Vaccine 28 (2010) 4588–4592

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Measles in the United Kingdom 1990–2008 and the effectiveness of measles vaccines

Hershel Jick*, Katrina Wilcox Hagberg

Boston Collaborative Drug Surveillance Program, Boston University School of Medicine, 11 Muzzey Street, Lexington, MA 02421, USA

ARTICLE INFO

Article history:
Received 30 June 2009
Received in revised form 12 April 2010
Accepted 28 April 2010
Available online 12 May 2010

Keywords:
Measles
MMR
Vaccination

ABSTRACT

We identified all children in the UK General Practice Research Database diagnosed with measles from 1990 to 2008 and calculated annual incidence according to age and geographic region by dividing the number of cases per year by the number of children who were active in the population. We evaluated the effectiveness of the measles vaccines by comparing the vaccination histories of children who were diagnosed with measles (cases) to children who were not (controls). The annual incidence of measles fell after the introduction of the MMR vaccine in late 1988. However, a modest outbreak of measles occurred in 1994, leading to large nationwide programs to immunize children. Since 1996, the incidence of measles has fallen by more than 80%. Prior measles vaccination is highly effective and has substantially reduced the risk of measles.

1. Introduction

From 1950 through 1968, the annual number of notified cases of measles in the United Kingdom (UK) varied from about 100,000 to 800,000 [1]. In 1968, routine immunization of children with one dose of a single measles vaccine was begun [1]. From 1968 to 1988 the number of notified cases of measles rapidly fell to a level of about 30,000 per year [1].

In October 1988, a comprehensive campaign of vaccination with combined measles, mumps, and rubella (MMR) vaccine was initiated, and in 1989 about 900,000 children age 12–35 months were vaccinated in the UK [2]. This campaign also provided MMR for over 800,000 children age 3–9 years [2]. Despite the early program of single measles vaccine, as well as the 1988 nationwide immunization with MMR, a modest outbreak of measles occurred in 1994 [1,3,4]. This led to a supplemental program of immunization with a vaccine against measles-rubella (MR) [1,3,4], as well as MMR, even though at that time the MMR vaccine was reported to be in short supply [1,3].

In this paper we describe, in detail, the incidence of measles in the UK and the effectiveness of the measles vaccines given prior to and after the 1994 measles outbreak.

2. Materials and methods

2.1. Data source

The study was based on information derived from the General Practice Research Database (the Database), a large automated UK medical record database. The source population for the study is some 3 million people enrolled in about 350 general practices since 1988. The size of the population is stable over time according to age, gender and general practice. The comprehensive nature of the information on clinical diagnoses and drug exposure recorded in this subset of the Database have been repeatedly validated and found to be of high quality for the purpose of conducting epidemiologic research [2,5–8]. The general practitioners (GPs), who contribute data to the Database use office computers in their routine practice, agreed to provide the data for research purposes, and have been trained to record medical information including demographic data, medical diagnoses, details of hospital stays, and deaths, in a standard, anonymous format. The GPs routinely record the administration of vaccines. Diagnoses, physical findings, symptoms, and administrative events such as referrals to specialists are recorded by using Oxford Medical Information System (OXMIS) or Read codes. All information we receive is anonymized.

The distribution of age, gender, and geography in the practices that contribute to the Database is closely similar to that of the UK except that London is somewhat underrepresented [9]. The UK population has been divided into regions by the Database group at the Medicines and Healthcare Products Regulatory Agency (MHRA) which is responsible for the data collection and storage.

* Corresponding author.
E-mail address: hjick@bu.edu (H. Jick).

0264-410X/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.vaccine.2010.04.084

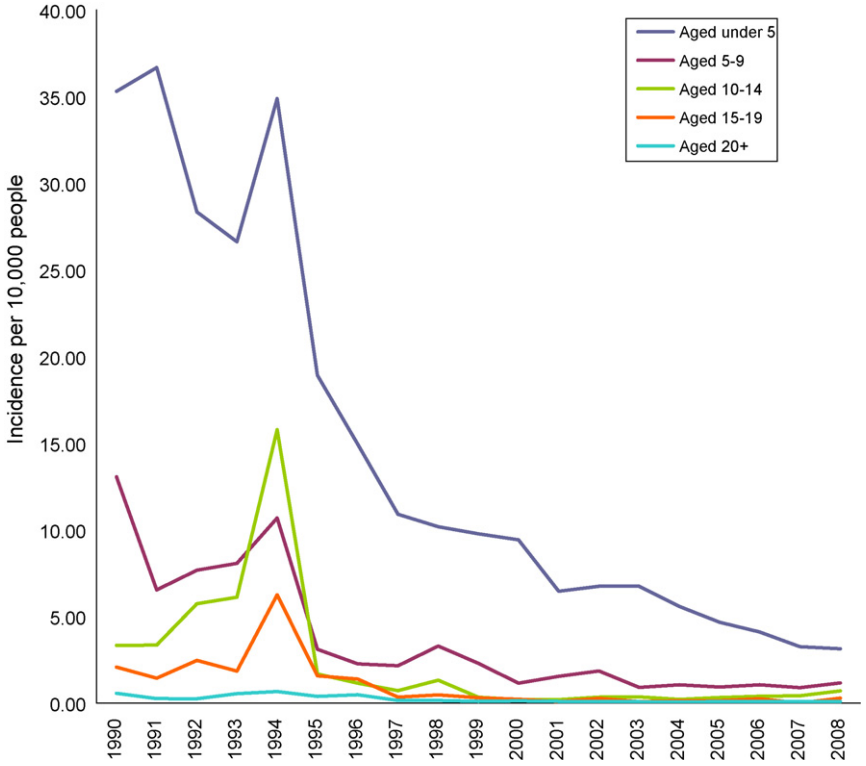

Fig. 1. The annual incidence of measles according to age and calendar year.

The protocol for this study was reviewed and approved by the Independent Scientific Advisory Committee (ISAC) of the MHRA.

2.2. Incidence estimation and source population

The first part of this study was conducted using a cohort design to estimate incidence of clinically diagnosed measles according to age, region, and calendar year. We identified all people for whom data were recorded in the Database from January 1, 1990 through December 31, 2008.

2.3. Case definition

We considered a person to be an incident case of measles if they had a clinical diagnosis of measles recorded in their computerized medical record. We could not obtain laboratory results to validate the measles diagnoses; however, the accuracy of diagnoses in the GPRD has been shown to be of high quality [2,5–8] and surveillance reports have indicated that accuracy of measles diagnosis in the UK is high, especially during outbreaks [10].

2.4. Measles vaccination use and effectiveness

A person was considered to have been vaccinated against measles if they had a measles-containing vaccination recorded in their computerized medical record.

We used a nested case–control design to estimate the risk of measles in relation to the receipt or non-receipt of a measles-containing vaccine. We included cases who were diagnosed with measles in 1994, age 1–19 at the time of the diagnosis, and who were born in or after 1982. We randomly selected up to 4 controls who had no prior diagnosis of measles, matched to each case on year of birth, gender, general practice attended, index date (the date of the case's measles diagnosis), and the duration of time the patient had been registered in the Database. We reviewed the immunization history for each case and control to determine receipt of a measles vaccine prior to the index date and how many prior measles vaccines had been received.

2.5. Data analyses

Annual incidence rates (IR) were calculated by dividing the number of cases of measles each year by the estimated population at risk active in the Database. Annual region specific rates were estimated by age and calendar year. Since the Database represents about 5% of the UK population [9], we estimated the number of cases in all of the UK by multiplying the number of cases recorded in the Database by 20.

We used conditional logistic regression in the case–control analysis to estimate the relative risk of measles infection in those who received a measles vaccination compared to those who did not. Odds ratios (OR) and 95% confidence intervals (CIs) are presented. The statistical analysis was conducted using the software program SAS, version 9.1 (SAS Institute, Inc., Cary, NC).

3. Results

3.1. Incidence of measles

The annual incidence of measles for years 1990–2008 is shown according to age in Fig. 1. There were over 8000 cases of measles recorded in the Database during the study period, of which 53% were male. The incidence of measles was highest in children less than 5 years old in 1990 and 1991 (about 36/10,000). It fell to about 28/10,000 in 1993, rose to 35/10,000 in 1994, and fell rapidly and progressively to less than 5/10,000 by 2005 and remained at this level through 2008. In children age 10–14, the incidence of measles rose more than 150%, from less than 5/10,000 in 1990–1991 to about 16/10,000 in 1994 (Fig. 1), after which it fell to levels below 2/10,000 in 1995 and remained at this level through 2008. The risk

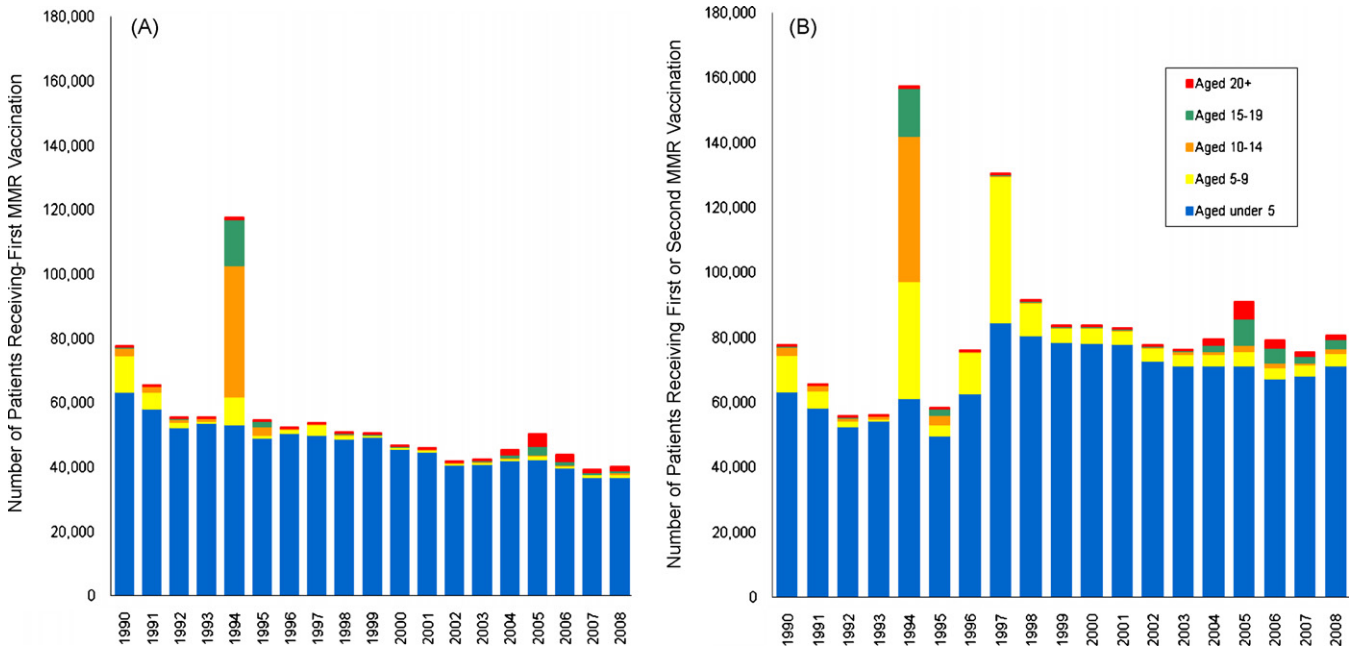

Fig. 2. (A) Number of people with first-time measles-containing vaccine by age and calendar year. (B) Number of people who received a first or second measles-containing vaccine by age and calendar year.

of measles in adults (age 20 or older) was less than 1/10,000 for the entire study period.

Based on the findings in the Database, we estimate that for those aged less than 15 years the number of cases of measles in the UK was stable at about 16,000 cases per year from 1990 through 1993. In 1994, the number of cases rose to an estimated 24,000 cases. As a result of the 1994 outbreak, a campaign of immunization with measles-containing vaccines (MR and MMR) was initiated (see vaccine frequency results).

In 1995, the number of notified cases of measles fell to around 10,000 per year, a level lower than the one that prevailed prior to the 1994 outbreak. In 1996, another large campaign of a two dose MMR vaccination regimen was initiated in the UK, primarily to help prevent an outbreak of mumps while at the same time providing additional protection against measles (see vaccine frequency results). In the years following 1996, the number of cases of measles in the GPRD fell to a low of around 100 per year—an estimated 2000 nationwide (Fig. 1).

The incidence was highest in Scotland's practices for years 1990–1995 after which it fell to levels of less than 5 per 10,000 in all regions. In addition to Scotland, the modest 1994 outbreak was mainly confined to Wales, the Northwest, and North Yorkshire.

3.2. Measles vaccine use and effectiveness

The distribution of the first-time measles-containing vaccine is provided in Fig. 2A by age and calendar year. As of 1994, about 90% of vaccinated children had received only one dose. We estimate that over 800,000 children age 5–14 years received a first-time measles-containing vaccination nationwide in 1994. Fig. 2B provides the total annual number of people who received a measles-containing vaccine (either first or second) according to age and calendar year. A substantial proportion of vaccinations in the later years were given to people who had already received a prior measles vaccination. The major vaccination campaigns in 1989–1990, 1994, 1996–1998 and 2004–2006 initiated in association with measles or mumps outbreaks are clearly demonstrated (Fig. 2A and B).

We evaluated the effectiveness of the measles-containing vaccines by comparing vaccination status in cases of measles to that in matched controls (Table 1). We identified 1261 recorded cases of measles in children less than age 20 in 1994, the year of the measles outbreak. The frequency of vaccination in the cases was compared to that of 4996 controls matched on year of birth, gender, general practice, date of diagnosis in the case, and duration of enrollment in the practice. The OR was 0.49 (95% CI 0.41–0.58) in children who had received one dose of a measles vaccine compared to those who received no vaccine. It was 0.39 (95% CI 0.26–0.58) in those who had received two vaccine doses compared to those who received none (Table 1).

Based on the controls, we estimate that, in 1994, 65% of children age 1–2 years had been vaccinated with the MMR vaccine, 87% of children age 3–4 years had been vaccinated, 77% of children age 5–9 years had been vaccinated, and 28% of those aged 10–19 years had been vaccinated.

4. Discussion

In the UK, routine immunization of children with one dose of the single measles vaccine began in 1968, with only moderate uptake [1]. Nevertheless, after 1968, the number of notified cases of measles fell to an estimated 30,000 per year from prior levels some ten times or higher. In October 1988, a comprehensive program of immunization against measles, mumps, and rubella with the MMR vaccine was initiated for children 1–9 years of age. By 1998, some

Table 1
Odds ratios for 1994 cases of measles and controls according to measles vaccination status.

Measles vaccination status	Cases (N = 1261)	Controls (N = 4996)	OR (95% CI)
0 Measles vaccinations received	812	2738	1.00 (reference)
1 Measles vaccination received	409	2012	0.49 (0.41–0.58)
2+ Measles vaccinations received	40	246	0.39 (0.26–0.58)

10 years later, the uptake of MMR was estimated to be 90% in the youngest children [1,2].

Despite the prior programs of immunization begun in 1968 and 1988, a mild outbreak of measles occurred in 1994. We estimate that an additional 8000 cases nationwide were diagnosed in that outbreak, primarily affecting children age 10–14 years, most of whom had not received prior vaccination with a measles-containing vaccine.

The 1994 outbreak of measles led to a new immunization campaign during that year (Fig. 2). Our results indicate that measles-containing vaccines distributed prior to 1994 and during this immunization campaign provided substantial protection against measles for children age 1–19 years and that two doses provided more protection than one (Table 1). The vaccination campaign of 1994 doubtless reduced the subsequent risk for measles, as did an additional large vaccination campaign begun in 1996 for children age 5–14 (Fig. 2B). After 1994, the incidence of measles continued to fall through 2008 when fewer than 100 cases were diagnosed in the Database in children less than 20 years of age. By that year, up to 90% of children less than 5 years of age had been vaccinated against measles at least once in general practices. Major vaccination campaigns in 1989–1990, 1994, 1996–1998 and 2004–2006 initiated in association with measles or mumps outbreaks are clearly demonstrated (Fig. 2A and B). In 1998, the frequency of first-time MMR vaccination began to fall in the youngest children as a result of public concern about possible side effects of the vaccine [1,2]. By 2002, first-time MMR vaccinations had fallen by about 25% in the youngest children (Fig. 2A).

Despite the vaccination of millions of children with a MMR vaccine by October 1998 and a subsequent substantial reduction in the incidence of measles, a large epidemic of mumps began in the UK in 2003 and lasted through 2006 [2]. More than 100,000 mumps cases were diagnosed by general practitioners [2]. The epidemic of mumps primarily affected young adults age 18–24, most of whom had not received prior MMR vaccination. The 2003 mumps epidemic led to yet another vaccination campaign in 2004 and 2005 (Fig. 2B) that demonstrably reduced, to some extent, the size of the mumps epidemic [2], while at the same time, it increased the number of children and young adults protected from measles. Nevertheless, there still remain some children in the UK who have not been vaccinated against measles (or mumps). Measles outbreaks similar to the one in 1994 may be expected in the future.

Reports have described UK outbreaks of measles in 2006–2008 [11–15]. We found no evidence for a widespread increased incidence of measles in the Database for these years indicating that these outbreaks were isolated and did not spread widely. In 2009 there was also an increase in the number of measles notifications reported to the government [16]. Our preliminary data suggest that this increase was also not widespread since there were fewer than 100 cases of measles recorded in the Database through September of 2009 in those less than 20 years of age. Limited local outbreaks of measles and mumps have not infrequently been reported in the past [4,12,13,16–18].

The accuracy of diagnoses made by the general practitioners has been established in numerous publications to be of high quality and completeness [2,5–8]. In addition, the recording of vaccinations in the Database has been found to be virtually complete and consistent with reported vaccine coverage [5]. Published studies on the incidence of mumps and influenza based on this Database have yielded results closely similar to those reported to the government, which rely on general practitioner reports [2,8,19]. The current measles study also provides incidence rates that are similar to those reported by the UK government [20–22]. The results, in relation to measles vaccination, are entirely consistent with the report and recommendations described by the World Health Organization [23].

In summary, the annual incidence of measles fell after the introduction of the MMR vaccine in late 1988. A modest outbreak of measles occurred in 1994 leading to large nationwide programs to immunize children. Since 1996, the incidence of measles has fallen by more than 80%. Prior measles vaccination is highly effective and has substantially reduced the risk of measles. This large UK computerized general practice data resource has provided comprehensive details about the incidence of measles in relation to the history of immunizations against this infectious disease. Standardized valid electronic population-based medical resources can provide real-time recording of infectious disease diagnoses, as well as vaccinations, rapidly and at low cost compared to other means that have been used to obtain this information [24–26].

References

[1] Asaria P, MacMahon E. Measles in the United Kingdom: can we eradicate it by 2010? BMJ 2006;333:890–5.
[2] Jick H, Chamberlin DP, Hagberg KW. The origin and spread of a mumps epidemic: United Kingdom, 2003–2006. Epidemiology 2009;20(September (5)):656–61.
[3] Gay N, Ramsay M, Cohen B, Hesketh L, Morgan-Capner P, Brown D, et al. The epidemiology of measles in England and Wales since the 1994 vaccination campaign. Commun Dis Rep CDR Rev 1997;7(February (2)):R17–21.
[4] Skinner R, Christie P, Cowden JM. The measles/rubella immunization campaign in Scotland. Health Bull (Edinb) 1996;54(January (1)):88–98.
[5] Kaye JA, Melero-Montes MM, Jick H. Mumps, measles, and rubella vaccine and the incidence of autism recorded by general practitioners: a time-trend analysis. BMJ 2001;322:460–3.
[6] Kaye JA, Derby LE, Melero-Montes MM, Quinn M, Jick H. The incidence of breast cancer in the General Practice Research Database compared with national cancer registration data. Br J Cancer 2000;83:1556–8.
[7] Jick SS, Kaye JA, Vasilakis-Scaramozza C, García Rodríguez LA, Ruigómez A, Meier CR, et al. Validity of the General Practice Research Database. Pharmacotherapy 2003;23:686–9.
[8] Meier CR, Napalkov PN, Wegmuller Y, Jefferson T, Jick H. Population-based study on incidence, risk factors, clinical complications and drug utilization associated with influenza in the United Kingdom. Eur J Clin Microbiol Infect Dis 2000;19:834–42.
[9] Hollowell J. General Practice Research Database (GRPD): scope and quality of data. Office of Population Censuses and Statistics. OPCS, now known as Office of National Statistics (ONS); 1994. pp. 1–20.
[10] Brown DW, Ramsay ME, Richards AF, Miller E. Salivary diagnosis of measles: a study of notified cases in the United Kingdom, 1991–3. BMJ 1994;308:1015–7.
[11] Muscat M, Bang Henrik, Wohlfahrt J, Glismann S, Molbak K. Measles in Europe: an epidemiological assessment. Lancet 2009;373:383–8.
[12] Health Protection Agency. Measles cases so far in 2006. Press release dated 15 June 2006. www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1231490136144?p=1158945065095 [accessed 21 December 2008].
[13] Health Protection Agency. Increase in measles cases in 2006, in England and Wales. Communicable Disease Report Weekly 2006;16:3. www.hpa.org.uk/cdr/archives/2006/cdr1206.pdf [accessed 21 December 2008].
[14] Health Protection Agency. Confirmed cases of measles in England and Wales—an update. Health Protection Report HPR [serial online] 2008;2(21): news. http://www.hpa.org.uk/hpr/archives/2008/news2108.htm#measls [accessed 2 February 2010].
[15] Eaton L. Measles cases in England and Wales rise sharply in 2008. BMJ 2009;338:b533.
[16] Health Protection Agency. Confirmed measles cases in England and Wales: update to end-April 2009. Health Protection Report HPR [serial online] 2009;3(24): news. http://www.hpa.org.uk/hpr/archives/2009/news2209.htm#msls [accessed 2 February 2010].
[17] Mackenzie DG, Hallam N, Stevenson J. Younger teenagers are also at risk of mumps outbreaks. BMJ 2005;330:1509.
[18] Morse D, O'Shea M, Hamilton G, Soltanpoor N, Leece G, Miller E, et al. Outbreak of measles in a teenage school population: the need to immunize susceptible adolescents. Epidemiol Infect 1994;113(October (2)):355–65.
[19] Jick H, Chamberlin DP, Hagberg KW. Vaccine policy and incidence of influenza. Epidemiology 2010;21(March (2)):270–1.
[20] Health Protection Agency. Notifications, by Age Group; 1989–2008. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733802298 [accessed 2 February 2010].
[21] Health Protection Surveillance Center. Epidemiology of measles in Ireland; 2006. http://www.ndsc.ie/hpsc/A-Z/VaccinePreventable/Measles/Publications/AnnualReportsonMeaslesinIreland/File,2648,en.pdf [accessed 2 February 2010].

[22] Health Protection Scotland. Measles notifications and laboratory reports, Scotland; 1988–2008. http://www.documents.hps.scot.nhs.uk/immunisation/measles/measles-notifications-lab-reports-1988-2008.pdf [accessed 2 February 2010].
[23] World Health Organization. Progress towards measles elimination in WHO's European region, 2005–2008. Wkly Epidemiol Rec 2009;84: 57–64.
[24] Ghebrehewet S, Falconer M, McDonald P, Schlecht B. MMR vaccine uptake rates: a data validation study. Commun Dis Public Health 2003;6(June (2)):144–6.
[25] Lyratzopoulos G, Aston R, Bailey K, Flitcroft J, Clarke H. Accuracy of routine data on MMR vaccination coverage and validity of parental recall of vaccination. Commun Dis Public Health 2002 Dec;5(4):305–10.
[26] Choi YH, Gay N, Fraser G, Ramsay M. The potential for measles transmission in England. BMC Public Health 2008;8(September):338.