Title

Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights

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Title: Can HCV direct-acting antiviral treatment as prevention reverse the HCV epidemic amongst men who have sex with men in the UK – epidemiological and modelling insights

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Key points:

- Epidemiological data and modelling suggest a continuing HCV epidemic among HIV-diagnosed MSM in the UK driven by high-risk individuals, despite high treatment rates.
- Substantial reductions in HCV transmission could be achieved through scale-up of DAA treatments and a moderately effective behavioural intervention.

Brief summary: Epidemiological data and modelling suggest a continuing HCV epidemic among HIV-diagnosed MSM in the UK driven by high-risk individuals, despite high treatment rates. Substantial reductions in HCV transmission could be achieved through scale-up of DAA treatments and a behavioural intervention.

ABSTRACT

Background: We report on the hepatitis C virus(HCV) epidemic among HIV-positive men who have sex with men(MSM) in the UK and model its trajectory with or without scaled-up HCV direct-acting antivirals(DAAs).

Methods: A dynamic HCV transmission model among HIV-diagnosed MSM in the UK was calibrated to HCV prevalence(Ab+ or RNA+), incidence, and treatment from 2004-2011 among HIV-diagnosed MSM in the UK collaborative HIV cohort(UK CHIC). The epidemic was projected with: current or scaled-up HCV treatment, with or without a 20% behavioral risk reduction.

Results: HCV prevalence among HIV-positive MSM in UK CHIC increased from 7.3% in 2004 to 9.9% in 2011, whereas primary incidence was flat(1.02-1.38 per 100 person-years). Over the next decade, modelling suggests 94% of infections are attributable to high-risk individuals, comprising 7% of the population. Without treatment, HCV chronic prevalence could have been 38% higher in 2015(11.9% vs 8.6%). With current treatment and SVR rates(status quo), chronic prevalence is likely to increase to 11% by 2025, but stabilize with DAA introduction in 2015. With DAAs scale-up to 80% within one year of diagnosis (regardless of disease stage), 20%/yr thereafter, chronic prevalence could reduce by 71% (to 3.2%) compared to status quo in 2025. With additional behavioural interventions, chronic prevalence could reduce further to <2.5% by 2025.

Conclusions: Epidemiological data and modelling suggest a continuing HCV epidemic among HIV-diagnosed MSM in the UK driven by high-risk individuals, despite high treatment rates. Substantial reductions in HCV transmission could be achieved through scale-up of DAAs and moderately effective behavioural interventions.

INTRODUCTION

An epidemic of hepatitis C virus (HCV) amongst HIV-positive men who have sex with men (MSM)[1, 2] has been documented in cities in Europe, Australia, and the US, but with little evidence of transmission amongst HIV-negative MSM[3, 4]. One of the key hubs of this epidemic is London[2]. However, the state and future of the UK epidemic is uncertain with reported incidence based on case notifications instead of longitudinal cohort trends[5, 6].

Modeling indicates HCV antiviral treatment for those at risk of transmission such as people who inject drugs (PWID) could have a primary prevention benefit[7-10]. HIV-positive MSM may be the ideal population to assess HCV treatment as prevention (particularly with interferon-free direct-acting antiviral therapy (IFN-free DAAs), which are highly effective in this population[11, 12]), because most patients are linked to care, frequently HCV tested, and the absolute numbers of HCV-HIV co-infected MSM are small. However, high reinfection rates (8-15 per 100 person-years(/100py)[13-15]) among HIV-positive MSM might limit the prevention benefits of HCV treatment.

To explore the potential impact of new treatments and other interventions on this epidemic, we took advantage of detailed available UK data and developed a dynamic model of HCV transmission among HIV-positive MSM in the UK, in order to assess the epidemic trajectory and project the impact of scaled-up HCV treatment as prevention.

METHODS

Epidemiological data analysis

The UK Collaborative HIV Cohort (UK CHIC) study is an ongoing observational study collecting clinical data from 16 HIV treatment centres across the UK[16]. Between 9/2012-9/2013, additional data were collected on HCV treatment from 11 participating centres. Individuals were included in the analysis if they had ever attended one of the 11 centres since 2004, had an HCV antibody (anti-HCV) or RNA test during follow-up, and were recorded as having acquired HIV through sex between men.

Cumulative HCV prevalence was calculated yearly as the number of men who had ever had a positive anti-HCV or HCV-RNA test by the end of that year as a proportion of all those who had been tested by that time. Incident infection was assessed among individuals with a negative anti-HCV test and either negative or missing HCV-RNA test after 1/1/2004 and at least one further test for anti-HCV or HCV-RNA. Individuals were followed-up until a positive anti-HCV or HCV-RNA test or their last date seen at a UK CHIC centre. The incidence rate was calculated by dividing the total number of incident infections (any positive anti-HCV or HCV-RNA test) by the total number of person years of follow-up. Receipt of HCV treatment (interferon (pegylated or non-pegylated) with or without ribavirin, telaprevir, or boceprevir) was assessed among all men who had ever received a positive HCV-RNA test.

Mathematical model

We developed a dynamic, deterministic model of HCV transmission, progression, and treatment among diagnosed HIV-positive MSM (**Figure 1**). Individuals enter at HIV diagnosis, a small proportion with existing HCV coinfection. As the model is dynamic, an individual's risk of acquiring HCV is related to background HCV prevalence and their risk behavior. The model tracks HCV disease progression and is stratified by HCV diagnosis status, treatment history, and transmission risk (high/low, based on factors associated with high-risk of HCV acquisition among MSM such as injecting drug use and methamphetamine use[17, 18]). We assume MSM who inject do so with other MSM, based on phylogenetic evidence indicating HCV MSM strains are clustered separately from PWID[19]. For our baseline analysis, we assume HCV uninfected HIV-diagnosed MSM are only at risk of HCV acquisition from HIV-diagnosed MSM because of the low HCV prevalence among HIV-negative MSM and HIV-positive undiagnosed MSM, proportional mixing between risk groups, and movement between high/low risk.

Model parameterization and calibration

The model was calibrated to annual UK CHIC data on HCV incidence, prevalence (Ab+ or RNA+) and proportion ever treated among diagnosed HIV-positive MSM in the UK from 2004-2011, and parameterized by data among HIV-diagnosed MSM in the UK (list of parameters in **Supplementary Table S1)**. The model was also calibrated to estimated HCV reinfection incidence among MSM in London (7.8/100py (95%CI 5.8-10.5) across 2004-2012)

[14] and the size of the HIV-diagnosed MSM population in 2013[20]. Model projections were validated against annual size estimates of the HIV-diagnosed MSM population from 2001-2013[20, 21].

Based on UK CHIC data, we model treatment rates (from 2003 onwards) of 46% (95%I 40-53) and 22% (95%I 20-24) treated within 1 year of an acute and chronic diagnosis, respectively. Using these rates and the cumulative proportion ever treated by 2011 (44%), the model estimates an annual treatment rate after the first year of diagnosis of 6.8% (95%I 3.8-9.9%). SVR rates for IFN-based therapy among HIV-infected individuals came from a published meta-analysis[22]; we assume 90% SVR with DAAs. We increased life expectancy from HIV diagnosis over calendar time based on UK data reflecting earlier diagnosis/treatment and more effective ART[23], and include excess liver-related mortality for MSM coinfected with HCV[24, 25].

To incorporate parameter uncertainty, 1000 parameter sets were randomly sampled from the parameter distributions shown in **Table S1**.

Intervention scenarios and sensitivity analyses

We model the UK epidemic from 1996 to 2015, assessing the population attributable fraction (PAF) of being high-risk by assessing the relative difference in cumulative new infections from 2015 to 2025 if the relative risk between high and low risk is set to 1 from 2015 and assuming status quo treatment rates and SVR. We explore the ten-year impact (to 2025) on HCV (Ab+ or RNA+) prevalence, chronic (RNA+) prevalence, primary incidence, and numbers treated for the following scenarios (summarized in **table 3**):

- **Baseline status quo with IFN/RBV:** Continuation of current treatment rates and SVR
- **Current treatment rates with DAAs for all:** Continuation of current treatment rates with DAAs (90% SVR) from 2015
- **DAA scale-up at diagnosis:** Scale-up DAA treatment rates to 60%/80%/100% treated within 1 year of diagnosis from 2015
- **DAA scale-up to all:** Scale-up DAA treatment rates to 80% treated within 1 year of diagnosis, and 20%/year thereafter from 2015

- **DAA scale-up to all and behavioral intervention: as above** and 20% behavioral risk reduction from 2015
- **No historical treatment from 1996**

We allow retreatment with DAAs for those who have previously failed IFN-based therapies and those who are reinfected.

One-way sensitivity analyses explore the impact of variations in SVR, retreatment eligibility, HCV testing rates, risk reductions post-treatment (50% and 100%) or post-diagnosis (20% for 1 year or until HCV treatment), assortative mixing, seeding of HCV from outside the HIV-diagnosed population on the mean chronic HCV prevalence in 2025 for the DAA scale-up to all scenario (details in **supplementary information**).

RESULTS

Epidemiological data from UK CHIC

Nearly all (98%) of MSM in UK CHIC under follow-up in 2011 had been tested for HCV (**Table 1**); the proportion of MSM not known to be infected who were annually HCV-tested increased from 31% in 2004 to 65% in 2011 **(Supplementary Table S2)**. The median number of diagnostic tests until the first positive result per individual was 4 (IQR: 2,6).

The cumulative HCV prevalence (Ab+ or RNA+) among HIV-positive MSM increased from 7.26% in 2004 to 9.86% in 2011 (**Table 1**). A total of 11,386 MSM, who were initially HCV uninfected and who had at least one further test during median 5 years follow-up, were included in the incidence analysis, contributing 54,619 person-years of follow-up. Incidence rates from 2004 to 2011 were relatively flat, varying from 1.02 to 1.38 per 100 person-years of follow-up (**Table 2**).

A total of 1,403 MSM had ever received a positive RNA result and were considered eligible for HCV treatment. Of these, 36 individuals were excluded as their treatment dates were prior to their first positive HCV tests. Therefore, a total of 1367 MSM were eligible for

inclusion in this analysis. Overall, 586/1367 (43%) were ever treated, the majority (60%) of treatments occurring within one year of diagnosis (**Supplementary tables S3, S4**).

Modelling projections

The model fits closely matched the number of HIV diagnosed MSM from 2000-2013 (**Figure 2a**) and HCV prevalence (Ab+ or RNA+) from 2004-2011 (**Figure 2b**). The projected HCV incidence (1.47/100py) was towards the upper bounds of the UK CHIC data (**Figure 2c**), and projected reinfection incidence (mean 7.8/100py for 2004-2012) was consistent with UK data[14]. In 2015, the modelled reinfection incidence ranged from 4-7 fold that of the primary incidence.

Population attributable fractions

The model fits estimate a high-risk population size of 7% (2.5%-97.5% Interval(95%I) 3-14%), consistent with the estimated proportion of HIV-positive MSM in the UK reporting injecting drug use or methamphetamine use in the previous 4 weeks[26]. These high-risk individuals contribute over one-third of prevalent (37%, 95%I 21-64%) and incident (36%, 95%I 13-78) infections in 2015. Over the next decade, 94% (95%I 91-97) of infections are attributable to high-risk individuals.

Projections of intervention impact to 2025

Treatment with IFN/RBV

If HCV treatment and SVR rates remain unchanged, the model predicts steadily increasing anti-HCV prevalence, and increasing chronic(RNA+) prevalence from 8.6% (95%CI 8.1-9.1) in 2015 to 11% (95%I 9.9-12.1%) in 2025 (**Figure 3a,b**). Due to the expanding epidemic, status quo treatment rates results in greater treatments required yearly (**Figure 4**). In contrast, incidence will remain relatively flat, at 1.5/100py (95%CI 1.4-1.7) in 2025 (**Figure 3c)**. However, if there was no treatment, chronic prevalence would have been over one-third (38%) higher in 2015 (11.9%, 95%I 11.1-12.6), and 17.4% (95%I 15.8-18.6) in 2025 (**Figure 3b**). Similarly, incidence would have been 24% higher (1.8/100py, 95%I 1.6-2).

Treatment with DAAs

If DAAs are provided from 2015 at current treatment rates, chronic prevalence will remain virtually unchanged over the next decade (8%, 95%I 7.4-8.6 in 2025), but could be a relative 27% lower in 2025 than if IFN/RBV is used (**Figure 3b).** Modest reductions in HCV incidence would be achieved (1.3/100py, 95%I 1.2-1.4 in 2025) (**Figure 3c**).

Treatment scale-up with DAAs

Substantial reductions in chronic prevalence can be achieved through scale-up of DAAs (**Figure 3b**). If 60%, 80%, or 100% of recently diagnosed (<1 year) individuals are treated the year of diagnosis (compared to 46% at baseline) but no change in treatment rates for non-recent diagnoses (>1 year), HCV RNA prevalence in 2025 could decrease to 7.4% (95%I 6.7-8.1), 6.2% (95%I 5.6-7), or 5.0% (95%I 4.4-6), respectively (a 33%, 44%, or 55% relative reduction compared to baseline, respectively). Similarly, incidence in 2025 could reduce relatively by 15%, 25%, and 36% compared to baseline, respectively. These treatment increases result in 15%, 30%, and 41% greater numbers treated for the first year, respectively, but the annual numbers treated drop below the status quo scenario by 2022 (**Figure 4**).

More impact is achieved if treatment is scaled-up among those with recent (<1 year) and non-recent (>1 year) diagnoses. If 80% of recent diagnoses and 20%/yr of non-recent diagnoses are treated (compared to 46%/7% for recent/nonrecent at baseline), RNA prevalence could reduce to 3.2% (95%I 2.8-4.1) by 2025 (71% lower than 2025 baseline), and incidence could reduce to 0.7/100py (95%I 0.6-1) (56% lower than 2025 baseline). Treatment numbers double the first year, but drop quickly, approaching the status quo scenario by 2022 (**Figure 4**).

If, DAA scale-up (80% <1 year from diagnosis and 20%/yr thereafter) is combined with a behavioral intervention that reduces transmission risk by 20% from 2015, HCV incidence decreases by 20% within 1 year to 1.2/100py (95%I 1.1-1.3), and to 0.4/100py (95%I 0.3-0.7) by 2025 (**Figure 3c).** This combined prevention intervention reduces chronic prevalence to 2.4% (95%I 2.1-3.3%) by 2025 (**Figure 3b**) and lowers the annual number of treatments (**Figure 4**).

Sensitivity analysis

Across our sensitivity analyses, all scenarios predict a chronic RNA prevalence of <4% in 2025 with DAA scale-up to all (compared to 3.2% for base-case). Less impact (35% relative reduction in chronic prevalence at 2025 compared to base-case) is achieved with no retreatment because high treatment rates are not sustainable due to many MSM already being treated. Although greater impact occurs if risk reductions occur post-treatment from 2015 (20% greater impact if risk is reduced by 100%) the effect is limited as retreatment of reinfections is high. Little additional impact (<3% relative difference) is achieved with a short term (<1 year) 20% reduction in risk behavior after diagnosis; more substantial impact by 2025 occurs with a sustained behavioral intervention targeting all MSM (chronic RNA 2.4% in 2025) than a short-term intervention targeting those post-diagnosis (chronic RNA 3.1% in 2025). Little difference (<15% relative difference) is seen with varied SVR, scaled-up diagnosis, partial assortative mixing of high-risk, or if HCV infections are seeded into the population (**Supplementary figure S1**).

DISCUSSION

HCV prevalence (Ab+ or RNA+) among HIV-diagnosed MSM in the UK CHIC study is projected to increase under current treatment rates from 9.9% in 2011 to 11% by 2025. We estimate that a small high-risk group (<10%) contributes over 90% of HCV infections over the next decade. In order to substantially reduce chronic prevalence (<3%), treatment scale-up amongst all diagnosed individuals is required, with behavior change interventions necessary to achieve immediate reductions in HCV incidence. The scaled-up rates we examine translate to a maximum of double the numbers of HIV-positive MSM treated (700/year in the UK) compared to the status quo initially, but these numbers drop below status quo levels by 2022 due to prevention benefits.

Comparison with other studies/Limitations

To our knowledge, this is the first study to model the HCV epidemic among HIV-infected MSM. Though our analysis is UK-focused, other settings have similar incidence [27-29]. The stable incidence levels found in UK are similar to Amsterdam[29] and USA[30], whereas increasing incidence is reported in Switzerland[28]. Given its large size and wide representation of UK clinics, UK CHIC is broadly representative of people living with HIV and attending for HIV care in the UK. Our UK CHIC estimate is slightly higher than reported previously in the UK[5, 6] based on case notification data but also slightly lower than projected by our modelling. Two potential sources of under-estimation by UK CHIC data could be due to incident infections without a previous negative test being excluded, or follow-up time being over-estimated for patients that cycle in/out of UK CHIC clinics, which if occurring among higher-risk individuals, could lead to true incidence being underestimated. On the other hand, it is possible those tested are at higher-risk of infection, which would overestimate true incidence.

The model projections are limited by several sources of uncertainty which remain even after the uncertainty analyses. First, we model HCV transmission among HIV-diagnosed MSM only, although we include inflow of HIV/HCV coinfected individuals at HIV diagnosis which are unaffected by our interventions. It is possible interventions for HIV-diagnosed MSM would also reduce incidence among HIV-undiagnosed MSM, in which case we would expect more impact than shown. Additionally, our sensitivity analysis suggests seeding of HCV infections from HIV undiagnosed or HIV-negative individuals would have minimal impact. It is unclear whether the higher HCV prevalence among HIV-diagnosed MSM compared to HIV undiagnosed or HIV-negative individuals is related to changing risk behavior upon HIV diagnosis, a longer time at risk, or individuals with elevated risk behaviors compared to the general MSM population acquiring both HIV and HCV.

Second, there are limited data defining HCV-related risk behaviours among HIV-positive MSM, and therefore we allowed details of the high-risk population (size, relative risk, time at risk) to vary as part of the model calibration. Additionally, although we include behavioural heterogeneity, we do not explicitly model the transmission network. It is possible that highly connected super-spreaders are responsible for many HCV transmission events and should be targeted for prevention. Similarly, we neglect international migration/travel due to a lack of

available data, movement which could seed infections and limit the impact of localized interventions. Better epidemiological data on these factors is critical to strengthening the model predictions.

Third, we explore a hypothetical 20% effective behavioral risk intervention, which was not based on a proven intervention in this population. Unfortunately, there is no empirical evidence that this level of HCV risk reduction is achievable. A Cochrane review found evidence for the effectiveness of behavior change interventions to reduce unprotected anal sex among MSM such as counseling, social and behavioral support, reporting an overall reduction by 27% (95%CI 15-37%)[31]. These interventions, though primarily aimed at reducing HIV risk, could be effective for HCV as well. Additionally, among people who inject drugs, opiate substitution therapy and high coverage needle and syringe programmes can reduce an individual's risk of HCV acquisition by 50% alone, or 80% in combination[32], but it is unclear how applicable these interventions are to the HCV epidemic among MSM. It is possible both sexual and injecting-related interventions could play an important role, such as prevention messaging training among sexual health/HIV clinic staff and the distribution of safe chemsex kits. One UK clinic is currently examining the impact of club drug behavior change intervention among MSM, but the impact is uncertain at present.

Fourth, we examine DAA scale-up for both acute and chronic infection as European[33] and US[34] guidelines recommend DAA therapy regardless of liver disease stage for HIV/HCV coinfected individuals. However, if DAAs are prioritized or restricted to those with more advanced liver disease then the prevention impact could be less than we predict. As such, the individual and population benefits achievable strongly support not restricting access to DAA therapy among HIV/HCV coinfected MSM. Nevertheless, even if IFN-free DAA therapy is prioritized to those with advanced liver disease, it is possible IFN-based treatment uptake among those with less advanced disease will remain high given historically high rates of uptake among HIV-coinfected MSM.

Conclusion

We report a continuing epidemic among HIV-diagnosed MSM in the UK, despite high rates of treatment, which is largely attributable to a high-risk population. Substantial reductions in

HCV transmission within a decade could be achieved through rapid DAA scale-up and moderately successful behavioural interventions. This impact could be achieved despite reinfection rates which are roughly five-fold higher than primary incidence, because the shortening and ease of delivery of new IFN-free DAAs enables scale-up with existing infrastructure. Given their importance in driving ongoing HCV transmission, there is a need to develop effective interventions to address high-risk behaviours associated with injecting and other drug use among MSM.

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TABLE LEGENDS

Table 1. Cumulative prevalence (Ab+ or RNA+) of hepatitis C among HIV-positive MSM in UK CHIC. UK CHIC: Collaborative HIV Cohort; MSM: men who have sex with men; HCV: hepatitis C virus

Table 2. Incidence of hepatitis C among HIV-positive MSM in UK CHIC. UK CHIC: Collaborative HIV Cohort; MSM: men who have sex with men; HCV: hepatitis C virus; CI: confidence interval

Table 3. Mathematical modeling scenarios. IFN/RBV: pegylated interferon+ribavirin, DAA: direct acting antivirals, SVR: sustained viral response

FIGURE LEGENDS

Figure 1. Mathematical model schematic. The model is also stratified by treatment naïve, IFN experienced, DAA experienced, and low/high risk states. HIV and non-HIV death occurs from all states. MSM: men who have sex with men; HCV: hepatitis C virus

Figure 2. Model fits to epidemiological data from the UK. (A) Number of HIV-diagnosed MSM, (B) HCV prevalence (Ab+ or RNA+) among diagnosed HIV-positive MSM, (C) HCV primary incidence among diagnosed HIV-positive MSM in the UK. Solid lines show the mean value of all 1000 simulations, dashed lines show the 2.5% and 97.5% range of the projections. Black diamonds show data from Public Health England (in Fig 2A, model calibrated to 2013 value, other values shown for validation) and UK CHIC (Fig 2B and 2C, model calibrated against all data points).

Figure 3. Model projections (mean value of 1000 simulations shown) with various treatment scenarios (A) HCV prevalence (Ab+ or RNA+) among HIV-positive MSM in the UK, (B) HCV chronic (RNA) prevalence among HIV-positive MSM in the UK, (C) HCV primary incidence among HIV-positive MSM in the UK

Figure 4. Model projections of the mean number of HCV treatments for HIV-infected MSM in the UK for different treatment scenarios.

Table 1. Cumulative prevalence (Ab+ or RNA+) of hepatitis C among HIV-positive MSM in UK CHIC. UK CHIC: Collaborative HIV Cohort; MSM: men who have sex with men; HCV: hepatitis C virus

Year	Total number of MSM under follow-up in that year in UK CHIC	Total number of MSM under follow-up in that year with a reported test by end of year	% with a HCV test reported by end of that year	Cumulative number HCV positive (Ab+ or RNA+)	Cumulative HCV prevalence (Ab+ or RNA+) (%)
2004	11012	6774	61.51	492	7.26
2005	11765	8398	71.38	641	7.63
2006	12335	9550	77.42	752	7.87
2007	12895	10808	83.82	896	8.29
2008	13262	11799	88.97	1049	8.89
2009	13693	12607	92.07	1195	9.48
2010	14147	13369	94.50	1293	9.67
2011	13101	12789	97.62	1261	9.86
Ever	17574	16533	94.08	1673	10.12

Table 2. Incidence of hepatitis C among HIV-positive MSM in UK CHIC. UK CHIC: Collaborative HIV Cohort; MSM: men who have sex with men; HCV: hepatitis C virus; CI: confidence interval

Year	Person years of follow-up of those HCV Ab negative	New infections	Incidence per 100 person years of follow-up (95% CI)
2004	1454	15	1.03 (0.58-1.70)
2005	4179	51	1.22 (0.91-1.60)
2006	6076	62	1.02 (0.78-1.31)
2007	7484	103	1.38 (1.12-1.67)
2008	8752	106	1.21 (0.99-1.46)
2009	9405	111	1.18 (0.97-1.42)
2010	9782	101	1.03 (0.84-1.25)
2011	7487	80	1.07 (0.85-1.33)

Table 3. Mathematical modeling scenarios. IFN/RBV: pegylated interferon+ribavirin, DAA: direct acting antivirals, SVR: sustained viral response

Model Scenario	SVR <1 year from HCV infection (sampled range)	SVR >1 year after acute infection (sampled range)	Proportion treated after acute diagnosis (sampled range)	Proportion treated the first year after chronic diagnosis (sampled range)	Proportion treated thereafter	Behavioral intervention
Baseline status quo with IFN/RBV	80% (70-90%)	30% (25-35%)	46% (40-53%)	22% (20-24%)	mean 5.9% (2.5%-97.5% fits 3.5-10)	no
Current treatment with DAA for all	90%	90%	As in baseline	As in baseline	As in baseline	no
DAA scale-up at diagnosis	90%	90%	60/80/100%	60/80/100%	As in baseline	no
DAA scale up to all	90%	90%	80%	80%	20%	no
DAA scale up to all and behavioral intervention	90%	90%	80%	80%	20%	20% reduction in risk for all
No historical treatment	N/A	N/A	0% (No treatment from 1996)	0% (No treatment from 1996)	0% (No treatment from 1996)	no

Figure 1. Mathematical model schematic. The model is also stratified by treatment naïve, IFN experienced, DAA experienced, and low/high risk states. HIV and non-HIV death occurs from all states. MSM: men who have sex with men; HCV: hepatitis C virus

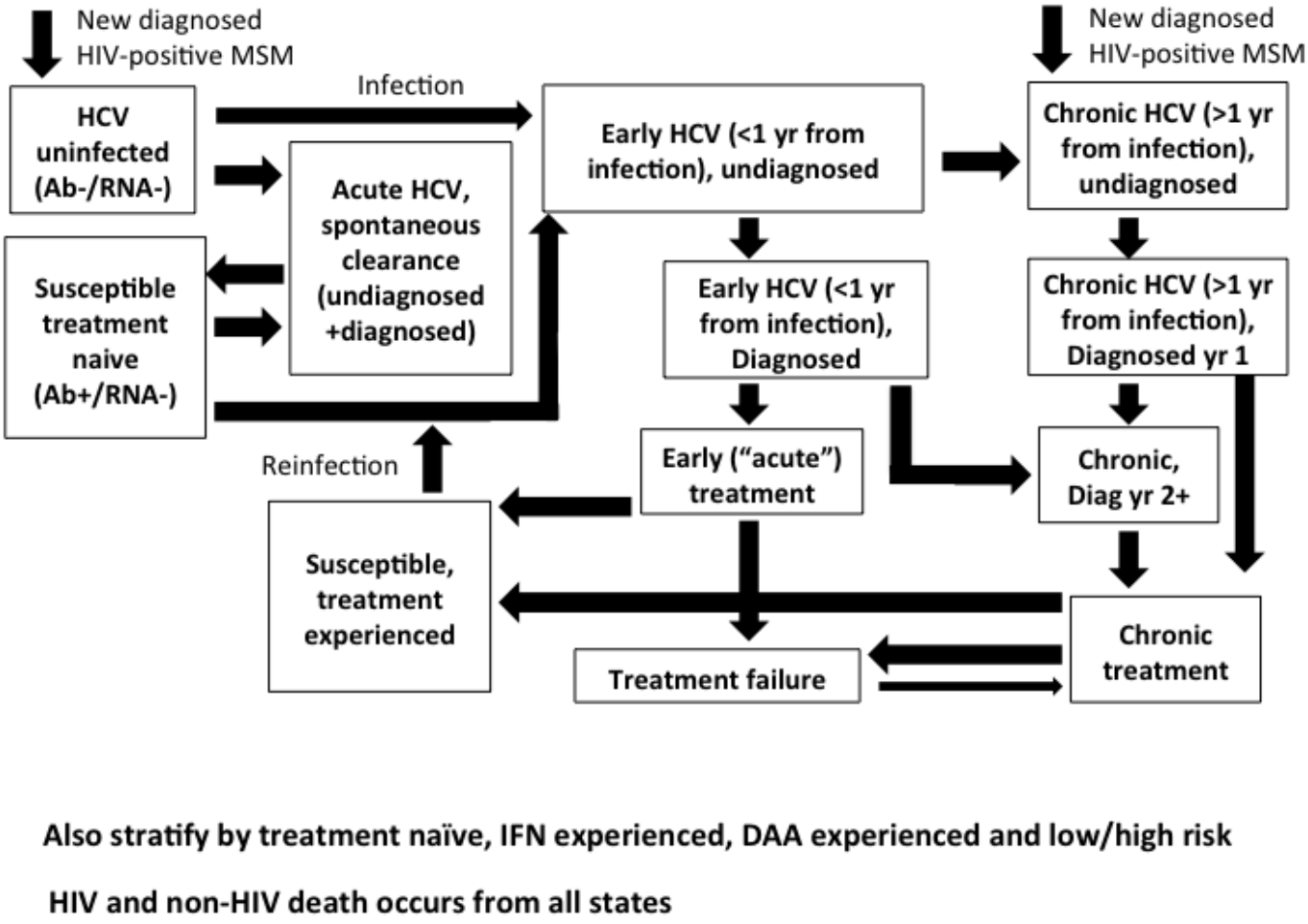
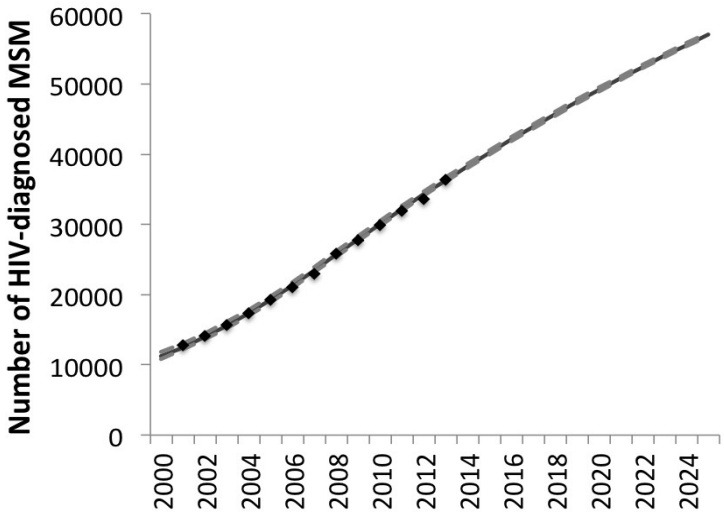
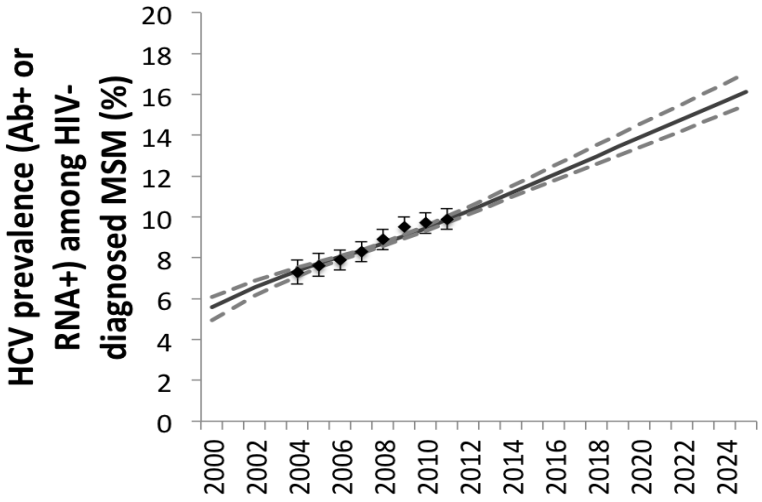


Figure 2. Model fits to epidemiological data from the UK. (A) Number of HIV-diagnosed MSM, (B) HCV prevalence (Ab+ or RNA+) among diagnosed HIV-positive MSM, (C) HCV primary incidence among diagnosed HIV-positive MSM in the UK. Solid lines show the mean value of all 1000 simulations, dashed lines show the 2.5% and 97.5% range of the projections. Black diamonds show data from Public Health England (in Fig 2A, model calibrated to 2013 value, other values shown for validation) and UK CHIC (Fig 2B and 2C, model calibrated against all data points).

(A)



(B)


HCV prevalence (Ab+ or RNA+) among HIV-diagnosed MSM (%)
0
2
4
6
8
10
12
14
16
18
20
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024

(C)

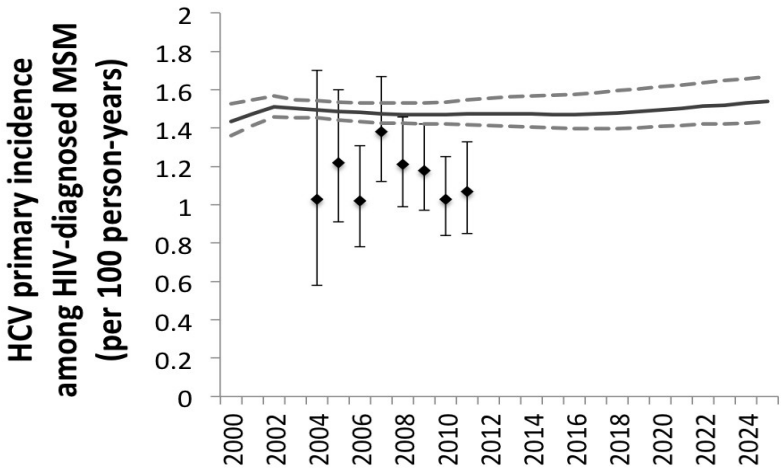


Figure 3. Model projections (mean value of 1000 simulations shown) with various treatment scenarios (A) HCV prevalence (Ab+ or RNA+) among HIV-positive MSM in the UK, (B) HCV chronic (RNA) prevalence among HIV-positive MSM in the UK, (C) HCV primary incidence among HIV-positive MSM in the UK

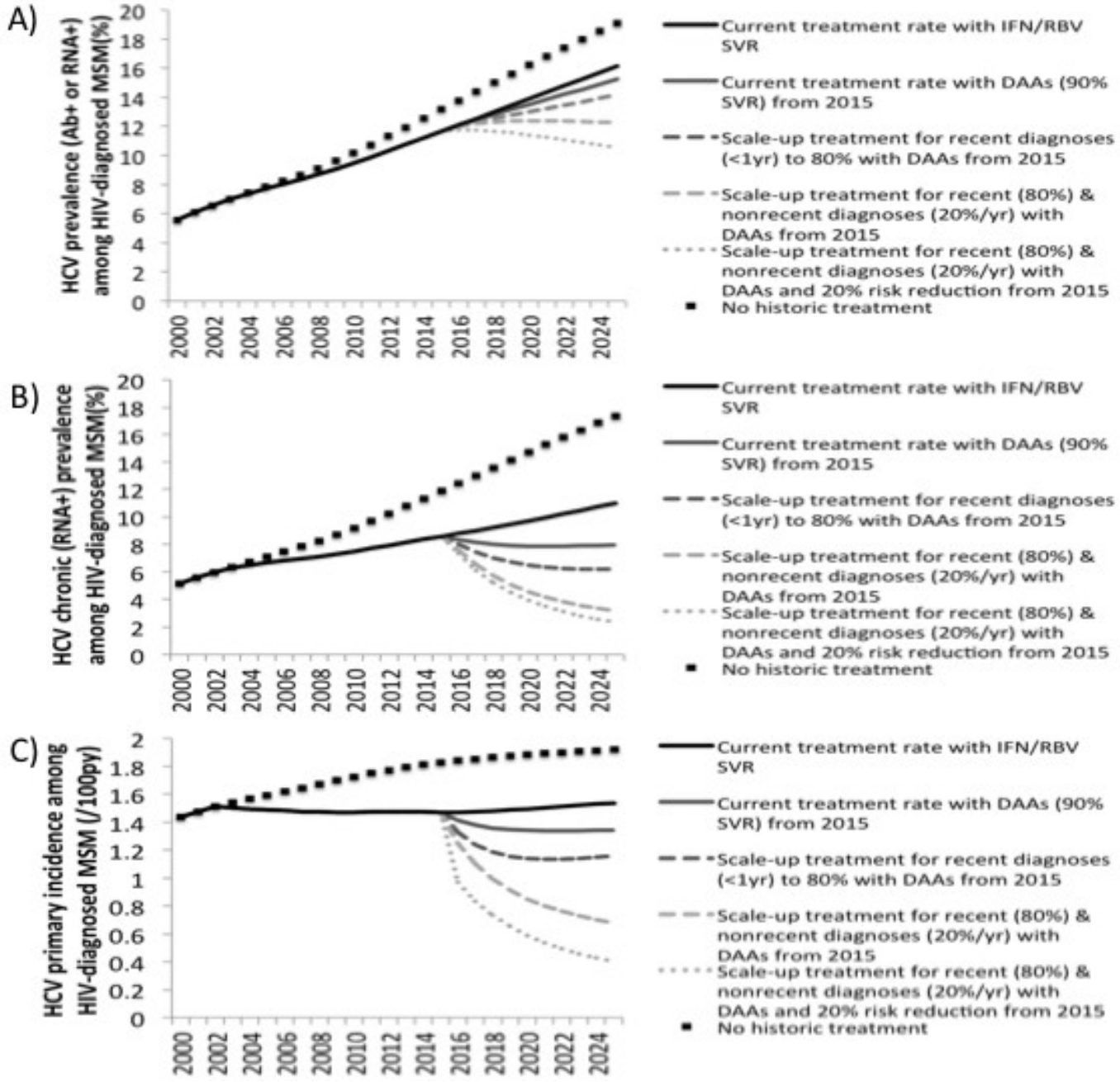
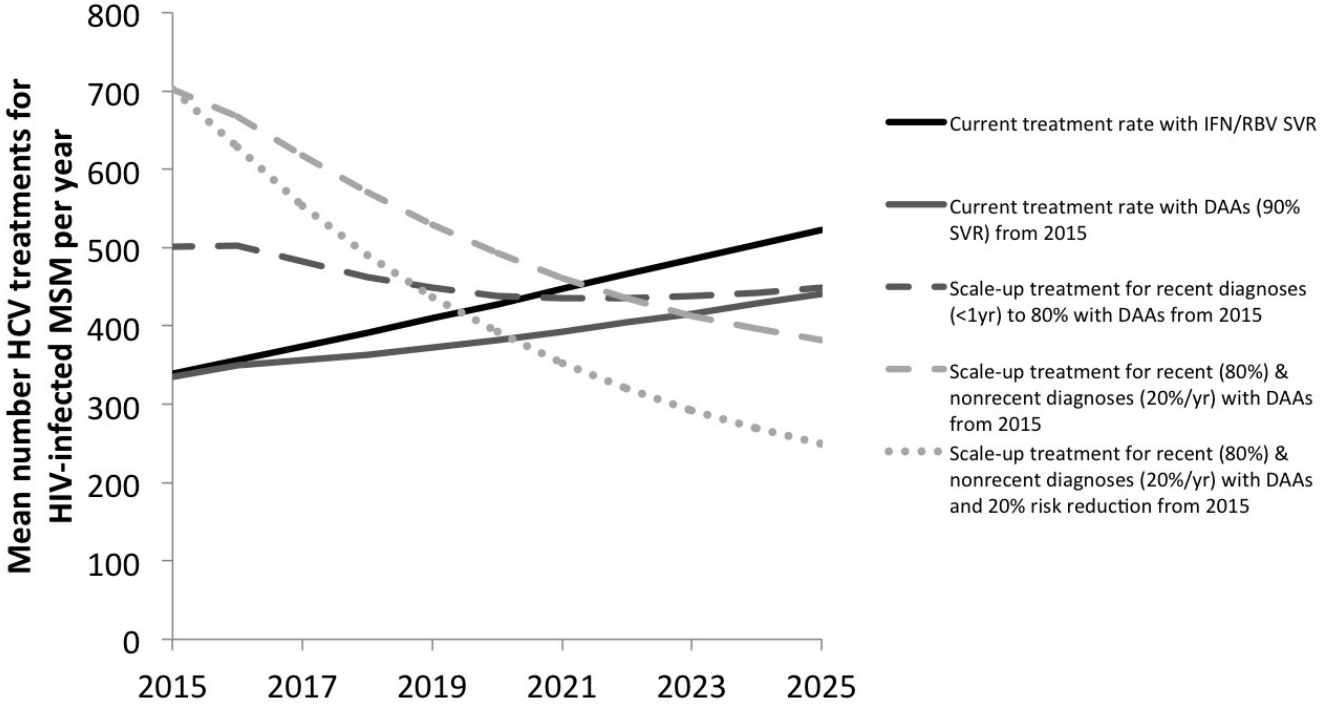


Figure 4. Model projections of the mean number of HCV treatments for HIV-infected MSM in the UK for different treatment scenarios.



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