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

Leber, Werner; Panovska-Griffiths, Jasmina; Martin, Peter; Morris, Stephen; Capelas Barbosa, Estela; Estcourt, Claudia; Hutchinson, Jane; Shahmanesh, Maryam; El-Shogri, Farah; Boomla, Kambiz; Delpech, Valerie; Creighton, Sarah; Anderson, Jane; Figueroa, Jose; Griffiths, Chris

Published in:
EClinicalMedicine

DOI:
10.1016/j.eclinm.2019.11.022

Publication date:
2020

Document Version
Publisher's PDF, also known as Version of record

Link to publication in ResearchOnline

Citation for published version (Harvard):
Leber, W, Panovska-Griffiths, J, Martin, P, Morris, S, Capelas Barbosa, E, Estcourt, C, Hutchinson, J, Shahmanesh, M, El-Shogri, F, Boomla, K, Delpech, V, Creighton, S, Anderson, J, Figueroa, J & Griffiths, C 2020, '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', EClinicalMedicine, vol. 19, 100229. https://doi.org/10.1016/j.eclinm.2019.11.022

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
If you believe that this document breaches copyright please view our takedown policy at https://edshare.gcu.ac.uk/id/eprint/5179 for details of how to contact us.
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 Leber1,*, Jasmina Panovska-Griffiths1,2,*, Peter Martinb, Stephen Morrisb,c, Estela Capelas Barbosab, Claudia Escourte,d, Jane Hutchinsofe, Maryam Shahmaneshf, Farah El-Shogria, Kambiz Boolmaa, Valerie Delpechb, Sarah Creightong, Jane Andersonh, Jose Figueroa1, Chris Griffithsb

1 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 Institute for Global Health, University College London, London, United Kingdom
f All East Sexual Health Services, Barts Health NHS Trust, 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

A B S T R A C T

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); 21% 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.

Keywords: HIV testing Implementation Interrupted time series

A R T I C L E   I N F O

Article History:
Received 1 August 2019
Revised 14 November 2019
Accepted 28 November 2019
Available online 10 January 2020

Keywords:
HIV testing
Implementation
Interrupted time series
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 disproportionately 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
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
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

---

**Table 1**

(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                   | 67,351                | 54,034            |
| Age (years)                             |                          |                       |                   |
| 16-24                                   | 15,608 (16%)             | 8,631 (13%)           | 6,423 (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.
| Characteristic | Pre-trial period (Apr 2009 – Mar 2010)a | Pre-trial control (N = 19) | Pre-trial non-participant (N = 4) | Trial period (Apr 2010 – Aug 2012)b | Pre-implementation (N = 13) | Pre-comparator (N = 10) | Post-trial implementation period (Sep 2012 – Dec 2014)c | Implementation (N = 13) | Comparator (N = 10) | Total (Apr 2009 – Dec 2014)d | All practices (N = 42) |
|---------------|----------------------------------------|---------------------------|---------------------------------|----------------------------------|---------------------------|-------------------------|---------------------------------|-------------------------|-------------------------|---------------------------------|-------------------|
| Practice      | Pre-trial intervention (N = 19)        | Pre-trial control (N = 19) | Pre-trial non-participant (N = 4) | Trial intervention (N = 19)     | Trial control & trial non-participant (N = 13) | Trial control & trial non-participant (N = 10) | Trial intervention + Implementation (N = 6) | Trial intervention, No implementation (N = 13) | Implementation & Trial non-participant (N = 13) | Comparator & Trial non-participant (N = 10) | |
| characteristic |                                        |                           |                                 |                                  |                          |                          |                                  |                          |                          |                                 |                  |
|               | HIV testing                            |                           |                                 |                                  |                          |                          |                                  |                          |                          |                                 |                  |
|               | Patients with rapid test               | 0                         | 0                               | 0                                | 4793                      | 0                       | 0                               | 2136                     | 1130                    | 2233                          | 0                 |
|               | Patients tested by serology            | 3566                      | 2583                            | 162                              | 10638                     | 4599                    | 2933                            | 4453                     | 6169                    | 5132                          | 4432              |
|               | HIV diagnosis                          | 9                         | 7                               | Nil                              | 32                        | 6                       | 8                               | 10                       | 19                      | 7                             | 3                 |
|               | By rapid testing                       | NA                        | NA                              | NA                               | 11                        | NA                      | 8                               | 2                        | 5                       | 3                             | NA                |
|               | By serology testing                    | 9                         | 7                               | Nil                              | 21                        | 6                       | 8                               | 8                        | 14                      | 4                             | 3                 |
|               | Median CD4 count (IQR)                 | 411 (238–461)             | 249 (110–354)                   | NA                               | 259 (168–374)             | 117 (30–374)            | 302 (151–383)                  | 411 (206–482)            | 387 (190–541)           | 459 (192–715)                  | 304 (238–439) |
|               | Mean CD4 count (STD)                   | 403 (191)                 | 241 (168)                       | NA                               | 351 (257)                 | 273 (372)              | 266 (152)                       | 378 (197)                | 396 (238)               | 425 (275)                      | 327 (102) |
|               | Black African                          | 7 (78%)                   | 6 (86%)                         | NA                               | 20 (63%)                  | 4 (67%)                 | 6 (75%)                        | 6 (60%)                  | 15 (79%)                | 4 (57%)                        | 1 (33%) |
|               | Heterosexuals                          | 8 (89%)                   | 5 (71%)                         | NA                               | 23 (72%)                  | 4 (67%)                 | 6 (75%)                        | 7 (70%)                  | 15 (79%)                | 3 (43%)                        | 3 (67%)  |
|               | Male                                   | 3 (22%)                   | 2 (29%)                         | NA                               | 19 (59%)                  | 3 (50%)                 | 4 (50%)                        | 7 (70%)                  | 10 (53%)                | 5 (71%)                        | 1 (33%)  |
| Mean Age (range) | 38 (17–67) | 47 (34–65) | 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 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.
intervention, and $T_{pre}$
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 implementa-
tion intervention periods are de-

test with the VIDAS HIV DUO
Quick assay (BioMerieux, UK) and the ImmunoComb II HIV 1 & 2 Bio-
Spot 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 implementa-
tion started and the last day of data available respectively. Then pre-
intervention periods are defined in Table 1 as $T_{pre}(T_0, T_1)$ for the trial
intervention, and $T_{pre}(T_1, T_2)$ for the implementation and compar-
ator practices respectively; while the intervention periods were $T_{during}
\in (T_1, T_2)$ for the trial intervention, and $T_{during}(T_2, T_3)$ for the im-
plementation 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 con-
sidered sufficient for statistical significance testing [19,20].

We used the raw, unsmoothed time series of the data over corre-
sponding $T_{pre}$ and $T_{during}$ periods to calculate the co-primary out-
comes as the monthly HIV testing rate (number of people who received
either rapid or serology HIV testing x 1000/number of regis-
tered patients), monthly HIV diagnosis rate (number of newly diag-
nosed people x 1000/number of registered patients); and CD4 count
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 sepa-
rately. 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 interven-
tion between cohorts, we used indicator variables for “during-interv-
vention” 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 (IRR), 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 coeffi-
cients ($r$) and the corresponding bootstrapped 95% CI (again using
200 replications) across all practices combined, over the entire 69-
month observation period.
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<0.001). 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

| Testing rate (per 1,000): mean (95% CI) | Diagnosis rate (per 1,000): mean (95% CI) | CD4 count at diagnosis: mean (95% CI) |
|----------------------------------------|-------------------------------------------|-------------------------------------|
| **Trial intervention practices**       |                                            |                                     |
| Pre-intervention                       | During intervention                        |                                     |
| 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)                        | 451 (256, 446)                            |                                     |
| **Implementation practices**          |                                            |                                     |
| Pre-intervention                       | During intervention                        |                                     |
| 1.798 (1.657, 1.938)                  | 3.681 (2.856, 3.306)                      |                                     |
| 0.0026 (0.0004, 0.0037)               | 0.0035 (0.0007, 0.0062)                   |                                     |
| 273 (12, 569)                         | 425 (216, 633)                            |                                     |
| **Comparator practices**              |                                            |                                     |
| Pre-intervention                       | During intervention                        |                                     |
| 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)                            |                                     |
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

| HIV Testing Rate | IRR   | 95% CI          | p value |
|------------------|-------|-----------------|---------|
| Trial intervention practices | 1.734 | 1.616-1.861 | <0.0001 |
| Implementation practices | 1.853 | 1.702-2.018 | <0.0001 |
| Comparator practices | 1.189 | 1.118-1.265 | <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 | <0.0001 |

| HIV diagnosis rate | IRR   | 95% CI          | p value |
|--------------------|-------|-----------------|---------|
| 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 | IRR   | 95% CI          | p value |
|-------------------------------------|-------|-----------------|---------|
| 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 |
to disclose.

Acknowledgements

We thank Keith Prescott, Martin A Sharp, Canan Ergulu, 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.

References

[1] PHE. Progress towards ending the HIV epidemic in the United Kingdom: 2018 report. London, UK: Public Health England; 2018 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/821273/ Progress_towards_ending_the_HIV_epidemic_in_the_UK.pdf (accessed November 09, 2019).
[2] Beck EJ, Mandalia S, Sangha R, et al. The cost-effectiveness of early access to HIV services and starting cART in the UK 1996-2008. PLoS ONE 2011;6(12):e27830.
[3] PHE. Towards elimination of HIV transmission, AIDS and HIV-related deaths in the UK: 2017 report. London, UK: Public Health England; 2017 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/675809/Towards_elimination_of_HIV_transmission_AIDS_and_HIV_related_deaths_in_the_UK.pdf (accessed November 09, 2019).
[4] BHIVA. UK national guidelines for HIV testing 2008. London, UK: British HIV Association; 2008 https://www.bhiva.org/file/RHNUJgIs DreadML/GlinesHIVTest08.pdf (accessed November 09, 2019).
[5] NICE. HIV testing: increasing uptake among people who may have undiagnosed HIV (Joint nice and public health England guideline). London, UK: National Institute for Health and Care Excellence; 2016 https://www.nice.org.uk/guidance/ng60 (accessed November 09, 2019).

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.

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.
Elmahdi R, Gerver SM, Gomez Guillen G, Fidler S, Cooke G, Ward H. Low levels of HIV test coverage in clinical settings in the U.K.: a systematic review of adherence to 2008 guidelines. Sex Transm Infect 2014;90(2):119–24.

Deblonde J, De Koker P, Hamers FP, Fontaine J, Luchters S, Temmerman M. Barriers to HIV testing in Europe: a systematic review. Eur J Public Health 2010;20(4):422–32.

Prost A, Griffiths CJ, Anderson J, Wight D, Hart CJ. Feasibility and acceptability of offering rapid HIV tests to patients registering with primary care in London (UK): a pilot study. Sex Transm Infect 2009;85(5):326–9.

Leber W, McMullen H, Anderson J, et al. Promotion of rapid testing for HIV in primary care (RHIVA2): a cluster-randomised controlled trial. The Lancet HIV 2015;2(6):e229–e35.

Baggaley RF, Irvine MA, Leber W, et al. Cost-effectiveness of screening for HIV in primary care: a health economics modelling analysis. Lancet HIV 2017;4(10):e465–74.

Eldh AC, Almost J, DeCorby-Watson K, et al. Clinical interventions, implementation interventions, and the potential greyness in between - a discussion paper. BMC Health Serv Res 2017;17(1):16.

Forsetlund L, Bjordal A, Rashidian A, et al. Continuing education meetings and workshops: effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2009;2:CD003030.

Griffiths C, Sturdy P, Brewin P, et al. Educational outreach to promote screening for tuberculosis in primary care: a cluster randomised controlled trial. Lancet 2007;369(9572):1528–34.

O’Brien MA, Rogers S, Jantvedt G, et al. Educational outreach visits: effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2007;4:CD000409.

Leber W, Beresford I, Nightingale C, et al. Effectiveness and cost-effectiveness of implementing HIV testing in primary care in East London: protocol for an interrupted time series analysis. BMJ Open 2017;7(12):e018163.

Sohal H, Creighton S, Figueroa J, Gibb A. The impact of establishing a local-enhanced service for treating sexually transmitted infections in primary care. Sex Transm Infect 2008;84(3):235–7 discussion 7–8.

Wellesley R, Whittle A, Figueroa J, et al. Does general practice deliver safe primary care to people living with HIV? A case-notes review. Br J Gen Pract 2015;65(639):e655–61.

Pinnock H, Epiphaniou E, Sheikh A, et al. Developing standards for reporting implementation studies of complex interventions (StaRI): a systematic review and e-Delphi. Implement Sci 2015;10(1):42.

Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. Int J Technol Assess Health Care 2003;19(4):613–23.

Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther 2002;27(4):299–309.

Tanton C, Geary RS, Clifton S, et al. Sexual health clinic attendance and non-attendance in Britain: findings from the third national survey of sexual attitudes and lifestyles (Natsal-3). Sex Transm Infect 2018;94(4):268–76.

ECDC. Public health guidance on HIV, hepatitis B and C testing in the EU/EEA. Stockholm, Sweden: European Centre for Disease Prevention and Control; 2018. https://www.ecdc.europa.eu/sites/default/files/documents/hiv-hep-testing-guidance_0.pdf (accessed November 9, 2019).