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Short communication

Surveillance methods to detect the impact of a significant cold chain breach

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ABSTRACT

In January 2015, a significant cold chain breach on a postnatal ward in a tertiary hospital in Sydney, Australia was noted to have been occurring since August 2013. Surveillance, amongst the 1178 mothers and 1178 babies affected, for vaccine-preventable diseases (VPDs) and adverse events following immunisation (AEFIs) using linkage with a notifiable diseases database was subsequently undertaken; no directly related instances of VPDs or AEFIs were detected. We evaluate this novel systematic surveillance method which has not been previously reported to determine whether it is effective in determining the impact of cold chain breaches on an individual and population level. The recommendation for revaccination of the affected mothers and subsequent surveillance was resource-intensive and future studies related to such incidents should focus on detailing the resources used to allow the costs versus benefits of such systematic surveillance to be determined.

1. Introduction

In Australia, vaccines are stored in accordance with national guidelines [1], with maintenance of the cold chain, the system of transporting and storing vaccines within the optimum temperature range of 2–8 °C, the most critical aspect for the preservation of vaccine potency [2]. Breaches of the cold chain outside of this recommended temperature range are managed by public health authorities, who determine the most appropriate course of action and may recommend discarding of the affected vaccines and possibly revaccination. There have been some ecological reports where known cold chain breaches have been suggested to have led to increases in certain vaccine-preventable diseases (VPDs) at a population level [3–5], but specific surveillance for VPDs or adverse events following immunisation (AEFIs) amongst cohorts affected by cold chain breaches has not been reported. As a result, the direct impact of cold chain breaches on the development of VPDs is unknown, and the utility of systematic surveillance for VPDs following cold chain breaches has not been evaluated.

In January 2015, it was noted that a refrigerator used to store vaccines that were administered to mothers and babies on a postnatal ward in a large tertiary hospital in metropolitan Sydney, Australia had experienced multiple cold chain breaches dating back to August 2013; this prompted an internal investigation. Case surveillance following long-term cold chain breaches is not routinely conducted and there is no protocol or requirement for such a process. A novel surveillance plan was therefore developed and implemented to determine if there were any episodes of VPDs or AEFIs as a result of this significant vaccine storage incident. This report describes and evaluates this surveillance method to determine whether it is effective in determining the impact of cold chain breaches on an individual and population level.

2. Methods

The postnatal refrigerator affected by the cold chain breach was found to be storing vaccines that included Boostrix® (pertussis/diphtheria/tetanus) and MMR® (measles/mumps/rubella) for mothers, and hepatitis B vaccine for children. At the time, it was standard postnatal practice in New South Wales (NSW), the state Sydney is located in, to offer Boostrix® to new mothers who had not received the vaccine during pregnancy, MMR® to rubella non-immune mothers, and hepatitis B to all newborn babies. An investigation, not detailed in this paper, determined that based on available documentation, temperature fluctuations, both to

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below 2 °C and above 8 °C, had been occurring intermittently in the fridge used to store these vaccines between 1 August 2013 and 13 January 2015.

A surveillance plan was developed with the aim of identifying any mothers or children that developed a VPD or AEFI as a result of receiving a vaccine on the ward during the period of interest. In NSW, diseases that are notifiable under the NSW *Public Health Act 2010* [6] are recorded in the electronic database 'Notifiable Conditions Information Management System' (NCIMS). For diseases which rely on laboratory confirmation for diagnosis (including pertussis, measles, and hepatitis B), NCIMS has a high capture rate when disease is severe enough to result in a healthcare presentation. A list of all mothers and babies vaccinated on the ward was cross-checked against all notifications of diphtheria, tetanus, pertussis, measles, mumps, rubella, hepatitis B, and AEFIs in NSW. This was done retrospectively for the period 1 August 2013 to 31 January 2015, and prospectively for the period from 1 February 2015 to 31 December 2016. Any matches were investigated further by reviewing case information in NCIMS and electronic medical records in the hospital database for notes on any related patient admissions and encounters. Prospective surveillance data were reviewed on a six-monthly basis. In addition, hepatitis B serology results for babies known to be born to mothers with hepatitis B infection, taken at 9–12 months of age, were obtained by contacting mothers and/or their general practitioners to determine whether they had evidence of hepatitis B immunity and whether further testing or referral was needed.

Based on the results of the surveillance, the pertussis age-specific prevalence rate amongst women aged 15–45 in 2015 living in Sydney Local Health District (SLHD), where this hospital was located, was calculated using NSW notifiable disease data taken from NCIMS (to calculate the number of confirmed notifications for pertussis in women aged 15–45 years) and Australian Bureau of Statistics Census data (to estimate the total population for this sub-group). This rate was used as the background rate to form a Poisson distribution to estimate the likelihood of seeing one or more cases of pertussis in this group of women.

3. Results

1178 mothers (representing 0.8% of the female population aged 15–45 living in SLHD in 2015) and 1178 babies were identified as having received vaccines on the ward during the time period of interest and these mothers were all contacted and recommended for revaccination with the vaccines they were documented as having received on the ward. The total number of mothers who were revaccinated was not known as the place of revaccination was at the discretion of mothers. However, 314 (27%) of the mothers were confirmed to have been revaccinated at a dedicated clinic set up by the hospital.

Cross-checking of the list of mothers and babies against all notifications of the diseases of interest (diphtheria, tetanus, pertussis, measles, mumps, rubella, hepatitis B, and AEFIs) on NCIMS found a positive match only for two cases of pertussis (in mothers) and no other diseases.

3.1. Mothers

The two mothers identified were diagnosed with pertussis in 2015 after the time this incident was detected. Both had received Boostrix® postnatally on the ward in 2014 and were diagnosed by a general practitioner more than one year following childbirth. Immunisation records for the two babies born to these mothers reveal that they both had received the full three dose primary vaccination schedule for pertussis (doses at 2,4, and 6 months) before their mothers were diagnosed, and no transmission to these babies, or other close household contacts, was recorded on NCIMS.

The 2015 pertussis rate amongst women aged 15–45 living in SLHD was calculated to be 88 per100 000 population. The Poisson distribution (Fig. 1) suggested at least one case of pertussis would likely be expected in the cohort of 1178 women, with one case being the most likely number (37%).

3.2. Babies

Twelve babies were identified as being born to mothers with hepatitis B infection during this period. Ten of these had documented hepatitis B immunity on serology conducted after 9 months of age. The remaining two were lost to follow-up, despite multiple attempts to contact the mothers via telephone and/or letter; they were known to have moved overseas.

4. Discussion

We describe the surveillance using linkage with a notifiable diseases database undertaken following a vaccine storage failure for over one year to determine if there were any resulting episodes of VPDs or AEFIs in the affected cohort. We used a systematic approach to identify that there were no instances of VPDs or AEFIs that could be directly attributed to the administration of potentially ineffective vaccines as a result of a cold chain breach impacting this defined population. Such extensive and systematic surveillance for VPDs and AEFIs using a notification database following a cold chain breach has not previously been described in the literature. This vaccine storage failure prompted public health authorities to contact and recommend revaccination for all 1178 affected women. The large scale of this response to the breach and the public attention it received resulted in a revision of the NSW guidelines regarding vaccine storage in hospitals [7].

Two cases of pertussis were identified in mothers who had been administered Boostrix® postnatally on the ward. Their diagnoses occurred in 2015 during a large pertussis epidemic in NSW [8]. The results of our Poisson distribution suggest that this observed number of two cases is above the most likely expected number of one case, however, it is not possible to determine if these two cases of pertussis could be attributed to potentially ineffective Boostrix® vaccines administered on this postnatal ward. The small

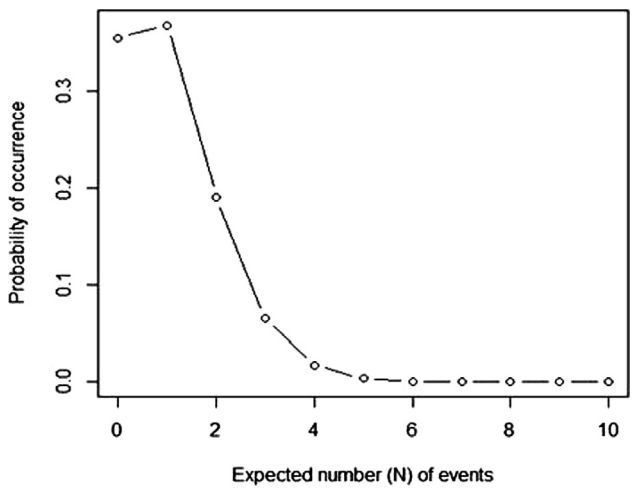

Fig. 1. The probability of an expected number (N) of pertussis cases in the cohort of women (n = 1178) affected by a cold chain breach on a post-natal ward in a Sydney tertiary hospital, 2015.

sample size does not provide high statistical power, vaccine coverage rates for this population are not available, and evidence shows that although the vaccine may be as high as 90% effective at preventing disease in adults, there is a rapid decline in the level of antibodies within the first two years after vaccination [9].

Cold chain breaches are regularly reported to public health authorities in Australia; any resulting vaccine wastage is recorded, and in 2016–17, 5.5% of all vaccines in NSW were discarded [10]. The vast majority of cold chain breaches are not known to result in adverse health outcomes, despite the associated known decrease in vaccine potency [1]. In NSW, this may be due to many of them being detected before the affected vaccines are administered to patients, and in the cases where these vaccines are administered, there is no surveillance system in place that would detect potential adverse health outcomes. A number of published ecological studies have linked population rates of vaccine-preventable diseases, including measles, pertussis, and hepatitis B, to problems with vaccine storage [3–5], but there are no reports of the use of a notifiable diseases database to systematically determine if a defined population affected by vaccine storage issues has subsequently developed a VPD. Our systematic surveillance of a large cohort of women found no instances of VPDs that could be attributed to this incident. The notification and revaccination of this group consumed significant resources, in line with previously reported revaccination efforts [11], as did the surveillance method used. The subsequent failure to detect any adverse outcomes brings into question the utility of such a systematic surveillance exercise; however, it is not possible for us to comment on whether such extensive surveillance is warranted in such incidents as we did not quantify the resources used. Future studies are needed that examine the level of resources required for this approach to such incidents; this would inform a discussion on the costs versus benefits of this resource intensive approach. One factor to consider in such studies would be the positive effect such systematic surveillance might have on reassuring the public that all efforts are made in these situations to determine if there are associated adverse outcomes.

There were a number of limitations to our surveillance process that may have affected its ability to identify a case. Mothers that developed pertussis following administration of the vaccine may not have sought medical attention if they had a mild illness, or may have visited a doctor but not had a pertussis test undertaken; these potential cases of pertussis would therefore have been missed using our surveillance method which relied on NCIMS. Mothers given a spoiled vaccine may have benefited from herd immunity and not developed a VPD. We do not know how many mothers in total were revaccinated as a result of the notification; notification and subsequent revaccination may have prevented further cases of VPDs that may otherwise have occurred following the initial administration of a potentially ineffective vaccine. We did not look at individual vaccine profiles and the likelihood of retaining efficacy given the recorded fridge temperatures; however, we did seek general advice from an expert panel. It is difficult to comment on the extent of potential vaccine ineffectiveness as we do not have detailed temperature monitoring records from the fridge involved, which was a standard bar fridge and not the recommended vaccine fridge. Some vaccines may not have been affected and may not have lost their potency; as individual vaccines affected could not be identified, a conservative approach was taken to consider all women and babies in the cohort to be affected.

We conducted systematic surveillance for instances of VPDs or AEFIs as a result of a long-term cold chain breach, a novel approach using linkage to a notifiable diseases database that has not previously been reported, to determine whether a vaccine storage error had resulted in an adverse outcome. We found no instances of a VPD or AEFI that could be conclusively attributed to the storage error. The revaccination and surveillance consumed a large amount of resources and it is worth considering the value of conducting such large-scale actions and surveillance in the event of future similar incidents We recommend that future studies of such incidents be designed that allow the costs versus benefits of such a systematic surveillance method to be determined.

Declaration of Competing Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no competing interests to declare

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.05.091.

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