Promotion of rapid testing for HIV in primary care (RHIVA2): a cluster-randomised controlled trial

Werner Leber, Heather McMullen*, Jane Anderson, Nadine Marlin, Andreia C Santos, Stephen Bremner, Kambiz Boomla, Sally Kerry, Danna Millett, Sifiso Mguni, Sarah Creighton, Jose Figueroa, Richard Ashcroft, Graham Hart, Valerie Delpech, Alison Brown, Graeme Rooney, Maria Sampson, Adrian Martineau, Fern Terris-Prestholt, Chris Griffiths*

Summary

Background **Many people with HIV are undiagnosed. Early diagnosis saves lives and reduces onward transmission. We assessed whether an education programme promoting rapid HIV testing in general practice would lead to increased and earlier HIV diagnosis.**

Methods **In this cluster randomised controlled trial in Hackney (London, UK), general practices were randomly assigned (1:1) to offer either opt-out rapid HIV testing to newly registering adults or continue usual care. All practices were invited to take part. Practices were randomised by an independent clinical trials unit statistician with a minimisation program, maintaining allocation concealment. Neither patients nor investigators were masked to treatment allocation. The primary outcome was CD4 count at diagnosis. Secondary outcomes were rate of diagnosis, proportion with CD4 count less than 350 cells per μL, and proportion with CD4 count less than 200 cells per μL. This study is registered with ClinicalTrials.gov, number ISRCTN63473710.**

Findings **40 of 45 (89%) general practices agreed to participate: 20 were assigned to the intervention group (44 971 newly registered adult patients) and 20 to the control group (38 464 newly registered adult patients), between April 19, 2010, and Aug 31, 2012. Intervention practices diagnosed 32 people with HIV versus 14 in control practices. Mean CD4 count at diagnosis was 356 cells per μL (SD 254) intervention practices versus 270 (SD 257) in control practices (adjusted difference of square root CD4 count 3·1, 95% CI –1·2 to 7·4; p=0·16);); in a pre-planned sensitivity analysis excluding patients diagnosed via antenatal care, the difference was 6·4 (95% CI, 1·2 to 11·6; p=0·017). Rate of HIV diagnosis was 0·30 (95% CI 0·11 to 0·85) per 10 000 patients per year in intervention practices versus 0·07 (0·02 to 0·20) in control practices (adjusted ratio of geometric means 4·51, 95% CI 1·27 to 16·05; p=0·021). 55% of patients in intervention practices versus 73% in control practices had CD4 count less than 350 cells per μL (risk ratio 0·75, 95% CI 0·53 to 1·07). 28% versus 46% had CD4 count less than 200 cells per μL (0·60, 0·32 to 1·13). All patients diagnosed by rapid testing were successfully transferred into specialist care. No adverse events occurred.**

Interpretation **Promotion of opt-out rapid testing in general practice led to increased rate of diagnosis, and might increase early detection, of HIV. We therefore recommend implementation of HIV screening in general practices in areas with high HIV prevalence.**

Funding **UK Department of Health, NHS City and Hackney.**

Introduction

Timely diagnosis of HIV is a major challenge. Undetected HIV and late diagnosis are associated with ill health, increased risk of death from HIV/AIDS, and onward viral transmission, constituting a substantial burden to public health budgets worldwide.[1–3] Of 107 800 people with HIV in the UK, almost one quarter are undiagnosed,[4] 42% are diagnosed late (after they should have begun antiretroviral treatment, CD4 cell count <350 cells per μL), and 24% are diagnosed very late (CD4 cell count <200 cells per μL).[4] Likewise, roughly half of the 2·2 million people with HIV in Europe and a sixth of the 1·1 million people with HIV in the USA are undiagnosed.[1,5,6]

Expansion of HIV testing is key to improving HIV outcomes. In 2008, the British HIV Association recommended universal HIV testing in primary care in areas with high prevalence (>0·2%), in addition to routine screening programmes in antenatal care and sexually transmitted infection clinics.[7] This approach was endorsed by the National Institute for Health and Clinical Excellence.[8,9] Pilot projects have shown the acceptability and feasibility of HIV testing in primary care.[10–12] However, HIV testing in these settings has not been widely adopted; there is no evidence about outcomes from robust screening trials. The US Preventative Services Task Force has noted that "no randomised trial or observational study compared clinical outcomes between adults and adolescents screened and not screened for HIV infection",[13] a conclusion also reached by the National Institute for Health and Clinical Excellence.[8,9] To our knowledge, no randomised trials have shown that HIV screening leads to increased and earlier diagnosis. This is a key evidence gap in current guidance.[14,15]

Primary care is ideally placed to offer HIV testing.[7] General practices provide health checks for newly

Lancet HIV 2015; 2: e229–35

Published Online
April 29, 2015
http://dx.doi.org/10.1016/S2352-3018(15)00059-4

See Comment page e217

*Contributed equally

Centre for Primary Care and Public Health (W Leber PhD, H McMullen MSc, N Marlin MSc, S Bremner PhD, K Boomla FRCP, S Kerry MSc, Prof A Martineau PhD, Prof C Griffiths DPhil)**, School of Law** (Prof R Ashcroft PhD)**, Queen Mary University of London, London, UK; Homerton Sexual Health Services, Homerton University Hospital NHS Foundation Trust, London, UK** (Prof J Anderson FRCP, D Millett MSc, S Mguni MSc, S Creighton FRCP)**; Department of Global Health and Development, London School of Hygiene & Tropical Medicine, London, UK** (A C Santos PhD, F Terris-Prestholt PhD)**; NHS City and Hackney, London, UK** (J Figueroa FRCPH)**; Faculty of Population Health Sciences, University College London, London, UK** (Prof G Hart PhD)**; Centre for Infectious Disease Surveillance and Control, Public Health England, London, UK** (V Delpech FPHM, A Brown PhD, G Rooney MSc)**; and Department of Virology, Barts Health NHS Trust, London, UK** (M Sampson MSc)

Correspondence to:
Dr Werner Leber, Centre for Primary Care and Public Health, Queen Mary University of London, London E1 2AB, UK
w.leber@qmul.ac.uk

Research in context

Evidence before this study

We searched PubMed for randomised controlled trials, published from Jan 1, 2000, to Jan 31, 2015, testing the effects of screening of adults for HIV in primary care compared with usual care on rate of diagnosis, CD4 count, and disease stage at diagnosis. We found no studies that met these criteria. The US Preventative Services Task Force did a similar search in 2011, as part of their evidence review to update their 2005 recommendations on HIV screening. They noted that "no randomised trial or observational study compared clinical outcomes between adults and adolescents screened and not screened for HIV infection".

Added value of this study

These findings provide, to our knowledge, the first robust evidence from a randomised study that a screening programme leads to increased rate of HIV diagnosis.

Implications of all the available evidence

Public health leaders should consider implementing screening for HIV in primary care in high prevalence areas.

registering patients and are a referral point to specialist care. HIV testing in general practice is feasible and acceptable[10–12] and might be preferable for people who would not normally attend traditional HIV testing settings such as sexual health clinics.[11]

We did a pragmatic cluster-randomised controlled trial to test the hypothesis that a multifaceted educational outreach programme promoting rapid HIV testing in general practice leads to increased and early diagnosis of HIV. We used a cluster-randomised design because the intervention was directed at practices, rather than individual patients.

Methods

Study design and participants

We did this cluster-randomised controlled trial in general practices in Hackney, a multiethnic, socioeconomically deprived inner London borough, which has the ninth highest prevalence of diagnosed HIV infection (eight patients per 1000 adults) in the UK.[1] We invited all general practices in Hackney to participate. At entry, practices offered incentivised serology testing for HIV to patients attending sexual health checks and did opportunistic serology testing when clinically indicated. Visiting midwives offered HIV screening for women receiving antenatal care. The study was approved by Camden and Islington Community Research Ethics Committee and ran from April 19, 2010, to Aug 31, 2012. An independent data monitoring committee was established.

We included patients aged 16 years (the age of consent for medical procedures in the UK) and older, who newly registered with study practices, and who were able to have a pretest discussion in English or with a suitable translator. Information sheets, available in English and eight locally spoken languages, were displayed at reception desks. The ethics committee approved a process of valid implied consent for patient participation.[12] We excluded patients who could not understand the information sheet or engage with the pretest discussion for HIV testing, and those who were HIV positive.

See Online for appendix

Randomisation and masking

Practices were randomly assigned (1:1) between April, 2010, and August, 2011, to either intervention or control, by an independent clinical trials unit statistician with use of a minimisation program (Minim, version 1.3),[16] maintaining allocation concealment. Minimisation criteria were practice list size (<5000, 5000–7000, or ≥7000 registered patients); practice deprivation (Index of Multiple Deprivation score: <47 or ≥47);[17] and male HIV testing rate (men tested between April and October, 2009/men registered×1000: less than seven or seven or more). Both total HIV testing rate and female HIV testing rate would have been confounded by the unknown contribution of antenatal HIV screening by midwives. Therefore, the male HIV testing rate offered the best representation of how actively each practice screened for HIV. Neither investigators nor clinical teams were masked to allocation.

For **Read codes** see http://systems.hscic.gov.uk/data/uktc/readcodes

Procedures

The intervention consisted of a practice-based outreach educational programme with follow-up training for a nominated HIV lead nurse or health-care assistant in each practice, integration of rapid HIV testing into the registration health check and management of reactive tests, and provision of free rapid HIV tests and payment of £10 per test completed. Control practices provided usual care only, which included an offer of serology HIV testing opportunistically and on patient request.

The educational programme was based on published clinician behaviour change strategies[18–20] together with our experience of delivering similar interventions. Initial training sessions were held at individual practices, lasted 90 min, targeted the whole practice team, and included didactic and interactive elements. Session leaders (WL, HM) were trained to ensure intervention fidelity (appendix p 1). Rapid HIV test operators completed competency-based training. An HIV lead was nominated in each practice to coordinate rapid testing and quality assurance (appendix p 2).

Registration health checks were done by a nurse or health-care assistant, who followed prompts on a template in patients' electronic health records. We added prompts to offer rapid HIV testing, linked to bespoke Read codes to record test outcomes: non-reactive, reactive, indeterminate, invalid, and test declined. Read

coding enabled remote data collection for testing activity (appendix p 2). The INSTI HIV1/HIV2 Rapid Antibody Test (bioLytical Laboratories, Canada) finger prick system was used for rapid testing.

The intervention was adaptable to each individual practice: staff could additionally offer rapid HIV testing in a range of clinical settings (eg, sexual health checks) and were encouraged to continue opportunistic HIV testing by serology. The core components of the testing process included an offer of a rapid HIV test as part of routine new registration health checks including a pretest discussion for patients to make informed decisions about testing; a rapid HIV test followed by a discussion for patients with non-reactive tests; and an immediate notification by the rapid test operator to the general practitioner of any patient with a reactive, indeterminate, or twice invalid test results with confirmatory serology sampling, and follow-up by a general practitioner (appendix p 2).

Any venous blood sample detected as reactive to HIV-1 or 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).

HIV-positive patients were referred to Homerton Hospital for specialist care. Practices implemented rapid testing immediately after the educational session. Ongoing support from the education team was available via telephone or email to practice staff for queries related to rapid testing. Control practices were informed by email about current national guidance on HIV testing. All study practices continued to provide standard care of HIV testing and were supported by a community HIV liaison nurse.

At Homerton Hospital, all patients who tested HIV positive at participating practices were allocated a unique study number. Newly diagnosed patients were distinguished from known HIV-positive patients already in care or defaulted from specialist care with the Genitourinary Medicine Clinical Activity Dataset.[21] The Homerton clinical team (JA, SM) extracted clinical record data into anonymised confidential clinical case report forms. AM, who was masked to study allocation, verified the accuracy of data extraction for all patients before data were passed to the study statistician (appendix p 4).

We generated rapid HIV antibody test result codes for the trial: EMISNQRE117 (reactive), EMISNQNO26 (non-reactive), EMISNQIN61 (indeterminate), and EMISNQIN62 (invalid). We also used the following Read codes: HIV (serology) screening test (4JR7) and rapid HIV test declined (8I3P). The Clinical Effectiveness Group at Queen Mary University of London (KP, MAS, AC, and JD) remotely extracted rapid HIV testing data and serology testing data from general practice computer systems (EMIS, Egton Medical Information Systems, UK; and Vision, In Practice Systems, UK).

Outcomes

The primary outcome was mean CD4 count of newly diagnosed patients (see appendix p 4 for a definition of a newly diagnosed patient). We included women newly diagnosed with HIV by the UK Antenatal HIV Screening Programme. We excluded patients who had not been tested for HIV before specialist referral, and patients who were referred by their general practitioner to secondary care at Homerton Hospital either for HIV testing or for further management of a suspected HIV-related illness. Secondary outcomes were rate of new HIV diagnoses (patients diagnosed/year/10 000 practice list size), percentage of patients with CD4 count less than 350 cells per µL, and percentage of patients with CD4 count less than 200 cells per µL.

The original primary outcome was the number of new HIV diagnoses. However, our initial assumptions were based on few data and the number of new diagnoses early in the study was lower than expected. Thus, on June 14, 2011, with the approval of the data monitoring committee, we recalculated statistical power with CD4 count as the primary outcome, retaining numbers of new diagnoses as the main secondary outcome.

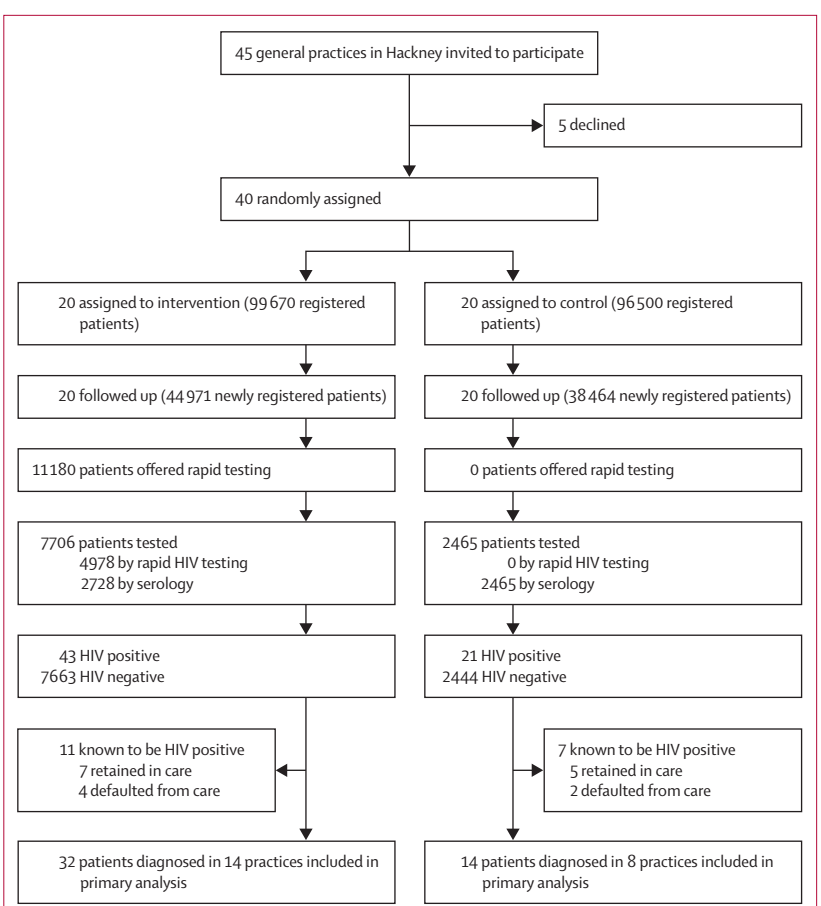

Figure: **Trial profile**

Statistical analysis

Allowing for clustering, and assuming 20 practices in each group and analysis of CD4 on the square root scale with an SD of 6 and an intracluster correlation coefficient of 0·05, we expected to identify 72 new HIV diagnoses, with 80% power and 5% significance. This would be sufficient to detect an increase in the mean CD4 count from 300 cells per µL to 470 cells per µL, corresponding to a reduction in the proportion of late presenters from 30% to 10%. We made allowances for practices to identify different numbers of patients or none at all.[22]

We compared intervention and control groups with logistic regression adjusted for clustering. We estimated the effect of the intervention on CD4 count and rate of diagnosis with a linear regression model adjusted for clustering of practices in Stata (version 12) by use of the cluster option (except for rate of diagnosis, for which we used practice summary data) and adjusted for minimisation factors.[23] We transformed CD4 count with a square root transformation and we log-transformed rate of diagnosis after adding 0·01 to zero counts. Using the intervention effect from the primary analysis and the normal distribution, we estimated the relative reduction in percentage of patients with both CD4 count less than 350 cells per µL and CD4 less than 200 cells per µL with a method developed by Peacock and colleagues.[24]

Although we originally planned an as-treated secondary analysis excluding practices that had done less than 50 tests, this was not feasible because only four practices did more than 50 tests and no patients from these practices had been diagnosed with HIV.

The UK Antenatal HIV Screening Programme offers all women in antenatal care an HIV test. We did a pre-planned sensitivity analysis excluding women diagnosed via this programme. Some HIV-positive patients had previously been diagnosed but had defaulted from specialist care: re-diagnosis in general practice therefore led to re-entry to specialist care. We did a second sensitivity analysis including such patients.

This study is registered with ClinicalTrials.gov, number ISRCTN63473710.

	Intervention practices (n=20)	Control practices (n=20)
General practices		
List size		
<5000 patients	8 (40%)	8 (40%)
5000–7000 patients	5 (25%)	5 (25%)
≥7000 patients	7 (35%)	7 (35%)
HIV testing rate in men*		
<7	13 (65%)	13 (65%)
≥7	7 (35%)	7 (35%)
Index of multiple deprivation score		
<47	11 (55%)	10 (50%)
≥47	9 (45%)	10 (50%)
Patients		
Number of registered patients	99 670	96 500
Age (years)		
16–24	15 623 (16%)	13 198 (14%)
25–34	28 200 (28%)	29 292 (30%)
35–49	31 218 (31%)	31 990 (33%)
≥50	24 629 (25%)	22 020 (23%)
Men	50 224 (50%)	48 929 (51%)
Ethnic origin		
White	40 250 (40%)	48 262 (50%)
Black	20 467 (21%)	17 690 (18%)
Asian	8487 (9%)	8002 (8%)
Mixed	3396 (3%)	4207 (4%)
Other	7134 (7%)	3562 (4%)
Unknown	19 936 (20%)	14 777 (15%)

Data are n (%). *Number of men tested April to October 2009/men registered × 1000.

Table 1: **Baseline characteristics**

Role of the funding source

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

Results

40 (89%) of 45 general practices agreed to take part (figure). The five practices that declined had similar characteristics to those that joined the study (data not shown). 20 practices were randomly assigned to intervention and 20 to control. Three practices in the intervention group withdrew during the study (one stopped offering registration health checks; one for workload reasons; and one closed), but all provided complete study data and were included in the intention-to-treat analyses. Practice and population characteristics and numbers of newly registering patients were well balanced at baseline (tables 1 and 2).

Baseline characteristics of study groups were similar for sex (p=0·742), age (p=0·0413), and ethnic origin (p=0·136). Baseline characteristics for newly registered patients were much the same in each treatment group: number of new registrants (p=0·935), sex (p=0·632), age (p=0·416), ethnic origin (p=0·136), and age (p=0·416).

Intervention practices offered 11 187 rapid tests, of which 4978 (45%) were accepted (table 3). Of these, 4964 were not reactive and 14 were reactive, including 11 that were confirmed HIV positive (true reactive) and three confirmed HIV negative (false reactive).

Overall, intervention practices identified 43 HIV-positive patients, of whom 11 had previously been diagnosed, giving a total of 32 new HIV diagnoses. Control practices identified 21 HIV-positive patients, of whom seven had previously been diagnosed, giving a total of 14 new HIV

	Intervention practices (n=20)	Control practices (n=20)
Total number of new registrants	44 971	38 464
Median number of new registrants per practice (IQR)	1379 (943–3238)	1802 (952–2732)
Age (years)		
16–24	7667 (17%)	6207 (16%)
25–34	19 491 (43%)	18 170 (47%)
35–49	10 950 (24%)	9016 (23%)
≥50	6863 (15%)	5071 (13%)
Men	20 219 (45%)	17 119 (45%)
Ethnic origin		
White	23 947 (53%)	22 365 (58%)
Black	6400 (14%)	5253 (14%)
Asian	3472 (8%)	3011 (8%)
Mixed	1296 (3%)	1442 (4%)
Other	2066 (5%)	1389 (4%)
Unknown	7790 (17%)	5004 (13%)

Data are n (%) unless stated otherwise.

Table 2: **Characteristics of newly registered patients**

	Intervention practices (n=20)	Control practices (n=20)
HIV testing		
New registrants	44 971	38 464
Patients offered rapid tests	11 187	NA
Patients accepting rapid tests	4978	NA
Patients with unreactive rapid tests	4964	NA
Patients with reactive tests	14	NA
Patients confirmed HIV positive	11	NA
Patients tested by serology test*	2728	2465
HIV diagnoses		
Total (new and previously diagnosed)	43	21
New diagnoses	32	14
By rapid testing	11	NA
By opportunistic serology	18	10
In antenatal screening	3	4
Previously diagnosed	11	7
Defaulted from care	4	2
Retained in care	7	5
Sensitivity analysis		
New diagnoses excluding antenatal screening	29	10
All new diagnoses plus those defaulted from care	36	16

Data are n. *Opportunistic testing, as part of antenatal screening, and confirmatory testing for rapid testing.

Table 3: **HIV testing and diagnoses**

diagnoses (figure, table 3). The UK Antenatal Screening Programme led to three new HIV diagnoses in intervention practices, and four in control practices.

Of the 32 newly diagnosed patients in the intervention group, 19 (59%) were men, 20 (63%) were of black African origin, and six (16%) were men who have sex with men. Of the 14 patients diagnosed in control practices, eight (57%) were men, and ten (71%) were of black African origin, and none were men who have sex with men, although we had no data for sexual orientation for three men. No adverse event occurred during the study.

CD4 count was available for 30 of 32 newly diagnosed patients from intervention practices, and in all 14 patients from control practices. Mean CD4 count was not significantly different between intervention practices and control practices (356 cells per µL [SD 254] *vs* 270 cells per µL [SD 257]; adjusted difference in square root transformed CD4 count 3·1, 95% CI –1·2 to 7·4; p=0·16; table 4). Mean CD4 count was significantly different when patients diagnosed via antenatal screening were excluded (6·4, 95% CI 1·2 to 11·6; p=0·017; table 4), and when patients who had been previously diagnosed with HIV but defaulted from care were included in the analysis (4·1, 0·0 to 8·1; p=0·049; table 4).

The rate of HIV diagnosis was 0·30 (95% CI 0·11 to 0·85) per 10 000 patients per year in the intervention group and 0·07 (95% CI 0·02 to 0·20) in the control group (adjusted ratio of geometric means 4·51, 95% CI 1·27 to 16·05; p=0·021). In a sensitivity analysis of newly diagnosed patients excluding those diagnosed during antenatal screening, the rate was 0·23 (95% CI 0·07 to 0·70) in the intervention group versus 0·04 (0·01 to 0·11) in the control group (adjusted ratio 5·88, 95% CI 1·71 to 20·17; p=0·006). For all new diagnoses plus those defaulted from care, the rates were 0·32 (0·11 to 0·91) versus 0·07 (0·02 to 0·21; ratio 4·53, 95% CI 1·25 to 16·38; p=0·023).

We estimated that 73% of patients in control practices had a CD4 count less than 350 cells per µL, compared with 55% of patients in intervention practices (risk ratio 0·75, 95% CI 0·53 to 1·07). 46% versus 28% had a CD4 count less than 200 cells per µL (risk ratio 0·60, 95% CI 0·32 to 1·13).

Discussion

We have shown that an educational outreach programme promoting opt-out rapid HIV testing of people newly registering in general practice leads to increased rates of diagnosis of HIV. Our study did not show significant differences between groups in CD4 counts at diagnosis, although diagnosis seemed to be non-significantly earlier in the intervention clinics. These are key goals of HIV-focused clinical and public health programmes. The effect of rate of diagnosis was greater in sensitivity analyses excluding women diagnosed through the UK's existing antenatal HIV screening programme. Practices used both rapid and opportunistic serology testing to make new diagnoses. A high proportion of newly diagnosed patients were of black African ethnic origin, showing successful integration of testing into a multiethnic community, recognised as a hard-to-reach

	Intervention practices (n=20)			Control practices (n=20)			Difference (95% CI)*
	Number of patients	Mean CD4 count (SD; cells per μL)†	Square root of mean CD4 count (SD)	Number of patients	Mean CD4 count (SD; cells per μL)	Square root of mean CD4 count (SD)	
New diagnoses	32	356 (254)	17·7 (6·6)	14	270 (257)	14·7 (7·7)	3·1 (–1·2 to 7·4)
All new diagnoses excluding antenatal screening	29	369 (262)	18·0 (6·7)	10	194 (169)	12·4 (6·7)	6·4 (1·2 to 11·6)
All new diagnoses plus those defaulted from care	36	411 (288)	19·0 (7·2)	16	259 (242)	14·5 (7·3)	4·1 (0·0 to 8·1)

*Calculated from square root of CD4 count and adjusted for minimisation factors. †CD4 cell count unavailable for two patients.

Table 4: **CD4 cell count of newly diagnosed patients**

population.[25] To our knowledge, this randomised trial is the first to show improvements in clinical outcomes from HIV screening.

Strengths of our study included a pragmatic real-world design that included almost all practices in the borough, improving the generalisability of our findings. Randomisation was robust, maintaining allocation concealment. Remote searching of practice computer systems ensured that data capture of testing activity and outcomes was consistent across practices. Access to test results from the regional laboratory ensured complete capture of all positive tests, minimising detection bias. The Public Health England national surveillance system enabled us to accurately distinguish between patients newly diagnosed in primary care from those who had previously tested positive. Validation of data extraction by an independent clinician, masked to allocation, of all newly diagnosed patients ensured accuracy and completeness of primary and secondary outcomes.

Our intervention was based on a successful screening intervention for tuberculosis in general practice,[18] which used various behaviour change techniques. Outreach visits, and clinician education combining mixed didactic and interactive elements, have been shown to be effective.[26] Computer prompts for testing and incentive fees might also have enhanced behaviour change.[27] A quality assurance scheme, which included competency-based training for rapid HIV testing, regular electronic monitoring of point-of-care results, and an assessment once every 2 months of staff using external control serum samples, enhanced patient safety by reducing the chances of incorrect rapid test results. All patients diagnosed by rapid testing were transferred to secondary care, showing that the links we established between general practice and specialist services were safe and effective. Some patients who had defaulted specialist care re-entered specialist services following a rediagnosis by their doctor, suggesting that primary care can play an important part in maintaining continuity of care.

A weakness of our study was that three intervention practices discontinued testing. These discontinuations are a consequence of the pragmatic study design. Nevertheless, we were able to include complete data from all practices in the analysis. Registration health checks are optional, thus only patients that attend (about 50% of all registering patients) can be offered a test. Increasing attendance at checks would increase the effect of our intervention. Although we could not mask clinical and research teams to allocation, validation of data extraction by a masked independent clinician helped ensure the validity of the study data. Our analysis accounted for differences between practices in the total list. An additional factor that could be used is the consultation rate for adult patients for each practice. Our study was potentially underpowered: increasing attendance at registration health checks would increase the effect of our intervention.

Observational studies[28] suggest that targeted community-based approaches to HIV testing achieve high uptake and a higher proportion of patients with CD4 count of more than 350 cells per μL at diagnosis. In community centres in the USA, nurse-initiated routine universal non-targeted rapid HIV testing achieved similar uptake and numbers of new diagnoses to those in our study.[29] Nurse-initiated rapid testing with streamlined counselling in primary care is feasible compared with traditional approaches.[29,30] These findings lend credibility to our results.

Our findings provide firm evidence that HIV screening in primary care leads to increased and earlier HIV diagnosis. This finding addresses a key gap in the evidence base for HIV testing, lending strong evidence in support of guideline recommendations.

Our results justify renewed efforts to implement community screening for HIV. This study builds on previous work showing that opt-out screening for tuberculosis using a multifaceted educational intervention and valid implied consent is effective in primary care.[18] Screening for multiple infectious agents in at-risk populations therefore seems justifiable.

Contributors

CG had the original idea for the study. WL, HM, CG, JA, SC, DM, SM, JF, GH, RA, KB, SB, SK, ACS, FT-P, and MS designed the study. WL, HM, DM, SC, JA, and CG trained and educated general practice staff. WL, HM, and MS undertook the quality assurance. SK and NM did the statistical analyses. RA provided advice on ethical aspects of the trial, including data management and data protection. AM completed data quality assurance checks. VD, AB, and GR validated HIV diagnoses data. WL and CG wrote the first draft of the report with input from ACS, HM, JA, SK, SB, JF, AM, VD, and FT-P. All authors have seen and approved the final version of the report.

Data monitoring committee
Claudia Estcourt, Karen Smith, Jill Zelin.

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

Acknowledgments
This study was funded by the UK Department of Health, and NHS City and Hackney. We thank all participants and general practices. We thank Keith Prescott, Arun Chinnaraj, Martin A Sharp, and Jack Dunne (Clinical Effectiveness Group, Queen Mary University of London, UK) for the extraction of demographic and HIV testing data. We are grateful to Damilola Awosika for her assistance in collating data of newly diagnosed patients. Many thanks to Clare Rutterford for the practice randomisation and for doing quality checks on the final analysis.

References

1 Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas. *HIV AIDS Surveill Rep* 2013; 25.
2 Gebo KA, Fleishman JA, Conviser R, et al. Contemporary costs of HIV healthcare in the HAART era. *AIDS* 2010; **24:** 2705–15.
3 Stover J, Korenromp EL, Blakley M, et al. Long-term costs and health impact of continued global fund support for antiretroviral therapy. *PLoS One* 2011; **6:** e21048.
4 Public Health England. HIV in the United Kingdom: 2014 report. London: Public Health England, 2014.
5 Hamers FF, Phillips AN. Diagnosed and undiagnosed HIV-infected populations in Europe. *HIV Med* 2008; **9** (suppl 2)**:** 6–12.
6 WHO Regional Office for Europe. HIV/AIDS. Copenhagen: World Health Organisation, 2014.
7 British HIV Association. UK National Guidelines for HIV testing. London: British HIV Association, 2008.
8 National Institute for Health and Care Excellence. Increasing the uptake of HIV testing to reduce undiagnosed infection and prevent transmission among men who have sex with men. London: National Institute for Health and Care Excellence, 2011.
9 National Institute for Health and Care Excellence. Increasing the uptake of HIV testing to reduce undiagnosed infection and prevent transmission among black African communities living in England. London: National Institute for Health and Care Excellence, 2011.
10 Health Protection Agency. Time to Test for HIV: expanding HIV testing in healthcare and community services in England. London: Health Protection Agency, 2011.
11 Prost A, Griffiths CJ, Anderson J, Wight D, Hart GJ. 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:** 326–29.
12 Rayment M, Thornton A, Mandalia S, et al. HIV testing in non-traditional settings—the HINTS study: a multi-centre observational study of feasibility and acceptability. *PLoS One* 2012; **7:** e39530.
13 Chou R, Selph S, Dana T, et al. Screening for HIV: systematic review to update the 2005 U.S. Preventive Services Task Force recommendation. *Ann Intern Med* 2012; **157:** 706–18.
14 Paltiel AD, Weinstein MC, Kimmel AD, et al. Expanded screening for HIV in the United States–an analysis of cost-effectiveness. *N Engl J Med* 2005; **352:** 586–95.
15 Yazdanpanah Y, Perelman J, DiLorenzo MA, et al. Routine HIV screening in Portugal: clinical impact and cost-effectiveness. *PLoS One* 2013; **8:** e84173.
16 Evans S, Royston P, Day S. Minim: allocation by minimisation in clinical trials. 2013. http://www-users.york.ac.uk/~mb55/guide/minim.htm (accessed Jan 6, 2010).
17 Department of Communities and Local Government. The English Indices of Deprivation 2008. London: UK Government, 2009.
18 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:** 1528–34.
19 O'Brien MA, Rogers S, Jamtvedt G, et al. Educational outreach visits: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2007; CD000409.
20 Forsetlund L, Bjorndal A, Rashidian A, et al. Continuing education meetings and workshops: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2009; CD003030.
21 Public Health England. Genitourinary medicine clinic activity dataset (GUMCADv2). 2013. https://www.gov.uk/genitourinary-medicine-clinic-activity-dataset-gumcadv2 (accessed April 30, 2013).
22 Eldridge SM, Ashby D, Kerry S. Sample size for cluster randomized trials: effect of coefficient of variation of cluster size and analysis method. *Intl J Epidemiol* 2006; **35:** 1292–300.
23 Kahan BC, Morris TP. Improper analysis of trials randomised using stratified blocks or minimisation. *Stat Med* 2012; **31:** 328–40.
24 Peacock JL, Sauzet O, Ewings SM, Kerry SM. Dichotomising continuous data while retaining statistical power using a distributional approach. *Stat Med* 2012; **31:** 3089–103.
25 Prost A, Elford J, Imrie J, Petticrew M, Hart GJ. Social, behavioural, and intervention research among people of Sub-Saharan African origin living with HIV in the UK and Europe: literature review and recommendations for intervention. *AIDS Behav* 2008; **12:** 170–94.
26 Flodgren G, Eccles MP, Shepperd S, Scott A, Parmelli E, Beyer FR. An overview of reviews evaluating the effectiveness of financial incentives in changing healthcare professional behaviours and patient outcomes. *Cochrane Database Syst Rev* 2011; CD009255.
27 Shojania KG, Jennings A, Mayhew A, Ramsay CR, Eccles MP, Grimshaw J. The effects of on-screen, point of care computer reminders on processes and outcomes of care. *Cochrane Database Syst Rev* 2009; CD001096.
28 Suthar AB, Ford N, Bachanas PJ, et al. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. *PLoS Med* 2013; **10:** e1001496.
29 Anaya HD, Butler JN, Solomon JL, et al. Implementation of nurse-initiated rapid HIV testing at high-prevalence primary care sites within the U.S. Veterans Affairs Health Care System. *Sex Transm Dis* 2013; **40:** 341–45.
30 Sanders GD, Anaya HD, Asch S, et al. Cost-effectiveness of strategies to improve HIV testing and receipt of results: economic analysis of a randomized controlled trial. *J Gen Intern Med* 2010; **25:** 556–63.