

# Canadian paediatricians' approaches to managing patients with adverse events following immunization: The role of the Special Immunization Clinic network

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**BACKGROUND:** When moderate or severe adverse events occur after vaccination, physicians and patients may have concerns about future immunizations. Similar concerns arise in patients with underlying conditions whose risk for adverse events may differ from the general population. The Special Immunization Clinic (SIC) network was established in 2013 at 13 sites in Canada to provide expertise in the clinical evaluation and vaccination of these patients.

**OBJECTIVES:** To assess referral patterns for patients with vaccine adverse events or potential vaccine contraindications among paediatricians and to assess the anticipated utilization of an SIC.

**METHODS:** A 12-item questionnaire was distributed to paediatricians and subspecialists participating in the Canadian Paediatric Surveillance Program through monthly e-mail and mail contacts.

**RESULTS:** The response rate was 24% (586 of 2490). Fifty-three percent of respondents practiced general paediatrics exclusively and 52% reported that they administer vaccines. In the previous 12 months, 26% of respondents had encountered children with challenging adverse events or potential vaccine contraindications in their practice and 29% had received referrals for such patients, including 27% of subspecialists. Overall, 69% of respondents indicated that they would be likely or very likely to refer patients to an SIC, and 34% indicated that they would have referred at least one patient to an SIC in the previous 12 months.

**CONCLUSIONS:** Patients who experience challenging adverse events following immunization or potential vaccine contraindications are encountered by paediatricians and subspecialists in all practice settings. The SIC network will be able to respond to a clinical need and support paediatricians in managing these patients.

**Key Words:** *Adverse events; Immunization; Referral*

Vaccination is one of the most effective public health interventions ever developed, having led to dramatic reductions in childhood morbidity and mortality (1). As vaccine-preventable diseases become increasingly uncommon, the public's focus has shifted to the safety of recommended vaccines (2). Although vaccines are generally safe, they have rarely been associated with moderate or severe adverse events (eg, febrile seizure, anaphylaxis) (3-5). An adverse event following immunization (AEFI) is any untoward medical event occurring after an immunization, regardless of whether the vaccine caused the event (6). For patients with

**Les approches des pédiatres canadiens pour la prise en charge des effets secondaires suivant l'immunisation : le rôle d'une clinique d'immunisation spéciale**

**HISTORIQUE :** Lorsque des effets secondaires modérés ou graves surviennent après l'immunisation, les médecins et les patients peuvent s'inquiéter des réactions éventuelles aux futurs vaccins. Des inquiétudes similaires sont soulevées au sujet des patients ayant une maladie sous-jacente et dont les risques d'effets secondaires sont différents de ceux de la population générale. Un réseau de cliniques spéciales en immunisation a été créé en 2013 dans 13 centres canadiens afin d'offrir des compétences dans l'évaluation clinique et la vaccination de ces patients.

**OBJECTIFS :** Chez les pédiatres, évaluer les profils d'aiguillage des patients présentant des effets secondaires suivant l'immunisation ou des contre-indications potentielles à la vaccination ainsi que l'utilisation prévue d'une clinique d'immunisation spéciale.

**MÉTHODOLOGIE :** Les pédiatres et les surspécialistes participant au Programme canadien de surveillance pédiatrique par des courriels et des envois postaux mensuels ont reçu un sondage de 12 questions.

**RÉSULTATS :** Le taux de réponse s'élevait à 24 % (586 répondants sur une possibilité de 2 490). Cinquante-trois pour cent d'entre eux exerçaient exclusivement en pédiatrie générale, et 52 % ont déclaré administrer des vaccins. Au cours des 12 mois précédents, 26 % des répondants avaient évalué des enfants ayant des effets secondaires problématiques ou une contre-indication potentielle à la vaccination dans leur pratique et 29 %, dont 27 % de surspécialistes, avaient reçu des demandes de consultation au sujet de tels patients. Dans l'ensemble, 69 % des répondants ont indiqué qu'ils seraient susceptibles ou très susceptibles d'orienter des patients vers une CIS, et 34 % qu'ils auraient orienté au moins un patient vers une CIS au cours des 12 mois précédents.

**CONCLUSIONS :** Les pédiatres et les surspécialistes en pédiatrie évaluent des patients ayant des effets secondaires problématiques suivant l'immunisation ou des contre-indications potentielles à la vaccination dans tous les milieux de pratique. Le réseau de cliniques spéciales en immunisation répondra à un besoin clinique et soutiendra les pédiatres dans leur prise en charge de ces patients.

AEFI that come to medical attention (approximately 13 to 22 per 100,000 population in an Australian study [7]), a careful evaluation is required to confirm the diagnosis, assess the probability that the vaccine caused the AEFI and assess the safety of future immunizations (8). This final step can be particularly challenging because there is a lack of scientific data regarding the risk of recurrence of AEFI. Patients with underlying medical conditions that may alter the risk of an adverse event and/or lead to reduced vaccine effectiveness also benefit from a detailed assessment by an expert clinician.

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**TABLE 1**  
**Description of the Special Immunization Clinic (SIC) network and locations of SIC sites**

What is the SIC network?	A Canadian network of paediatric and adult infectious disease specialists and allergists with expertise in the assessment and management of patients who experienced a 'challenging' AEFI or who have underlying conditions that may put them at higher risk of an AEFI (eg, immunocompromise). Patients seen in one of the 13 SICs are assessed and managed using a standardized approach and are included in a central registry, with consent. This registry will permit the evaluation of patient outcomes with current management protocols and build a scientific basis for developing improved practice guidelines.
What are the network's objectives?	To guide best practice regarding investigation, diagnosis and management of patients presenting with AEFI or potential contraindications to immunization. To estimate the safety of vaccinating patients with potential contraindications. To determine the probability of recurrence of AEFIs upon revaccination and identify risk factors for recurrence. To develop expert resources that will enhance public health capacity to respond to new or emerging vaccine safety concerns. To provide a platform for prospective multicentre studies on AEFI or potential contraindications to immunization.

**SIC locations and contact information (current as of March 2014)**

City	Hospital	Contact telephone number
Halifax, Nova Scotia	IWK Health Centre	902-470-7859
Quebec City, Quebec	Centre hospitalier universitaire de Québec (CHUL)	418-525-4444 ext 48290
Montreal, Quebec	Centre hospitalier universitaire Sainte-Justine	514-345-4931 ext 5862
	Montreal Children's Hospital	514-624-7855
Sherbrooke, Quebec	Centre hospitalier universitaire de Sherbrooke	819-346-1110 ext 70337
Ottawa, Ontario	Children's Hospital of Eastern Ontario	613-737-7600 ext 2651
Toronto, Ontario	Hospital for Sick Children	416-813-8097 ext 208097
Hamilton, Ontario	McMaster Children's Hospital	905-521-2100 ext 76947
Sudbury, Ontario	Health Sciences North	705-523-7300 ext 3219
Saskatoon, Saskatchewan	Royal University Hospital	306-844-1159
Edmonton, Alberta	Stollery Children's Hospital	780-248-5540
Calgary, Alberta	Alberta Children's Hospital	403-955-2200
Vancouver, British Columbia	BC Children's Hospital	604-875-2422

*AEFI Adverse event following immunization*

Specialized clinical services for patients with previous AEFI or potential contraindications to immunization (eg, egg allergy) have been established in several locations (9-11). In Canada, the Special Immunization Clinic (SIC) network was established in 2013 to provide expertise in the clinical care of patients with AEFI and potential contraindications to immunization (Table 1). Because immunization programs in Canada are the jurisdiction of each province and territory, resources available for managing these patients and patterns of referral may vary across the country. In anticipation of establishing the SIC network, we sought to describe the current referral patterns for children with AEFI or potential vaccine contraindications among paediatricians and subspecialists in Canada, and to assess paediatricians' willingness to refer such patients to an SIC.

### METHODS

A survey of paediatricians and paediatric subspecialists was conducted through the Canadian Paediatric Surveillance Program (CPSP). The CPSP conducts active surveillance for rare diseases and distributes one-time surveys through monthly e-mail or mail contacts to approximately 2500 actively practicing paediatricians and subspecialists across Canada, of whom approximately 75% are members of the Canadian Paediatric Society. Response rates to the monthly mailings averaged 77% in 2012 (12). The survey was distributed in English and French in April 2013. Survey reminders were included in the monthly e-mails in May and June 2013, after which the survey was closed.

The survey instrument was developed by the authors, reviewed by experts in the field for content validity and piloted among seven paediatricians and subspecialists to assess face validity, readability and time to completion. The questionnaire was then reviewed by the CPSP Steering Committee for content validity.

The survey was translated into French by CPSP staff. The final questionnaire consisted of 12 items including type of practice (eg, general paediatrics, subspecialty), province, whether they provided vaccines, referrals received regarding patients with AEFI and their management, satisfaction with current resources for managing these patients and likelihood of referring patients to a special immunization clinic.

The analysis was descriptive. Proportions were compared using the  $\chi^2$  test;  $P < 0.05$  was considered to be statistically significant.

### RESULTS

In total, 462 online and 124 mailed-in responses were received. The overall response rate was 24% (586 of 2490). The online response rate was 30% (462 of 1540) compared with the mailed-in response rate of 13% (124 of 950). Most respondents (312 of 586 [53%]) practiced general paediatrics exclusively, 4% practiced infectious diseases (ID) or allergy subspecialties, 25% practiced general paediatrics and a subspecialty other than ID or allergy, and 16% practiced another subspecialty only. Among CPSP members for whom the information was available (70%), 52% practiced general paediatrics exclusively, 14% practiced general paediatrics and a subspecialty, and 35% were subspecialists (including ID and allergy). Compared with the total CPSP membership, survey respondents were more likely to practice in academic settings (35% versus 45%) and less likely to be exclusively hospital-based (8% versus 6%). Fifty-two percent (303 of 586) of respondents reported administering vaccines in their practice. Respondents had been in practice for a median of 18 years (interquartile range nine to 27 years) and 81% (475 of 586) practiced within 150 km of a paediatric tertiary care centre. Respondents practiced in all regions of the country: 7% in the Atlantic provinces, 58% in Quebec or Ontario, and 27% in the Western provinces and

**TABLE 2**  
**Frequency of referrals for adverse events following immunization (AEFI) and anticipated utilization of a Special Immunization Clinic (SIC) according to practice type and vaccine provider status, n=583**

	Type of practice			Vaccine provider	
	General paediatrics only	ID or allergy	Other subspecialty ± general paediatrics	Yes	No
In the past 12 months, did you encounter patients with challenging AEFI or contraindications to vaccination?					
Yes	86 (28)	15 (60)	47 (20)	102 (34)	50 (18)
No	209 (68)	10 (40)	168 (70)	193 (63)	201 (72)
Did not answer	13 (4)	0	23 (10)	8 (3)	29 (10)
Did you receive questions/referrals about challenging AEFI or contraindications?					
Yes	96 (31)	21 (84)	51 (21)	97 (32)	71 (25)
No	199 (65)	3 (12)	173 (73)	198 (65)	180 (64)
Did not answer	13 (4)	1 (4)	14 (6)	8 (3)	29 (10)
Sources of referrals*					
	n=89	n=14	n=46	n=91	n=57
Family physicians	69 (76)	11 (79)	34 (74)	70 (77)	43 (75)
Paediatrician	10 (11)	12 (86)	25 (54)	31 (34)	16 (28)
Public health professional†	23 (26)	2 (14)	10 (22)	17 (19)	20 (35)
Other	34 (38)	5 (36)	21 (46)	34 (37)	26 (46)
Did you refer patients with challenging AEFI or potential contraindications? (n=438)‡					
Yes	74 (30)	8 (32)	28 (18)	67 (22)	46 (34)
No	75 (30)	15 (60)	52 (34)	100 (33)	43 (32)
Did not answer	97 (40)	2 (8)	75 (48)	136 (45)	46 (34)
To whom did you refer patients?*					
	n=74	n=8	n=28	n=67	n=46
Public health officials	16 (22)	1 (13)	3 (11)	12 (18)	20 (43)
Allergist	51 (69)	5 (63)	14 (50)	58 (87)	40 (87)
ID specialist	18 (24)	2 (25)	16 (57)	23 (34)	34 (74)
General paediatrician + other	5 (7)	2 (25)	2 (7)	7 (10)	6 (13)
Level of satisfaction with local resources for patients with AEFI (n=438)‡					
Very/somewhat satisfied	118 (48)	21 (84)	67 (43)	133 (44)	75 (56)
Very/somewhat dissatisfied	26 (11)	1 (4)	10 (7)	25 (8)	12 (9)
Did not answer	102 (41)	3 (12)	78 (50)	145 (48)	48 (35)
How likely would you be to refer patients to an SIC?					
Very/somewhat likely	242 (78)	16 (64)	146 (61)	207 (68)	198 (71)
Very/somewhat unlikely	48 (16)	6 (24)	69 (29)	72 (24)	53 (19)
Did not answer	18 (6)	3 (12)	23 (10)	24 (8)	29 (10)
In the past 12 months, how many patients would you have referred to an SIC, if available?					
0	163 (53)	11 (44)	154 (65)	169 (56)	163 (58)
≥1	120 (39)	14 (56)	67 (28)	107 (35)	94 (34)
Did not answer	25 (8)	0 (0)	17 (7)	27 (9)	23 (8)

Data presented as n (%) unless otherwise indicated. \*Respondents could give more than one response; †Includes Public Health nurse, Medical Officer of Health; ‡Respondents who indicated that they did not provide vaccines, encounter patients with AEFI, or receive questions or referrals about AEFI were excluded from answering this question. ID Infectious diseases

Northern territories. The geographical distribution of survey respondents was similar to the total CPSP membership.

Children with potential vaccine contraindications or 'challenging' AEFI (defined as events that raised uncertainty about how to proceed with future immunizations such as large injection site reactions, neurological or allergic symptoms) had been encountered in the previous 12 months by 60% of ID or allergy specialists compared with 28% of general paediatricians and 20% of other subspecialists (Table 2). Respondents who indicated that they administer vaccines were more likely than nonproviders to encounter children with AEFI (34% versus 18%;  $P < 0.001$ ). However, 25% of nonproviders and 21% of non-ID/allergy subspecialists reported that they had received questions or referrals regarding challenging AEFI or vaccine contraindications in the past year. Among general paediatricians, family physicians were the most frequent source of referrals, followed by public health professionals. Subspecialists, including ID and allergy, received referrals primarily from family physicians and general paediatricians. Referrals from public health professionals were

more frequently reported by paediatricians practicing in regions where public health nurses administer most childhood vaccines (eg, Quebec: 33% [n=30]; Western and Northern regions: 20% [n=44]) than by paediatricians practicing in regions with primarily physician-delivered immunization programs (eg, Ontario: 3% [n=53]). Respondents who indicated that they had referred patients with AEFI to another specialist were most likely to have referred them to an allergist, followed by an ID specialist or public health official.

Few respondents expressed dissatisfaction with available resources for managing patients with AEFI (8% overall) compared with the proportion that was satisfied (47% overall), but there was a high frequency of nonresponse (up to 50%). Overall, 69% of respondents indicated that they would be likely or very likely to refer patients to an SIC if available, with no differences noted between vaccine providers versus nonproviders, type of practice or region of practice (data not shown). More than one-third of vaccine providers and nonproviders, and a majority of ID and allergy specialists (56%), indicated that they would have referred at least

one patient to an SIC in the previous 12 months. Among 70 respondents who indicated why they would be somewhat or very unlikely to refer patients to an SIC, 34 (49%) stated that they do not manage immunization-related issues in their practice and 19 (27%) stated that they are comfortable managing patients with AEFI and potential contraindications themselves.

## DISCUSSION

More than one-quarter of Canadian paediatricians and subspecialists who responded to the present cross-sectional survey had encountered patients with AEFI or potential vaccine contraindications in the previous year. Family physicians were the most frequent source of referrals overall. Although <10% of respondents indicated dissatisfaction with the resources currently available to manage patients with previous AEFI or vaccine contraindications, nearly 70% reported that they would be likely or very likely to refer patients to an SIC, if available, and 34% would have referred at least one patient to an SIC in the previous 12 months. Importantly, anticipated uptake of an SIC was high in all regions of the country among general paediatricians and subspecialists, including ID specialists and allergists, suggesting that such a service would receive wide acceptance among physicians.

The published experience of specialized immunization services in Australia, Italy and the United Kingdom has demonstrated that a systematic approach to patient assessments is associated with high acceptance of reimmunization (9-11). More than 70% of patients were safely immunized and <1% experienced a serious adverse event (9,10). The current study provides further evidence that vaccine providers and specialists who care for patients with AEFI are highly interested in having access to specialized immunization services, emphasizing the need to expand these services.

Specialized immunization services have also helped to educate local physicians and the public about vaccine adverse events (10). This role is important because there is growing evidence to suggest that the occurrence of an AEFI significant enough to require medical attention may adversely affect a family's confidence in the safety of immunization and lead to refusal of future immunizations (13-15). For these reasons, a specialized service for patients with previous AEFI or potential contraindications to immunization should be considered to be an essential component of every universal immunization program (9-11,16,17).

There is currently limited scientific evidence to guide management of patients with AEFI and potential contraindications to vaccination. Current recommendations for management after an AEFI are based largely on expert opinion, with a few exceptions (18). The Canadian SIC network, with clinics at 13 sites in six provinces (Table 1), provides clinical expertise and will serve as a platform for research on vaccine safety. Specific research interests include evaluating outcomes of patients with AEFI after reimmunization, assessing vaccine safety in immunocompromised patients and studying etiologies of AEFI. Patients are assessed and managed using a standardized approach based on the best available evidence. The development of a registry of patients seen in the SIC will facilitate the evaluation of patient outcomes, thus creating a better scientific basis to guide management of this group of patients. The network also provides expert resources to enhance public health capacity to respond to new or emerging vaccine safety concerns. The majority of Canadians live within 150 km of an SIC; therefore, this service will be widely accessible. Future plans include expansion of the SIC network to secondary referral centres and creation of an information hotline for providers in more remote areas.

The present study had limitations. The response rate was low (24%), but was similar to other one-time CPSP surveys conducted

in 2011 to 2012, which had a mean response rate of 27% (range 21% to 34%) (12,19). The proportion of incomplete responses was high for some questions. Both factors could have contributed to significant response bias and led to an overestimation of the anticipated utilization of an SIC. The high proportion of nonresponse to the question regarding level of satisfaction with resources for managing patients with AEFI could indicate a high proportion of individuals with a neutral opinion, or may suggest greater satisfaction or dissatisfaction than the results indicate. Additionally, the restrictions on survey length limited the number of questions that could be asked (eg, types of patients that respondents would be more likely to refer, willingness to follow common protocols and contribute data to the registry, anticipated utilization of an AEFI hotline). However, the strength of the present study was the broad representation from paediatricians and subspecialists in all regions of the country practicing in a range of settings.

## CONCLUSION

There appears to be broad support for an SIC network to standardize the assessment and management of patients with challenging vaccine concerns such as previous adverse events after vaccination and potential contraindications to immunization. With the current number of sites and their distribution across the country, this service will be accessible to most Canadians. Further expansion of this service over time will broaden its reach even further.

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**ETHICS STATEMENT:** This was a professional survey regarding current practice conducted by the Canadian Paediatric Surveillance Program, which does not require ethical review under Tri-Council Policy Statement 2.

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