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Feasibility study for identifying adverse events attributable to vaccination by record linkage

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SUMMARY

To investigate the feasibility of using a record linkage method for identifying vaccine attributable adverse events, computerized hospital admissions and vaccination records from South East Kent district were linked and checked for accuracy. Records for 90% of children under 2 years of age admitted to hospital over a 2-year period were matched with vaccination records using a computer algorithm based on name, date of birth, sex, and post-code supplemented by visual inspection. Relative to this gold standard, matching on date of birth, sex and postcode alone had a sensitivity of 60% and an incorrect match rate of 0·2% after matches to more than one vaccine recipient were excluded. Manual checking of a sample of admissions showed that only 4% had been assigned incorrect International Classification of Disease (ICD) codes. Routine record linkage of ICD admission codes to vaccination records therefore yields data of good quality which may be used for surveillance purposes.

INTRODUCTION

The detection of an increased risk of aseptic meningitis after vaccines containing the Urabe mumps strain by linking laboratory and vaccination records has demonstrated the advantages of active surveillance over the existing system based on passive reporting of adverse events to the Department of Health Committee on Safety of Medicines (the 'Yellow Card' system) [1]. This finding has recently been confirmed using record linkage of hospital admissions with selected ICD codes with district vaccination data [2], the value of the method being further reinforced

by the confirmation of a significantly raised risk of idiopathic thrombocytopenic purpura (ITP) after MMR vaccine [2].

Computerization of hospital admissions and immunization records provides an opportunity to extend this methodology to surveillance of any potentially vaccine related hospital admissions. To this end, all admissions in a defined age group were linked to vaccination records to provide a complete description of the temporal relationship between vaccination and any event type, as defined by its ICD classification. The validity of such a system relies on accurate coding of admissions, and accurate matching of admission and vaccination records.

The present paper reports on a pilot study undertaken in South East Kent to assess the feasibility of using record linkage for surveillance. The specific aims of the study were to estimate the sensitivity and accuracy of different matching algorithms, and to validate the accuracy of ICD codes for events temporally related to vaccination.

METHODS

With the approval of the local ethics committee, computer records of all inpatient admissions in children aged between 1 month and 2 years of age for the period 1 January 1991 to 28 February 1993 were extracted from the administrative systems of Buckland hospital (Dover) and William Harvey hospital (Ashford), the two District General Hospitals in former South East Kent Health Authority. The data for each admission included patient name, sex, date of birth, postcode, date of admission, and up to three International Disease Classification Version 9 (ICD-9) diagnosis codes which form part of the routine hospital summary.

Vaccination records of all children in South East Kent born between 1 January 1989 and 28 January 1993 and who received at least one dose of diphtheria, tetanus and pertussis (DTP), polio or measles, mumps and rubella (MMR) vaccine were downloaded from the South East Thames Regional Health Authority Child Health Vaccine database. These records included name, sex, date of birth, postcode, vaccine type and vaccination dates.

Records were matched on combinations of name or phonetic alphanumeric ('soundex') code, date of birth, sex and postal code as shown in Fig. 1, using computerized procedures supplemented by visual inspection of a line listing of potential date of birth matches. This matching constituted the 'gold standard' against which other matching algorithms were evaluated. All data manipulations were performed using the relational database DataEase [3] running on a personal computer.

A computer-generated list of ICD-9 diagnosis codes for a subset of the admissions occurring within 5 weeks of MMR vaccination were checked by a consultant paediatrician who examined the case notes.

RESULTS

Computer records for 2410 hospital admissions involving 1670 patients were obtained. Vaccination records for 14944 children with a total 72811 vaccinations were extracted. Of these, 31134 were doses of oral poliovirus vaccine; the

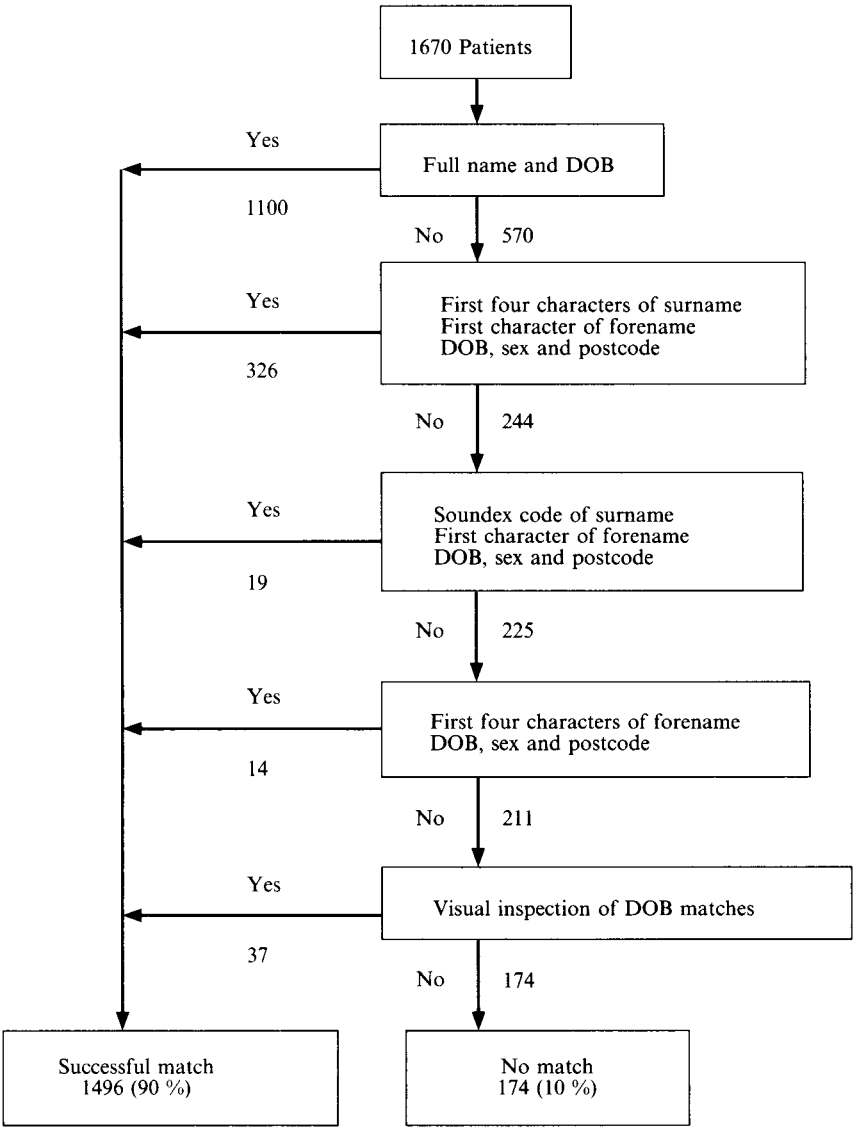

Fig. 1. Matching algorithm.

remainder were doses of DTP or MMR vaccines (Table 1). The 'gold standard' matching algorithm successfully matched 1496/1670 (90%) patients admitted; 1459 (87%) were identified by computerized procedures alone. Of the 174 patients with no matches, 77 (44%) lived outside the catchment area of the vaccine database. Further details are given in Fig. 1.

Of the total 1496 successful matches, 1100 (74%) were matched using only full name and date of birth, and 1459 (98%) using computer matching alone. An alternative strategy using only date of birth, sex and postcode correctly identified 910 (61%) matches but mismatched 17 patients, an incorrect match rate of 17/927 (2%). Fifteen of these occurred when patients legitimately shared dates of birth and postcodes (13 of these matched pairs were same sex twins). After

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Table 1. *Number of doses of DTP and MMR vaccines administered to 14944 children in study population*

Vaccine	Number of doses
Total MMR doses	10544
Total DTP doses	31133
1st DTP	10912
2nd DTP	10419
3rd DTP	9802

Table 2. *Principal discharge diagnosis in 78 admissions within 5 weeks of MMR vaccine identified by the record linkage method*

	Onset after vaccination (days)		
Diagnosis	0–5	6–14	15–34
Vaccine reaction	2	0	0
Febrile convulsion	1	3	5
Idiopathic thrombocytopenic purpura	0	0	1
Respiratory tract or viral infection/PUO	2	9	16
Gastro/cardiac/genitourinary disorder	2	2	8
Other*	1	7	19
Total admissions	8	21	49

* Includes accidents, congenital disorders and surgical admissions.

eliminating the 32 matches where the hospital admission was matched to more than one vaccine recipient the sensitivity was 60% and the number of incorrect matches fell to two, an incorrect match rate of 2/895 (0·2%). Failure to match was largely caused by missing post code information in the hospital records.

Review of the case notes for 78 admissions within 5 weeks of MMR vaccine revealed six admissions which had not been assigned ICD codes (one occurrence each of allergy, burn, bronchiolitis, circumcision, squint surgery, upper respiratory tract infection). Of the 72 with ICD-9 codes, 3 (4%) were assigned incorrect codes (urinary tract infection as chest infection, bronchiolitis as otitis media, diarrhoea as pyrexia of unknown origin). Two admissions correctly coded as febrile convulsions were found also to have chickenpox and intussusception respectively which had not been coded. Another four correctly coded patients had skin rashes which had not been coded.

Table 2 shows the range of ICD-9 codes found in admissions temporally related to MMR vaccination. Two admissions were coded as vaccine reactions. One occurred 1 day after vaccination and had cough coded as a second diagnosis. The other, coded as a reaction to the measles component of the vaccine, occurred 2 days after vaccination and had febrile convulsion coded as a second diagnosis. The onsets of the three convulsions in the 6–14 day period were 8, 9 and 11 days. Altogether, 10 (6%) of the total of 163 admissions for convulsions, and 1 of the total of 2 admissions for idiopathic thrombocytopenic purpura (ITP) occurred within 5 weeks of MMR vaccination.

One child for whom no linked vaccination record was found was coded as having 'post-immunization encephalitis'. Vaccination records for this case, who lived outside the South East Kent district were traced and showed that admission

occurred 6 days after MMR vaccine. The symptoms were consistent with a simple febrile convulsion; a transient macular rash was also present.

An analysis of admissions temporally related to DTP vaccination identified one for an injection site reaction following a second dose and a further two in which a causal connection with vaccination was probable. One of the latter was a febrile convulsion on the day of vaccination and the other was a PUO on the day after vaccination; both admissions were after a third dose. There were no admissions for collapse after any dose. The accuracy of the ICD discharge codes for the three admissions with a definite or probable causal association with vaccination was confirmed by examination of the hospital notes. The convulsion and PUO had both been attributed to vaccination.

DISCUSSION

The high proportion (90%) of successful matches of hospital admission and vaccination records achieved by combined computer matching and visual inspection demonstrates the quality of admission and vaccination data. The success rate of computer matching alone (87%) together with the low error rate in ICD coding (4%) shows that identification of adverse events using record linkage is feasible. Matching only on date of birth, sex and postcode and excluding multiple matches produces a very low proportion of false matches (0·2%), though at the cost of reduced sensitivity (60%). This method is therefore effective in situations where named admission data is unavailable or its use is precluded by confidentiality restraints. The excluded admissions were largely those without postcode information. Bias is, therefore, unlikely to be introduced by use of the less sensitive matching method unless absence of postcode is related to timing of admission relative to vaccination. A substantial increase in sensitivity could be achieved with this method by more complete recording of post code information in hospital records. This is likely to improve due to administrative needs in the purchaser/provider environment. Use of the new NHS number as a unique patient identifier in hospital records should also facilitate matching in the future.

The risk estimates for adverse events derived from record linkage studies have been shown to be far more reliable than those based on 'Yellow Card' reports [1, 2]. This pilot study picked up one admission for ITP temporally associated with MMR vaccination which had not been reported on a 'Yellow Card'. Only one of the four children admitted with a febrile convulsion 6–11 days after MMR vaccination was diagnosed as having a vaccine reaction, although this is the characteristic time of onset for convulsions attributable to the measles component [1]. However, two children admitted within 48 h of MMR vaccination were incorrectly diagnosed as having a vaccine reaction, the time interval being too short for the symptoms to have been caused by a live viral vaccine. These examples illustrate the shortcomings of a passive reporting system for identifying vaccine attributable events. For DTP vaccine, where the interval to onset of symptoms is much shorter, recognition by clinicians of probable reactions is better although such cases are not always reported on a 'Yellow Card'.

The record linkage method described here allows all events occurring in temporal relation to vaccination to be captured, and with appropriate statistical

methods, can be used to identify any with a significantly increased incidence in a defined post-vaccination period [4]. The method therefore enables previously unsuspected vaccine reactions to be identified. Since the data is routinely available the method has the potential to form the basis for a surveillance system for adverse reactions attributable to vaccination. The data must, however, be interpreted with some care to avoid identifying spurious risks resulting from chance associations. Hypotheses generated by the surveillance system should be tested formally on separate prospective or retrospective linked datasets. If associations are confirmed, such data can be used to estimate the absolute and attributable risk of specific adverse events using the number of vaccine doses administered in the study population as a denominator [2]. Despite the small size of our study, the absolute risks of a convulsion after a third dose of DTP vaccine of 1 in 9800 approximately, and of a convulsion 6–11 days after MMR vaccine of 1 in 2850 (matched admissions only) were consistent with other estimates [2]. The absence of admissions for collapse, which have been reported after American DTP vaccines in association with pyrexia [5], is consistent with an earlier study of British DTP vaccine in which recipients were actively followed up after each dose [6].

In order to achieve sufficient power for robust statistical analyses, admission data must be captured on a regional rather than district level. Following this pilot study, a surveillance system is being set up on a trial basis in the South East Thames region. Since patient names are not held on regional admission files record matching will be by date of birth, sex and postcode with exclusion of multiple matches. The performance of the system will be evaluated by monitoring events known to be causally associated with vaccination.

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