40 | [38, 41] |
| Victimization (out-of-pocket expenses): | | |
| Household (break & enter, theft, vandalism) | 453.78 | [42] |
| Pain and suffering (violent crime) | 4,771.09 | [42] |

SPHCM: St. Paul's Hospital Cost Model. * Including drug possession, trafficking, other acquisitive, vandalism/loitering/vagrancy, legal status violations, other offenses.

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**Table A12. Health resource utilization (rate per 100 person months) NAOMI trial [N=226]**

| | MMT state | DAM state | Relapse state |
|---|---|---|---|
| Total patient months | 296.9 | 364.6 | 182.6 |
| *Inpatient Care** | | | |
| Hospital admission | 5.7 | 4.4 | 15.9 |
| ED admission | 4.7 | 3.8 | 12.1 |
| Days, Inpatient care | 13.1 | 20.7 | 74.9 |
| *Outpatient Care** | | | |
| ED visit | 2.0 | 2.5 | 2.2 |
| GP visit | 53.6 | 33.5 | 91.5 |
| Addiction counselling | 0.3 | 0.0 | 0.0 |
| Mental health | 6.4 | 0.8 | 4.4 |
| Other specialists | 15.5 | 14.3 | 21.9 |
| Other non-specialists | 33.3 | 27.2 | 72.3 |

ED: Emergency department; GP: General physician * Based on self-reported data.

**Table A13. Self-reported property theft and violent crime rates per patient month. NAOMI trial [N=226]**

| | MMT state | DAM state | Relapse state |
|---|---|---|---|
| Total patient months | 296.9 | 364.6 | 182.6 |
| Property theft | 0.72 | 0.75 | 1.39 |
| Violent crime | 0.13 | 0.09 | 0.26 |

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**Table A14. Results of generalized least squares regression to estimate the costs of health resource utilization, criminal involvement, criminal charges and health utility from NAOMI dataset (N=226): pooled treatment estimates**

| | Mean | β | SE | p-value | Variance-covariance matrix | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Health resource utilization* | | | | | | | | | |
| Intercept | | 5.469 | 1.544 | <0.01 | Intercept | 2.383 | | | |
| Age | | 0.047 | 0.032 | 0.15 | Treatment | -0.577 | 0.527 | | |
| Female | | 0.448 | 0.528 | 0.40 | HIV - | 0.014 | -0.328 | 0.374 | |
| HIV - | | -1.146 | 0.612 | 0.06 | Female | -0.361 | 0.276 | -0.212 | 0.278 |
| No treatment | 695.98 | Ref | | | Age | -0.046 | 0.007 | 0.003 | 0.004 | 0.001 |
| Treatment | 72.10 | -2.267 | 0.726 | <0.01 | | | | | |
| *Criminal activity* | | | | | | | | | |
| Intercept | | 8.838 | 1.286 | <0.01 | Intercept | 1.654 | | | |
| Age | | 0.013 | 0.028 | 0.66 | Treatment | -0.105 | 0.153 | | |
| Female | | -0.599 | 0.456 | 0.19 | Female | -0.338 | -0.018 | 0.208 | |
| No treatment | 8981.28 | Ref | | | Age | -0.035 | 0.000 | 0.007 | 0.001 |
| Treatment | 4273.11 | -0.743 | 0.391 | 0.06 | | | | | |
| *Criminal charges* | | | | | | | | | |
| Intercept | | 7.690 | 0.533 | <0.01 | Intercept | 0.284 | | | |
| Age | | -0.031 | 0.015 | 0.03 | Treatment | 0.076 | 0.096 | | |
| Female | | -0.225 | 0.497 | 0.65 | Female | -0.099 | -0.115 | 0.247 | |
| No treatment | 590.05 | Ref | | | Age | -0.007 | -0.003 | 0.003 | 0.000 |
| Treatment | 398.82 | -0.392 | 0.310 | 0.21 | | | | | |
| *Health utility* | | | | | | | | | |
| Intercept | | 0.828 | 0.069 | <0.01 | Intercept | 0.005 | | | |
| Age | | -0.002 | 0.002 | 0.15 | Treatment | 0.000 | 0.000 | | |
| Female | | 0.004 | 0.033 | 0.90 | Female | -0.001 | 0.000 | 0.001 | |
| No treatment | 0.739 | Ref | | | Age | 0.000 | 0.000 | 0.000 | 0.000 |
| Treatment | 0.841 | 0.102 | 0.020 | <0.01 | | | | | |

Ref: reference group; Tx: Treatment; Mean: estimated mean value, given mean age, gender and HIV-status (in health resource utilization model) mix of the NAOMI study; β: estimated coefficient value; SE: standard error.

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**Table A15. Results of generalized least squares regression to estimate the costs of health resource utilization, criminal involvement, criminal charges and health utility from NAOMI dataset (N=226): treatment-specific estimates**

| | Mean | β | SE | P-value | Variance-covariance matrix | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Health resource utilization* | | | | | | | | | | |
| Intercept | | 5.489 | 1.763 | <0.01 | Intercept | 3.107 | | | | |
| Age | | 0.046 | 0.036 | 0.21 | DAM | -0.716 | 0.522 | | | |
| Female | | 0.444 | 0.597 | 0.46 | MMT | -0.759 | 0.364 | 0.593 | | |
| HIV + | | Ref | | | HIV - | 0.389 | -0.258 | -0.290 | 0.288 | |
| HIV - | | -1.108 | 0.537 | 0.03 | Female | -0.820 | 0.269 | 0.271 | -0.207 | 0.356 |
| No treatment | 689.94 | Ref | | | Age | -0.061 | 0.011 | 0.011 | -0.007 | 0.014 | 0.001 |
| DAM | 36.83 | -2.930 | 0.723 | <0.01 | | | | | | |
| MMT | 109.18 | -1.844 | 0.770 | 0.02 | | | | | | |
| *Criminal activity* | | | | | | | | | | |
| Intercept | | 8.727 | 1.258 | <0.01 | Intercept | 1.584 | | | | |
| Age | | 0.016 | 0.028 | 0.57 | DAM | -0.242 | 0.167 | | | |
| Female | | -0.610 | 0.444 | 0.17 | MMT | 0.006 | 0.099 | 0.253 | | |
| Relapse | 9121.45 | Ref | | | Female | -0.302 | -0.017 | -0.026 | 0.197 | |
| DAM | 3935.46 | -0.841 | 0.409 | 0.04 | Age | -0.033 | 0.004 | -0.002 | 0.006 | 0.001 |
| MMT | 4673.13 | -0.669 | 0.503 | 0.18 | | | | | | |
| *Criminal charges* | | | | | | | | | | |
| Intercept | | 7.753 | 0.550 | <.001 | Intercept | 0.302 | | | | |
| Age | | -0.032 | 0.015 | 0.03 | DAM | 0.113 | 0.123 | | | |
| Female | | -0.241 | 0.506 | 0.63 | MMT | 0.067 | 0.054 | 0.118 | | |
| No treatment | 707.65 | Ref | | | Female | -0.107 | -0.094 | -0.126 | 0.256 | |
| DAM | 342.39 | -0.637 | 0.350 | 0.07 | Age | -0.008 | -0.003 | -0.003 | 0.003 | 0.000 |
| MMT | 492.23 | -0.322 | 0.343 | 0.35 | | | | | | |
| *Health utility* | | | | | | | | | | |
| Intercept | | 0.828 | 0.070 | <0.01 | Intercept | 0.005 | | | | |
| Age | | -0.002 | 0.002 | 0.15 | DAM | 0.000 | 0.001 | | | |
| Female | | 0.005 | 0.033 | 0.89 | MMT | 0.000 | 0.000 | 0.001 | | |
| No treatment | 0.738 | Ref | -- | -- | Female | -0.001 | 0.000 | 0.000 | 0.001 | |
| DAM state | 0.857 | 0.119 | 0.026 | <0.01 | Age | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| MMT state | 0.826 | 0.088 | 0.023 | <0.01 | | | | | | |

Ref: reference group; Mean: estimated mean value, given mean age, gender and HIV-status (in health resource utilization model) mix of the NAOMI study; β: estimated coefficient value; SE: standard error.

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**Table A16. Results of generalized least squares regression to estimate the costs of criminal involvement and criminal charges from NAOMI dataset (N=226): pooled treatment estimates, Third party payer perspective***

| | Mean | β | SE | p-value | Variance-covariance matrix | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Criminal activity* | | | | | | | | | |
| Intercept | | 8.330 | 1.213 | <0.01 | Intercept | 1.472 | | | |
| Age | | 0.020 | 0.027 | 0.47 | Treatment | -0.121 | 0.148 | | |
| Female | | -0.640 | 0.459 | 0.16 | Female | -0.319 | 0.004 | 0.210 | |
| No treatment | 6489.38 | Ref | | | Age | -0.031 | 0.001 | 0.006 | 0.001 |
| Treatment | 3216.18 | -0.702 | 0.385 | 0.07 | | | | | |
| *Criminal charges* | | | | | | | | | |
| Intercept | | 7.655 | 0.550 | <0.01 | Intercept | 0.302 | | | |
| Age | | -0.032 | 0.015 | 0.03 | Treatment | 0.065 | 0.069 | | |
| Female | | -0.311 | 0.432 | 0.47 | Female | -0.072 | -0.069 | 0.186 | |
| No treatment | 515.66 | Ref | | | Age | -0.008 | -0.002 | 0.002 | 0.000 |
| Treatment | 361.41 | -0.355 | 0.263 | 0.18 | | | | | |

Ref: reference group; Tx: Treatment; Mean: estimated mean value, given mean age, gender mix of the NAOMI study; β: estimated coefficient value; SE: standard error. *excluding out-of-pocket costs due to criminal victimization from

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**Table A17. Reported general-population EQ-5D estimates from Johnson et al. (2000)**

| Age stratum | N | EQ-5D Index [Mean (SD)] | Difference in EQ-5D Index [Mean (SD)] |
|---|---|---|---|
| 18-24 | 31 | 85.9 (20.9) | -- |
| 25-34 | 151 | 91.3 (15.3) | 0.913 |
| 35-44 | 330 | 87.4 (19.1) | -0.039 |
| 45-54 | 321 | 86.4 (18.4) | -0.049 |
| 55-64 | 237 | 82.8 (20.6) | -0.085 |
| 64-74 | 230 | 79.0 (23.7) | -0.123 |
| ≥ 75 | 190 | 70.5 (24.5) | -0.208 |

**Table A18: Estimated variance covariance matrix of differences in EQ-5D scores**

| | Age stratum | | | | | |
|---|---|---|---|---|---|---|
| | **25-34** | **35-44** | **45-54** | **55-64** | **64-74** | **≥ 75** |
| 25-34 | 0.000155 | | | | | |
| 35-44 | -0.000155 | 0.000266 | | | | |
| 45-54 | -0.000155 | 0.000155 | 0.000260 | | | |
| 55-64 | -0.000155 | 0.000155 | 0.000155 | 0.000334 | | |
| 64-74 | -0.000155 | 0.000155 | 0.000155 | 0.000155 | 0.000399 | |
| ≥ 75 | -0.000155 | 0.000155 | 0.000155 | 0.000155 | 0.000155 | 0.000471 |

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**Table A19. Complete results of sensitivity analyses**

| Time Horizon | | Costs ($C1,000s) [Mean (95% CI)] | Cost component (%) Tx | HRU | Crime | QALYs [Mean (95% CI)] | ICER ($C1,000s) [Mean (95% CI)] |
|---|---|---|---|---|---|---|---|
| *Third party payer perspective* | | | | | | | |
| 1 year | DAM | 73.9 (55.6, 100.5) | 20.5 | 4.9 | 74.6 | 0.86 (0.83, 0.90) | 58.6 (CS, 544.6) |
| | MMT | 72.9 (53.4, 100.7) | 4.5 | 7.8 | 87.7 | 0.85 (0.81, 0.89) | |
| 5 years | DAM | 333.0 (251.5, 448.6) | 14.3 | 9.5 | 76.1 | 3.43 (3.26, 3.59) | CS (CS, 138.3) |
| | MMT | 351.5 (251.7, 490.0) | 3 | 13.3 | 83.7 | 3.32 (3.14, 3.47) | |
| 10 years | DAM | 603.9 (439.0, 839.7) | 12 | 12.6 | 75.3 | 5.61 (5.29, 5.90) | CS (CS, 94.3) |
| | MMT | 634.6 (446.5, 906.0) | 2.6 | 16.3 | 81.1 | 5.39 (5.08, 5.67) | |
| Lifetime | DAM | 971.5 (642.1, 1,489.9) | 10.5 | 15.7 | 73.8 | 7.92 (7.32, 8.53) | CS (CS, 129.9) |
| | MMT | 993.6 (635.6, 1,546.3) | 2.4 | 18.9 | 78.7 | 7.46 (6.91, 8.01) | |
| *Ministry of Health perspective* | | | | | | | |
| 1 year | DAM | 18.3 (16.8, 20.6) | 80.9 | 19.1 | - | 0.86 (0.83, 0.90) | 573.7 (346.8, 945.0) |
| | MMT | 8.8 (6.3, 14.3) | 37.8 | 62.2 | - | 0.85 (0.81, 0.89) | |
| 5 years | DAM | 78.0 (63.6, 101.1) | 60.5 | 39.5 | - | 3.43 (3.26, 3.59) | 194.7 (45.7, 380.8) |
| | MMT | 56.5 (34.7, 95.0) | 19.6 | 80.4 | - | 3.32 (3.14, 3.47) | |
| 10 years | DAM | 146.2 (111.5, 203.5) | 49.3 | 50.7 | - | 5.61 (5.29, 5.90) | 125.2 (CS, 308.0) |
| | MMT | 118.4 (69.8, 198.3) | 14.7 | 85.3 | - | 5.39 (5.08, 5.67) | |
| Lifetime | DAM | 247.6 (170.8, 401.9) | 41.1 | 58.9 | - | 7.92 (7.32, 8.53) | 85.6 (CS, 363.1) |
| | MMT | 208.0 (113.9, 386.3) | 12.1 | 87.9 | - | 7.46 (6.91, 8.01) | |
| *Equalize mortality in MMT to mortality in DAM (using DAM estimates)* | | | | | | | |
| 1 year | DAM | 85.9 (63.8, 116.7) | 17.7 | 4.2 | 78.1 | 0.86 (0.83, 0.90) | CS (CS, 468.5) |
| | MMT | 87.6 (63.9, 119.8) | 3.7 | 6.5 | 89.8 | 0.85 (0.81, 0.89) | |
| 5 years | DAM | 387.5 (293.3, 511.4) | 12.3 | 8.2 | 79.5 | 3.42 (3.26, 3.59) | CS (CS, 103.9) |
| | MMT | 417.0 (296.8, 575.4) | 2.5 | 11.2 | 86.2 | 3.31 (3.14, 3.47) | |
| 10 years | DAM | 695.3 (504.2, 958.4) | 10.4 | 11.1 | 78.5 | 5.60 (5.28, 5.90) | CS (CS, 83.3) |
| | MMT | 739.7 (515.0, 1,054.3) | 2.2 | 14 | 83.7 | 5.36 (5.07, 5.65) | |
| Lifetime | DAM | 1,091.2 (721.5, 1,703.7) | 9.3 | 14.1 | 76.6 | 7.89 (7.29, 8.53) | CS (CS, 115.4) |
| | MMT | 1,118.1 (724.7, 1,758.9) | 2.1 | 16.7 | 81.2 | 7.35 (6.86, 7.87) | |
| *Mortality estimates from Gronbladh et al (1990)* | | | | | | | |
| 1 year | DAM | 85.8 (63.7, 116.6) | 17.7 | 4.2 | 78.1 | 0.86 (0.83, 0.90) | CS (CS, 426.4) |
| | MMT | 87.0 (63.5, 118.9) | 3.7 | 6.5 | 89.8 | 0.84 (0.81, 0.88) | |
| 5 years | DAM | 377.1 (284.8, 498.7) | 12.7 | 8.1 | 79.3 | 3.39 (3.22, 3.55) | CS (CS, 119.2) |
| | MMT | 394.5 (282.2, 543.1) | 2.7 | 11.1 | 86.3 | 3.21 (3.06, 3.37) | |
| 10 years | DAM | 653.0 (477.4, 897.5) | 11 | 10.8 | 78.3 | 5.44 (5.11, 5.74) | CS (CS, 111.8) |
| | MMT | 665.2 (466.7, 943.9) | 2.4 | 13.8 | 83.8 | 5.04 (4.77, 5.30) | |
| Lifetime | DAM | 941.2 (640.8, 1,435.4) | 10.3 | 13.5 | 76.2 | 7.33 (6.65, 8.01) | 44.8 (CS, 146.6) |
| | MMT | 904.2 (604.4, 1,377.4) | 2.4 | 16.2 | 81.4 | 6.50 (6.09, 6.90) | |

*Starting age = 30*

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1 year | DAM | 83.0 (50.2, 137.9) | 19.2 | 3.6 | 77.2 | 0.89 (0.85, 0.94) | CS (CS, 554.6) |
| | MMT | 83.7 (45.6, 146.5) | 4.2 | 5.5 | 90.4 | 0.88 (0.83, 0.92) | |
| 5 years | DAM | 376.0 (236.8, 591.5) | 13.5 | 6.9 | 79.6 | 3.65 (3.48, 3.81) | CS (CS, 160.1) |
| | MMT | 402.9 (235.5, 673.4) | 2.8 | 9.5 | 87.6 | 3.55 (3.38, 3.73) | |
| 10 years | DAM | 684.2 (459.1, 1,016.8) | 11.4 | 9.4 | 79.3 | 6.17 (5.89, 6.45) | CS (CS, 111.8) |
| | MMT | 730.0 (466.1, 1,120.9) | 2.5 | 11.9 | 85.6 | 6.00 (5.72, 6.28) | |
| Lifetime | DAM | 1,292.7 (966.5, 1,736.6) | 9.5 | 13.1 | 77.4 | 10.27 (9.69, 10.85) | CS (CS, 123.1) |
| | MMT | 1,345.1 (965.5, 1,852.2) | 2.2 | 15.3 | 82.5 | 9.83 (9.27, 10.38) | |
| *Starting age = 50* | | | | | | | |
| 1 year | DAM | 95.2 (57.9, 159.0) | 16.3 | 5.6 | 78.1 | 0.82 (0.77, 0.88) | CS (CS, 425.6) |
| | MMT | 99.4 (57.1, 168.3) | 3.4 | 8.7 | 87.9 | 0.81 (0.75, 0.86) | |
| 5 years | DAM | 405.8 (233.5, 708.9) | 11.5 | 10.5 | 78 | 3.03 (2.80, 3.25) | CS (CS, 95.0) |
| | MMT | 438.4 (237.1, 802.1) | 2.4 | 14.2 | 83.4 | 2.88 (2.65, 3.10) | |
| 10 years | DAM | 674.8 (360.4, 1,251.5) | 9.9 | 13.6 | 76.5 | 4.56 (4.17, 4.95) | CS (CS, 94.0) |
| | MMT | 712.2 (360.5, 1,370.8) | 2.2 | 17 | 80.8 | 4.26 (3.87, 4.64) | |
| Lifetime | DAM | 840.7 (421.7, 1,653.9) | 9.4 | 15.1 | 75.4 | 5.37 (4.82, 5.94) | CS (CS, 148.3) |
| | MMT | 864.3 (420.4, 1,754.2) | 2.1 | 18.3 | 79.6 | 4.92 (4.40, 5.46) | |
| *Treatment - specific cost and utilities* | | | | | | | |
| 1 year | DAM | 82.5 (59.4, 115.6) | 18.5 | 3.8 | 77.7 | 0.88 (0.84, 0.92) | CS (CS, 1,828.2) |
| | MMT | 96.4 (62.9, 152.1) | 3.5 | 6.4 | 90.1 | 0.84 (0.79, 0.88) | |
| 5 years | DAM | 382.3 (277.2, 526.7) | 12.5 | 7.7 | 79.8 | 3.46 (3.31, 3.62) | CS (CS, 450.2) |
| | MMT | 449.5 (306.4, 658.7) | 2.4 | 10.6 | 87 | 3.28 (3.10, 3.46) | |
| 10 years | DAM | 694.6 (487.8, 994.6) | 10.5 | 10.4 | 79.1 | 5.66 (5.37, 5.95) | CS (CS, 380.6) |
| | MMT | 797.8 (543.6, 1,157.9) | 2.1 | 13.2 | 84.7 | 5.33 (5.01, 5.66) | |
| Lifetime | DAM | 1,109.3 (712.1, 1,754.0) | 9.3 | 13.1 | 77.6 | 7.99 (7.41, 8.60) | CS (CS, 417.3) |
| | MMT | 1,229.2 (790.0, 1,838.1) | 2 | 15.8 | 82.2 | 7.38 (6.81, 7.98) | |
| *Time to discontinuation of relapse for DAM from NAOMI trial data* | | | | | | | |
| 1 year | DAM | 84.0 (61.2, 115.9) | 18.7 | 3.8 | 77.4 | 0.87 (0.83, 0.91) | CS (CS, 628.5) |
| | MMT | 84.7 (61.3, 116.0) | 4 | 6.1 | 89.9 | 0.85 (0.81, 0.89) | |
| 5 years | DAM | 355.9 (265.8, 480.2) | 15.5 | 6.3 | 78.2 | 3.49 (3.33, 3.65) | CS (CS, 290.7) |
| | MMT | 372.0 (267.4, 509.5) | 3.5 | 9.3 | 87.2 | 3.40 (3.22, 3.57) | |
| 10 years | DAM | 624.2 (450.1, 860.6) | 14.2 | 8.2 | 77.6 | 5.80 (5.49, 6.10) | CS (CS, 240.9) |
| | MMT | 650.2 (448.9, 905.0) | 3.3 | 11.4 | 85.3 | 5.62 (5.25, 5.97) | |
| Lifetime | DAM | 1,018.7 (673.4, 1,629.1) | 13 | 10.8 | 76.1 | 8.58 (7.87, 9.29) | CS (CS, 847.5) |
| | MMT | 1,042.6 (664.1, 1,678.3) | 3.1 | 14 | 82.9 | 8.18 (7.32, 9.09) | |
| *Time to discontinuation of MPH for DAM from NAOMI trial data* | | | | | | | |
| 1 year | DAM | 86.2 (64.3, 117.2) | 17.6 | 4.2 | 78.2 | 0.86 (0.82, 0.90) | CS (CS, 311.6) |
| | MMT | 93.4 (67.5, 128.3) | 3.1 | 7.3 | 89.6 | 0.84 (0.80, 0.88) | |
| 5 years | DAM | 395.7 (296.7, 526.4) | 12.1 | 8.6 | 79.4 | 3.41 (3.25, 3.57) | CS (CS, 69.7) |
| | MMT | 443.6 (311.7, 618.3) | 2.1 | 12.3 | 85.7 | 3.26 (3.09, 3.41) | |
| 10 years | DAM | 713.4 (515.9, 980.5) | 10.2 | 11.6 | 78.2 | 5.57 (5.26, 5.87) | CS (CS, 60.1) |
| | MMT | 782.6 (536.7, 1,131.0) | 1.8 | 15.1 | 83.1 | 5.27 (4.96, 5.55) | |

Appendix to: Nosyk B, Guh DP, Bansback NJ, et al. Cost-effectiveness of diacetylmorphine versus methadone for chronic opioid dependence refractory to treatment. *CMAJ* 2012. DOI:10.1503/cmaj.110669.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Lifetime | DAM | 1,113.3 (739.7, 1,728.5) | 9.2 | 14.6 | 76.2 | 7.79 (7.18, 8.40) | CS (CS, 106.7) |
| | MMT | 1,172.9 (759.1, 1,864.5) | 1.7 | 17.7 | 80.6 | 7.19 (6.68, 7.71) | |
| *Exponential distributions set for time to discontinuation curves* | | | | | | | |
| 1 year | DAM | 85.4 (63.2, 115.8) | 17.8 | 4.1 | 78.1 | 0.86 (0.82, 0.90) | 339.5 (CS, 2,465) |
| | MMT | 82.3 (58.8, 113.2) | 4.3 | 5.6 | 90 | 0.86 (0.81, 0.89) | |
| 5 years | DAM | 391.5 (291.5, 528.6) | 11 | 8.8 | 80.2 | 3.41 (3.23, 3.58) | CS (CS, 200.1) |
| | MMT | 416.9 (294.8, 581.3) | 2.6 | 11 | 86.4 | 3.33 (3.15, 3.49) | |
| 10 years | DAM | 706.7 (507.2, 994.1) | 9 | 11.9 | 79.1 | 5.56 (5.23, 5.88) | CS (CS, 143.1) |
| | MMT | 749.3 (515.6, 1,083.8) | 2.2 | 14.1 | 83.7 | 5.38 (5.07, 5.71) | |
| Lifetime | DAM | 1,103.5 (728.7, 1,712.1) | 7.9 | 15.2 | 76.9 | 7.77 (7.14, 8.44) | CS (CS, 330.7) |
| | MMT | 1,145.5 (737.8, 1,812.3) | 2 | 17.1 | 80.9 | 7.38 (6.78, 8.06) | |
| *Probability of HIV seroconversion: set to zero* | | | | | | | |
| 1 year | DAM | 85.6 (63.5, 116.1) | 17.7 | 3.8 | 78.5 | 0.86 (0.83, 0.90) | CS (CS, 514.2) |
| | MMT | 86.9 (63.1, 118.7) | 3.8 | 5.6 | 90.7 | 0.85 (0.81, 0.89) | |
| 5 years | DAM | 376.3 (279.5, 503.6) | 12.7 | 5.4 | 81.9 | 3.43 (3.26, 3.59) | CS (CS, 170.0) |
| | MMT | 399.7 (281.2, 559.4) | 2.7 | 7 | 90.3 | 3.32 (3.14, 3.47) | |
| 10 years | DAM | 661.1 (469.9, 921.3) | 11 | 6.3 | 82.8 | 5.62 (5.30, 5.91) | CS (CS, 133.8) |
| | MMT | 694.1 (470.7, 1,000.6) | 2.4 | 7.7 | 89.9 | 5.39 (5.08, 5.68) | |
| Lifetime | DAM | 1,017.9 (652.7, 1,624.6) | 10 | 7.3 | 82.7 | 7.94 (7.33, 8.54) | CS (CS, 147.1) |
| | MMT | 1,039.3 (647.1, 1,692.6) | 2.3 | 8.6 | 89.1 | 7.46 (6.91, 8.02) | |
| *Discount rate: 0%* | | | | | | | |
| 1 year | DAM | 88.1 (65.4, 119.6) | 17.6 | 4.2 | 78.2 | 0.89 (0.85, 0.92) | CS (CS, 482.0) |
| | MMT | 90.0 (65.7, 122.9) | 3.7 | 6.5 | 89.8 | 0.87 (0.83, 0.91) | |
| 5 years | DAM | 439.2 (331.2, 581.5) | 12.1 | 8.4 | 79.5 | 3.86 (3.66, 4.04) | CS (CS, 96.5) |
| | MMT | 474.5 (336.6, 657.1) | 2.5 | 11.4 | 86.1 | 3.73 (3.53, 3.91) | |
| 10 years | DAM | 887.1 (637.9, 1,231.5) | 10 | 11.6 | 78.4 | 7.02 (6.61, 7.39) | CS (CS, 73.0) |
| | MMT | 946.9 (650.2, 1,359.6) | 2.2 | 14.5 | 83.3 | 6.73 (6.33, 7.10) | |
| Lifetime | DAM | 1,802.9 (1,114.6, 3,040.9) | 8.6 | 15.8 | 75.5 | 12.16 (11.04, 13.37) | CS (CS, 223.4) |
| | MMT | 1,837.5 (1,128.1, 3,112.3) | 2 | 18.3 | 79.7 | 11.29 (10.27, 12.37) | |
| *No improvement in HRQoL from treatment to abstinence* | | | | | | | |
| 1 year | DAM | 85.9 (63.8, 116.7) | 17.7 | 4.2 | 78.1 | 0.86 (0.82, 0.90) | CS (CS, 519.1) |
| | MMT | 87.7 (63.9, 119.8) | 3.7 | 6.5 | 89.8 | 0.85 (0.81, 0.89) | |
| 5 years | DAM | 387.7 (293.4, 511.6) | 12.3 | 8.2 | 79.5 | 3.42 (3.24, 3.59) | CS (CS, 114.8) |
| | MMT | 418.3 (297.0, 579.0) | 2.5 | 11.2 | 86.2 | 3.31 (3.14, 3.47) | |
| 10 years | DAM | 696.0 (504.9, 960.0) | 10.4 | 11.1 | 78.5 | 5.60 (5.27, 5.90) | CS (CS, 82.2) |
| | MMT | 743.8 (515.1, 1,059.7) | 2.3 | 14 | 83.8 | 5.38 (5.07, 5.67) | |
| Lifetime | DAM | 1,096.1 (724.1, 1,707.2) | 9.3 | 14.1 | 76.7 | 7.90 (7.28, 8.52) | CS (CS, 131.3) |
| | MMT | 1,137.6 (736.8, 1,776.5) | 2.1 | 16.7 | 81.2 | 7.46 (6.90, 8.01) | |

DAM: Diacetylmorphine; MMT: methadone maintenance treatment; QALY: Quality-adjusted life years; ICER: incremental cost-effectiveness ratio: ICER = $(Cost_{DAM} - Cost_{MMT}) / (QALY_{DAM} - QALY_{MMT})$; Tx: Treatment cost; HRU: health resource utilization cost; CRIME: costs of criminal activity. CS: Cost Saving.

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