MAJOR ARTICLE



Testing and Treatment Interventions in Community Settings Key to Controlling a Recent Human Immunodeficiency Virus Outbreak Among People Who Inject Drugs in Glasgow: A Modeling Study

Lara I. Allen,^{1,2,0} Hannah Fraser,¹ Jack Stone,¹ Andrew McAuley,^{2,3} Kirsten M. A. Trayner,^{2,3} Rebecca Metcalfe,^{3,4} S. Erica Peters,⁵ Sharon J. Hutchinson,^{2,3,a} Peter Vickerman,^{1,a} and Matthew Hickman^{1,a}

¹Population Health Sciences, Bristol Medical School, University of Bristol; ²Clinical and Protecting Health Directorate, Public Health Scotland; ³School of Health and Life Sciences, Glasgow Caledonian University; ⁴Sandyford Sexual Health Service, National Health Service Greater Glasgow and Clyde; and ⁵Brownlee Centre for Infectious Diseases, National Health Service Greater Glasgow and Clyde; Glasgow, United Kingdom

Background. A human immunodeficiency virus (HIV) outbreak was identified among people who inject drugs (PWID) in Glasgow in 2015, with >150 diagnoses by the end of 2019. The outbreak response involved scaling up HIV testing and improving HIV treatment initiation and retention.

Methods. We parameterized and calibrated a dynamic, deterministic model of HIV transmission among PWID in Glasgow to epidemiological data. We use this model to evaluate HIV testing and treatment interventions. We present results in terms of relative changes in HIV prevalence, incidence, and cases averted.

Results. If the improvements in both testing and treatment had not occurred, we predict that HIV prevalence would have reached 17.8% (95% credible interval [CrI], 14.1%–22.6%) by the beginning of 2020, compared to 5.9% (95% CrI, 4.7%–7.4%) with the improvements. If the improvements had been made on detection of the outbreak in 2015, we predict that peak incidence would have been 26.2% (95% CrI, 8.8%–49.3%) lower and 62.7% (95% CrI, 43.6%–76.6%) of the outbreak cases could have been averted. The outbreak could have been avoided if the improvements had already been in place.

Conclusions. Our modeling suggests that the HIV testing and treatment interventions successfully brought the HIV outbreak in Glasgow under control by the beginning of 2020.

Keywords. HIV; modeling; antiretroviral treatment; HIV testing.

The potential for human immunodeficiency virus (HIV) transmission via sharing injecting equipment means that people who inject drugs (PWID) are at particular risk of acquiring HIV [1], with an estimated 15% of PWID globally living with the infection [2]. Harm reduction interventions, such as opioid agonist therapy (OAT) and needle and syringe programs (NSPs), can reduce the risk of blood-borne virus (BBV) transmission among this population [3]. OAT effectively reduces transmission by reducing injecting frequency, while NSPs reduce the number of needle/syringe sharing events. Suboptimal harm reduction coverage has contributed to several recent HIV outbreaks among PWID internationally [4].

The Journal of Infectious Diseases[®]

Despite high levels of harm reduction coverage [4], an HIV outbreak among PWID was identified in the Greater Glasgow and Clyde (GGC) region of Scotland in 2015 [5, 6], leading to an HIV prevalence of more than 10% in Glasgow City Centre (GCC), approximately 10 times pre-outbreak levels [5].

Analysis of the GGC outbreak found associations between HIV and multiple risk factors, including cocaine injecting (which increased rapidly over the course of the outbreak), homelessness, frequent incarceration, and public injecting [5, 7]. Stimulant injecting has been associated with many recent outbreaks of HIV [4] and is linked with higher injecting frequency [8].

Before detection of the outbreak, HIV testing rates among PWID in GCC were low, with approximately 30% tested in the last year prior to the outbreak [9]. To increase HIV testing, key interventions included the systematic expansion of testing in drug treatment services and opt-out BBV testing in prisons. The proportion of PWID reporting a recent HIV test in GCC more than doubled (from 30% to nearly 70%), but was slow to rise during the first years of the outbreak [9]. Testing rates in the Rest of Greater Glasgow and Clyde (RoGGC) also increased but to a lesser extent [9].

Received 10 January 2024; editorial decision 09 April 2024; accepted 18 April 2024; published online 22 May 2024

^aS. J. H., P. V., and M. H. contributed equally to this work as joint senior authors. Correspondence: Lara I. Allen, MSc, Population Health Sciences, Bristol Medical School, University of Bristol, Oakfield House, Bristol BS8 2BN, UK (lara.gordon.2019@bristol.ac.uk).

 $[\]textcircled{\sc 0}$ The Author(s) 2024. Published by Oxford University Press on behalf of Infectious Diseases Society of America.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited. https://doi.org/10.1093/infdis/jiae206

Antiretroviral treatment (ART) is a highly effective treatment for HIV. When adherence to treatment is good, the virus will be suppressed and HIV transmission does not occur [10]. Treatment as prevention is effective because it reduces the population-level viral load, which reduces the number of onward transmissions. ART was available for PWID in GGC prior to 2015, but treatment and viral suppression rates were low among the early outbreak cases in 2014–2015 [11]. The original treatment model, which was delivered via hospitals, was found to be insufficient to meet the needs of the population. Therefore, the Glasgow Enhanced Care HIV Outreach (GECHO) treatment model was developed, which involved recruiting a BBV clinical nurse specialist and implementing a consultant-led HIV clinical service in close proximity to the target population. Community pharmacy services were also adapted to enhance ART adherence by providing ART alongside OAT, which was supervised and delivered daily for the majority of people. This approach to improving HIV treatment successfully reduced the time from diagnosis to ART initiation from 264 days in 2015 to 23 days in 2019 [11], which contributed to viral suppression rates (viral load <200 copies/mL) among those diagnosed reaching nearly 90% by mid-2019. GECHO also included intensive contact tracing to identify new cases.

In this study, we use mathematical modeling to evaluate the impact of the systematic expansion of HIV testing for PWID, and the GECHO treatment and contact tracing interventions. We refer to these interventions collectively as GECHO+, meaning GECHO plus enhanced testing.

METHODS

The Model

We constructed a dynamic, deterministic, compartmental model of HIV transmission among PWID. The population is stratified by injecting status and duration, HIV progression, diagnosis and treatment status, homelessness, cocaine injecting, OAT status, and geographical region; see model schematics illustrated in Figure 1.

PWID enter the model when they initiate injecting drug use. They enter as susceptible to HIV acquisition, never tested for HIV, and not accessing OAT. They may enter in any homelessness or cocaine injecting state and into either GCC or RoGGC. PWID leave the model through background mortality, drug-related mortality (which has substantially increased in Scotland over the period of the outbreak [12]), AIDS-related mortality, or permanent cessation of injecting.

PWID can transition between currently injecting and temporarily ceased injecting. Currently injecting PWID are defined to be those who have injected in the last 6 months and are categorized by the duration of their current injecting period (<1 year/ \geq 1 year) due to the association between duration of injecting period and temporary cessation [13]. When temporarily

ceased, PWID may relapse, or leave the model by permanently ceasing injecting. We assume PWID on OAT are more likely to temporarily cease injecting [13], unless they inject cocaine.

In the model, once HIV is acquired, PWID progress through the HIV infection stages (acute/latent/pre-AIDS/AIDS). PWID on ART experience slower HIV progression and reduced AIDS mortality. PWID acquire HIV at a rate dependent on the number of PWID in each infection stage, the proportion of PWID living with HIV accessing ART, the proportions of PWID with risk factors for HIV acquisition and transmission (homelessness/cocaine injecting), and the proportion accessing OAT. HIV transmission varies by infection stage [14], and is higher for those who are homeless and/or injecting cocaine but reduced if on OAT. The effectiveness of ART at preventing transmission improves throughout the outbreak as a greater proportion of PWID become virally suppressed. We assume partial assortative population mixing based on homelessness, cocaine injecting, and geography.

PWID can be tested for HIV either through systematic testing, with different rates depending on first/subsequent test, or contact tracing. Systematic testing rates increase over time and are dependent on homelessness and OAT, to account for the targeted testing interventions in homeless services and pharmacies respectively, and geographical region. Contact tracing moves PWID with undiagnosed HIV into the "diagnosed" category. We assume that contact tracing does not necessarily lead to engagement with systematic testing services, and so susceptible PWID tested through contact tracing are not moved from "never" to "ever" tested. Further details about the implementation of contact tracing in the model are described in the Supplementary Material.

PWID diagnosed with HIV initiate ART at a time-dependent rate to reflect the improvements made to the time from HIV diagnosis to treatment initiation throughout the outbreak. Attrition from ART is not included in the model due to the high levels of viral suppression among PWID diagnosed as part of the outbreak [11, 15] and the short time scale being modeled.

PWID can move from being "never" homeless to "recently homeless," defined as those who have been homeless in the last 6 months. Those who have been "recently homeless" can move between the "recently homeless" and "previously but not recently homeless" compartments. Different rates are used for becoming homeless first and subsequent times to capture patterns in the data relating to the proportions of PWID who have ever been homeless or been homeless in the last 6 months [16]. A similar structure is used for the OAT component, as shown in Figure 1, with "recently on OAT" defined as being on OAT in the last 6 months. The rates for becoming homeless depend on geography.

In the model, PWID can start injecting cocaine, but cannot leave the "injecting cocaine" compartment, unless they stop



Figure 1. Model schematics: injecting status (*A*), human immunodeficiency virus (HIV) progression (*B*), testing and treatment (*C*), homelessness (*D*), cocaine injecting (*E*), opioid agonist therapy (*F*), and geography (*G*). Red arrows illustrate how people who inject drugs (PWID) are recruited into and leave the model. Note that non-HIV mortality and permanent cessation of injecting have been explicitly labeled in (*A*), whereas red outflow arrows in (*B*–*G*) refer to combined background mortality, drug-related mortality, and permanent cessation of injecting. The total number of PWID diagnosed with HIV who have not yet been asked about contacts is also tracked to inform the contact tracing rate. Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus; OAT, opioid agonist therapy.

injecting entirely. They may temporarily cease, but those who relapse will continue in the "injecting cocaine" compartment. This is because the time frame where cocaine injecting started increasing in Glasgow (2015–2020) [16] is relatively short. The rate for initiating cocaine injecting varies over time and by geographical region to account for the increase in cocaine injecting over the course of the outbreak, which was particularly marked in GCC.

The model does not account for PWID movement between GCC and RoGGC due to the short time scale being modeled.

Downloaded from https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiae206/7676520 by guest on 03 July 2024

Submodels were used to calibrate injecting cessation and relapse rates; further information can be found in the Supplementary Material.

Parameterization and Calibration

Most of the data used to parameterize and calibrate the model came from the biennial cross-sectional Needle Exchange Surveillance Initiative (NESI) surveys [16] undertaken among PWID in contact with services. Data collected relate to injecting behavior, use of harm reduction services, BBVs, and other drug-related health harms. The participants complete a questionnaire administered by an interviewer and are asked to provide a voluntary dried blood spot sample, which is used to test for the presence of BBV markers, including HIV. The modeled population reflects the population of PWID participating in this survey, who are likely at higher risk of BBV transmission than the wider group of people who have ever injected drugs. Public Health Scotland and National Health Service Greater Glasgow and Clyde provided data on annual numbers of HIV diagnoses (from the data sources used to produce the "HIV in Scotland" update [17]), annual numbers of HIV tests in drug services [18], and data related to viral suppression and ART [11, 15] within GGC. Literature sources were used for the remaining parameters.

There is inconsistency in the data regarding estimated PWID population sizes in GCC [19], the HIV prevalence from NESI [16], and the reported number of diagnoses [17], with the population size estimates and HIV prevalence suggesting there should have been more diagnoses. As the population participating in NESI is likely to be at higher risk of BBV transmission, and this is the population we wish to model, we have allowed a wide prior distribution for the population size estimate so it calibrates to fit the HIV prevalence and diagnosis data. Further details can be found in the Discussion and in the Supplementary Material.

We implemented an approximate Bayesian computation sequential Monte Carlo algorithm [20] to calibrate the model parameters to data relating to HIV prevalence, HIV diagnoses, history of HIV testing, prevalence of homelessness and cocaine injecting, and coverage of OAT. The algorithm was run with 7500 parameter sets to give 7500 model fits, which were used to give the median and 95% credible interval (CrI; 2.5th to 97.5th percentile range) for all model projections. Further details, including specifics about the model fit, are provided in the Supplementary Material.

Table 1 provides information on the data used to parameterize and calibrate the aspects of the model relating to the interventions. Full details about the model parameters and calibration data are provided in Supplementary Tables 1 and 2.

Estimating the Impact of the Interventions

All calibrated parameter sets are used to investigate the impact of the interventions on the outbreak. The time horizon for the analysis spans from the beginning of 2015 to the beginning of 2020. We compare the GECHO+ scenario, which was calibrated to data on the outbreak, with multiple counterfactual scenarios where improvements in testing/treatment interventions are absent (scenarios R1, R2, R3) or implemented earlier (scenarios I1, I2, I3, P1). The scenarios and their definitions are listed in Table 2. For each of these scenarios, we calculate the prevalence and incidence at the beginning of 2015 and 2020. We also calculate the relative increase in prevalence and incidence for each scenario at the beginning of 2020 compared to GECHO+, the annual number of new HIV cases and the total number of excess cases for each scenario.

Sensitivity analysis methods and results are provided in the Supplementary Material.

All coding and analysis was performed in MATLAB.

RESULTS

Results for each of the modeled scenarios are presented in Tables 3–5 and illustrated in Figures 2 and 3.

GECHO+

In line with the observed public health surveillance data, Figures 2 and 3 show that under the GECHO+ scenario (S0), the HIV prevalence increased from 1.6% (95% CrI, 1.2%– 2.1%) at the beginning of 2015 to 5.9% (95% CrI, 4.7%–7.4%) by the beginning of 2020. The modeling suggests that incidence peaked around 2016 at a value of 2.1/100 person-years (PY) (95% CrI, 1.6–2.8) before declining to 0.7/100 PY (95% CrI, .4–1.2) by the beginning of 2020, with 142 (95% CrI, 105–190) cases in the years 2015–2019 inclusive.

Impact of the Outbreak Response

If the GECHO+ improvements in testing and treatment had not been implemented (R1), the modeling suggests that HIV prevalence would be 201.7% (95% CrI, 147.6%–279.6%) greater by 2020 compared to the GECHO+ scenario, likely exceeding 14.1%, and still increasing. Incidence would be 832.0% (95% CrI, 469.7%–1571.2%) greater by 2020 and is unlikely to have peaked by this point, reaching a value of 6.6/100 PY (95% CrI, 4.9–8.8), as illustrated in Figure 2*B*. Table 5 suggests there would have been 294 (95% CrI, 213–441) additional infections between 2015 and 2020 if GECHO+ had not been implemented, an increase of 210.1% (95% CrI, 154.4%–292.2%).

Breaking this down, we can see that without the improvements in HIV treatment (R2), HIV prevalence would be 113.1% (95% CrI, 76.3%–164.9%) greater by 2020 and incidence would be 500.9% (95% CrI, 294.7%–936.7%) greater. Over the study period, there would have been 160 (95% CrI, 104–255) additional infections compared to the GECHO+ scenario, an increase of 113.9% (95% CrI, 76.4%–167.4%). The outbreak would have had a similar profile to the scenario where both testing and treatment improvements are removed (R1),

Table 1. Data Used to Inform How the Interventions Are Modeled

Description	Value	Source	Notes	Posteriors: Median (95% Crl)
Time from HIV diagnosis to ART initiation (days) by year	2015: 264 (Q1–Q3: 94–556) 2016: 139 (Q1–Q3: 49–280) 2017: 73 (Q1–Q3: 25–156) 2018: 28 (Q1–Q3: 18–51) 2019: 23 (Q1–Q3: 12–38)	[11, 15] Included in model as parameter		2015: 298 (198–406) 2016: 143 (93.9–193) 2017: 75.2 (45.0–111) 2018: 28.0 (22.3–34.8) 2019: 23.3 (17.0–30.8)
Proportion of HIV-positive PWID on ART who are virally suppressed	Pre-mid-2016: Range, 0.61–0.68 Post-mid-2018: Range, 0.84–0.89	[11, 15]	Included in model as parameter	Pre: 0.65 (.62–.67) Post: 0.87 (.85–.89)
No. of HIV tests carried out in drug services in GGC by year	2013: 746 2014: 912 2015: 1673 2016: 2616 2017: 2308 2018: 3610 2019: 4939	West of Scotland Specialist Virology Centre [18]	Specialist Virology Calibrating model parameters to between 50% and 100% of these data values (see Discussion for more details)	
Proportion who have ever had an HIV test among PWID who have never been homeless	Pre: 0.69 (95% Cl, .62–.76) Early: 0.81 (95% Cl, .76–.87) Mid: 0.78 (95% Cl, .71–.85) Late: 0.84 (95% Cl, .79–.89)	NESI [16]	Calibrating model parameters to these data	Pre: 0.74 (.70–.79) Early: 0.75 (.69–.80) Mid: 0.80 (.76–.84) Late: 0.84 (.79–.88)
Proportion who have ever had an HIV test among PWID who have previously been homeless but are not recently homeless	Pre: 0.83 (95% Cl, .79–.87) Early: 0.89 (95% Cl, .86–.93) Mid: 0.93 (95% Cl, .90–.96) Late: 0.95 (95% Cl, .92–.97)	NESI [16]	Calibrating model parameters to these data	Pre: 0.84 (.81–.87) Early: 0.87 (.84–.90) Mid: 0.92 (.90–.94) Late: 0.95 (.93–.96)
Proportion who have ever had an HIV test among PWID who are recently homeless	Pre: 0.81 (95% Cl, .76–.87) Early: 0.86 (95% Cl, .80–.91) Mid: 0.91 (95% Cl, .87–.96) Late: 0.92 (95% Cl, .89–.96)	NESI [16]	Calibrating model parameters to these data	Pre: 0.80 (.76–.84) Early: 0.84 (.80–.87) Mid: 0.90 (.87–.91) Late: 0.92 (.90–.94)
Proportion who have ever had an HIV test among PWID who have never been on OAT	Pre: 0.36 (95% Cl, .16–.56) Early: 0.38 (95% Cl, .21–.55) Mid: 0.41 (95% Cl, .24–.59) Late: 0.51 (95% Cl, .38–.64)	NESI [16]	Calibrating model parameters to these data	Pre: 0.31 (.25–.37) Early: 0.33 (.27–.39) Mid: 0.42 (.37–.48) Late: 0.48 (.42–.54)
Proportion who have ever had an HIV test among PWID who have previously been on OAT but are not recently on OAT	Pre: 0.77 (95% Cl, .62–.93) Early: 0.83 (95% Cl, .64–1.00) Mid: 0.93 (95% Cl, .84–1.00) Late: 0.88 (95% Cl, .76–1.00)	NESI [16]	Calibrating model parameters to these data	Pre: 0.87 (.84–.89) Early: 0.89 (.86–.91) Mid: 0.94 (.92–.95) Late: 0.96 (.95–.97)
Proportion who have ever had an HIV test among PWID who are recently on OAT	Pre: 0.81 (95% Cl, .78–.84) Early: 0.89 (95% Cl, .86–.91) Mid: 0.92 (95% Cl, .90–.95) Late: 0.95 (95% Cl, .93–.97)	NESI [16]	Calibrating model parameters to these data	Pre: 0.85 (.82–.88) Early: 0.88 (.85–.90) Mid: 0.93 (.91–.94) Late: 0.95 (.94–.96)
Proportion of HIV diagnoses made in drugs services	2014: 0.22 (95% Cl, .0354) 2015: 0.39 (95% Cl, .2848) 2016: 0.39 (95% Cl, .2652) 2017: 0.31 (95% Cl, .2042) 2018: 0.41 (95% Cl, .2358) 2019: 0.32 (95% Cl, .1749) 2020: 0.53 (95% Cl, .3367) ⁸	Estimate derived from proportion of HIV diagnoses in drugs services and prisons [17], and proportion of HIV tests carried out in drugs services vs drugs services and prisons [18]	Calibrating model parameters to these data	2014: 0.34 (.2147) 2015: 0.40 (.2948) 2016: 0.47 (.3952) 2017: 0.50 (.4555) 2018: 0.52 (.4756) 2019: 0.53 (.4957)
In response to the outbreak, people diagnosed with HIV asked about contacts within approximately 1 mo of diagnosis	398 unique contacts reported from 184 HIV cases, of whom 150/398 (38%) had HIV (includes 2020 data)	Personal correspondence relating to [11]	NA	NA

Outbreak eras are defined as follows: Pre, 2013–2014; Early, 2015–2016; Mid, 2017–2018; Late, 2019–2020.

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; Crl, credible interval; GGC, Greater Glasgow and Clyde; HIV, human immunodeficiency virus; NA, not applicable; NESI, Needle Exchange Surveillance Initiative; OAT, opioid agonist therapy; PWID, people who inject drugs; Q1, quartile 1; Q3, quartile 3.

^aIncluded to show general trend over time.

with HIV prevalence continuing to increase throughout the study period, and incidence unlikely to peak before the end of 2019, as shown in Figure 2*D*.

Without the improvements in HIV testing (R3), HIV prevalence would be 128.1% (95% CrI, 82.3%–195.0%) greater and incidence would be 496.0% (95% CrI, 260.1%–972.3%) greater

Table 2. Definitions for Each Scenario Investigated

Scenario	Details			
S0: GECHO+	Testing and treatment interventions are modeled as they actually happened.			
R1: Removing HIV testing and treatment improvements	Combination of R2 and R3 described below.			
R2: Removing improvements in HIV treatment	The time from diagnosis to treatment initiation is set to the 2015 value for all years. The proportion of PWID diagnosed with HIV achieving viral suppression is fixed to the pre/early outbreak value.			
R3: Removing improvements in HIV testing	The increase in testing rates during the outbreak is set to 0, so that testing rates remain at pre-outbreak levels. The homeless and OAT effects on testing are set to their pre-outbreak values. The contact tracing rate is set to zero.			
I1: Immediate improvements in HIV testing and treatment interventions	Combination of I2 and I3 below.			
I2: Immediate improvement in HIV treatment	From the beginning of 2015, the time from diagnosis to treatment initiation is increased from the 2015 value to the 2019 value over the course of 1 y.			
I3: Immediate improvement in HIV testing	The full increase in testing rates during the outbreak is set to occur immediately. From the beginning of 2015, the testing rate increases from the pre-outbreak value to the late-outbreak value over the course of 1 y. Targeted testing toward those who are homeless and/or on OAT is adjusted to start at the beginning of 2015.			
P1: Preemptive improvements in HIV testing and treatment interventions	The time from diagnosis to treatment initiation is set to the 2019 value for all time. Testing rates are set to their highest value for all time. Targeted testing interventions for those who are homeless and/or on OAT are set to start before the modeled time period. The contact tracing rate is set to zero because this intervention is typically implemented in response to an outbreak instead of being in place permanently.			
Outbreak eras are defined as follows: Pre, 2013–2014; Early	, 2015–2016; Mid, 2017–2018; Late, 2019–2020.			

Abbreviations: GECHO+, Glasgow Enhanced Care HIV Outreach plus enhanced testing; HIV, human immunodeficiency virus; OAT, opioid agonist therapy; PWID, people who inject drugs.

Table 3. Prevalence Results

Scenario	Prevalence in 2015, %	Prevalence in 2020, %	Relative Increase in Prevalence From S0 in 2020 (%)
S0: GECHO+	1.6 (1.2–2.1)	5.9 (4.7–7.4)	NA
R1: Removing HIV testing and treatment improvements	1.6 (1.2–2.1)	17.8 (14.1–22.6)	201.7 (147.6–279.6)
R2: Removing improvements in HIV treatment	1.6 (1.2–2.1)	12.6 (9.7–16.3)	113.1 (76.3–164.9)
R3: Removing improvements in HIV testing	1.6 (1.2–2.1)	13.5 (10.2–17.9)	128.1 (82.3–195.0)
I1: Immediate improvements in HIV testing and treatment interventions	1.6 (1.2–2.1)	2.8 (1.8-4.2)	-53.0 (-66.4 to -36.4)
12: Immediate improvement in HIV treatment	1.6 (1.2-2.1)	3.5 (2.4–5.0)	-41.0 (-55.3 to -25.8)
I3: Immediate improvement in HIV testing	1.6 (1.2–2.1)	5.1 (3.9–6.5)	-13.5 (-22.5 to -7.3)
P1: Preemptive improvements in HIV testing and treatment interventions	0.2 (.1–.3)	0.2 (.1–.5)	-97.0 (-98.8 to -92.3)

Values given are the median (95% credible interval).

Abbreviations: GECHO+, Glasgow Enhanced Care HIV Outreach plus enhanced testing; HIV, human immunodeficiency virus; NA, not applicable

by 2020. The modeling suggests there would have been 189 (95% CrI, 118–311) more infections without this intervention, an increase of 134.4% (95% CrI, 87.0%–205.5%). Again, we see a similar outbreak profile to the case where neither testing nor treatment improvements are accounted for.

Impact of Intervening Earlier

If the GECHO+ improvements in testing and treatment had been implemented to their peak capacity immediately in 2015 (I1), when the outbreak was first detected, then Figure 3A and 3B suggests the outbreak could have been immediately reduced and controlled. The prevalence would have plateaued, reaching a value of 2.8% (95% CrI, 1.8%–4.2%) by the beginning of 2020, which is 53.0% (95% CrI, 36.4%–66.4%) lower than the GECHO+ scenario. The incidence would have peaked in 2015, at a value 26.2% (95% CrI, 8.8%–49.3%) lower compared to the GECHO+ scenario, before rapidly returning to pre-outbreak levels. The modeling suggests there would have been 87 (95% CrI, 58–125) fewer infections, a 62.7% (95% CrI, 43.6%–76.6%) reduction.

A similar situation is shown in Figures 2*C* and 3*D* when we consider what would have happened if only the treatment interventions had been scaled up immediately (I2), with prevalence reaching 3.5% (95% CrI, 2.4%-5.0%) by the beginning of 2020, which is 41.0% (95% CrI, 25.8\%-55.3\%) lower than the GECHO+ scenario. The decline in incidence also follows a similar pattern, with 69 (95% CrI, 44–102) fewer infections over the modeled time period, which is a decrease of 49.5% (95% CrI, 31.9%-64.8%).

However, when we consider the situation when only the improvements in testing are implemented immediately (I3), and the improvements in treatment follow their historical course,

Table 4. Incidence Results

Scenario	Incidence in 2015 per 100 PY	Incidence in 2020 per 100 PY	Relative Increase in Incidence From S0 in 2020, %	Peak Incidence per 100 PY	Relative Increase in Peak Incidence From S0, %
S0: GECHO+	1.4 (1.0–1.9)	0.7 (.4–1.2)	NA	2.1 (1.6–2.8)	NA
R1: Removing HIV testing and treatment improvements	1.4 (1.0–1.9)	6.6 (4.9–8.8)	832.0 (469.7–1571.2)	6.8 (5.0–9.0)	222.1 (131.5–346.0)
R2: Removing improvements in HIV treatment	1.4 (1.0–1.9)	4.3 (3.0–6.1)	500.9 (294.7–936.7)	4.4 (3.1–6.2)	109.7 (47.8–197.0)
R3: Removing improvements in HIV testing	1.4 (1.0–1.9)	4.3 (2.7–6.2)	496.0 (260.1–972.3)	4.5 (3.1–6.4)	111.1 (50.2–213.2)
I1: Immediate improvements in HIV testing and treatment interventions	1.4 (1.0–1.9)	0.4 (.1–.9)	-46.9 (-69.5 to -22.9)	1.5 (1.1–2.1)	-26.2 (-49.3 to -8.8)
I2: Immediate improvement in HIV treatment	1.4 (1.0–1.9)	0.5 (.2–1.0)	-26.5 (-46.9 to -8.5)	1.5 (1.1–2.1)	-25.7 (-48.6 to -8.2)
I3: Immediate improvement in HIV testing	1.4 (1.0–1.9)	0.6 (.3–1.1)	-17.4 (-33.4 to -7.4)	1.9 (1.4–2.5)	-10.0 (-22.8 to6)
P1: Preemptive improvements in HIV testing and treatment interventions	0.0 (.0–.0)	0.0 (.0–.2)	-95.3 (-98.7 to -79.6)	0.1 (.0–.2)	-97.5 (-98.9 to -89.8)

Values given are the median (95% credible interval).

Abbreviations: GECHO+, Glasgow Enhanced Care HIV Outreach plus enhanced testing; HIV, human immunodeficiency virus; NA, not applicable; PY, person-years.

Table 5. New Cases Results

Scenario	New Cases in 2015	New Cases in 2016	New Cases in 2017	New Cases in 2018	New Cases in 2019	Total New Cases	Total Excess Cases
S0: GECHO+	32 (22–45)	38 (28–50)	34 (23–47)	22 (14–33)	16 (8–26)	142 (105–190)	NA
R1: Removing HIV testing and treatment improvements	35 (25–50)	62 (45–87)	94 (68–136)	119 (86–173)	127 (91–184)	437 (327–612)	294 (213–441)
R2: Removing improvements in HIV treatment	32 (23–45)	46 (33–64)	63 (44–93)	78 (53–116)	83 (56–124)	303 (220–429)	160 (104–255)
R3: Removing improvements in HIV testing	35 (24–50)	58 (42–80)	75 (53–111)	81 (54–127)	82 (52–131)	332 (237–481)	189 (118–311)
 Immediate improvements in HIV testing and treatment interventions 	20 (14–29)	9 (5–17)	8 (3–17)	7 (3–17)	7 (2–17)	53 (30–92)	-87 (-125 to -58)
I2: Immediate improvement in HIV treatment	21 (15–30)	13 (8–22)	13 (7–23)	12 (6–22)	11 (5–21)	71 (43–112)	-69 (-102 to -44)
I3: Immediate improvement in HIV testing	31 (22–44)	33 (24–45)	26 (17–38)	16 (9–27)	12 (6–22)	120 (86–164)	-21 (-37 to -11)
P1: Preemptive improvements in HIV testing and treatment interventions	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–2)	1 (0–4)	2 (0–9)	-139 (-185 to -103)

Values given are the median (95% credible interval). A negative value for excess cases indicates that cases were averted rather than in excess. Abbreviations: GECHO+, Glasgow Enhanced Care HIV Outreach plus enhanced testing; HIV, human immunodeficiency virus; NA, not applicable.

the outbreak shows a similar profile to the GECHO+ scenario. The prevalence by the beginning of 2020 is only 13.5% (95% CrI, 7.3%–22.5%) lower, and the incidence is 17.4% (95% CrI, 7.4%–33.4%) lower, with 21 (95% CrI, 11–37) fewer infections corresponding to a 15.0% (95% CrI, 8.2%–24.8%) decrease.

Figure 3E and 3F shows that if the testing and treatment interventions, excluding contact tracing, had already been in place prior to the outbreak beginning (P1), then the outbreak could have been avoided.

DISCUSSION

We use a mathematical modeling approach to evaluate the impact of the GECHO+ intervention in response to an HIV outbreak among PWID, which consisted of a novel HIV care outreach approach to treating PWID living with HIV and the scale-up of HIV testing among PWID. Our results show that GECHO+ was effective at bringing the outbreak under control by the beginning of 2020, likely preventing hundreds of infections. If the improvements to the interventions had been implemented to their peak capacity upon detection of the outbreak in



Figure 2. Human immunodeficiency virus prevalence and incidence among current people who inject drugs for counterfactual scenarios where interventions have been removed (R1, R2, R3); see Table 2 for scenario definitions. The Glasgow Enhanced Care HIV Outreach plus enhanced testing scenario (S0) is illustrated using dark gray shading and a solid black line to indicate the median; the counterfactual scenarios are illustrated using light gray shading and a dashed black line to indicate the median. The boundaries of the shading indicate the 95% credible intervals. Validation data are illustrated in blue. Abbreviations: HIV, human immunodeficiency virus; PY, person-years.

2015, the outbreak would have been immediately controlled. Furthermore, the outbreak could have been avoided if the interventions had been at peak capacity in the years before 2015.

A key strength of this model is that it was fitted to rich epidemiological data using Bayesian methods that account for uncertainty in model parameters.

However, there are limitations to consider. First, we use a deterministic, compartmental model because these models are flexible, allowing us to use a variety of data types to account for multiple features of the outbreak and population, and are computationally feasible even for large model complexity. However, these models do not account for network structure in the population, which may impact the epidemic profile and estimated impact of interventions [21, 22]. Therefore, it may be appropriate for further modeling of this outbreak to utilize phylogenetic analysis of the outbreak [6], particularly for assessing network-based interventions such as contact tracing.

Second, the majority of the outbreak-specific data used to parametrize and calibrate the model come from the NESI surveys. These surveys may have a greater response rate in GCC compared to RoGGC. Furthermore, by recruiting from sites supplying injecting equipment, the surveys target individuals who are actively injecting and represent PWID with higher HIV risk compared to those in recovery or on long-term OAT. This may contribute to the observed inconsistency between the data regarding HIV prevalence [16], HIV diagnoses [17], and



Figure 3. Human immunodeficiency virus prevalence and incidence among current people who inject drugs for counterfactual scenarios where interventions are implemented immediately on detection of the outbreak (I1, I2, I3) or prior to the start of the outbreak (P1); see Table 2 for scenario definitions. The Glasgow Enhanced Care HIV Outreach plus enhanced testing scenario (S0) is illustrated using dark gray shading and a solid black line to indicate the median; the counterfactual scenarios are illustrated using light gray shading and a dashed black line to indicate the median. The boundaries of the shading indicate the 95% credible intervals. Validation data are illustrated in blue. Abbreviations: HIV, human immunodeficiency virus; PY, person-years.

historical estimates for the PWID population size in Glasgow [19]. As we are modeling a higher-risk population than is reflected in the PWID population size estimates, we calibrated the population size using a wide uninformed prior, which results in a smaller population size compared to the data estimates. Assuming a smaller population size would impact the ratio of HIV tests per person. To account for this, we adjusted the metric used to compare the annual number of HIV tests to data in the calibration process; model predictions within 50%– 100% of the data value are considered an equally good fit. This leads to wider posterior distributions for the testing rates. This uncertainty propagates to the model results and is reflected in the reported credible intervals.

Third, certain features of the outbreak were necessarily excluded to minimize model complexity. For example, sexual transmission was not explicitly modeled because high prevalence of hepatitis C virus among the outbreak cohort suggests transmission occurred mainly via sharing of injecting equipment [6]. Incarceration dynamics were not included because the data from NESI suggest that cocaine and homelessness are more important risk factors to include [5, 16]. The impact of NSPs was not explicitly included in the model because provision remained relatively stable over the course of the outbreak [5, 16].

Fourth, though we have detailed data for the number of HIV tests carried out in drugs services, there were diagnoses among PWID in the outbreak cohort made in other locations, where fewer data are available specifically relating to PWID. We were able to use the 2019–2020 NESI survey [16] to estimate the proportion of HIV tests carried out in other locations at 1 time point, but relied on approximate estimates for the proportion of HIV diagnoses made in drugs services to estimate how this changed over time. Further details are provided in the Supplementary Material.

Finally, the modeling does not extend past the beginning of 2020; therefore, we cannot evaluate the longer-term impact of the interventions on the outbreak. A key reason for this is that that the coronavirus disease 2019 (COVID-19) pandemic reached the United Kingdom in 2020, which disrupted interventions and data collection [23]. Further data are required to understand the impact of COVID-19 on the HIV outbreak.

Previous modeling work also demonstrates the benefits of testing and treatment interventions in combination. Gonsalves et al [24] modeled the impact of testing, treatment, and harm reduction interventions on an HIV outbreak that began in Scott County, United States, in 2014. Some modeled scenarios suggest that earlier intervention could have had a substantial impact on the outbreak, preventing it from happening. The modeling by Flountzi et al [25] of the 2012–2013 HIV outbreak in Athens, Greece, demonstrated the beneficial impact of a combined harm reduction and targeted testing/care outreach intervention. Cepeda et al [26] found a beneficial impact of combined harm

reduction and treatment interventions when HIV is increasing among PWID.

CONCLUSIONS

The HIV outbreak in Glasgow occurred under the backdrop of moderate to high levels of OAT and NSP coverage, alongside an increase in cocaine injecting and initially suboptimal HIV testing and treatment interventions.

The GECHO clinical outreach approach to improving HIV treatment in response to the outbreak managed to achieve viral suppression in nearly 90% of PWID diagnosed with HIV by mid-2019, a large improvement compared to 2015 where no more than 40% were virally suppressed. In combination with increased HIV testing (GECHO+), the modeling suggests these interventions brought the outbreak under control before 2020. However, our results highlight the importance of a combined approach; improvements in either testing or treatment alone would not have controlled the outbreak.

HIV testing and treatment interventions should be maintained even when HIV apparently is endemically low, as had been the case prior to the outbreak in GGC. Given the financial pressures facing the healthcare system, analysis of the costeffectiveness of GECHO+ should be carried out as soon as possible to understand the health economic benefit of a rapid clinical intervention at the outset.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Author contributions. L. I. A., H. F., P. V., M. H., and S. J. H. conceived the study. L. I. A., H. F., J. S., and P. V. contributed to model design. L. I. A., supervised by H. F., J. S., P. V., M. H., and S. J. H., performed all the modeling and undertook all formal analysis. S. J. H., A. M., K. M. A. T., R. M., and S. E. P. provided the survey and other epidemiological data to parameterize the model. Analysis of the survey and other epidemiological data that informed the model was performed by L. I. A., K. M. A. T., and R. M. All authors interpreted the findings. L. I. A. wrote the first and subsequent drafts of the manuscript and all remaining authors contributed to critical review of the manuscript.

Acknowledgments. We acknowledge the contributions of Julie Craik and Daniel Carter, who provided data for model parameterization and facilitated interpretation of the findings.

Data sharing. Supplementary Material relating to this study are available online, which include the data used to parameterize and calibrate the model. Aggregate-level survey data are available at https://publichealthscotland.scot/publications/needle-exchange-surveillance-initiative-nesi/n

Financial support. This work was supported in part by grant MR/N0137941/1 for the GW4 BIOMED Medical Research Council (MRC) doctoral training partnership, awarded to the Universities of Bath, Bristol, Cardiff, and Exeter from the MRC/UK Research and Innovation. This study was also supported in part by Public Health Scotland and the National Institute for Health and Care Research (NIHR). NIHR funding was through the Programme Grants for Applied Research (Evaluating the Population Impact of Hepatitis C Direct Acting Antiviral Treatment as Prevention for People Who Inject Drugs (EPIToPe) grant number RP-PG-0616-20 008) and NIHR Health Protection Research Unit (HPRU) in Behavioural Science and Evaluation (NIHR200877). The intervention evaluated and associated administrative data used were funded by NHS Greater Glasgow and Clyde. The Needle Exchange Surveillance Initiative was funded by Public Health Scotland and NIHR EPIToPe. H. F., P. V., and M. H. acknowledge support from the NIHR HPRU in Evaluation of Interventions and Behavioural Science. J. S. and P. V. acknowledge funding from the Wellcome Trust (WT 226619/Z/22/Z). This work was carried out using the computational facilities of the Advanced Computing Research Centre, University of Bristol (http://www.bristol.ac.uk/acrc/). For the purpose of open access, the authors have applied a Creative Commons Attribution (CC BY) license to any Author Accepted Manuscript version arising.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Degenhardt L, Charlson F, Stanaway J, et al. Estimating the burden of disease attributable to injecting drug use as a risk factor for HIV, hepatitis C, and hepatitis B: findings from the Global Burden of Disease Study 2013. Lancet Infect Dis **2016**; 16:1385–98.

- Degenhardt L, Webb P, Colledge-Frisby S, et al. Epidemiology of injecting drug use, prevalence of injecting-related harm, and exposure to behavioural and environmental risks among people who inject drugs: a systematic review. Lancet Glob Health **2023**; 11:e659–72.
- Palmateer N, Hamill V, Bergenstrom A, et al. Interventions to prevent HIV and hepatitis C among people who inject drugs: latest evidence of effectiveness from a systematic review (2011 to 2020). Int J Drug Policy 2022; 109:103872.
- 4. Des Jarlais DC, Sypsa V, Feelemyer J, et al. HIV outbreaks among people who inject drugs in Europe, North America, and Israel. Lancet HIV **2020**; 7:e434–42.
- McAuley A, Palmateer NE, Goldberg DJ, et al. Re-emergence of HIV related to injecting drug use despite a comprehensive harm reduction environment: a crosssectional analysis. Lancet HIV 2019; 6:e315–24.
- Ragonnet-Cronin M, Jackson C, Bradley-Stewart A, et al. Recent and rapid transmission of HIV among people who inject drugs in Scotland revealed through phylogenetic analysis. J Infect Dis 2018; 217:1875–82.
- Trayner KMA, McAuley A, Palmateer NE, et al. Increased risk of HIV and other drug-related harms associated with injecting in public places: national bio-behavioural survey of people who inject drugs. Int J Drug Policy 2020; 77: 102663.
- Leri F, Stewart J, Tremblay A, Bruneau J. Heroin and cocaine co-use in a group of injection drug users in Montréal. J Psychiatry Neurosci 2004; 29:40–7.
- Trayner KMA, Palmateer NE, McAuley A, et al. Evaluation of the scale-up of HIV testing among people who inject drugs in Scotland in the context of an ongoing HIV outbreak. Int J Drug Policy 2021; 96:103304.
- Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med 2016; 375:830–9.
- Metcalfe R, Ragonnet-Cronin M, Bradley-Stewart A, et al. From hospital to the community: redesigning the human immunodeficiency virus (HIV) clinical service model to respond to an outbreak of HIV among people who inject drugs. J Infect Dis 2020; 222:S410–9.
- McAuley A, Fraser R, Glancy M, et al. Mortality among individuals prescribed opioid-agonist therapy in Scotland, UK, 2011–20: a national retrospective cohort study. Lancet Public Health 2023; 8:e484–93.
- 13. Xia Y, Seaman S, Hickman M, et al. Factors affecting repeated cessations of injecting drug use and relapses during the entire injecting career among the Edinburgh Addiction Cohort. Drug Alcohol Depend 2015; 151:76–83.
- Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. J Infect Dis 2008; 198: 687–93.

- NHS Greater Glasgow and Clyde. ART and viral suppression data for NHS Greater Glasgow and Clyde. GGC HIV database. Glasgow, UK: NHS Greater Glasgow and Clyde, 2020.
- 16. Public Health Scotland, Glasgow Caledonian University and the West of Scotland Specialist Virology Centre. The Needle Exchange Surveillance Initiative (NESI): prevalence of blood-borne viruses and injecting risk behaviours among people who inject drugs attending injecting equipment provision services in Scotland, 2008 to 2020. Edinburgh, UK: Public Health Scotland, 2022.
- Public Health Scotland. HIV in Scotland: update to 31 December 2022. UK: Public Health Scotland, 2023.
- West of Scotland Specialist Virology Centre. HIV testing data for Greater Glasgow and Clyde. UK: NHS Greater Glasgow and Clyde, 2020.
- Hay G, Gannon M, Casey J, et al. Estimating the national and local prevalence of problem drug misuse in Scotland. Glasgow, UK: University of Glasgow, 2009.
- Toni T, Welch D, Strelkowa N, et al. Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. J R Soc Interface 2009; 6:187–202.
- 21. Haw DJ, Pung R, Read JM, et al. Strong spatial embedding of social networks generates nonstandard epidemic

dynamics independent of degree distribution and clustering. Proc Natl Acad Sci U S A **2020**; 117:23636-42.

- 22. House T, Keeling MJ. The impact of contact tracing in clustered populations. PLoS Comput Biol **2010**; 6:e1000721.
- 23. Trayner KMA, McAuley A, Palmateer NE, et al. Examining the impact of the first wave of COVID-19 and associated control measures on interventions to prevent blood-borne viruses among people who inject drugs in Scotland: an interrupted time series study. Drug Alcohol Depend **2022**; 232:109263.
- 24. Gonsalves GS, Crawford FW. Dynamics of the HIV outbreak and response in Scott County, IN, USA, 2011–15: a modelling study. Lancet HIV **2018**; 5:e569–77.
- 25. Flountzi E, Lim AG, Vickerman P, et al. Modeling the impact of interventions during an outbreak of HIV infection among people who inject drugs in 2012–2013 in Athens, Greece. Drug Alcohol Depend **2022**; 234:109396.
- 26. Cepeda JA, Eritsyan K, Vickerman P, et al. Potential impact of implementing and scaling up harm reduction and antiretroviral therapy on HIV prevalence and mortality and overdose deaths among people who inject drugs in two Russian cities: a modelling study. Lancet HIV 2018; 5: e578–87.



EVIDENCE SUPPORTS THE HIGH BARRIER TO RESISTANCE OF DOVATO UP TO 5 YEARS¹⁻³



IS IT TIME TO **RECONSIDER THE VALUE OF THE 2ND NRTI?** LEARN MORE ()

DOVATO is indicated for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.1

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellowcard in the Google Play or Apple App store. Adverse events should also be reported to GSK on 0800 221441

REFERENCES

- 1. Maggiolo F et al. BMC Infect Dis 2022; 22(1); 782.
- 2. Taramasso L et al. AIDS Patient Care STDS 2021; 35(9): 342-353.
- 3. Ciccullo A et al. JAIDS 2021; 88(3): 234-237
- 4. ViiV Healthcare. Data on File. REF-223795. 2024. 5. Cahn P et al. AIDS 2022; 36(1): 39–48.
- 6. Rolle C et al. Open Forum Infect Dis 2023; 10(3): ofad101.
- 7. Cordova E et al. Poster presented at 12th IAS Conference on HIV Science. 23–26 July 2023. Brisbane, Australia. TUPEB02.
- 8. De Wit S et al. Slides presented at HIV Glasgow. 23-26 October 2022. Virtual and Glasgow, UK. M041.
- 9. Llibre J et al. Clin Infect Dis 2023; 76(4): 720-729.
- ViiV Healthcare. Data on File. REF-220949. 2024.
 Rolle C et al. Poster presented IDWeek. 11–15 October 2023. Virtual and Boston, USA. 1603.
- 12. Slim J et al. Abstract presented IDWeek. 11–15 October 2023. Virtual and Boston, USA. 1593.
- 13. DOVATO. Summary of Product Characteristics. June 2023.

PRESCRIBING INFORMATION

Dovato Prescribing Information

Legal Notices

Privacy Policy

Contact Us

ViiV Healthcare, 980 Great West Road, Brentford, Middlesex, London, UK.

ViiV trademarks are owned by or licensed to the ViiV Healthcare group of companies. Non-ViiV trademarks are owned by or licensed to their respective owners or licensors ©2024 ViiV Healthcare group of companies or its licensor. All rights reserved Intended for healthcare professionals only.

ABBREVIATIONS

3TC, lamivudine; CD4, cluster of differentiation 4; DTG, dolutegravir; FDA, United States Food and Drug Administration: FTC. emtricitabine: HIV. human immunodeficiency virus: ITT-E, intention-to-treat exposed; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; RCT, randomised controlled trial; RNA, ribonucleic acid; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate; XTC, emtricitabine.

FOOTNOTES

*Data extracted from a systematic literature review of DTG+3TC real-world evidence. Overlap between cohorts cannot be fully excluded.

**The reported rate reflects the sum-total of resistance cases calculated from GEMINI I and II (n=1/716, through 144 weeks), STAT (n=0/131, through 52 weeks), and D2ARLING (n=0/106, through 24 weeks).5-7

†GEMINI I and II are two identical 148-week, phase III, randomised, double-blind, multicentre, parallel-group, non-inferiority, controlled clinical trials testing the efficacy of DTG/3TC in treatment-naïve patients. Participants with screening HIV-1 RNA ≤500,000 copies/mL were randomised 1:1 to once-daily DTG/3TC (n=716, pooled) or DTG + TDF/FTC (n=717, pooled). The primary endpoint of each GEMINI study was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 48 (ITT-E population, snapshot algorithm).¹³

\$STAT is a phase IIIb, open-label, 48-week, single-arm pilot study evaluating the feasibility, efficacy, and safety of DTG/3TC in 131 newly diagnosed HIV-1 infected adults as a first line regimen. The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 24.6

§D2ARLING is a randomised, open-label, phase IV study designed to assess the efficacy and safety of DTG/3TC in treatment-naïve people with HIV with no available baseline HIV-1 resistance testing. Participants were randomised in a 1:1 ratio to receive DTG/3TC (n=106) or DTG + TDF/XTC (n=108). The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 48.7 Results at week 24 of the study.

||The reported rate reflects the sum-total of resistance cases calculated from TANGO (n=0/369, through 196 weeks) and SALSA (n=0/246, through 48 weeks).89

¶TANGO is a randomised, open-label, trial testing the efficacy of DOVATO in virologically suppressed patients. Participants were randomised in a 1:1 ratio to receive DOVATO (n=369) or continue with TAF-containing regimens (n=372) for up to 200 weeks. At Week 148, 298 of those on TAF-based regimens switched to DOVATO. The primary efficacy endpoint was the proportion of subjects with plasma HIV-1 RNA ≥50 copies/mL (virologic non-response) as per the FDA Snapshot category at Week 48 (adjusted for randomisation stratification factor).8,1 #SALSA is a phase III, randomised, open-label, non-inferiority clinical trial evaluating the efficacy and safety of switching to DTG/3TC compared with continuing current antiretroviral regimens in virologically suppressed adults with HIV. Eligible participants were randomised 1:1 to switch to once-daily DTG/3TC (n=246) or continue current antiretroviral regimens (n=247). The primary endpoint was the proportion of subjects with plasma HIV-1 RNA ≥50 copies/mL at Week 48 (ITT-E population, snapshot algorithm).9