Continuous active surveillance of adverse events following immunisation using SMS technology

Darren W Westphal^{a,b,c,*}, Stephanie A Williams^c, Alan Leeb^d, Paul V Effler^{a,e}

^aCommunicable Disease Control Directorate, Western Australian Department of Health, Perth, WA, Australia

^bWestfarmer's Centre for Vaccines and Infectious Diseases, Telethon Kids Institute, University of Western Australia, Subiaco, WA Australia

^cNational Centre of Epidemiology and Population Health, Research School of Population Health, The Australian National University, ACT Australia

^dIllawarra Medical Centre, Ballajura, WA, Australia

^eSchool of Pathology and Laboratory Medicine, University of Western Australia, Nedlands, WA, Australia

*Corresponding author: Tel +618 9388 4841.

Email addresses: darren.westphal@health.wa.gov.au, darren.westphal@anu.edu.au (D.W. Westphal)

Abstract

Introduction

On-going post-licensure surveillance of adverse events following immunisation (AEFI) is critical to detecting and responding to potentially serious adverse events in a timely manner. SmartVax is a vaccine safety monitoring tool that uses automated data extraction from existing practice management software and short message service (SMS) technology to follow-up vaccinees in real-time. We report on childhood vaccine safety surveillance using SmartVax at a medical practice in Perth, Western Australia.

Methods

Parents of all children under age five years who were vaccinated according to the Australian National Immunisation Schedule between November 2011 and June 2015 were sent an SMS three days post administration to enquire whether the child had experienced a suspected vaccine reaction. Affirmative replies triggered a follow up SMS requesting details of the reaction(s) via a link to a survey that could be completed using a smartphone or the web. Rates of reported AEFI including fever, headache, fatigue, rash, vomiting, diarrhoea, rigors, seizures, and local reactions were calculated by vaccination time point.

Results

Overall, 239 (8.2%; 95% CI 7.2%—9.2%) possible vaccine reactions were reported for 2,897 vaccination visits over the 44 month time period. The proportion of children experiencing a possible AEFI, mostly local reactions, was significantly greater following administration of diphtheria-tetanus-pertussis-poliomyelitis vaccine at 4 years of age (77/441; 17.5%; 95% CI 13.9%—21.0%) compared to the vaccinations given at 2-18 months ($p<0.001$). Across all time points, local reactions and fatigue were the most frequently reported AEFI.

Conclusion

Automated SMS-based reporting can facilitate sustainable, real-time, monitoring of adverse reactions and contribute to early identification of potential vaccine safety issues.

Keywords: Adverse events following immunisation, vaccine safety, surveillance, SMS, paediatric vaccination

Introduction

Post-marketing surveillance of vaccines is critical to identify potential safety issues [1, 2] as quickly as possible, so that changes in practice can occur in a timely manner. Important policy responses to safety signals identified through post-marketing surveillance include the withdrawal of the first rotavirus vaccine because of increased rates of intussusception [3, 4] and a contraindication for administering one brand of influenza vaccine to children less than 5 years of age due to the increased risk of severe febrile reactions [5].

Ongoing monitoring is also important for maintaining public confidence in the safety of vaccines. While pre-licensure safety studies are critical, they can be limited by relatively small sample sizes, may not reflect use of the vaccine outside the clinical trial setting (e.g. use with other vaccines or in alternate patient cohorts), and do not capture changes to the vaccine that may occur after licensure (e.g. annual strain changes in the influenza vaccine) [1, 2, 6]. Post-marketing vaccine safety surveillance is therefore important, however current mechanisms are mostly passive and may be unfavourably affected by underreporting, reporting biases, and the lack of accurate denominators for determining rates [7, 8]. To help address the limitations of passive surveillance, routine, active vaccine safety monitoring has recently been established in the United States [9, 10]. Here we describe ongoing efforts to develop a system for active post-marketing vaccine safety surveillance in Australia. SmartVax is a vaccine safety monitoring tool that uses automated data extraction from provider-based electronic patient records and short message service (SMS) technology to follow-up vaccinees in real-time. This report describes how SmartVax was used to establish reactogenicity profiles for paediatric vaccine combinations and assess the impact of changes to the childhood immunisation schedule.

2. Methods

2.1 Setting

In Australia, more than 70% of vaccinations are given by general practitioners (GPs) [9]. SmartVax has been used at a single GP practice in metropolitan Perth, the capital of Western Australia (WA), since 2011. The practice has approximately ten full-time practitioners, 21,000 active patients, and administers approximately 2,000 paediatric vaccinations each year. Details on operational aspects of the SmartVax system have been previously described [11].

In brief, parents or guardians of vaccinated children (hereafter patients) were explained the risks and benefits of vaccination prior to consenting, as per routine clinic practice. Patients were informed that they would be contacted by SMS in three days, those who preferred not to be contacted by SMS could opt-out of SMS communication by advising their provider; no patients declined participation. Each weekday the SmartVax tool extracted vaccination data from the practice's commercially available management software. SMS text messages were sent to patients three days post-vaccination to query whether they had experienced any perceived reactions following their vaccination. The SMS read, *"Thank you for caring to have a vaccination. We would like to know if there were any reactions. Kindly reply Y or N only."* Affirmative replies to this query were followed up by two additional SMSs, the first to ascertain whether the reported adverse event was medically attended and the second with a link to a survey that could be completed on a smartphone to obtain details of the nature, duration and severity of the possible AEFI [11]. All SMS replies received from patients were automatically written back into the tool database. Medically attended reactions were automatically sent to the correspondence inbox of the practice software where they were entered into the electronic patient record.

Patients who indicated they had experienced a reaction but did not reply to the survey request, as well as those who did not respond to the first SMS, were telephoned by a practice nurse or doctor.

Ethics approval for analysis of AEFI data from SmartVax was received by the WA Department of Health Human Research Ethics Committee.

2.2 Participants

All children under five years of age who received one or more vaccines recommended in the Australian Childhood Immunisation Schedule [12] at 2, 4, 6, 12, 18 and/or 48 months between 9 November 2011 and 9 June 2015 were included in this analysis. Since SmartVax is intended to be an SMS/Smartphone-based system, the responses of those who did not reply by SMS but were subsequently reached by telephone were not included in the primary analysis. However, a secondary analysis compared the age, sex and reactions reported using SMS/Smartphones and those who required follow-up by voice telephone call.

2.3 Outcome measures

Possible AEFI were defined as a patient's affirmative reply to the first SMS. Patients reporting a possible AEFI were then asked if they sought medical attention and whether they experienced any of the following symptoms: fever, headache, fatigue, rash, vomiting, diarrhoea, rigors, seizures, and local reactions (pain or swelling at the injection site). A serious adverse event (SAE) was defined using the US Vaccine Adverse Events Reporting System criteria; an event where the patient experienced a health-risk, a life-threatening illness, was hospitalised, had a permanent disability, or died [7].

2.4 Statistical Analysis

The response rate was defined as the proportion of patients who responded to the clinic's SMS with a reply SMS. Patients who provided an incorrect or disconnected mobile number or did not answer after three attempted phone calls were classified as uncontactable. Duplicate observations and SMS replies that were unrelated to the vaccination event (e.g. "wrong number" or "stop and get milk on your way home") were removed prior to analysis.

The proportion of patients reporting each clinical symptom, or possible AEFI, at each time point on the vaccination schedule was defined as the number of patients reporting the symptom divided by the total number of vaccinations given for that age time point $\times 100$.

We compared proportions of possible AEFI by year for each time point to determine if there were differences in reports by year. On 1 July 2013, measles-mumps-rubella-varicella (MMRV) vaccine replaced the varicella-only vaccine dose at 18 months and the dose of MMR vaccine at four years of age was removed on the national immunisation schedule. We report the proportion of reported reactions at 18 months of age prior to and after this change using a two-sample test of proportions assuming equal variances.

We also looked at individual patients to calculate SMS response times; this sub-analysis was restricted to the first vaccination visit only so each patient would contribute equally. In addition we determined whether individuals who had more than one visit, and who reported a possible AEFI after their first visit, were more likely to report a possible AEFI at a subsequent visit.

Finally, we compared demographic characteristics of those who did not reply by SMS to determine whether they were different to all those who did reply by SMS (i.e. voice telephone only respondents and those who were uncontactable).

Data were analysed using Stata 14 (Stata Corp. College Station, TX). Descriptive data are presented as proportions with 95% confidence intervals (CI). Logistic regression was used with reaction (Y/N) as the dependent variable, sex and scheduled time point as independent variables. Subsequent logistic regression was used with each reaction type (fever, local reaction, fatigue, etc.) as the dependent variable. Results were considered significant at $\alpha < 0.05$.

3. Results

Between November 2011 and June 2015, 1,667 patients who were aged five years or under had a total of 3,922 vaccination visits. Post-visit SMSs were sent to 3,906/3,922 (99.6%) of these patients and 2,897/3,906 (74.2%) SMS replies were received. Of the 1,009/3,906 (25.8%) patients sent an SMS who did not reply to the initial SMS, 284/1,009 (28.1%) were reached through follow-up telephone calls. Post-vaccination information on possible reactions was unavailable for the remaining 725/3,906 (18.6%) vaccination visits.

There was no significant difference in age, sex or reporting of possible AEFI between those patients who replied to the initial SMS and those who provided information only after being telephoned (Table 1); there was also no significant difference in terms of age, sex and number of vaccination visits between patients who were uncontactable and those who replied by SMS (Table 2). The final dataset for primary analysis included a total of 2,897 SMS replies from 1,216 unique patients, of whom 564/1,216 (46.4%) were female. Of the patients with race recorded, approximately 1% were identified as Aboriginal and/or Torres Strait Islander. The mean number of visits per patient was 1.8 (range 1-6).

Responses to the first SMS were prompt: 988/1,216 (81.3%) individual patients replied within two hours. Of those responding within two hours, 602/988 (60.9%) responded within 10 minutes after the outgoing SMS was sent. A significantly higher proportion of people who reported “no” to any reaction responded within 2 hours 896/1,216 (82.2%) compared with those who reported “yes” 92/1,216 (73.0%), Pearson’s chi-square $p=0.03$.

3.1 Reported Reactions

Overall, 239 (8.2%; 95% CI 7.2—9.2) possible vaccine reactions were reported for all 2,897 vaccination visits over the 44 month time period. The most frequently reported reactions were local reactions (2.5%; 95% CI 2.0—3.2) and fatigue (2.1%; 95% CI 1.6—2.7) across all time points. Local reactions were higher at the 48-month time point (8.6%, 95% CI 6.0—11.2). The odds of a patient having a local reaction at the 48-month scheduled time point was nine times that of the two-month time point (OR 9.2, 95% CI 3.6—23.6) (Table 3). The results were similar when other time points were used as the reference. Frequency of fever was 2.5%, 95% CI 1.0—4.0 (11/441) at the 48-month time point but ranged between 0.6%—1.2% for all other time points. There were a total of 20 GP or after-hours doctor visits and two reported visits to an emergency department (Table 4).

There was no significant difference between the proportion of possible AEFI reported before and after the change from varicella as a single antigen to MMRV at 18 months, i.e. 8.9% vs. 5.9% respectively, $p=0.24$ (Table 5).

When assessing proportions of reported AEFI by year (2012-2014) using each time point on the schedule we found no significant differences across years for any vaccination time points (Figure 1).

One possible serious adverse reaction, a seizure, was reported, however at medical follow-up the patient denied having had a seizure and suggested an accidental affirmative response.

Of 130 individual patients who reported a possible AEFI at their first visit, 68 were age-eligible to attend a subsequent vaccination visit during the period of our study (i.e. 48-month time point excluded). Of these patients, 54/68 (79.4%) were documented to have returned for one or more subsequent vaccinations. Rate of reactions reported at a subsequent visit was significantly higher among those who reported a reaction at their first visit 17/54 (31.5%, 95% CI 19.1-43.9) vs. those who did not report a reaction at their first visit, 71/847 (8.4%, 95% CI 6.5-10.3).

4. Discussion

Our report on a novel vaccine safety surveillance system that uses automatically-generated SMS to actively monitor AEFI in children has three important findings: first, the participation rate by parents is high (>70%); second, the responses are timely (81% reply within two hours); third, the program is sustainable with high rates of participation over time.

The overall rate of possible AEFI of 8.3% was within the range of AEFI reported from passive surveillance [13]. The most common reported reactions, i.e. local (2.5%) and fatigue (2.1%) were below rates reported in the Australian

Immunisation Handbook (handbook) [12] and other sources [13]. At each vaccination time point, the proportions of possible adverse events observed in our study were below those reported in the United States [14]. Thus it appears using SMS technology has made it possible to actively solicit information in near real-time without leading to an over-estimation of AEFI.

Although reactogenicity of individual antigens could not be calculated because the majority of vaccines are combination vaccines, we were able to establish profiles of these vaccine combinations given at each time point.

We identified that the proportion of reactions reported at the 48 month time point may be higher than that for vaccinations administered at younger ages, and this finding is consistent with data collected by the state's passive AEFI monitoring program, the Western Australian Vaccine Safety Surveillance System [15]. Also consistent with our finding, an increased incidence of reactions following booster doses of acellular pertussis-containing vaccines have been reported in a Cochrane review of clinical trials [16] and post-marketing surveillance of 4-6 year olds receiving their fifth dose in Canada [17].

Reassuringly, we found no evidence that changing the immunisation schedule from varicella as a single antigen to MMRV affected reactogenicity experienced at the 18 month time point. Our finding of no increased reaction after MMRV is consistent with others who demonstrated the same for the first dose of MMRV [18, 19].

Adjustments to the childhood immunisation schedule or changes in the lots of vaccine distributed do occur. Having a pre-existing system that can quickly and efficiently assess a change's impact on reactogenicity may be useful to regulatory authorities and providers.

Our findings on rates of specific reactions should be interpreted in context. Although they describe possible adverse events that occurred following vaccination, they do not necessarily prove that the events were caused by the vaccination. Some reported adverse reactions can be the result of coincidence with the timing of the vaccination and not causally-linked [16]. Even so, the rates of possible reactions reported via SmartVax in this analysis are generally reassuring as they do not exceed rates from previous published studies using different methodologies.

We were not able to ascertain why patients were more likely to report a possible AEFI at a subsequent visit if they reported a possible AEFI at their first visit. It could be that these patients were more likely to experience a

substantive reaction after vaccination and report it, or alternatively, that they had, on average, a lower threshold for reporting post-vaccination symptomatology than other patients.

The fact that there was no significant difference in the proportion of patients reporting reactions between those who replied by SMS or who were followed-up by telephone in our study implies that relying only on responses that are received by SMS and smartphone survey are likely to be representative of the broader patient population.

Follow-up telephone calls to non-responders are resource intensive and removing this arm of the program would substantially reduce the staff time required to actively monitor AEFI [11]. Bexelius and colleagues found similar results to ours when they compared SMS with telephone interviews in collecting data about influenza vaccinations from a random sample of the Swedish population registry and found no significant difference between the data obtained by SMS and that obtained by telephone interview [20].

The need to individually follow-up some patients is inevitable; for example, a person who replies affirmatively to the SMS asking about whether their reaction was medically attended may fail to complete the smartphone/web survey. The system only collects self-reported reaction information, it does not evaluate it.

In our assessment, using automated data extraction and SMS/smartphone surveys to actively monitor vaccinees has the potential to make major contributions to vaccine safety surveillance, particularly in countries lacking programs like the Vaccine Safety Datalink in the United States [21]. To help realise this potential in Australia, there have been several enhancements to the SmartVax program since the data in this report were collected. First, the number of practices participating in SmartVax has been expanded. At present there are more than 90 practices which include government and hospital immunisation clinics using SmartVax; increasing the number of vaccinations under surveillance means that any significant deviations from established rates of AEFI will be able to be detected more quickly. Second, SmartVax has been configured to aggregate de-identified patient data across practices so it can be regularly reviewed by vaccine safety professionals. Third, there is flexibility in the timing of when the system sends an SMS, depending on which vaccine was administered; this flexibility should enable SmartVax to actively survey vaccinees about potential reactions other than reactogenicity. For example, it would likely be more meaningful to inquire about fever and rash 7-10 days post-vaccination for patients receiving MMR/V vaccines. Last, in order to ensure the program remains sustainable as it grows in scope, we are examining the concept of tiered-reporting, i.e. having all participating practices report details for every medically attended possible AEFI, but a smaller number routinely supplying information on those events not serious enough in the patients mind to necessitate medical

attention. Future research can focus on how this system can be used to quickly assemble adverse event profiles for newly released vaccine lots and assess differences across vaccine brands to evaluate the impact of recommended changes to the timing of vaccine doses. Further work will evaluate the extent to which these enhancements make SmartVax capable of contributing to robust, national AEFI surveillance.

5. Conclusions

We described a system for active post-marketing vaccine safety surveillance in Western Australia that demonstrated our ability to establish reactogenicity profiles for paediatric vaccine combinations at a practice and assess the impact of changes to the childhood immunisation schedule on reported rates of AEFI. Automated SMS-based reporting can facilitate sustainable, real-time, monitoring of adverse reactions and contribute to early identification of potential vaccine safety issues.

Acknowledgements

We would like to acknowledge Ian Peters who provided technical guidance and support through the development of the tool and collection of data. We would like to thank Asha Bowen for critically reviewing early versions of the manuscript.

Authors Contributions: DWW, SAW & PVE designed the study. DWW reviewed the literature, conducted the statistical analyses, analysed the data and wrote the initial draft of the manuscript. SAW & PVE supervised the analysis and assisted with writing the manuscript. AL collected and assisted with the interpretation of the data. All authors contributed by making critical revisions to the manuscript and all have approved the final article.

Conflict of interest statement: DWW, SAW, & PVE have no conflict of interest to disclose. AL is a co-developer of the SmartVax system. SmartVax is a registered trademark but is not commercially available nor is it under copyright. If this software were to be licensed and sold commercially, he may derive financial benefit.

Funding: This work was supported by the Western Australia Department of Health.

References

- [1] World Health Organization. Promoting Safety of Medicines in Children. France: World Health Organization; 2007.
- [2] Woo E, Labadie J, Braun MM. Vaccine Safety Surveillance. In: Andrews EM, Nicholas; Mann, Ronald D, editor. Mann's Pharmacovigilance. 3rd ed. West Sussex UK: Wiley Blackwell; 2014.
- [3] Murphy TV, Gargiullo PM, Massoudi MS, Nelson DB, Jumaan AO, Okoro CA, et al. Intussusception among infants given an oral rotavirus vaccine. The New England journal of medicine. 2001;344:564-72.
- [4] Galazka AM, Robertson SE, Kraigher A. Mumps and mumps vaccine: a global review. Bulletin of the World Health Organization. 1999;77:3-14.
- [5] Armstrong P, Dowse G, Effler P, Carcione D, Blyth C, Richmond P, et al. Epidemiological study of severe febrile reactions in young children in Western Australia caused by a 2010 trivalent inactivated influenza vaccine. BMJ open. 2011;1:e000016.
- [6] Chen RT, Mootrey G, DeStefano F. Safety of routine childhood vaccinations. An epidemiological review. Paediatric drugs. 2000;2:273-90.
- [7] Zhou W, Pool V, Iskander JK, English-Bullard R, Ball R, Wise RP, et al. Surveillance for safety after immunization: Vaccine Adverse Event Reporting System (VAERS)--United States, 1991-2001. Morbidity and mortality weekly report Surveillance summaries. 2003;52:1-24.
- [8] Gold MS, Effler P, Kelly H, Richmond PC, Buttery JP. Febrile convulsions after 2010 seasonal trivalent influenza vaccine: implications for vaccine safety surveillance in Australia. Med J Aust. 2010;193:492-3.
- [9] Davis RL, Kolczak M, Lewis E, Nordin J, Goodman M, Shay DK, et al. Active surveillance of vaccine safety: a system to detect early signs of adverse events. Epidemiology. 2005;16:336-41.
- [10] Yih WK, Kulldorff M, Fireman BH, Shui IM, Lewis EM, Klein NP, et al. Active surveillance for adverse events: the experience of the Vaccine Safety Datalink project. Pediatrics. 2011;127 Suppl 1:S54-64.
- [11] Leeb A, Regan AK, Peters IJ, Leeb C, Leeb G, Effler PV. Using automated text messages to monitor adverse events following immunisation in general practice. Med J Aust. 2014;200:416-8.
- [12] Australian Technical Advisory Group on Immunisation. The Australian Immunisation Handbook 10th edition 2013 (updated January 2014). Canberra ACT: Australian Government Department of Health and Aging;; 2014.
- [13] Clothier HJ, Crawford NW, Kempe A, Buttery JP. Surveillance of adverse events following immunisation: the model of SAEFVIC, Victoria. Commun Dis Intell Q Rep. 2011;35:294-8.
- [14] Zimmerman RK, Middleton DB, Burns IT, Clover RD, Kimmel SR. Routine vaccines across the life span, 2005. J Fam Pract. 2005;54:S9-26.
- [15] Prevention and Control Program CDCD, Western Australia Department of Health. Western Australia Vaccine Safety Surveillance--Annual Report, 2014. Department of Health, Western Australia; 2014.
- [16] Zhang L, Prietsch SO, Axelsson I, Halperin SA. Acellular vaccines for preventing whooping cough in children. The Cochrane database of systematic reviews. 2014;9:CD001478.
- [17] Skowronski DM, Remple VP, Macnabb J, Pielak K, Patrick DM, Halperin SA, et al. Injection-site reactions to booster doses of acellular pertussis vaccine: rate, severity, and anticipated impact. Pediatrics. 2003;112:e453.
- [18] Czajka H, Schuster V, Zepp F, Esposito S, Douha M, Willems P. A combined measles, mumps, rubella and varicella vaccine (Priorix-Tetra): immunogenicity and safety profile. Vaccine. 2009;27:6504-11.
- [19] Nolan T, McIntyre P, Robertson D, Descamps D. Reactogenicity and immunogenicity of a live attenuated tetravalent measles-mumps-rubella-varicella (MMRV) vaccine. Vaccine. 2002;21:281-9.
- [20] Bexelius C, Merk H, Sandin S, Ekman A, Nyren O, Kuhlmann-Berenzon S, et al. SMS versus telephone interviews for epidemiological data collection: feasibility study estimating influenza vaccination coverage in the Swedish population. Eur J Epidemiol. 2009;24:73-81.
- [21] Baggs J, Gee J, Lewis E, Fowler G, Benson P, Lieu T, et al. The Vaccine Safety Datalink: a model for monitoring immunization safety. Pediatrics. 2011;127 Suppl 1:S45-53.

Figure 1. Proportion of patients reporting a possible AEFI using SMS by year and vaccination time point with error bars indicating 95% confidence intervals

Abbreviations: AEFI, adverse events following immunisation; SMS, short message service

Table 1. Comparison of patients who replied to the SmartVax SMS and those who did not reply but were contacted by telephone.

	Replied to SMS n=2,898	Telephoned n=284	P Value
Mean age, months (median [IQR])	14.6 (9 [4-18])	17.0 (12 [4-19])	0.28
Sex, Female N (%; 95% CI)	1,359 (46.9; 44.2—49.6)	133 (46.8; 38.3—55.3)	0.98
Any reaction N (%; 95% CI)	239 (8.3; 4.8—11.8)	27 (9.5; 1.6—20.6)	0.83

Abbreviations: IQR, Interquartile Range; SMS, short message service; 95% CI, 95% confidence interval

Table 2. Comparison of demographic characteristics of individual patients who responded to SMS and those who did not respond

	Replied to SMS (n=1,216)	Unable to be contacted (n=725)	P Value
Age, months mean	18.1	16.7	0.10 ^a
Median [IQR]	6 [2-48]	12 [4-19]	
Gender			
Female n (%)	564 (46.4)	342 (47.2)	0.82
Male n (%)	652 (53.6)	383 (52.8)	0.80
No. of vaccination visits, mean	2.1	2.2	0.78 ^a
Median [IQR]	2 [1-3]	2 [1-3]	

^aCompared using an independent t-test with equal variances

Table 3. Patient reported local reactions using SmartVax at each scheduled vaccination time point at a general practice in Perth, Western Australia 2011-2015

Vaccination time point	Odds ratio	95% confidence interval
2 month	[1] Reference	[1] Reference
4 month	1.1	0.31—3.7
6 month	2.3	0.82—6.7
12 month	1.2	0.36—3.9
18 month	1.4	0.45—4.6
48 month	9.2	3.6—23.7

Table 4. Parental reports of possible AEFI by vaccination time point using SmartVax, a SMS adverse events monitoring system in General Practice

	2 month n=494	4 month n=459	6 month n=515	12 month n=505	18 month n=483	48 month n=441	Total ^b n=2,897
Scheduled vaccinations (vaccinations administered concomitantly)	Diphtheria, Tetanus, Pertussis, Hepatitis B, Poliomyelitis, Haemophilus influenza type b, Pneumococcal & Rotavirus	Diphtheria, Tetanus, Pertussis, Hepatitis B, Poliomyelitis, Haemophilus influenza type b, Pneumococcal & Rotavirus	Diphtheria, Tetanus, Pertussis, Hepatitis B, Poliomyelitis, Haemophilus influenza type b, Pneumococcal & Rotavirus	Measles, Mumps, Rubella, Haemophilus influenza type b & Meningococcal C	Before 1 July 2013 Varicella After 1 July 2013 Measles, Mumps, Rubella & Varicella	Diphtheria, Tetanus, Pertussis & Poliomyelitis	
Any reaction ^a N (%; 95% CI)	29 (5.9, 3.8—8.0)	37 (8.1, 5.6—10.6)	39 (7.6, 5.3—9.9)	24 (4.8, 2.9—6.6)	33 (6.8, 4.6—9.1)	77 (17.5, 13.9—21.0)	239 (8.2, 7.2—9.2)
Fever ≥38°C	5 (1.0)	4 (0.9)	3 (0.6)	6 (1.2)	3 (0.6)	11 (2.5)	32 (1.1)
Headache	0	0	0	0	0	2 (0.5)	2 (0.1)
Fatigue	12 (2.4)	8 (1.7)	11 (2.1)	11 (2.2)	1 (0.2)	13 (2.0)	60 (2.1)
Rash	0	1 (0.2)	1 (0.2)	3 (0.6)	3 (0.6)	1 (0.2)	9 (0.3)
Vomiting	3 (0.6)	2 (0.4)	4 (0.8)	2 (0.4)	4 (0.8)	3 (0.7)	18 (0.6)
Diarrhoea	8 (1.6)	3 (0.7)	6 (1.2)	3 (0.6)	0	2 (0.5)	22 (0.8)
Rigors	0	0	0	0	0	0	-
Seizure	0	1 (0.2)	0	0	0	0	1 (0.03)
Local reaction	5 (1.0)	5 (1.1)	12 (2.3)	6 (1.2)	7 (1.5)	38 (8.6)	73 (2.5)
Attended GP or after hours service	3 (0.6)	4 (0.9)	0	5 (1.0)	2 (0.4)	6 (1.4)	20 (0.7)
Attended an emergency department	0	0	1 (0.2)	0	1 (0.2)	0	2 (0.06)

Abbreviations: AEFI, adverse events following immunisation; SMS, short message service text message; 95% CI, 95% confidence interval; GP, general practitioner

n= number of SMS responses received per scheduled vaccination

^a“Any reaction” refers to a patient responding by SMS to, “Thank you for caring to have a vaccination. We would like to know if there were any reactions. Kindly reply Y or N only.”

^bTotal reactions may not equal the sum of individual symptoms reported as patients were allowed to report multiple symptoms.

Table 5. Parental reported proportions of AEFI before and after MMR booster and varicella vaccination schedule changes in July 2013

	Prior to 1 July 2013 N (%) 95% CI	After 1 July 2013 N (%) 95% CI	P Value ^a
18 months			
Varicella-only (n=158)	16 (8.9) 4.5—13.3		0.24
18 months			
Measles, Mumps, Rubella, Varicella (n=272)		17 (5.9) 3.1—8.7	

^aUsing a two-sample test of proportions