Cost-effectiveness of screening for HIV in primary care: a health economics modelling analysis

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Summary

Background Early HIV diagnosis reduces morbidity, mortality, the probability of onward transmission, and their associated costs, but might increase cost because of earlier initiation of antiretroviral treatment (ART). We investigated this trade-off by estimating the cost-effectiveness of HIV screening in primary care.

Methods We modelled the effect of the four-times higher diagnosis rate observed in the intervention arm of the RHIVA2 randomised controlled trial done in Hackney, London (UK), a borough with high HIV prevalence (≥0·2% adult prevalence). We constructed a dynamic, compartmental model representing incidence of infection and the effect of screening for HIV in general practices in Hackney. We assessed cost-effectiveness of the RHIVA2 trial by fitting model diagnosis rates to the trial data, parameterising with epidemiological and behavioural data from the literature when required, using trial testing costs and projecting future costs of treatment.

Findings Over a 40 year time horizon, incremental cost-effectiveness ratios were £22 201 (95% credible interval 12 662–132 452) per quality-adjusted life-year (QALY) gained, £372 207 (268 162–1 903 385) per death averted, and £628 874 (434 902–4 740 724) per HIV transmission averted. Under this model scenario, with UK cost data, RHIVA2 would reach the upper National Institute for Health and Care Excellence cost-effectiveness threshold (about £30 000 per QALY gained) after 33 years. Scenarios using cost data from Canada (which indicate prolonged and even higher health-care costs for patients diagnosed late) suggest this threshold could be reached in as little as 13 years.

Interpretation Screening for HIV in primary care has important public health benefits as well as clinical benefits. We predict it to be cost-effective in the UK in the medium term. However, this intervention might be cost-effective far sooner, and even cost-saving, in settings where long-term health-care costs of late-diagnosed patients in high-prevalence regions are much higher (≥60%) than those of patients diagnosed earlier. Screening for HIV in primary care is cost-effective and should be promoted.

Funding NHS City and Hackney, UK Department of Health, National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care.

Lancet HIV 2017; 4: e465–74

Published Online July 30, 2017 http://dx.doi.org/10.1016/S2352-3018(17)30123-6

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Introduction

Increased testing for HIV is crucial to the identification of the large numbers of people living with HIV who are as yet undiagnosed. Perhaps as many as half of the 2·3 million people living with HIV in Europe and up to a sixth of the 1·1 million in the USA are undiagnosed.[1,2] In the UK, where an estimated 13% (n=13 500) of people living with HIV are undiagnosed,[3] recent recommendations propose expansion of existing testing provision to offer routine testing of all adults in high-prevalence (≥0·2%) areas.[4–7] Most testing remains concentrated in sexual health and antenatal clinics.[8]

Treatment for HIV is expensive and its initiation is being recommended progressively earlier in the course of infection owing to increased recognition of the benefits of starting earlier treatment.[9] Increased testing therefore has the potential to increase treatment costs. Health-care planners need reliable estimates of cost-effectiveness of screening but estimates are few and have not yet been based on data from randomised control trials of screening interventions.[10–12] We have previously reported the first randomised controlled trial assessing the effect of HIV screening in general practice (RHIVA2),[13] showing increased and possibly earlier detection of HIV. Our trial was pragmatic in design and covered a large inner-London primary care population, providing a real-life picture of the effect of screening. Its cost-effectiveness should be evaluated to ensure resources are optimally allocated.[14]

We calculated the costs of screening and, using a cost-effectiveness model of HIV testing for the trial setting fitted to trial data, we evaluated the costs, benefits, and cost-effectiveness of this intervention. We took account of the increased diagnosis rate and benefits to the population of reduced HIV transmission through earlier diagnosis. We also compared the cost savings of averting HIV infections with the costs accrued by the intervention and by earlier initiation of HIV treatment for diagnosed patients.

Research in context

Evidence before this study

Screening for HIV is recommended in national guidelines in the USA, Canada, and the UK, but cost-effectiveness of various screening and testing approaches is unclear. RHIVA2 was the first randomised controlled trial of HIV screening in primary care. The intervention quadrupled the HIV diagnosis rate. Calls have been made by public health and primary care physicians, as well as the National Institute for Health and Care Excellence, for its cost-effectiveness to be evaluated, to ensure limited resources are appropriately employed. We searched PubMed for studies published from inception up to May 31, 2017, estimating the cost-effectiveness of primary care-based HIV screening interventions, and including effects on onward transmission. We combined search terms for HIV screening ("HIV", "screening", and "testing") with health economic terms ("cost-effectiveness", "cost effectiveness", "ICER", "cost–benefit", "cost benefit", "cost–utility", "cost utility", "health economics") and "transmission". We found just one relevant study, screening for HIV in community-based settings in the USA, but screening was for acute HIV infection only.

Added value of this study

We report the first health economic modelling study informed by real-world data from a randomised controlled trial of primary care-based screening for all HIV infections. We include the costs accrued from earlier treatment of individuals who have been diagnosed earlier. By taking account of the full cost implications of the intervention, this study illustrates how a successful primary care-based HIV screening intervention, resulting in increased diagnosis rates, becomes cost-effective in the medium term (33 years) or sooner.

Implications of all the available evidence

General practice-based HIV screening leads to increased and probably earlier diagnosis of HIV, which improves the length and quality of life of people who are HIV positive and might reduce onward transmission. Primary care-based HIV screening becomes cost-effective over the medium term according to National Institute for Health and Care Excellence criteria, under current UK HIV treatment cost estimates. Using findings from Canada of long-term higher health-care costs for patients diagnosed late, our model predicts RHIVA2 will become a cost-effective intervention far sooner and even to become cost saving.

Methods

Data sources

RHIVA2 was set in Hackney, a multiethnic, socioeconomically deprived inner London borough with a prevalence of diagnosed HIV infection of 0·8% (eight of 1000 adults).[15] The intervention involved training of practices to integrate opt-out rapid point-of-care HIV testing into the practice registration health check. For rapid testing, the INSTI HIV1/HIV2 Rapid Antibody Test (bioLytical Laboratories, Richmond, BC, Canada) finger prick system was used (sensitivity 99·6%, specificity 99·3%). Most (40 [89%]) of the 45 general practices in Hackney took part.

HIV diagnosis rates in intervention (20 practices with 44 971 new registrants) and control (20 practices with 38 464 new registrants) practices over the 28 month trial duration informed the cost-effectiveness model. Intervention practices newly diagnosed 32 people living with HIV compared with 14 in control practices. The overall rate of HIV diagnosis was four times higher in the intervention group than in the control group: 0·30 (95% CI 0·11-0·85) per 10 000 patients per year in intervention practices versus 0·07 (0·02–0·20) in control practices. Mean CD4 count at diagnosis was 356 cells per µL (SD 254) in intervention versus 270 (SD 257) in control practices. Full details of the intervention, study design, and analysis are available.[13]

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See Online for appendix

Costs for the RHIVA2 intervention were estimated with standard methods, in which the mean use of a resource was multiplied by the unit cost of that resource to produce the estimated direct mean cost incurred by the intervention.[16] The analysis was done from the perspective of the National Health Service (NHS) and thus only considered costs directly incurred by the NHS; overhead costs were not included.

Direct start-up and recurrent costs for the RHIVA2 intervention were collected by the RHIVA2 team. Each participating surgery was offered a £300 (US$484) enrolment incentive. Additionally, an incentive of £10 ($16·14) was offered for each rapid HIV test done (intervention only).

We annualised start-up costs over the lifetime of the programme to reflect utility beyond the period of the trial (duration 28 months). Using our best judgment as managers of the RHIVA2 intervention and our experience of working within the NHS, we estimated programme lifetime to be 5 years.

When necessary, we adjusted the price of commodities (eg, HIV rapid test, confirmatory tests) by inflation to reflect the year of the costing analysis, 2012. Costs and quality-adjusted life-years (QALYs) were discounted at a rate of 3·5% per year. We used an average annual exchange rate of $1·6143 per £1 for 2012 as calculated by OANDA but this rate has changed substantially in recent years ($1·29448 per £1 as of July 7, 2017). Further details of costing are in the appendix (p 1).

We took quality of life estimates by CD4 cell count band and diagnosis and treatment status from the scientific literature (appendix pp 16–18). We calculated QALYs gained by the intervention by comparing total

QALYs of the model population (ie, the population of Hackney) under the control scenario with total QALYs under the intervention scenario. We estimated QALYs as the product of the utility estimate assigned to each model compartment and the average duration that an infected individual remains in that compartment.

HIV-related health-care cost data used in the model included costs of antiretroviral treatment (ART) and CD4, viral load, and resistance testing, as well as use of health-care services (appendix pp 3, 19). Little information is available on how long-term HIV health-care costs are related to CD4 cell count at diagnosis. Therefore, we explored three plausible scenarios in which patients diagnosed with late infection have increased health-care costs. Scenario 1 is based on UK data[17] and models 25% higher costs for long-term diagnosed (ie, patients in long-term HIV care after the first year of diagnosis) patients on ART who were diagnosed at CD4 counts of 200 cells per µL or less. Scenarios 2 and 3 are based on data from Canada[18] where those diagnosed at CD4 counts of 350 cells per µL or less had direct medical costs 1·6 times higher than did other patients, up to 15 years after diagnosis. Scenario 2 assumes 1·6-times higher costs for long-term diagnosed who were diagnosed at 350 cells per µL or less. Scenario 3 assumes 1·6-times higher costs for all long-term diagnosed who were diagnosed at CD4 counts of 350 cells per µL or less, but costs for those diagnosed at counts of 200 cells per µL or less are twice those of patients diagnosed at counts of 200–349 cells per µL. In each case, we calculated weights so that total costs of all long-term diagnosed are the same as in scenario 1. We report scenario 1 results as our base case because it is based on UK data. We also explored scenarios in which ART costs reduce with future drug price reductions after patent expiry. Further information on health-care costs is provided in the appendix (pp 4–5, 19).

Cost-effectiveness model

We developed a dynamic, compartmental model to represent the HIV epidemic and the effect of screening within the borough of Hackney. The model was parameterised with epidemiological and behavioural data, some of which were obtained from a previous cost-effectiveness model of HIV screening in the UK[19]

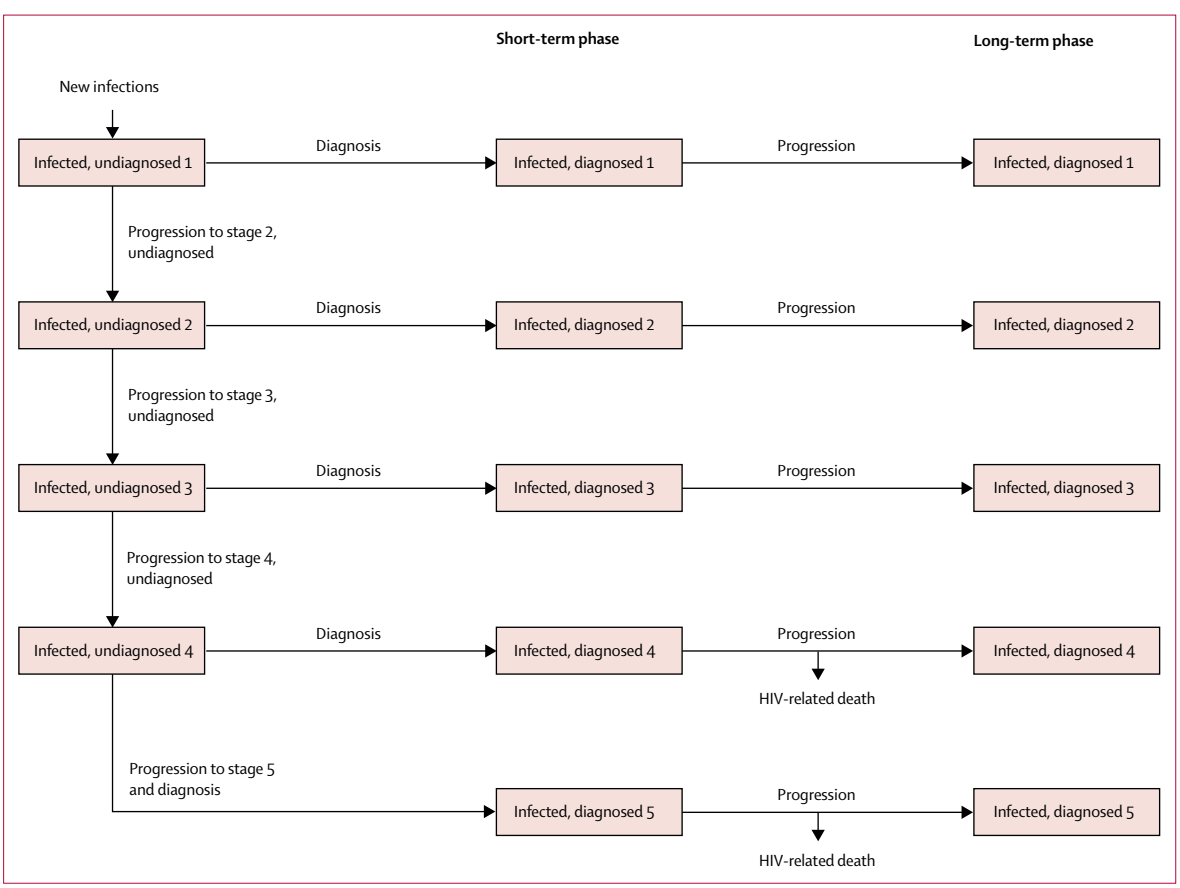

Figure 1: **Schematic illustrating HIV screening model structure**
Background death rate is applied to each compartment but, for clarity, is not shown. Numbers refer to stages of HIV infection: 1=acute infection; 2=CD4 count of more than 500 cells per µL; 3=CD4 count of 350–500 cells per µL; 4=CD4 count of 200–349 cells per µL; and 5=CD4 count of less than 200 cells per µL. Diagnosis rate for compartment 1 is assumed to be zero (ie, no diagnoses occur during acute infection). Model assumed diagnosis upon progression to AIDs (appendix p 3).

	Total or unit cost
Total resource costs	
Start-up costs assumed to be used by RHIVA2 trial	£26 099 ($42 132)
Rapid HIV testing (recurrent)	£78 354 ($126 486)
Indeterminate or twice-invalid rapid HIV test results (recurrent)	£208 ($336)
Quality assurance and additional rapid HIV test kits used (recurrent)	£21 054 ($33 988)
Reactive rapid HIV test results (recurrent)	£1288 ($2078)
Marginal increase in serology testing resulting from the RHIVA2 intervention (recurrent)	£721 ($1165)
Average costs	
Per rapid HIV test done*	£25·25 ($40·77)
Per additional patient newly diagnosed by the intervention†	£7096 ($11 455)

Data are 2012 prices given in UK£ and US$. *Calculated as sum of first four resource types listed divided by 4978 tests. †Calculated as sum of all listed resource types divided by 18 patients (11 confirmed patients diagnosed via HIV rapid test plus seven patients diagnosed through serology because of the RHIVA2 intervention).

Table 1: **Average cost per HIV rapid test done and per additional newly diagnosed patient attributable to the intervention**

and HIV infection progression rates by CD4 cell count band taken from a recent modelling study of ART.[20]

The model defines HIV infection progression according to five stages, the first representing the short period of acute infection after HIV acquisition, and the remaining four defined by the following CD4 count bands: more than 500 cells per μL (not acute), 350–500 cells per μL, 200–349 cells per μL, and less than 200 cells per μL (figure 1). The state variables and transmission equations for the model are shown in the appendix (pp 1–3).

We defined three phases of infection: undiagnosed, diagnosed short-term (representing the first year after diagnosis), and diagnosed long-term (time thereafter). Quality of life estimates are lower during the first year after diagnosis compared with subsequent years, and so time diagnosed is divided into a first phase averaging 1 year and a long-term phase thereafter.

After diagnosis, individuals are assumed to have a long life expectancy because of effective treatment and care, and reductions in HIV infectiousness are assumed to result from ART-induced reductions in viral load.[21] For each behavioural risk group, we assigned an average number of partners per year for those undiagnosed. As used previously,[19] we assumed that once these individuals are diagnosed, they permanently reduce their number of sexual partners by 25%. HIV mortality is modelled as a fraction of patients diagnosed at CD4 count of less than 350 cells per μL who die after the first year of diagnosis, followed by a small mortality rate for the long-term diagnosed phase (figure 1).

Individuals tracked by the model (referred to as primary infections) are assumed to represent the following three population groups: men who have sex with men (MSM), heterosexual males, and heterosexual females. We did not include injecting drug users because needle reuse is in decline in the UK and HIV prevalence in this group is low (0·38% in the UK in 2015).[3]

We modelled secondary infections by estimating the proportion of those infected in Hackney in each of the three population groups, and for each of these, estimating annual onward HIV transmission events per year according to their HIV status (infection stage, diagnosis status, and circumcision status of partners). HIV status and population group determine an individual's risk behaviour (number of partners and condom use) and infectiousness (higher infectiousness for MSM resulting from more frequent anal sex practice and reduced infectiousness of those diagnosed because of ART). We estimated HIV prevalence among partners from Public Health England data.[19]

Diagnosed HIV incidence and prevalence for Hackney have been relatively stable since 2008,[19] therefore we assumed a constant HIV incidence in the model. We fitted the equilibrium state of the model to incidence in the control arm of the trial to calculate number of HIV-positive individuals in the model. Diagnosis rates for control and intervention scenarios were fitted to the number of infections diagnosed and the proportions diagnosed at each CD4 cell count band to trial data for intervention and control practices. We fitted the model using Bayesian inference done with Markov Chain Monte Carlo, with 95% credible intervals (95% CrIs) sampled from the posterior distribution.

We explored the sensitivity of model predictions to uncertainty in model parameters in univariate analysis by constructing a tornado diagram of incremental cost-effectiveness ratio (ICER) estimates at 40 years after the start of the trial, using ranges of values for key parameters (appendix p 21) and plotting sensitivity of ICER estimates over time to plausible ranges for those parameters identified as influential through the tornado analysis. Parameter values were not varied by a fixed percentage above and below the base case value as used in a typical tornado plot; reasonable parameter ranges were selected as informed by data sources. Uncertainty in model outcomes was expressed as 95% CrIs that were generated by use of probabilistic, multivariate sensitivity analysis, selecting model inputs from the model parameter ranges and with the 2·5–97·5th percentile range of all results generated. The model was double-programmed in R version 3.0.3 and Berkeley Madonna Version 8.3.18 to ensure robustness of the results. All other analyses were done with R.

Cost-effectiveness of the intervention was assessed with the ICER at different time horizons (durations since start of the intervention). We assessed cost-effectiveness for the duration of the trial only rather than as an ongoing intervention (ie, the model simulated a higher diagnosis rate for the first 28 months of the simulation, before reducing to the control rate for the remainder of the model run). This result was compared with a simulation by use of the control arm diagnosis rate for the entire simulation. The ICER is defined as the difference in cumulative costs

	30 years	40 years	50 years
Total QALYs gained	8·7 (0·8–27·0)	11·7 (1·1–33·6)	14·3 (1·3–39·6)
Cost per QALY gained	£34 425 (18 241–187 671)	£22 201 (12 662–132 452)	£16 543 (9616–109 026)
Total deaths averted	0·70 (0·07–1·75)	0·70 (0·07–1·75)	0·70 (0·07–1·75)
Cost per death averted	£429 083 (323 909–1 959 830)	£372 207 (268 162–1 903 385)	£339 526 (238 218–1 869 219)
Total secondary HIV infections averted	0·41 (0·03–0·89)	0·41 (0·03–0·88)	0·41 (0·03–0·88)
Cost per secondary HIV infection averted	£721 693 (513 253–4 755 138)	£628 874 (434 902–4 740 724)	£575 720 (390 053–4 773 379)

Intervention diagnosis rates last for 28 months (ie, for the duration of the RHIVA2 trial). Numbers in parentheses are 95% credible intervals: the 2·5–97·5th percentile range of all results generated through probabilistic sensitivity analysis, varying model parameters through the ranges shown in the appendix (p 22). QALY=quality-adjusted life-year.

Table 2: **Estimated benefits of RHIVA2 and cost-effectiveness outcomes reached by 30 years, 40 years, and 50 years after intervention, under scenario 1 (long-term diagnosed health-care costs based on evidence from UK data)**

in the intervention minus the control model scenarios, divided by the difference in their cumulative effect on QALYs.[22] The ICER for the intervention was evaluated as cost-effective if it lay within or below the £20 000–30 000 threshold of cost-effectiveness of interventions used by the National Institute for Health and Care Excellence (NICE) in the UK.[23]

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. JF, a clinician employed by NHS City and Hackney, which part-funded the study, was involved in designing the RHIVA2 trial, data interpretation, and writing the report, but had no role in data collection or analysis. The corresponding author had full access to all the study data and had final responsibility for the decision to submit for publication.

Results

Total cost of the intervention is estimated to be £127 724 (appendix pp 14–15). Estimated mean cost per rapid test performed was £25 and mean cost per additional patient newly diagnosed because of the intervention was £7096 (table 1).

With model parameters based on UK cost data (scenario 1) over a 40 year time horizon, ICERs are £22 201 (95% CrI 12 662–132 452) per QALY gained, £372 207 (268 162–1 903 385) per death averted, and £628 874 (434 902–4 740 724) per HIV transmission averted (table 2). RHIVA2 reaches the upper NICE cost-effectiveness threshold (~£30 000 per QALY gained[23]) after 33 years. Costs are high during the first 10 years after the RHIVA2 trial because increased medical costs are incurred by earlier diagnosis of infected individuals. However, this effect decreases over time because it is compensated by the benefits of reduction of onward HIV transmission and reduced health-care costs for people living with HIV who are diagnosed earlier.

Total QALYs gained because of the intervention are negative until 8·5 years after the start of the trial (figure 2A) because quality of life decreases in the model upon diagnosis of the cohort (green line), having an immediate effect, whereas the benefits of deaths and secondary infections averted (blue line) take 8·5 years to balance out this effect.

By 50 years, cost per QALY gained under scenario 1 is well below the lower NICE cost-effectiveness threshold (figure 2B, table 2). ICER estimates for scenarios 2 and 3, based on evidence from Canada, show that the higher the HIV-related health-care costs are for long-term patients who were diagnosed late compared with those diagnosed earlier, the more rapidly RHIVA2 becomes cost-effective, reaching the upper NICE threshold in as little as 13 years (figure 2B).

The results presented in the cost-effectiveness plane (figure 2C) show the initial QALY loss resulting from early diagnosis over the first 8·5 years. However, the intervention continues to derive benefits in terms of QALYs gained as well as costs saved for decades, because earlier testing reduces HIV transmission (table 2).

Predictions of the ICER of the RHIVA2 trial are most sensitive to incidence of new HIV infections in Hackney, closely followed by uncertainty in the estimate of quality of life of patients when in the acute stage of HIV infection (figure 3, appendix p 21). A higher incidence produced a lower model-predicted ICER (cost per QALY gained). A higher incidence leads to more cases in the community, so the intervention averts more secondary infections, thus increasing QALYs gained and reducing costs. The model is sensitive to acute-stage HIV quality of life because of its large range of uncertainty. Ribbon plots show how uncertainty in ICER estimates to these two key parameters change over time since the start of the intervention (appendix pp 11–12). Notably, model uncertainty resulting from the acute-stage infection quality of life multiplier decreases substantially over time since the start of intervention. This result is because at the start of screening, QALYs are gained through prevention of new infections that start in the acute stage, but over time, QALYs gained are from prevention of QALY loss as a result of chronic HIV infection. Importantly, the ribbon plots (appendix pp 11–12) show that uncertainty in ICER predictions decreases hugely over time and by 40 years after

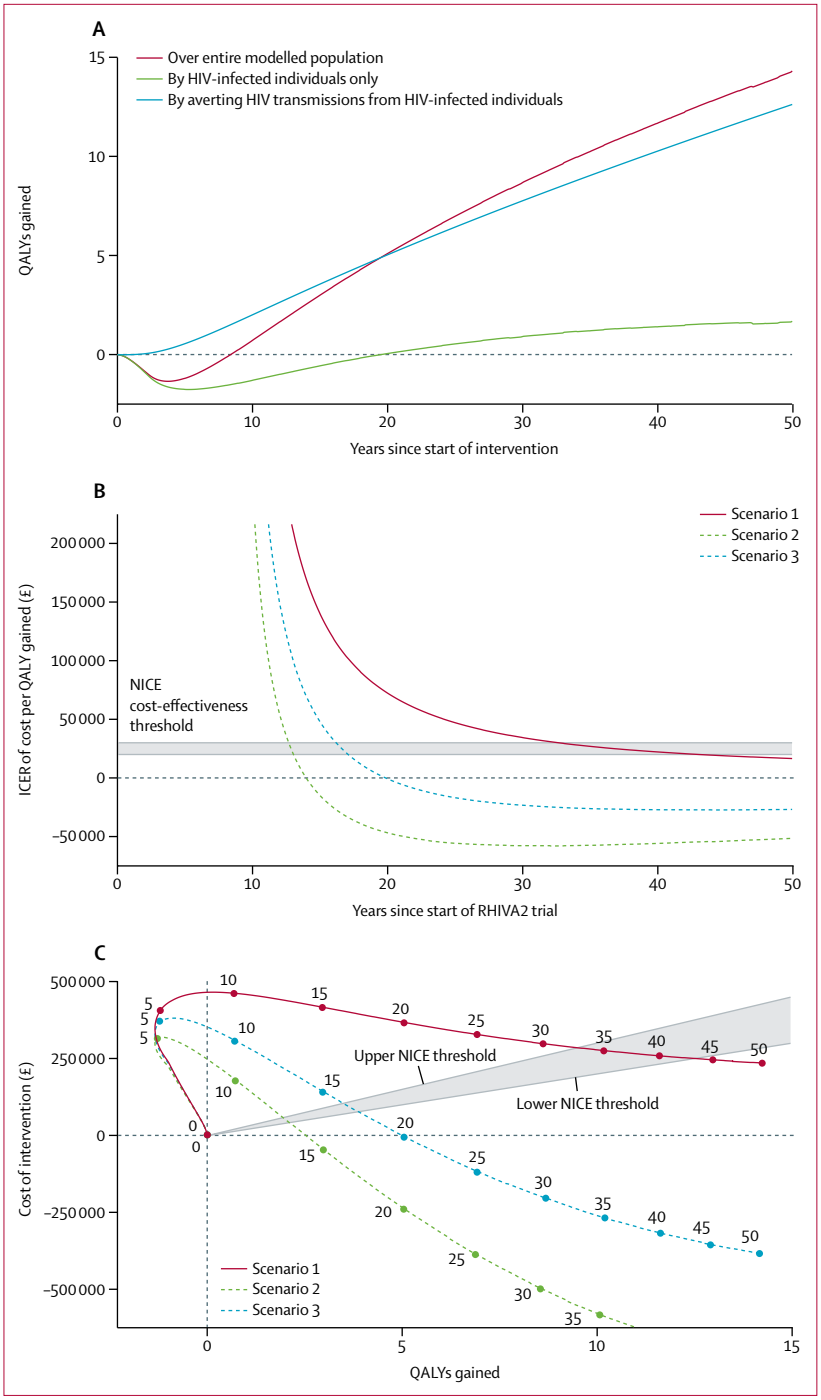

Figure 2: **Outcomes of the RHIVA2 intervention**
(A) Cumulative QALYs gained as a result of the RHIVA2 trial over time. The intervention is continued for 28 months only (the duration of the RHIVA2 trial). (B) ICER of cost per QALY gained as a result of the RHIVA2 trial, over time, for the three explored scenarios of increased long-term health-care costs for patients diagnosed with late infection. The grey band represents the £20 000–30 000 threshold of cost-effectiveness of interventions used by NICE in the UK. (C) Scenario lines show additional cost of RHIVA2 against QALYs gained, over time, highlighting each 5 year increment since start of the intervention (shown as coloured dots). Shaded grey area represents the NICE threshold of cost-effectiveness. QALY=quality-adjusted life-year. ICER=incremental cost-effectiveness ratio. NICE=National Institute for Health and Care Excellence.

RHIVA2 start, ICER values become centred on the NICE cost-effectiveness threshold.

Modelled ICER predictions over time are not substantively affected by assumptions regarding the reduction in risk-taking behaviour that individuals with HIV adopt once they are diagnosed (figure 4A) or by assumptions regarding quality of life after diagnosis (figure 4B). Changes in sexual behaviour have relatively little effect on the ICER because the most diagnosed patients with HIV are receiving ART, which substantially reduces HIV infectiousness, so different patterns of sexual risk do not much influence transmission. Varying QALY and cost yearly discount rates from 1·5% to 5·0% varies the duration before RHIVA2 reaches the upper cost-effectiveness threshold by 10 years (figure 4C). Reductions in ART costs do not meaningfully affect RHIVA2 ICER predictions (appendix p 13).

Discussion

Screening for HIV in primary care is cost-effective in the medium term in settings of high HIV incidence such as Hackney because of lower health-care costs of people living with HIV if diagnosed earlier and ongoing reductions in HIV transmission. Our model-based predictions are sensitive to assumptions regarding the increased cost of managing late-diagnosed HIV infection, for which UK-based data are scarce. If HIV health-care costs remain permanently elevated by at least 60% for patients diagnosed late (CD4 count ≤350 cells per μL), RHIVA2 becomes cost-effective more rapidly (between 13 years and 18 years in our modelled scenarios) and even becomes cost-saving. Therefore, general practice-based HIV screening is an important public health intervention deserving of scaling up.

Our study has a number of strengths. To our knowledge, ours is the first study to use data from a randomised controlled trial of HIV screening in primary care. That RHIVA2 was a pragmatic trial including almost all general practices in a large inner city borough strengthens the generalisability of our findings. We have done a full uncertainty analysis involving tornado plots for univariable analysis and probabilistic sensitivity analysis to provide 95% CrIs that provide a range for each model output to reflect the uncertainty in our model inputs. For some of the more potentially influential model inputs, we did scenario analyses to explore how different assumptions changed the model outputs.

Our study also has limitations, reflecting uncertainties regarding the values of inputs for modelling the transmission of a sexually transmitted disease. The paucity of reliable data to inform sexual behaviour and HIV transmission parameters means we designed our model to track secondary infections, as opposed to a full transmission model that accounts for all HIV

transmissions. This approach has been used by others,[19] and slightly underestimates benefits of the intervention because tertiary HIV infections onwards are not included. Given the small influence that onward HIV transmission has on intervention cost (appendix p 10) and the insufficient sensitivity of the model to sexual risk behaviour assumptions, we would not anticipate tertiary transmissions and beyond to affect our findings substantially. Further detail of limitations is given in the appendix (p 5).

Our analysis estimated the cost-effectiveness of the RHIVA2 trial, lasting 28 months, rather than that of an ongoing intervention. If RHIVA2 were to continue or have the residual effect of prolonged, increased HIV diagnosis rates, the intervention would take slightly longer to reach cost-effectiveness, but would be even more cost-effective overall. This result would be because the reduced quality of life of patients immediately following diagnosis initially counteracts QALYs saved through limiting transmission, but ultimately prevention of new infections has the greatest effect.

Our findings show the importance of the collection of accurate data on actual costs of HIV treatment to the NHS to produce more reliable cost-effectiveness estimates. Uncertainty about how long-term HIV health-care costs vary by HIV stage at diagnosis substantially affects our cost-effectiveness predictions. However, NHS England still does not have consistent information on costs for many specialised services.[24]

Previous HIV testing cost-effectiveness studies from high-income countries have produced contrasting results, depending on the nature of the testing intervention investigated and the assumptions made in the analysis. Sanders and colleagues[10] estimated that screening for symptomatic HIV patients was highly cost-effective. However, they assumed ART initiation at CD4 counts of 350 cells per μL or less and focused on identification of late-stage patients, whereas treatment in the UK generally occurs earlier than this (83% of all people living with HIV in 2015 were on treatment[3]). Our model assumes increased diagnosis rates across all HIV-infected individuals, regardless of CD4 cell count. Therefore, earlier diagnosis of asymptomatic patients will not produce great QALY gains but substantially increases treatment costs, making our cost-effectiveness predictions more modest.

Long and colleagues[19] assessed annual HIV testing of UK adults, concluding it to be very cost-effective when targeted to key populations (such as MSM). Phillips and colleagues[25] evaluated increased HIV testing in MSM in the UK and presented scenarios in which substantial increases in HIV testing (ie, in which more than 90% of MSM are diagnosed within a year of infection) were cost-effective. Such scenarios represent a highly intensive and targeted intervention which would probably have a major effect on the MSM HIV epidemic. Restriction of RHIVA2 to screening self-identifying MSM only would probably increase its cost-effectiveness but at the expense of missing large numbers of diagnoses (for example, in northeast London, 34% of new HIV diagnoses in 2015 were in women,[26] which calls into question the equity of targeted interventions).

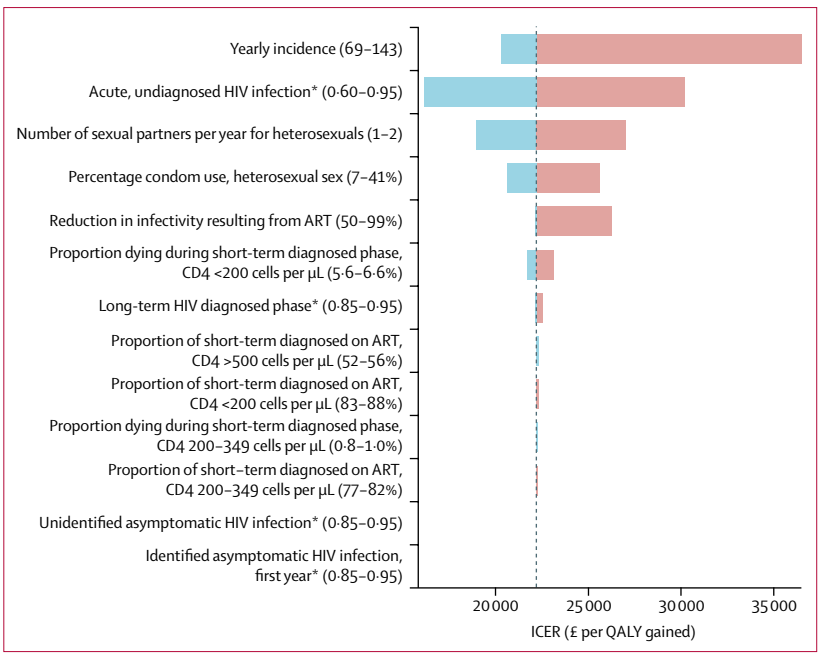

Figure 3: **Tornado plot of model parameters varied in univariate sensitivity analysis of scenario 1**
Parameters are arranged from widest range of model outcome, with range of model input values shown in parentheses. Dashed line represents ICER estimate for 40 years after RHIVA2 intervention using base case values of all parameters (appendix pp 16–18). Model parameters varied in univariate sensitivity analysis with minimal effect on the ICER (ie, even less than the parameter quality of life multiplier for identified asymptomatic infections, first year) are not shown. ART=antiretroviral therapy. ICER=incremental cost-effectiveness ratio. *Quality of life multiplier.

The START[27] and ANRS TEMPRANO[28] trials have shown reduced morbidity and mortality with earlier treatment, even in patients with high CD4 cell counts (>500 cells per μL); such benefits of earlier HIV treatment initiation would make RHIVA2 cost-effective at an even earlier time horizon.

The estimated cost-effectiveness of RHIVA2 is comparable to that of pre-exposure prophylaxis (PrEP) among MSM, implementation of which in high-income countries has been the subject of several health economic analyses.[29–31] PrEP cost-effectiveness estimates have ranged from cost-saving (Canada[30]) to US$160 000 per QALY gained (USA[29]). Preliminary cost-effectiveness results of MSM PrEP in the UK have also varied, from £26 300[32] to cost-saving per QALY gained[33] in base case scenarios. The latter ICER used an 80 year time horizon,[33] whereas we report cost-effectiveness at 40 years after the start of the intervention. Cost-effectiveness of these HIV prevention interventions increase with time and so RHIVA2 is of comparable cost-effectiveness.

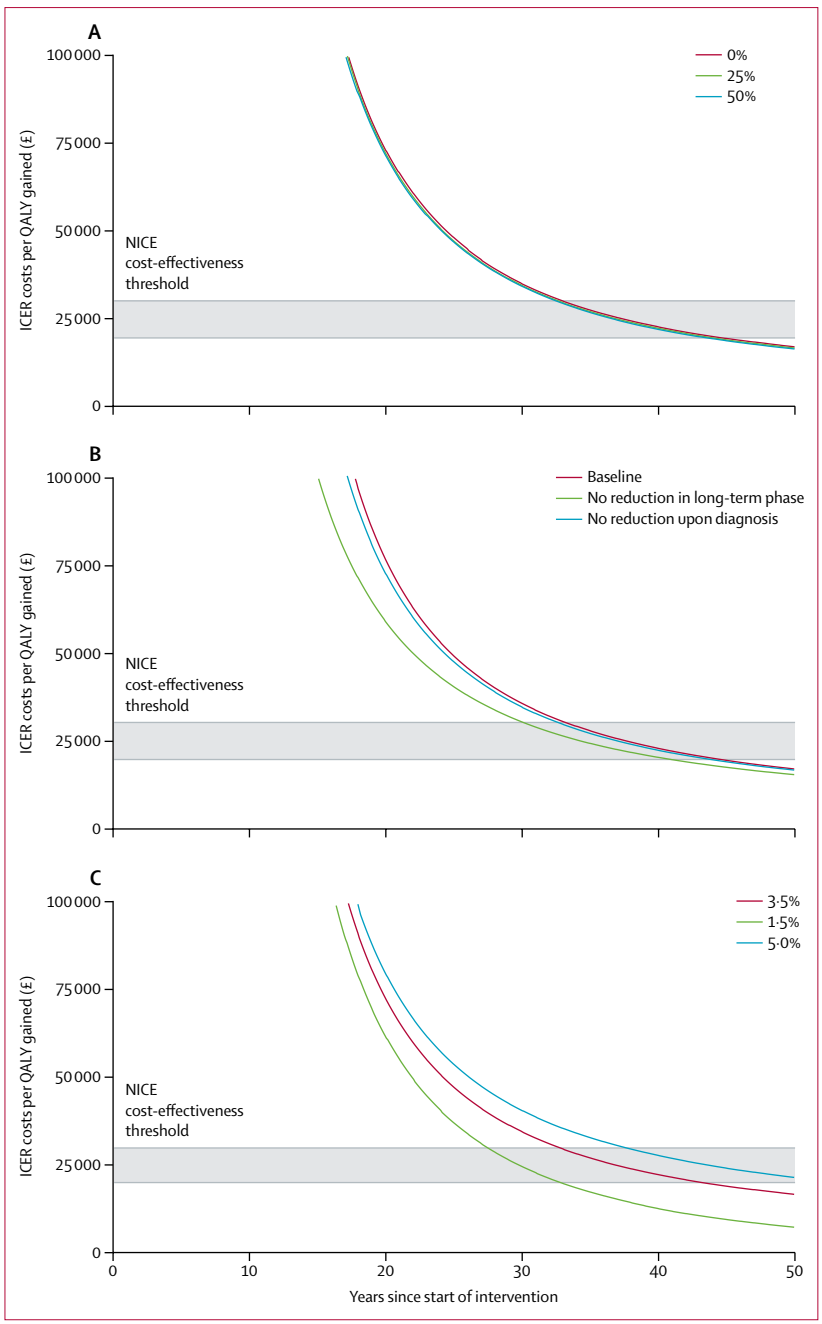

Figure 4: **Model sensitivity to assumptions on change in sexual behaviour after diagnosis, quality of life, and QALY and cost discount rates**

Scenario analyses exploring the sensitivity of model results to different (A) levels of reduction in sexual behaviour among people upon HIV diagnosis; (B) assumptions regarding quality of life after diagnosis; and (C) QALY and cost discount rates. The NICE threshold for cost-effectiveness of £20 000–30 000 is shown in grey. QALY=quality-adjusted life-year. NICE=National Institute for Health and Care Excellence.

Our cost-effectiveness analysis is relatively unusual because we are considering a public health intervention involving therapeutic drug use, thus providing both individual-level and population-level benefits. Early diagnosis of people who are HIV-positive has benefits for the individual in terms of improved prognosis, reduces inequalities, and improves access to effective ART, while also benefiting the wider community by reducing onward HIV transmission. The community benefit is because people living with HIV who are diagnosed earlier are treated earlier, thus reducing their infectiousness, and might also reduce their risk-taking behaviour, thus reducing population exposure to HIV. Our results suggest that most of the HIV prevention benefit of RHIVA2 is due to earlier ART initiation rather than changes in behaviour. They highlight the need for further UK health-care cost data, by CD4 cell count band at diagnosis, for HIV economic evaluations.

Translation of the findings of the RHIVA2 trial and this accompanying cost-effectiveness analysis into action is crucial. We have evaluated the effectiveness and cost-effectiveness of RHIVA2 in a high HIV-prevalence local authority. RHIVA2 is probably less cost-effective in low-prevalence authorities (defined as <0·2%, which is the NICE and British HIV Association threshold for routine HIV testing in primary care) and we would currently recommend primary care-based HIV screening in high-prevalence regions only. 11 authorities have HIV prevalence similar to Hackney (0·80–1·46%) and 74 of 325 authorities in England are defined as high prevalence and could benefit from screening.[15] We are currently comparing the implementation of RHIVA2 with different HIV testing interventions in neighbouring London boroughs with slightly lower prevalences. Further analyses with these data might identify a cutoff HIV prevalence below which screening is not cost-effective, but it is more likely for recommendations for screening to tally with low-prevalence cutoff defined by Public Health England of less than 0·2%. Furthermore, cost-effectiveness is affected by other factors varying by region, such as proportion of infections undiagnosed. Daily PrEP for 10 000 MSM has been estimated to cost £54 million per year.[32] The RHIVA2 trial intervention, covering half of Hackney general practices, cost £127 724 over 28 months. Thus, estimated annual screening programme costs for roll-out to all 11 Hackney-level HIV-prevalence authorities is about £600 000, and £4 million for roll-out to all high-prevalence authorities. RHIVA2 therefore represents an affordable prevention measure across all high-prevalence authorities in England. These figures are screening programme costs and do not include the increased HIV health-care costs resulting from earlier HIV diagnosis and treatment, which would fall under other NHS budgets (our analysis is of the 28 month trial rather than an ongoing, continuous intervention, so we cannot estimate an average health-care cost of the intervention per year).

Although ART as a prevention intervention is very effective, and treatment coverage in the UK is high, the estimated number of people living with undiagnosed HIV remains substantial and the number of people

living with HIV continues to increase.[3] Patients should be diagnosed and treated earlier to effect meaningful reductions in transmission, along with ensuring that for those with a negative HIV test other prevention interventions, such as condom use and PrEP, are accessible and promoted.[34,35]

Contributors

RFB designed and analysed the cost-effectiveness model with input from TDH, MAI, WL, CJG, and AM. RFB and MAI coded the model. RFB, TDH, WL, CJG, and AM designed the sensitivity analysis. WL, CJG, JA, JF, and HM designed and undertook the RHIVA2 HIV screening trial. FT-P designed the costing of RHIVA2. ACS, HM, and WL collected costs from the trial. TDH and MAI carried out the model fitting procedure. VC summarised the data available on the cost of care for people who are HIV positive in the UK. AM provided technical support on cost-effectiveness analysis. RFB drafted the manuscript with substantial input from all coauthors. All authors approved the submitted version of the manuscript.

Declaration of interests

JA reports fees and non-financial support from Bristol-Myers Squibb; grants and personal fees from Gilead Sciences; personal fees from ViiV, Merck Sharp & Dohme, and AbbVie; and grants from Janssen, outside the submitted work. VC and ACS report grants from Merck Sharp & Dohme, outside the submitted work. The other authors declare no competing interests.

Acknowledgments

This research was funded by the NHS City and Hackney, UK Department of Health, and supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care North Thames at Barts Health NHS Trust (CLAHRC). WL received a Walport NIHR clinical lectureship. HM was supported by an NIHR Doctoral Fellowship from 2013 to 2016. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health. We thank all participants and general practices, Zheng Yin (Public Health England), and Kevin Kelleher (London, UK) for providing additional data, and Steve Morris (University College London) for helpful comments.

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