

# Poor uptake of primary healthcare registration among recent entrants to the UK: a retrospective cohort study

Helen R Stagg,<sup>1</sup> Jane Jones,<sup>2</sup> Graham Bickler,<sup>3</sup> Ibrahim Abubakar<sup>1,4</sup>

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<sup>1</sup>TB Section, Respiratory Diseases Department, Health Protection Services, Health Protection Agency, Colindale, UK

<sup>2</sup>Travel and Migrant Health Section, Respiratory Diseases Department, Health Protection Services, Health Protection Agency, Colindale, UK

<sup>3</sup>South East Region, Health Protection Agency, London, UK

<sup>4</sup>Norwich Medical School, University of East Anglia, Norwich, UK

## Correspondence to

Professor Ibrahim Abubakar; [ibrahim.abubakar@hpa.org.uk](mailto:ibrahim.abubakar@hpa.org.uk)

## ABSTRACT

**Objectives:** Uptake of healthcare among migrants is a complex and controversial topic; there are multiple recognised barriers to accessing primary care. Delays in presentation to healthcare services may result in a greater burden on costly emergency care, as well as increased public health risks. This study aimed to explore some of the factors influencing registration of new entrants with general practitioners (GPs).

**Design:** Retrospective cohort study.

**Setting:** Port health screening at Heathrow and Gatwick airports, primary care.

**Participants:** 252 559 new entrants to the UK, whose entry was documented by the port health tuberculosis screening processes at Heathrow and Gatwick. 191 had insufficient information for record linkage.

**Primary outcome measure:** Registration with a GP practice within the UK, as measured through record linkage with the Personal Demographics Service (PDS) database.

**Results:** Only 32.5% of 252 368 individuals were linked to the PDS, suggesting low levels of registration in the study population. Women were more likely to register than men, with a RR ratio of 1.44 (95% CI 1.41 to 1.46). Compared with those from Europe, individuals of nationalities from the Americas (0.43 (0.39 to 0.47)) and Africa (0.74 (0.69 to 0.79)) were less likely to register. Similarly, students (0.83 (0.81 to 0.85)), long-stay visitors (0.82 (0.77 to 0.87)) and asylum seekers (0.46 (0.42 to 0.51)) were less likely to register with a GP than other migrant groups.

**Conclusions:** Levels of registration with GPs within this selected group of new entrants, as measured through record linkage, are low. Migrant groups with the lowest proportion registered are likely to be those with the highest health needs. The UK would benefit from a targeted approach to identify the migrants least likely to register for healthcare and to promote access among both users and service providers.

## INTRODUCTION

The Office of National Statistics estimates that 567 000 migrants were documented as entering the UK for a year or more between January and December 2009 and 575 000

## ARTICLE SUMMARY

### Article focus

- Previous studies have suggested that access to health services for refugees and asylum seekers is difficult.
- There are limited data on access to primary care among other migrant groups.
- This study aimed to explore some of the factors influencing registration of new entrants with GPs.

### Key messages

- Our study indicates that less than a third (32.5%) of new entrants who are eligible for tuberculosis screening at ports register with a GP.
- Registration rates need to be improved by targeting resources to particular subgroups (eg, students and asylum seekers) and increasing awareness of eligibility for primary care among both migrants and GPs.

### Strengths and limitations of this study

- Previous studies have largely focused on asylum seekers and refugees, whereas we examined a range of migrant groups.
- Primary care registration uptake may have been underestimated for those who migrated to Scotland or Northern Ireland, although these individuals represented only a small proportion (2.7%) of our data set.
- Port health services only screen entrants from countries with a high incidence of tuberculosis; thus, our results are not generalisable beyond these countries. However, these populations are likely to represent those with the greatest health needs.

between January and December 2010.<sup>1 2</sup> During this time period, the top eight non-UK countries of birth of migrants remained the same: India, Poland, Pakistan, Ireland, Germany, South Africa, Bangladesh and the USA.<sup>3 4</sup> Although the majority of new entrants to the UK are likely to be young and healthy, certain groups are at higher risk of infectious diseases. The risk of communicable and chronic diseases differs by country of origin, so primary care services need to tailor individual care to the conditions that

each new entrant is most likely to suffer from. Ensuring that new entrants to the UK access healthcare services while resident in the country is essential to avoid delayed treatment of transmissible conditions, which can impact upon the health of population groups with social or domestic contact with new entrants.

Certain forms of healthcare are provided free to all entrants, including immediately necessary treatment from Accident and Emergency departments or walk-in centres, treatment for certain communicable diseases, family planning services and compulsory psychiatric treatment.<sup>5</sup> Furthermore, general practitioners (GPs) may, at their discretion, register all persons who apply to them.<sup>5</sup> However, not all those entering the country will access the services available as a result of uncertainties surrounding their entitlements, a perceived lack of need for healthcare or fears about an overlap between health and immigration services.<sup>6 7</sup> Cultural and linguistic barriers can also have detrimental effects, but problems with access may also be service provider related, particularly as recent migrants may be perceived to be greater than average primary care users.<sup>6 8 9</sup> Delayed access, for whatever reason, may shift the burden of care onto inpatient and emergency services, often at a greater expense than primary and secondary outpatient care.<sup>10 11</sup> A lack of registration with primary care provides a barrier to being referred to other healthcare services and limits exposure to the health promotional resources often found in GP surgeries.

We sought to explore the factors that influenced registration with primary healthcare services using a data set of individuals screened by port health teams at Gatwick and Heathrow airports for tuberculosis between June 2009 and November 2010, linked to the Personal Demographics Service (PDS). Identification of the factors that influence registration could lead to (1) better targeting of awareness-raising efforts designed to encourage new entrants to register upon entering the UK and (2) improved knowledge among healthcare providers of the rights of new entrants to register. Ultimately, promoting earlier presentation to healthcare services may save NHS resources.

## METHODS

We undertook a retrospective cohort study, following STROBE guidelines.<sup>12</sup> A database of all individuals screened for tuberculosis by chest x-ray at Gatwick or Heathrow port health services between 10 June 2009 and 10 November 2010 (252 559 records) was linked to the PDS database (August 2011) of NHS registrations in England and Wales. Thus, the most recent migrants in our data set had a minimum of 9 months to register in order to be found in the PDS. Individuals were selected for screening as they were subject to immigration controls into the UK, staying for more than 6 months and from a country with high rates of tuberculosis. Individuals are subject to immigration control if they are not nationals of the UK, Ireland, Channel Islands, Isle of

Man, another country in the European Economic Area or Switzerland and also have not been given permission to stay as refugees or a permanent right to remain.<sup>13</sup> The Demographics Batch Service undertakes the automatic linking of records to the PDS by first name, surname, gender and date of birth. The potential for the reversal of first names and surnames during record compilation was compensated for by linking both fields to each other. Exact linking of names, gender and dates of birth that is not sensitive to case is performed. Spaces and punctuation are included in the linking traces. Records with multiple links were included in the data set as single linked records, as we required a yes/no linking outcome. Eighty-two thousand one hundred and fifteen records were linked and 170 253 not linked; 191 records had insufficient information for linking.

The outcome of interest was registration with a GP practice. Exposure variables included age, gender, nationality, immigration status and year of entry. These variables were collected by the port health team at the time of screening from the individual and their travel documents. The nationality of individuals was classified into world regions by WHO standards. When 'UK-Europe', 'UK-Hong Kong' or 'UK-India' was recorded, individuals were classified into the same categories as other European nationals, individuals from Hong Kong or India, respectively. Four age groups were created: 16 and under (children), 16-30 (young adults), 30-65 (adults) and 65 or more (older individuals). A single immigration variable was generated from visa information—entrants were divided into students and their dependants (collectively 'students'), refugees/asylum seekers/detainees and their dependants (collectively 'asylum seekers'), long-stay visitors and 'other', which in the majority represented individuals entering with work visas and their dependants.

Generally, few variables were missing; the greatest proportion was in the nationality field (4.0% of 252 368). Univariate analysis was undertaken and a stepwise forward technique (predefining gender and age) used to assess which variables to include in the final model. All variables were significant and thus included. Age was non-linear. Sensitivity analysis was carried out on 2009 data alone, excluding detainees, or excluding individuals in the 'other' category who were not clearly designated as having a work visa or being a dependant of someone who did. Analysis was undertaken in STATA V.11 (StataCorp).

## RESULTS

Of the 252 559 original records of individuals screened by port health tuberculosis services, 191 (0.08% of 252 559) were excluded due to having insufficient data for linking, leaving 252 368 for the descriptive analysis (82 115 linked and 170 253 not linked). Ten thousand nine hundred and fifty records had missing information, thus 241 418 were included in the regression model (79 206 linked and 162 212 not linked).

Of the new entrants screened for tuberculosis who met our inclusion criteria, the majority were men (56.7% of 252 368), between 16 and 30 years of age (71.0% of 252 368), of Southeast Asian nationality (48.3% of 252 368) and students or their dependants (65.4% of 252 368) (table 1). The gender and age distributions seen in our data were similar to those documented by the Office for National Statistics (ONS) in 2009 and 2010, albeit with more males in their teens and early twenties in 2009.<sup>14</sup> This may reflect the differing criteria for defining an immigrant between the two studies—a 6-month stay is required for screening by the port health service and 12 months by ONS. Very few new entrants were asylum seekers or their dependants (1.2% of 252 368).

Less than a third (32.5%) of the 252 368 individuals analysed were linked to the PDS, suggesting low levels of registration with a GP within this study sample. A higher proportion of women were linked than men (36.5% of 109 391 and 29.5% of 142 977, respectively) (table 2). A greater proportion of individuals who entered in 2009 had registered than those who entered in 2010. Individuals of a nationality from the Americas had the lowest

proportion linked of all the world regions (table 2). The age group with the lowest proportion linked was the over 65s (23.6% of 1376). Asylum seekers and their dependants had the lowest proportion linked of all the migrant groups (19.1% of 3071).

Within the entire data set, women were more likely to register than men (RR ratio 1.44 (95% CI 1.41 to 1.46),  $p < 0.005$ ) (table 3, multivariable model). Anyone over 16 years of age was less likely to register, particularly the over 65s (0.51 (0.45 to 0.59), Wald  $p$  value  $< 0.005$ ). Individuals of nationalities from the Americas were the least likely group to register (0.43 (0.39 to 0.47), Wald  $p$  value  $< 0.005$ ). Southeast Asian nationalities were significantly more likely to register than Europeans (1.41 (1.33 to 1.50), Wald  $p$  value  $< 0.005$ ). Asylum seekers and their dependants (0.46 (0.42 to 0.51), Wald  $p$  value  $< 0.005$ ) were less likely to register than other immigration categories.

As year of entry was associated with registration in the multivariable model, reflecting the fact that individuals entering the UK in 2010 had less time to register, sensitivity analysis was performed solely on 2009 data. This multivariable analysis demonstrated similar trends, confirming the validity of our conclusions. The system for detainees to access healthcare may be different from that of other individuals within the asylum seeker category, thus sensitivity analysis excluding them from the data set was also undertaken. These individuals made up a very small proportion of the overall linked data set (0.5% of 252 368); exclusion did not appreciably alter our findings. Finally, exclusion of individuals not clearly designated as having a work visa or as dependants of individuals with work visas from the ‘other’ category of immigration status also did not significantly alter our conclusions.

**Table 1** Descriptive analysis of screened new entrants 2009–2010

Exposure variables	Overall	
	N	% (column)
Age (years)		
0–16	21 027	8.3
16–30	179 087	71.0
30–65	50 868	20.2
65+	1376	0.5
Missing	10	0.0
Year of entry		
2009	101 655	40.3
2010	150 713	59.7
Missing	0	0.0
Gender		
Male	142 977	56.7
Female	109 391	43.3
Missing	0	0.0
World region of nationality		
Europe	5194	2.1
Africa	27 443	10.9
Americas	5879	2.3
Eastern Med	27 552	10.9
Southeast Asia	121 885	48.3
Western Pacific	54 222	21.5
Stateless	38	0.0
Missing	10 155	4.0
Immigration status		
Other	77 630	30.8
Student	165 022	65.4
Asylum seeker	3071	1.2
Long-stay visitor	5751	2.3
Missing	894	0.4

Overall total 252 368.  
N, number in category; %, column percentage.

## DISCUSSION

### Principal findings and comparison with other studies

Although there is a body of literature on the barriers to accessing healthcare among refugees, asylum seekers and detainees,<sup>15–20</sup> relatively little has been published on access among migrants who do not fit into these categories.<sup>6 8 21 22</sup> European and global reviews of migrant access to healthcare, although often hampered by difficulties comparing between countries, have provided a varied picture, but have recommended assessing the impact of immigration status and ethnicity, as well as instigating policies that adequately respond to these differences.<sup>9 23–26</sup>

We linked data from the port health tuberculosis screening service between June 2009 and November 2010 to the PDS in order to explore some of the factors influencing registration with GP practices. Our results showed that only 32.5% of 252 368 individuals had registered. The proportion of migrants registered in this study is very low compared with other estimates of registration among migrants. For example, the Patient Register Data Service provided by NHS Connecting for

**Table 2** Descriptive analysis of screened new entrants 2009–2010, by linking results

Exposure variables	Unlinked		Linked	
	N	% (row)	N	% (row)
Age (years)				
0–16	13 598	64.7	7429	35.3
16–30	121 486	67.8	57 601	32.2
30–65	34 108	67.1	16 760	32.9
65+	1051	76.4	325	23.6
Missing	10	100.0	0	0.0
Year of entry				
2009	65 788	64.7	35 867	35.3
2010	104 465	69.3	46 248	30.7
Missing	0	0.0	0	0.0
Gender				
Male	100 815	70.5	42 162	29.5
Female	69 438	63.5	39 953	36.5
Missing	0	0.0	0	0.0
World region of nationality				
Europe	3625	69.8	1569	30.2
Africa	20 736	75.6	6707	24.4
Americas	4929	83.8	950	16.2
Eastern Med	18 924	68.7	8628	31.3
Southeast Asia	77 160	63.3	44 725	36.7
Western Pacific	37 336	68.9	16 886	31.1
Stateless	25	65.8	13	34.2
Missing	7518	74.0	2637	26.0
Immigration status				
Other	49 406	63.6	28 224	36.4
Student	113 821	69.0	51 201	31.0
Asylum seeker	2483	80.9	588	19.1
Long-stay visitor	3955	68.8	1796	31.2
Missing	588	65.8	306	34.2

170 253 individuals were unlinked and 82 115 were linked.

N, number in category; %, row percentage linked or unlinked as a proportion of overall numbers in subcategory.

Health compiles yearly data on Flag 4s for ONS. Flag 4s mark an individual who has registered with a GP in England and Wales as previously living overseas. This includes UK nationals whose previous address was outside the UK and non-UK nationals entering the England or Wales for the first time. From August 2009 to July 2010, 622 178 Flag 4s were registered in England and Wales; 572 000 long-term (for more than a year) migrants entered the UK between July 2009 and June 2010.<sup>27 28</sup> Thus, during similar time frames, ONS data suggest that there were comparable numbers of new entrants and new registrants with a previous overseas address. This might indicate that registration of new entrants is generally high and is in distinct contrast to our data. However, in comparison to ONS data, we have sought to link the records of individuals entering the country directly to GP registrations. Additionally, the individuals included in this study were from a particular section of new entrants (those screened for tuberculosis) who are nationals of countries with a high burden of tuberculosis. The two apparently conflicting indications may therefore be compatible, that is, registration of new entrants may be generally high, but much lower in certain at-risk groups. Indeed, a proportion of those with

Flag 4s are UK citizens who have lived abroad (or are nationals from high-income countries), thus their inclusion with non-UK-born migrants may mask underlying trends. Approximately 15% of long-term migrants to the UK are known to be British.<sup>28</sup>

Furthermore, although linking may underestimate the number of identical individuals in both databases, this should be a more accurate method than simply counting registrations, as indicated by recent research.<sup>29</sup> Previous studies that have surveyed a cross section of GP registrations among users of other healthcare services have indicated higher levels of GP registration (68.8%–89.2%), likely reflecting a greater time spent living in the UK and increased health-seeking behaviour.<sup>21 22</sup> The low level of GP registration found in this study is particularly interesting, given the relatively broad access to primary healthcare currently available for most migrants to the UK, albeit at the discretion of the practitioner.

The study is unable on its own to provide a satisfactory explanation for its findings but they may be, in part, related to the nature of the selected study group. The individuals screened may represent a population less aware of their healthcare rights in the UK who face service-related barriers to access at the local level,



**Table 3** Univariate and multivariable regression of screened new entrants 2009–2010

Exposure variables	Univariate		Multivariable	
	RRR (95% CI)	p Value	RRR (95% CI)	p Value
Age (years)				
0–16	1	<0.005	1	<0.005
16–30	0.87 (0.85 to 0.90)		0.90 (0.87 to 0.93)	
30–65	0.90 (0.87 to 0.93)		0.91 (0.88 to 0.95)	
65+	0.56 (0.50 to 0.64)		0.51 (0.45 to 0.59)	
Year of entry				
2009	1	<0.005	1	<0.005
2010	0.82 (0.81 to 0.84)		0.80 (0.79 to 0.82)	
Gender				
Male	1	<0.005	1	<0.005
Female	1.37 (1.35 to 1.40)		1.44 (1.41 to 1.46)	
World region of nationality				
Europe	1	<0.005	1	<0.005
Africa	0.75 (0.70 to 0.80)		0.74 (0.69 to 0.79)	
Americas	0.44 (0.41 to 0.49)		0.43 (0.39 to 0.47)	
Eastern Mediterranean	1.05 (0.99 to 1.12)		1.11 (1.04 to 1.18)	
Southeast Asia	1.34 (1.26 to 1.42)		1.41 (1.33 to 1.50)	
Western Pacific	1.05 (0.98 to 1.11)		1.05 (0.99 to 1.12)	
Stateless	1.20 (0.61 to 2.36)		1.53 (0.77 to 3.04)	
Immigration status				
Other	1	<0.005	1	<0.005
Student	0.80 (0.78 to 0.81)		0.83 (0.81 to 0.85)	
Asylum seeker	0.42 (0.38 to 0.46)		0.46 (0.42 to 0.51)	
Long-stay visitor	0.80 (0.75 to 0.84)		0.82 (0.77 to 0.87)	

p Values quoted represent likelihood ratio test across entire category. RRR, RR ratio.

including the variable methods used by GP practices to identify and register overseas visitors versus individuals who are ordinarily resident.<sup>8</sup> Cultural and linguistic factors might also play a part for both users and service providers, and some migrants might be disinclined to engage with health services because of concerns related to their immigration status.<sup>6 7</sup> In this study, those of male gender, from Africa or the Americas or over 65 years of age were much less likely to register, as were students, and asylum seekers and their dependants. Men are generally recognised to be lower users of primary healthcare than women.<sup>30</sup> Differences by world region may reflect expectations of the UK health system, based on previous experiences in an individual's country of origin. Younger migrants (eg, students, who had an average age in our data set of 24 years) might also be expected to have a lower registration rate associated with a reduced need for healthcare. Indeed, the 'healthy migrant' effect, hypothesising that only the healthiest individuals migrate, has been well described.<sup>31–33</sup> Young individuals may additionally delay registration until they have a need for healthcare. However, the lowest rates of registration in this study were in people over 65 years, who might be expected to have the highest healthcare needs. Previous studies have documented that elderly migrants are just as likely to access a GP as their British-born counterparts, but did not specifically select recent entrants.<sup>34</sup> Other

studies have noted that refugees and asylum seekers are frequently not registered with a GP.<sup>21</sup>

### Limitations

In discussing the implications of our results, some limitations of the study need to be considered. The PDS records registration with the NHS in England and Wales, thus individuals registering in Scotland and Northern Ireland will not have been linked. However, only 2.7% (6848 of 252 368) of new entrants registered an intended address outside England and Wales, so the impact is likely to be minimal. A destination address was missing for 30.7% of records (77 574 of 252 368), but 32.3% of these were linked during our analysis, that is, an almost identical proportion to the overall linking rate. Our data will not include undocumented migrants, who represent the most vulnerable proportion of the new entrant population and who are the least likely to gain access to services. This will have likely led to an overestimate of the proportion of total migrants registered. On the other hand, nationals of high-income countries are unlikely to have been included in this study (although some Western Europeans were screened), which would have biased the results in the opposite direction. Our results will also not include short-term 'health tourists', although these visits may present only a minimal economic burden.<sup>35</sup> Service data show that not all eligible new entrants are screened, partly due to the

variable caseload at screening facilities (which may have resulted in selection bias towards certain groups of migrants), for example, during the peak season for student entry. Notably, port health services screened 165 658 individuals between July 2009 and June 2010, that is, 29% of the migrants chartered by the ONS.<sup>28</sup> It should be noted, however, that long-term migrants enter for at least 12 months by ONS standards, but entry for 6 months or more results in eligibility to be screened.

Our results are not generalisable beyond entrants from countries with high tuberculosis incidence (usually low- and middle-income countries). Nevertheless, these are likely to be the very populations with the highest healthcare needs. A study on the same data set, but restricted to migrants entering between June 2009 and September 2010, has demonstrated that <0.5% had screening results suggestive of active tuberculosis.<sup>36</sup> As this is a very small proportion of our data set, it is unlikely that these individuals would have biased our results by increasing the likelihood of their registration due to concerns surrounding their health.

Individuals entering in 2010 will have had less time to register than their counterparts in 2009. To ensure that our analysis was not biased by the relatively short time frame available for registration following arrival in the UK, we performed a sensitivity analysis using 2009 data alone, which gave very similar results (with a small increase in the proportion of people registered, from 30.7% of 150 713 in 2010 to 35.3% of 101 655 in 2009). We excluded individuals for whom migration status was unknown. Sensitivity analysis was also performed to exclude detainees, who may have variable routes to access healthcare, and individuals not clearly designated to have had a work permit or as the dependant of someone who did. Neither of the analyses appreciably altered our results. Inevitably, the linking process will not have perfectly identified all the individuals who registered for care due to incorrect recording of personal details. Using a linking technique that did not rely on exact links may have improved our results. However, both during port health screening and upon registering with a GP, individuals are likely to have presented a form of identification; reading these documents should have reduced the likelihood of typographical errors. Nevertheless, even if linking only succeeded in identifying 50% of those registered, our results would suggest that a large proportion of migrants in the particular risk group studied do not access primary care services. It would be instructive to determine how long individuals took to register and what initiates registration, but this information was not available. Furthermore, registration with a GP indicates an intention to access healthcare services but not the extent of that access; ultimately, healthcare use can be a more significant indicator.

### Implications of findings

While we are unable to determine from this study the reasons why certain groups of migrants have low registration rates, we might hypothesise that this is likely to be

due to a combination of patient- and service-related factors. The UK would benefit from a targeted approach to identify the migrants least likely to register for healthcare and promote their access among both users and service providers. However, registration is only the first step for adequate provision of healthcare.<sup>6</sup> Supporting practitioners is particularly crucial, especially given the autonomy of GPs in registering patients. The Health Protection Agency maintains a free to use online Migrant Health Guide, which brings together a range of guidelines, information and resources that a busy practitioner looking after migrant patients can access during a standard consultation.<sup>37</sup> It provides detailed information on a country-specific basis so that practitioners can tailor healthcare to the needs of an individual patient and assists practitioners in performing an expanded 'new patient check'.<sup>38</sup>

If new entrants do not register for primary care, they are not exposed to the awareness-raising and case-finding campaigns that often target specific vulnerable population groups via GP surgeries. Screening programmes in primary care have proved successful for tuberculosis and may be extended beyond pilot studies for post-entry screening for latent infection and active disease.<sup>39</sup> Case finding could also be undertaken for other infectious diseases, such as HIV and hepatitis C, as well as conditions such as diabetes. Delayed diagnosis of HIV, rates of which will be high in many of the countries of origin of the new entrants included in this data set, has been shown to significantly shorten life expectancy.<sup>40</sup> Clearly case-finding interventions will be ineffective, and excessively costly, if the majority of migrants are not registered for primary care services and thus cannot be approached.

### Conclusions and future research

By improving the access of migrant patients to primary healthcare delayed presentation, transmission risks and the burden on emergency services should be decreased. Further research on the mechanisms that best improve the proportion of migrants registering with GPs and the speed with which they do would be advantageous, for example, prospective cohort studies of publicity surrounding welcome health checks, lists of GP practices provided by local councils, employers or after successfully receiving a visa.<sup>41</sup> Furthermore, the effect of highlighting the eligibility rights of new migrants with GP practices (eg, via the Health Protection Agency's Migrant Health Guide),<sup>37</sup> in order to ensure that migrants are not erroneously turned away by active or passive discrimination, should be trialled.<sup>8</sup> Such research could inform international governments of mechanisms to ensure that they operate the 'migrant-sensitive health policies' that the World Health Assembly called for in 2008.<sup>42</sup>

**Contributors** HRS and IA designed the study. The Demographics Batch Service undertook the matching of records via the Health Protection Agency. HRS carried out the analysis and wrote the manuscript, with input from all authors. All authors, external and internal, had full access to all the data (including

statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. IA is the guarantor of this work.

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**Competing interests** None.

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	<b>Item No</b>	<b>Recommendation</b>
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract <i>p1, lines 1-2</i> (b) Provide in the abstract an informative and balanced summary of what was done and what was found <i>p2, lines 2-24</i>
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported <i>p3, lines 2-26</i>
Objectives	3	State specific objectives, including any prespecified hypotheses <i>p3, lines 28-34</i>
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper <i>p4, lines 2-17</i>
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection <i>p4, lines 2-11</i>
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed <i>(a-b) p4, lines 2-17</i>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable <i>p4, lines 20-30</i>
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group <i>p4, lines 20- p5, line 2</i>
Bias	9	Describe any efforts to address potential sources of bias <i>Potential bias covered in discussion</i>
Study size	10	Explain how the study size was arrived at <i>p4, lines 1-18</i>
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why <i>p4, lines 16-27</i>
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses <i>(a-e) p4, lines 32- p5, line2</i>
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed



		(b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram <i>(a-c) p6 lines 2-5</i>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount) <i>(a-c) p6 line 7- p6 line 13</i>
Outcome data	15*	Report numbers of outcome events or summary measures over time <i>p6 lines 2-5</i>
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <i>(a-c) p7 line 1-10, tables 2 and 3</i>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <i>p8, lines 2- p9, line 10</i>
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives <i>p10 line 10-25</i>
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias <i>p11 line 27-p12 line 33</i>
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence <i>p12 line 35- p 13 line 19</i>
Generalisability	21	Discuss the generalisability (external validity) of the study results <i>p12 line 9-16</i>
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based <i>p14, lines 13-15</i>

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.