EClinicalMedicine 000 (2019) 100229

Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Research Paper

Evaluating the impact of post-trial implementation of RHIVA nurse-led HIV screening on HIV testing, diagnosis and earlier diagnosis in general practice in London, UK

Werner Leber[a,1,*], Jasmina Panovska-Griffiths[b,1,*], Peter Martin[b], Stephen Morris[b,c], Estela Capelas Barbosa[b], Claudia Estcourt[d,e], Jane Hutchinson[e], Maryam Shahmanesh[f], Farah El-Shogri[a], Kambiz Boomla[a], Valerie Delpech[g], Sarah Creighton[g], Jane Anderson[h], Jose Figueroa[i], Chris Griffiths[a]

[a] *Institute of Population Health Sciences, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London United Kingdom*
[b] *Department of Applied Health Research, University College London, London, United Kingdom*
[c] *Institute of Public Health, University of Cambridge, Cambridge United Kingdom*
[d] *School of Health and Life Sciences, Glasgow Caledonian University, Glasgow, United Kingdom*
[e] *All East Sexual Health Services, Barts Health NHS Trust, London, United Kingdom*
[f] *Institute for Global Health, University College London, London, United Kingdom*
[g] *Department of HIV and STI, National Infection Service, Public Health England, London, United Kingdom*
[h] *Homerton Sexual Health Services, Homerton University Hospital NHS Foundation Trust, London, United Kingdom*
[i] *Specialised Commissioning Team, NHS England, London, United Kingdom*

ARTICLE INFO

Article History:
Received 1 August 2019
Revised 14 November 2019
Accepted 28 November 2019
Available online xxx

Keywords:
HIV testing
Implementation
Interrupted time series

ABSTRACT

Background: UK and European guidelines recommend HIV testing in general practice. We report on the implementation of the Rapid HIV Assessment trial (RHIVA2) promoting HIV screening in general practice into routine care.

Methods: Interrupted time-series, difference-in-difference analysis and Pearson-correlation on three cohorts comprising 42 general practices in City & Hackney (London, UK); covering three periods: pre-trial (2009–2010), trial (2010–2012) and implementation (2012–2014). Cohorts comprised practices receiving: "trial intervention" only (n = 19), "implementation intervention" only (n = 13); and neither ("comparator") (n = 10). Primary outcomes were HIV testing and diagnosis rates per 1000 people and CD4 at diagnosis.

Findings: Overall, 55,443 people were tested (including 38,326 among these cohorts), and 101 people were newly diagnosed HIV positive (including 65 among these cohorts) including 74 (73%) heterosexuals and 69 (68%) people of black African/Caribbean background; with mean CD4 count at diagnosis 357 (SD=237). Among implementation intervention practices, testing rate increased by 85% (from 1·798 (95%CI=(1·657,1·938) at baseline to 3·081 (95%CI=(2·865,3·306); p = 0·0000), diagnosis rate increased by 34% (from 0·0026 (95%CI=(0·0004,0·0037)) to 0·0035 (95%CI=(0·0007,0·0062); p = 0·736), and mean CD4 count at diagnosis increased by 55% (from 273 (SD=372) to 425 (SD=274) cells per μL; p = 0·433). Implementation intervention and trial intervention practices achieved similar testing rates (3·764 vs. 3·081; 6% difference; 95% CI=(-5%,18%); p = 0·358), diagnosis rates (0·0035 vs. 0·0081; -13% difference; 95%CI=(-77%,244%; p = 0·837), and mean CD4 count (425 (SD=274) vs. 351 (SD=257); 69% increase; 95% CI=(-61%,249%); p = 0·359). HIV testing was positively correlated with diagnosis (r = 0·114 (95% CI=[0·074,0·163])), and diagnosis with CD4 count at diagnosis (r = 0·011 (95% CI=[-0·177,0·218])).

Interpretation: Implementation of the RHIVA programme promoting nurse-led HIV screening into routine practice in inner-city practices with high HIV prevalence increased HIV testing, and may be associated with increased and earlier diagnosis. HIV screening in primary care should be considered a key strategy to reduce undiagnosed infection particularly among high risk persons not attending sexual health services.

Date: 09/11/2019
* Corresponding authors.
E-mail addresses: w.leber@qmul.ac.uk (W. Leber), j.panovska-griffiths@ucl.ac.uk (J. Panovska-Griffiths).
[1] WL and JPG are joint first authors and contributed equally to the manuscript

https://doi.org/10.1016/j.eclinm.2019.11.022

Funding: National Institute for Health Research ARC North Thames, and Barts and The London School of Medicine and Dentistry.

Research in context

Evidence before this study

We searched PubMed for implementation of a cluster randomised trial, published from Jan 01, 2000, to July 31, 2019, testing the impact of HIV screening of adults in primary care compared with usual care on rates of HIV testing and diagnosis, and CD4 count at diagnosis. We found no studies that met these criteria.

Added value of this study

These findings provide, to our knowledge, evidence that implementation of nurse-led HIV screening in general practices with HIV high prevalence into routine care leads to increased HIV testing, and may be associated with increased and earlier diagnosis.

Implications of all available evidence.
Public health leaders should consider implementing HIV screening in primary care in high prevalence areas.

Introduction

HIV prevalence continues to rise globally. In the UK, 101,600 people were estimated to be living with HIV (PLWH) in 2017. In the same year, 4,363 people were newly diagnosed with HIV and 1,879 of them (43%) were diagnosed at a late stage of infection, i.e. with CD4 count below 350 cells per μL blood [1]. Early diagnosis and treatment are associated with improved clinical outcomes, reduced transmission, and lower treatment costs [2].

In London, testing interventions have largely reached men who have sex with men (MSM); however, late diagnosis remains disproportionally high among people who are heterosexual (54% vs. 32% in MSM), people of black African/Caribbean origin (65%), and those older than 65 years (63%) [3].

To promote earlier diagnosis, in the UK, more routine HIV testing is recommended in non-traditional settings including general practices located in high prevalence areas [4,5]. However, a recent systematic review suggested that uptake of HIV testing in primary care remains low [6]. Furthermore, barriers to HIV testing in primary care remain across Europe [7], although France and the Netherlands have reported gradual rises in HIV testing since national recommendations for GP-led testing were issued [7].

Our group has tested the feasibility, acceptability and the impact of implementing nurse-led routine HIV testing in general practice under the Rapid HIV Assessment (RHIVA) umbrella intervention. Our pilot study in 2009 (RHIVA1) demonstrated that rapid point-of-care HIV testing offered by a health care assistant at general practice registration was feasible and acceptable to both patients and staff [8]. Subsequently, using a pragmatic cluster randomised controlled trial (RHIVA2), we showed that an educational training and support package promoting nurse-led HIV screening at general practice registration resulted in increased and earlier diagnosis of HIV [9], and furthermore, was cost-effective [10].

However, outside of a clinical trial, evidence of the impact of implementing routine HIV testing in general practice is still lacking. After completing the RHIVA2 trial in September 2012, we offered the RHIVA intervention to all practices in City and Hackney, two high HIV prevalence areas in inner London, irrespective of their participation in the original trial. The local public health authority welcomed the positive impact of RHIVA on population health and commissioned it as a clinical service in April 2013. The "RHIVA" intervention is defined as a routine offer of HIV testing by competency-trained non-medical staff in general practice, either as part of the RHIVA2 research trial (the "trial intervention") or via its post-trial implementation (the "implementation intervention"); whereas the term implementation refers to the methods used to support the adoption of RHIVA in the practices [11].

This paper evaluates the RHIVA implementation across City and Hackney general practices not previously exposed to the trial intervention, by investigating changes in HIV testing rate, HIV diagnosis rate, and CD4 count at diagnosis. We aimed to answer the following three questions: (a) Is there a difference in outcomes between the RHIVA trial intervention and its post-trial implementation? (b) Is there a difference in outcomes between the RHIVA implementation and usual care in comparator practices? (c) What is the association between HIV testing and diagnosis rates, and between diagnosis rate and CD4 count at diagnosis, in the presence of RHIVA?

Methods

Setting

The study was conducted in the City of London and the London borough of Hackney (UK), where the estimated local diagnosed HIV prevalence rates are 11·23 and 7·67 per 1000 per adult population respectively [3]. All general practices within the borough (44 practices, September 2012) were invited to implement RHIVA, including practices that had previously participated in the RHIVA2 trial (2010–2012). All adults aged 16 and above registered with a general practice were included.

Design

We conducted a service evaluation comprising a pragmatic cohort using an interrupted time series analysis (ITS) to examine the longitudinal impact of the implementation in the borough. HIV testing, diagnosis and CD4 count at diagnosis data were collected for the period between April 01, 2009 and December 31, 2014.

Ethics approval

The study utilised secondary anonymised data for which approval was granted from Camden and Islington NHS Research Ethics Committee, London and no informed consent from patients was required.

Intervention

Between April 2010 and August 2012, we delivered the RHIVA2 trial intervention across 20 general practices randomised to the intervention arm of the trial (See Fig. 1). This theory-based intervention [12–14] previously described [9,15] includes an initial practice-based education and training session (tailored to nurses and health care assistants) to offer nurse-led routine rapid HIV testing at registration, competency assessment and certification for the completion of

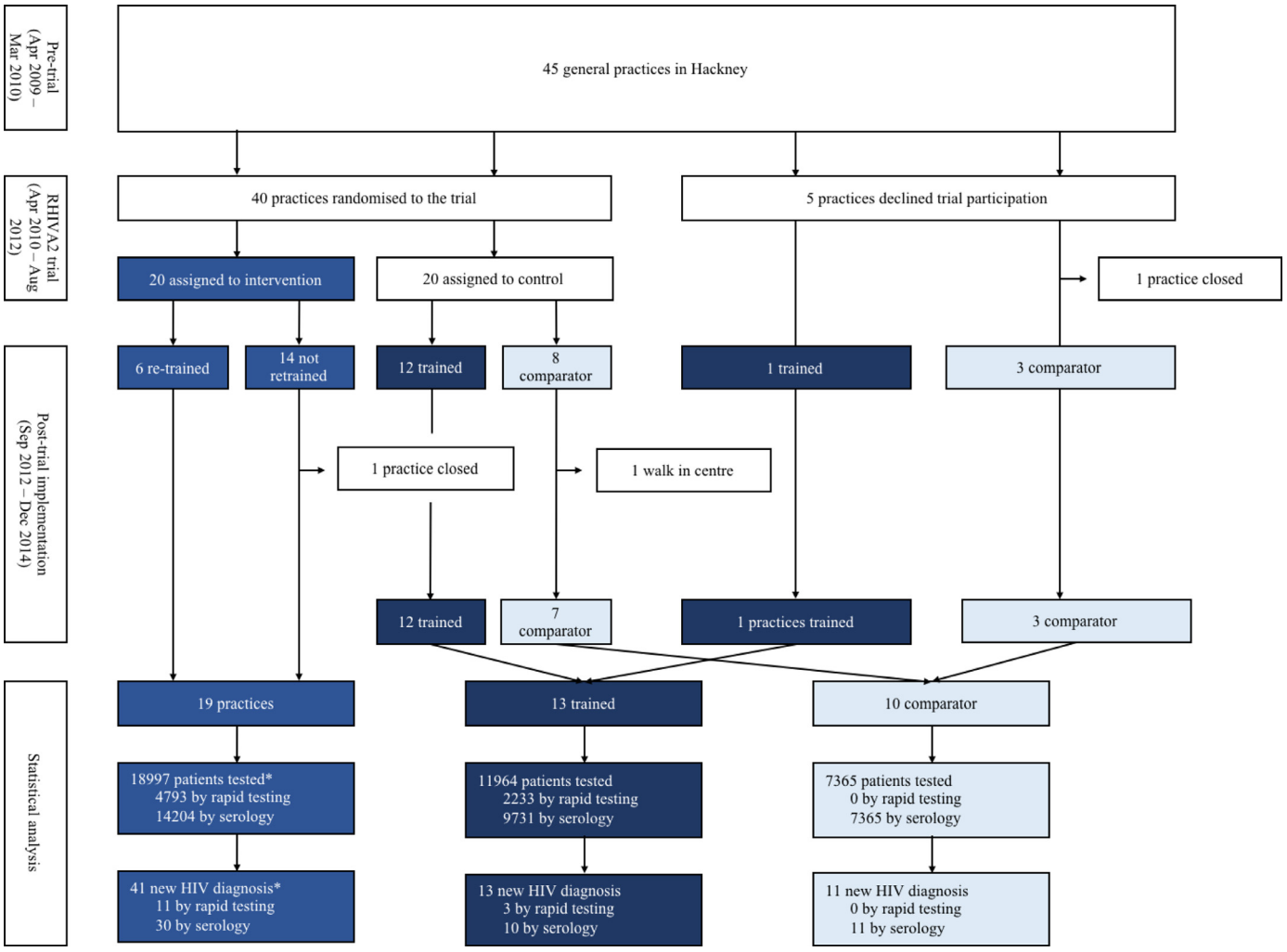

Fig. 1. Consort flow diagram. RHIVA trial and implementation profile.

training, a follow up meeting with a nominated practice HIV-lead nurse, external quality assurance including regular support by the research team, integration of prompts to offer rapid HIV testing with the primary care computer template, and incentive payments to the practices (£10 per rapid test performed and recorded on the template). Practices were also able to offer rapid testing in other clinical encounters, such as contraception or sexual health screening appointments. This intervention supplemented existing national antenatal HIV screening and a general practice sexual health local enhanced service (LES) promoting HIV case detection (incentive payments of £265 per newly diagnosed patient including referral to the HIV clinic) introduced in 2006/07 [16].

Forty-five practices were operating at the beginning of the trial, including 40 practices that took part in the trial and five practices that declined participation. Of the latter, one practice closed during the trial period resulting in 44 practices available during implementation. Forty-two of 44 practices were included in this analysis; two practices were excluded: one trial intervention practice closed, and one comparator practice offered walk-in services to homeless people resulting in disproportionally high testing rates compared to their small practice list size (see Fig. 1).

Of the 44 practices invited to participate in the implementation, 20 practices had received the intervention during RHIVA2 (trial intervention practices) and 24 had not (20 trial control practices, and 4 non-participating practices) (see Fig. 1). A total of 19 practices were trained, including 13 de novo trained practices (12 trial control, 1 non-participating practice) and six trial intervention practices for whom this implementation constituted a reinforcement, i.e. they received two analogous RHIVA interventions, 28 months apart [12–14]. Since this work focuses on evaluating the impact of the implementation intervention, in comparison to the trial intervention or no intervention, we stratified the practices into three cohorts of interest:

- Trial intervention practices (comprising 19 practices that received RHIVA during the trial between April 2010 and August 2012).
- Implementation intervention practices (henceforth implementation practices and comprising 13 de novo trained practices that received only the implementation intervention between September 2012 and December 2014).
- Implementation comparator practices (henceforth comparator practices and comprising 10 practices that received no intervention, either during either the trial or the implementation).

Details of the practice cohorts and their characteristics are given in Tables 1 and 2.

RHIVA implementation

Informed by our previous work [8,9], we modified the intervention prior to implementation as follows: promotion of both rapid or serology testing in any GP clinical setting (instead of rapid testing at GP registration only as per trial); discontinuation of regular research

Table 1
a and b: Summary of the descriptive statistics for the baseline cohorts and the people who had an HIV tests across the three practice cohorts.

(a) Baseline characteristics across the three practice cohorts

Practice cohort (N=number of practices)	Trial intervention (N=19)	Implementation (N=13)	Comparator (N=10)
Search date*	01/04/2010	01/09/2012	01/09/2012
Total number of people registered on search date	98,351	67,551	54,034
Age (years)			
16-24	15,608 (16%)	8,631 (13%)	6,425 (12%)
25-34	29,196 (30%)	20,532 (30%)	17,210 (32%)
35-49	30,263 (31%)	22,021 (33%)	17,192 (32%)
≥50	23,284 (24%)	16,367 (24%)	13,207 (24%)
Gender			
Men	49,396 (50%)	34,860 (52%)	26,806 (50%)
Ethnic origin			
White	18,624 (38%)	17,667 (51%)	13,866 (52%)
Black	10,016 (20%)	6,666 (19%)	4,968 (19%)
Mixed	345 (1%)	241 (1%)	219 (1%)
Asian	3,337 (6·8%)	2,518 (7·2%)	1,489 (5·6%)
Other	4,121 (8%)	1,643 (5%)	1,536 (6%)
Unknown	12,953 (26%)	6,125 (18%)	4,728 (18%)

(b) Characteristics of people with an HIV test

Practice cohort (N=number of practices)	Trial intervention (N=19)	Implementation (N=13)	Comparator (N=10)
Period	01/04/2010 to 31/08/2012	01/09/2012 to 31/12/2014	01/09/2012 to 31/12/2014
Total number of people with an HIV test	15,431	7,365	4,432
Age (years)			
16-24	96 (1%)	175 (2%)	81 (2%)
25-34	4,228 (29%)	2,883 (39%)	1,642 (35%)
35-49	7,803 (54%)	3,465 (47%)	2,406 (52%)
≥50	2,392 (16%)	784 (11%)	499 (11%)
Gender			
Men	4,486 (31%)	2,423 (33%)	1,336 (29%)
Ethnic origin			
White	1,841 (41%)	960 (40%)	469 (35%)
Black	839 (19%)	231 (10%)	118 (9%)
Mixed	24 (1%)	24 (1%)	14 (1%)
Asian	205 (5%)	73 (3%)	33 (2%)
Other	250 (6%)	128 (5%)	47 (4%)
Unknown	1,327 (30%)	1,007 (42%)	655 (49%)

* Search date for the trial intervention cohort (highlighted in royal blue) was April 01, 2010;
and for the implementation (dark blue) and comparator (light blue) cohorts September 09, 2012 respectively.

team support to the practices; and provision of external quality assurance through the UK National External Quality Assessment Service (https://ukneqas.org.uk/). In parallel, we also conducted an evaluation of "missed opportunities" for HIV diagnosis commissioned by NHS City and Hackney, across 31 practices (11 trial intervention, 15 control) [17]. This evaluation demonstrated evidence of late diagnosis in general practices preceding the trial. In April 2013, the existing general practice sexual health service [16] was updated to include incentive payments between £7 and £10 for any rapid or serology test performed in addition to the existing payments for case-detection (£258).

Clinical data

We retrospectively collected anonymised HIV testing data in primary care, as per the RHIVA2 protocol, using remote searches on the

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Table 2
Characteristics of practice cohorts studied during three periods: pre-trial (April 2009 to March 2010), trial (Apr 2010 to Aug 2012), and implementation (September 2012 to December 2014).

	Pre-trial period (Apr 2009 – Mar 2010)[a]			Trial period (Apr 2010 – Aug 2012)[a]			Post-trial implementation period (Sep 2012 – Dec 2014)[a]				Total (April 2009 – Dec 2014)[a]
Cohort characteristics Practice characteristic	Pre-trial intervention Pre-trial intervention (*N* = 19)	Pre-trial control (*N* = 19)	Pre-trial non-participant (*N* = 4)	Trial intervention Trial intervention (*N* = 19)	Pre-implementation Trial control & trial non-participant (*N* = 13)	Pre-comparator Trial control & trial non-participant (*N* = 10)	Trial intervention + Implementation (*N* = 6)	Trial intervention, No implementation (*N* = 13)	Implementation Trial control & Trial non-participant + Implementation (*N* = 13)	Comparator Trial control & Trial non-participant, No Implementation (*N* = 10)	All practices (*N* = 42)
Patient characteristic											
HIV testing											
Patients with rapid test	0	0	0	4793	0	0	2136	1130	2233	0	**10,292**
Patients tested by serology[d]	3566	2583	162	10638	4599	2933	4453	6169	5132	4432	**45,151**
HIV diagnosis											
New HIV diagnoses	9	7	Nil	32	6	8	10	19[c]	7	3[b]	**101[b,c]**
By rapid testing	NA	NA	NA	11	NA	NA	2	5	3	NA	**21[c]**
By serology testing	9	7	Nil	21	6	8	8	14[c]	4	3[b]	**80[b,c]**
Median CD4 count (IQR)	411 (238–461)	249 (110–354)	NA	259 (168–478)[e]	117(30–374)	302((151–383)	411 (206–482)[f]	387 (190–541)	459 (192–715)[g]	304 (238–439)	**318 (186–477)**
Mean CD4 count (STD)	403 (191)	241 (168)	NA	351 (257)[e]	273(372)	266(152)	378 (197)[f]	396 (238)	425 (275)[g]	327 (102)	**357 (237)**
Black African	7 (78%)	6 (86%)	NA	20 (63%)	4 (67%)	6 (75%)	6 (60%)	15 (79%)	4 (57%)	1 (33%)	**69 (68%)**
Heterosexuals	8 (89%)	5 (71%)	NA	23 (72%)	4 (67%)	6 (75%)	7 (70%)	15 (79%)	3 (43%)	3 (67%)	**74 (73%)**
Male	3 (22%)	2 (29%)	NA	19 (59%)	3 (50%)	4 (50%)	7 (70%)	10 (53%)	5 (71%)	1 (33%)	**54 (53%)**
Mean Age (range)	38 (17–67)	47 (34–65)	NA	40 (21–62)	37 (21–49)	38.5 (26–53)	38 (23–62)	41 (22–65)	37 (21–54)	39 (35–42)	**39.5 (17–67)**

All practice and patient data for these periods are shown. Practice cohorts included in the interrupted time series and difference-in-difference analyses are trial intervention practices including their pre-trial control (highlighted in royal blue), implementation practices including their pre-implementation control (highlighted in dark blue) and implementation comparator practices and their pre-comparator control (highlighted in light blue).

[a] Two practices were excluded from this analysis; a trial intervention practice closed down during the implementation period, and a comparator practice offering walk-in services where the number of people tested was higher than the practice list size.

[b] As a result of (a) two people newly diagnosed in this comparator practice were excluded from the analysis.

[c] One potentially newly diagnosed patient from an implementation practice was excluded as we were unable to match their data with Public Health England records.

[d] Total number of people tested by serology for opportunistic or diagnostic reasons, antenatal screening, or confirmatory testing for rapid testing.

[e] CD4 count data at diagnosis for four people were not available due to missing data.

[f] CD4 count data missing due to lack of patient consent.

EMIS Web (Egton Medical Information Systems, UK) primary care computer systems of READ codes used for rapid and serology testing [9]. A master case report form (CRF), detailing a list of people with a positive HIV test result confirmed by the local pathology laboratory (Homerton University Hospital), was generated by the lead HIV clinician (JA) at Homerton Sexual Health Services [9]. CD4 count at the time of diagnosis were included. Patient data were linked to practices, and the master CRF was shared with the study team in an anonymised fashion, as per the RHIVA2 protocol. In collaboration with Public Health England (PHE), we externally validated data categorising people confirmed HIV positive into those with a new HIV diagnosis and those previously known to have HIV infection using the national HIV and AIDS database. The INSTI HIV1/HIV2 Rapid Antibody Test (bioLytical Laboratories, Canada) finger prick system was used for rapid testing. Any venous blood sample detected as reactive to HIV-1or HIV-2 on an Abbott Architect ci8200 analyser (Abbott Diagnostics, UK) at Homerton Hospital (London, UK) was sent on to Barts Health Virology for confirmatory testing with the VIDAS HIV DUO Quick assay (BioMerieux, UK) and the ImmunoComb II HIV 1 & 2 BioSpot kit assay (Alere, UK). The study has been reported in accordance with the STARI reporting guidelines for implementation studies [18].

Outcome measures

We constructed time series of the HIV testing data, combining data from serology and rapid tests, HIV diagnosis and CD4 count associated to diagnosis separately for each of the three practice cohorts between April 2009 and December 2014. Using the data, we truncated the 69-month observation period into periods of pre-intervention and intervention as per Table 1.

We separately considered the pre/during-trial periods for trial intervention practices, and the pre/during-implementation periods for implementation and comparator practices respectively, as described before. To aid visualisation of the temporal trajectory of testing and diagnosis rates, we smoothed the corresponding time series of the pooled monthly data for each group using a symmetric moving average filter with span 5 (testing data) and 8 (diagnosis data). As illustrated in Figure 2, we defined T_0 as the time when data collection started, T_1, T_2 as the times when trial intervention started and ended respectively; and T_2, T_3 as the times when implementation started and the last day of data available respectively. Then pre-intervention periods are defined in Table 1 as $T_{pre} \epsilon (T_0, T_1)$ for the trial intervention, and $T_{pre} \epsilon (T_1, T_2)$ for the implementation and comparator practices respectively; while the intervention periods were $T_{during} \epsilon (T_1, T_2)$ for the trial intervention, and $T_{during} \epsilon (T_2, T_3)$ for the implementation and comparator practices. We note that we only had 12 months of pre-trial data, whereas we utilised 28 months of trial, pre-implementation and implementation data. These data sizes are considered sufficient for statistical significance testing [19,20].

We used the raw, unsmoothed time series of the data over corresponding T_{pre} and T_{during} periods to calculate the co-primary outcomes as the monthly HIV testing rate (number of people who received either rapid or serology HIV testing x 1000/number of registered patients), monthly HIV diagnosis rate (number of newly diagnosed people x 1000/number of registered patients); and CD4 count at diagnosis for people newly diagnosed with HIV across the three different practice cohorts. In addition, we calculated the correlation between rates of HIV testing and HIV diagnosis, and between HIV diagnosis rate and CD4 count at diagnosis across all practice cohorts.

Statistical analysis

We used mixed effects negative binomial regression models with random intercepts for GP practices and an offset term for practice size (number of registered patients) to analyse each outcome separately. To estimate the difference in outcomes associated with the intervention period, we fitted a random intercept model with a single indicator variable for "during-intervention" in each cohort. For the purpose of comparing the differences associated with the intervention between cohorts, we used indicator variables for "during-intervention" and "cohort" as well as their interaction, so the interaction term estimated the between-cohort difference in the change over time. Details of the statistical analysis are presented in Appendix A. For each analysis we calculated incidence rate ratios (IRRs), and used bootstrapping with 200 replications to estimate standard errors, 95% confidence intervals (95% CI), and p-values. Finally, we explored whether increased HIV testing was associated with increased and earlier HIV diagnosis by calculating the Pearson correlation coefficients (r) and the corresponding bootstrapped 95% CI (again using 200 replications) across all practices combined, over the entire 69-month observation period.

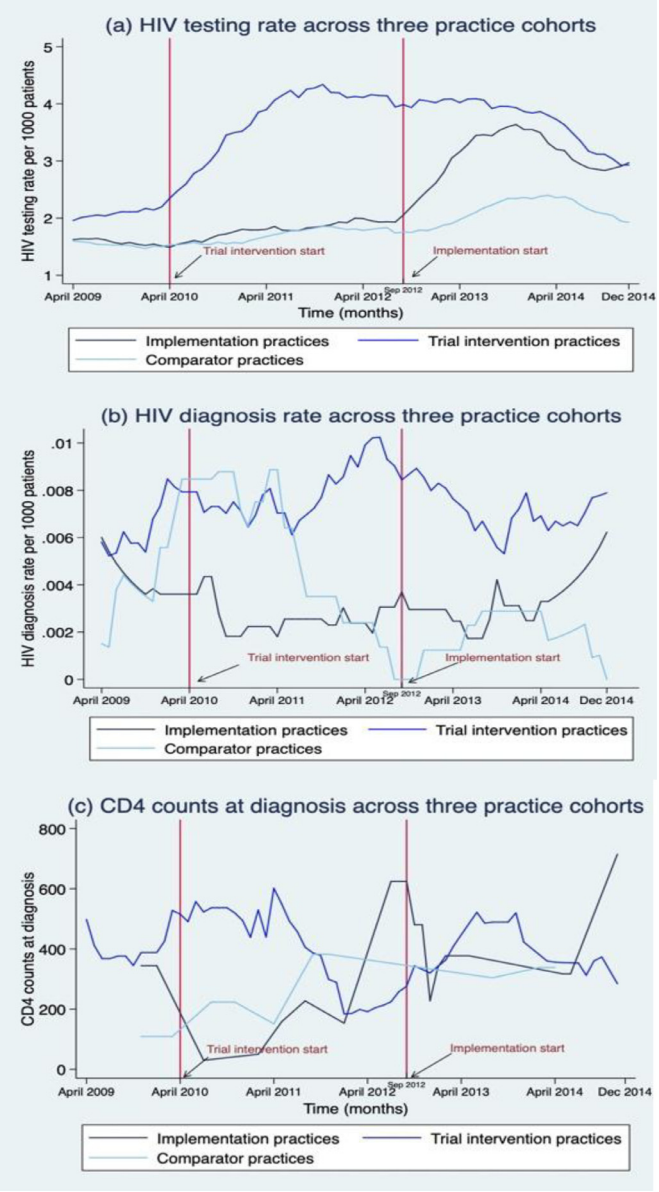

Fig. 2. (a–c). Smoothed time-series of three outcomes: HIV testing rate (a), HIV diagnosis rate (b) and (c) CD4 count at diagnosis over the period April 2009 to December 2014 across 19 trial intervention practices (royal blue line), 13 implementation practices (dark blue line) and 10 comparator practices (light blue line). The vertical red lines denote the times of the start of the trial intervention and the implementation respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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Results

Baseline characteristics were similar for sex, age, and ethnic origin across all three practice cohorts (Table 1). Table 1 shows that in implementation and comparator practices, people aged 50 and above and people of black African or Caribbean origin were underrepresented among those tested. There was less evidence of such underrepresentation in trial intervention practices.

Across all practices and over the entire 68-month study period (April 2009 to December 2014), 55,443 people had an HIV test, of which 45,151 had a serology test and 10,292 a rapid test (Table 2). Some people may have received both. Across our cohorts, 11,964 people were tested in implementation practices (N = 13) (7,365 during the implementation period), 18,997 in trial intervention practices (N = 19, 15,431 during the trial) [9], and 7,365 in comparator practices (n = 10, 4,432 during implementation) (Tables 1 and 2).

Across all practices, a total of 101 people were newly diagnosed with HIV, of whom 21 (21%) were diagnosed by rapid testing; 74 (73%) were heterosexual and 69 (68%) were people of black African/Caribbean background. Among the three cohorts, 65 people were newly diagnosed, including 13 people (three diagnosed by rapid testing) in implementation practices, 41 (11 diagnoses by rapid testing) in trial intervention practices, and 11 in comparator practices (Table 2).

During the implementation period, a total of 26 patients had a reactive test result recorded on the EMIS template; of which 10 were confirmed HIV positive (true positive), two were confirmed HIV negative (false reactive), two patients were known to Homerton Sexual Health to be HIV positive, and one patient was unobtainable for confirmatory testing; the remaining 11 reactive results were entry errors. Three patients had an indeterminate result recorded; two were confirmed HIV negative, and one patient was unobtainable for confirmatory testing.

Overall, mean CD4 count at diagnosis was 357 (SD=237) (Table 1); in implementation practices the mean CD4 count was 425 (SD=274) during implementation, 351 (SD=257) in trial intervention practices during the trial, and 327 (SD=102) in comparator practices during implementation. Furthermore, 44% of people diagnosed in implementation practices had a CD4 count of less than 350 cells per μL, compared to 57% in trial intervention practices, and 71% in comparator practices.

Fig. 2(a–c) show the smoothed time-series of HIV testing rates, HIV diagnosis rates and CD4 count at diagnosis across the three practice cohorts. Table 3 contains the testing rates, diagnosis rates, and mean CD4 counts in the pre-implementation and implementation periods, by cohort. Testing rates rose in all three cohorts, but were greater in trial intervention and implementation practices than in comparator practices. Testing rates declined somewhat in trial intervention practices after the end of the trial. Diagnosis rates increased in trial intervention and implementation practices, but decreased in comparator practices. Mean CD4 count at diagnosis increased in implementation and comparator practices, but decreased among trial intervention practices. Confidence intervals for diagnosis rates and mean CD4 counts are wide, reflecting the relatively small number of diagnoses overall.

Table 4 reports the results from statistical models estimating the difference between intervention and pre-intervention periods for each of the three cohorts, and difference-in-difference analyses for the two comparisons of interest. HIV testing increased more in implementation practices compared to comparator practices by 55% (95% CI=(40%, 72%); $p<0{\cdot}001$). Diagnosis rate also increased more in implementation practices compared to comparator practices by 106% (95% CI=(−40%, 754%); p = 0·17), as did CD4 count at diagnosis by 35% (95%CI=(−70%, 502%)). Although the direction of the difference was as hypothesised for all three outcomes, the differences in diagnosis rates and CD4 counts had very wide confidence intervals that included zero difference, hence not giving conclusive results on the direction or approximate size of the difference.

Compared to trial intervention practices, in implementation practices both testing rates (6%; 95%CI=(−5%, 18%)) and CD4 count at diagnosis (69%, 95%CI=(−61%,249%)) increased to a larger extend, while diagnosis rates increased to a smaller extend (−13%; 95%CI=(−77%, 244%)). For all three outcomes, the confidence intervals included zero difference.

Across the whole dataset, increased HIV testing was associated with increased diagnosis (r = 0·114; 95% CI=(0·074, 0·163)) (Fig. 3(a)), while the association between HIV diagnosis and CD4 count at diagnosis, although positive, was negligible (r = 0·011; 95% CI=(−0·177, 0·218)) (Fig. 3(b)).

Discussion

Our analysis suggests that implementation of an educational programme promoting nurse-led HIV screening in inner-city high prevalence general practices leads to increased HIV testing, compared to comparator practices. Change in testing rates among implementation practices was similar to trial intervention practices, suggesting that promotion of testing in real life settings can be as effective as under research conditions.

Increased and earlier diagnosis are key clinical and public health outcomes. In our data, implementation practices had a higher increase in diagnostic rates in the implementation period compared to comparator practices, and patients in these practices were, on average, diagnosed earlier than in comparator practices. These differences were not statistically reliable. Because rates of new diagnoses were generally low, we had low statistical power despite our

Table 3
HIV testing and diagnosis rates, and mean CD4 count at diagnosis before and during intervention periods across trial intervention, implementation and comparator practices. These periods are defined in Table 2.

	Testing rate (per 1,000): mean (95% CI)		Diagnosis rate (per 1,000): mean (95% CI)		CD4 count at diagnosis: mean (95% CI)	
	Pre-intervention	During intervention	Pre-intervention	During intervention	Pre-intervention	During intervention
Trial intervention practices	2·084 (1·905,2·267)	3·764 (3·539,3·989)	0·0062 (0·0016,0·0106)	0·0081 (0·0054,0·0112)	403 (273,532)	351 (256,446)
Implementation practices	1·798 (1·657,1·938)	3·081 (2·856,3·306)	0·0026 (0·0004,0·0037)	0·0035 (0·0007,0·0062)	273 (12,569)	425 (216,633)
Comparator practices	1·695 (1·582,1·808)	2·107 (1·922,2·291)	0·0052 (0·0014,0·0097)	0·0017 (0·0003,0·0037)	266 (167,367)	327 (228,425)

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Table 4
Model-based interrupted time series estimates of the difference in testing rate, diagnosis rate, and CD4 count at diagnosis: incidence rate ratios (IRR) for difference between implementation and pre-implementation periods, and difference-in-difference analyses comparing cohorts.

	IRR	95% CI	p value
HIV Testing Rate			
Trial intervention practices	1·734	1·616-1·861	p<0·0001
Implementation practices	1·853	1·702-2·018	p<0·0001
Comparator practices	1·189	1·118-1·265	p<0·0001
Difference-in-difference between implementation and trial intervention practices	1·055	0·941-1·184	0·358
Difference-in-difference between implementation and comparator practices	1·548	1·391-1·722	p<0·0001
HIV diagnosis rate			
Trial intervention practices	1·391	0·652-2·967	0·393
Implementation practices	1·341	0·398-3·673	0·736
Comparator practices	0·432	0·000001-5·183	0·832
Difference-in-difference between implementation and trial intervention practices	0·868	0·225-3·437	0·837
Difference-in-difference between implementation and comparator practices	2·059	0·596-8·540	0·170
CD4 count for newly diagnosed people			
Trial intervention practices	0·882	0·559-1·502	0·728
Implementation practices	1·552	0·516-4·661	0·433
Comparator practices	1·226	0·507-2·963	0·651
Difference-in-difference between implementation and trial intervention practices	1·69	0·388-3·497	0·359
Difference-in-difference between implementation and comparator practices	1·353	0·304-6·021	0·691

relatively long observation periods. Nonetheless, we did show that increased testing rates are associated with higher diagnosis rates in our data set overall.

Similar to the RHIVA2 trial, the majority of patients diagnosed during the implementation were heterosexuals and people of black African/Caribbean origin. These at-risk groups are less likely to attend sexual health clinics [21], and might benefit most from testing in general practice. Therefore, testing in these settings may be considered as an important adjunct to achieving the UNAIDS strategy of reducing new infections and HIV-related death by 2030. This would particularly apply to countries with less efficient HIV services than the UK, where HIV testing in primary care can be expected to be cost-saving [10].

Continuous training and support may be required for sustained testing and diagnosis in practices. Unlike trial intervention practices, implementation practices did not receive any ongoing clinical support and although their testing rates were similar, diagnosis rates were relatively low, perhaps reflecting low uptake of testing among people of black African/Caribbean origin and among those aged 50 and above. This could indicate a training issue and suggest that regular facilitation to practices may be needed to reach key populations at risk. Alternatively, the low diagnosis rates may be due to successes of prevention efforts, gentrification and changes to governmental immigration policies. Of note, national strategies such as TasP policy and a PrEP pilot in sexual health centres were unlikely to have impacted on local HIV infection, as these were not available before July 2015. Finally, loss of follow up of patients with a reactive or indeterminate result in implementation (but not in the trial) suggests that a failsafe, including regular data monitoring and feedback to practices, may be required for delivery of safe care.

Our study has many strengths. Firstly, we used a comprehensive longitudinal data set covering over five years, comprising HIV testing and diagnosis data, from all practices within a large health system, allowing incorporation of the RHIVA2 trial data set with implementation data, and enabling data stratification into practice cohorts for statistical analysis. Secondly, data management was consistent during the whole study period and across the care continuum, including usage of the same primary care computer system, confirmation of HIV positive tests by the same hospital, and external validation of new diagnoses by PHE using the national HIV and AIDS database. Finally, this research is underpinned by a strong multi-disciplinary team of academic GPs, HIV specialists, public health and academic researchers, showing importance of collaboration to drive implementation post-trial.

The main weakness of the implementation period is lack of randomisation, allowing less certainty about causality. Cross-contamination of comparator practices might have occurred during the pre-trial, trial, and implementation periods. During implementation, contamination of comparator practices might have occurred through clustering effects by geographical proximity with intervention practices and by joint working in general practice commissioning consortia established in 2012. The temporary initial peak in both testing and diagnosis observed in comparator practices, might have also resulted from an audit of “missed opportunities for diagnosis” conducted in 31 practices at that time [17]. During the trial and implementation, comparator practices might have additionally been contaminated by the Hawthorne effect (i.e. knowing you are in an HIV testing trial (or in a comparator group) may cause a change in practice) or by dissemination of the National testing guidelines via the media and the local health authority at commencement of the trial. Pre-trial, engagement of the local sexual health department with the practices focussing on testing at-risk populations could have resulted in increased diagnostic rates observed during this period. Finally, cross-contamination might have also occurred due to people switching practices, as electronic HIV testing records (but not diagnosis data that we obtained

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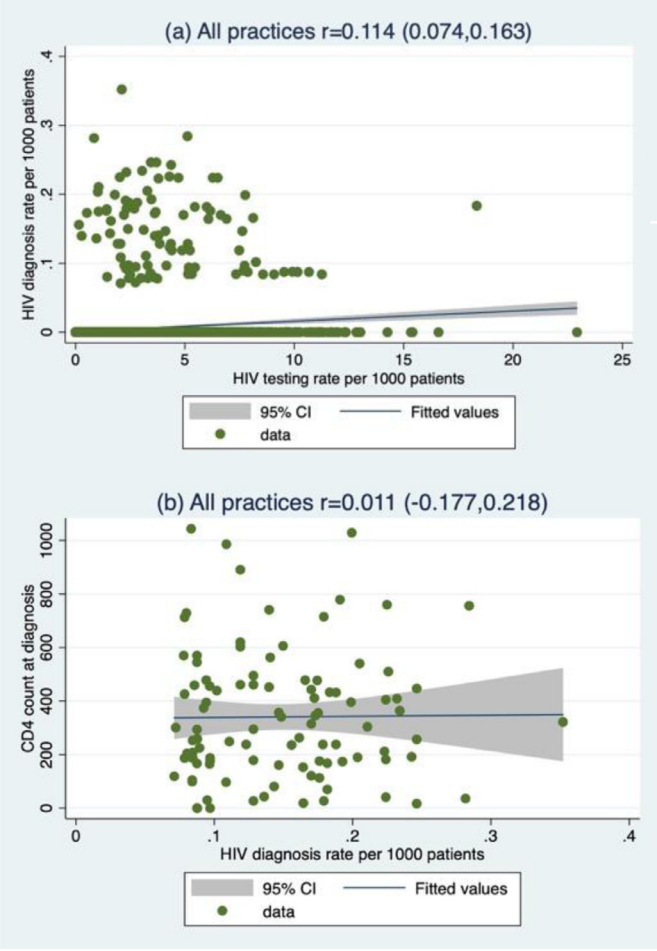

Fig. 3. (a-b). Pearson correlation coefficient showing the correlation between data on (a) testing rate and diagnosis rate, and (b) diagnosis data and CD4 count at diagnosis over the entire time period (April 2009 to December 2014) and across all practice cohorts combined. The data from Fig. 2(a-b) are pooled together for this correlation calculation. The confidence intervals were determined using bootstrapping with 200 replications.

from the local laboratory) would follow people when re-registering with a new practice.

To our knowledge, this is the first study to demonstrate the impact of implementing nurse-led HIV screening after a cluster randomised controlled trial into routine primary care.

Our study findings have important implications for people, populations, and health care systems internationally. Our data suggests that routine implementation of a trial intervention delivers equivalent improvements on HIV testing and diagnosis rates, and CD4 count at diagnosis. People, particularly those from at-risk key populations, are likely to benefit from both increased access to testing in a familiar primary care setting, linkage to prompt treatment and care for those testing positive, and increased access to effective prevention strategies including PrEP for those testing negative. For public health, RHIVA provides an additional tool for reducing undiagnosed HIV in the community. Given its pragmatic and collaborative nature, the intervention may facilitate sexual health service development in primary care, knowledge transfer to practice staff, and safe patient transfer to the HIV clinic. RHIVA has been included in the ECDC public health guidance on HIV, hepatitis B and C testing (2018) as an example of good clinical practice [22], and key research priorities include: implementation of RHIVA among other high prevalence areas nationally and internationally, expansion of RHIVA to include multiple chronic infection screening among migrant communities, and application of digital technology to enhance uptake of testing.

Declaration of Competing Interest

Dr. Anderson reports unremunerated support from Gilead Sciences and from Merck Sharp & Dohme Corp outside the submitted work; and she co-chairs the HIV Outcomes Initiative unremunerated. Dr. Shahmanesh reports grants from the US National Institute for Health, the UK National Research Institute for Health, the Medical Research Council, the Bill and Melinda Gates Foundation, Unitaid, 3ie, ViiV Health Care, the Engineering Physical Science Research Council, and grants from the Wellcome Trust, outside the submitted work. WL, JPG, PM, SM, ECB, CE, JH, FES, KB, VD, SC, JA, JF and CG have nothing to disclose.

Acknowledgements

We thank Keith Prescott, Martin A Sharp, Canan Eroglu, and Jack Dunne (Clinical Effectiveness Group, Queen Mary University of London, UK) for the extraction of demographic and HIV testing data. We thank Sambasivarao Pelluri for providing the data on people testing HIV positive. We are grateful to Heather McMullen and Danna Millett for conducting the implementation training sessions, and to Renata Spinelly Martins for her managerial assistance in the implementation roll out.

Author's contributions

WL, JPG, PM, SM, ECB, JF and CG significantly contributed to designing the study and drafted the paper. CE, JH, MS, HM, KB, JA, FJ contributed to designing the study. FE-S constructed the HIV testing data base. All co-authors read and approved the submitted version of the manuscript.

Funding

This report is independent research funded by the National Institute for Health Research ARC North Thames. The views expressed in this publication are those of the author(s) and not necessarily those of the National Institute for Health Research or the Department of Health and Social Care. HM was supported by an NIHR Doctoral Fellowship from 2013 to 2016. The funders had no role in the study design, data collection and analysis, interpretation and writing of the report.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2019.11.022.

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