

Weekly Influenza Update

December 4, 2008

Wisconsin:

Influenza activity continues to be at baseline in Wisconsin. The prevalence of influenza-like illness [fever of 100oF or higher and either cough or sore throat] in Wisconsin's primary care patients is an estimated to be 1.2%.

13.0% of last week's primary care patients had acute respiratory infections (ARI).

The prevalence of acute diarrheal illness (ADI) in Wisconsin's primary care patients is at 1.6%.

CLINICAL NOTES:

Prophylaxis

Continue to offer influenza vaccine to anyone interested. Full immunity is achieved within 2 weeks of vaccination.

Vaccination is targeted towards:

- all high risk individuals
- children from 6 months to 18 years
- adults 50 years and above
- pregnant women
- healthcare workers

Diagnosis

- influenza infections are rare at this time
- PPV of rapid influenza tests is poor, NPV is excellent

Treatment

- a limited number of viruses have been tested for neuraminidase inhibitor resistance this season
 - 20 out of 21 A(H1) viruses were resistant to Oseltamivir (95%)
 - 0/5 A(H3) and 0/8 B viruses have been resistant to oseltamivir.

All viruses tested have been sensitive to zanamivir

- a limited number of viruses have been tested for adamantane resistance this season
 - 0/6 A(H1N1) viruses were resistant to adamantanes
 - 4/4 A(H3N2) viruses were resistant to Adamantanes
 - Adamantane antivirals are ineffective against influenza B viruses

Other

- Rhinovirus, parainfluenza type 3 and adenovirus continue to circulate in Wisconsin
- RSV prevalence is increasing
- rotavirus isolations are at low levels

Across the U.S.:

As of November 22nd, 309 positive surveillance cultures have been recorded in the United States. 2.5% of respiratory specimens during week 47 (November 16-22) were positive for influenza.

- 78.6% of isolates have been type A
 - 87.8% of all sub-typed A viruses have been H1N1
 - 12.2% of A viruses have been H3N2
- 21.4% of isolates have been type B

- 6.4% of deaths during week 47 (November 16-22) were due to pneumonia or influenza [below the epidemic threshold of 7.0%] -no pediatric influenza deaths have been reported to CDC this season

Global News [from the WHO]: There have been no new cases of Avian influenza (A-H5N1) reported since 9/10/08.

Since 2003, there have been 387 laboratory-confirmed cases of Avian influenza (A-H5N1). The cases been confined to Laos, Viet Nam, Thailand, Indonesia, Cambodia, the People's Republic of China, Turkey, Iraq, Azerbaijan, Egypt, Djibouti Nigeria,

Myanmar and Pakistan. There have been 245 associated deaths (case fatality rate= 63.3%). There is enhanced avian influenza surveillance in Wisconsin. Contact Tom Haupt at the Wisconsin Division of Public Health (608-266-5326) prior to submitting specimens for fee-exempt testing for patients with influenza-like illness returning from Southeast Asia within 10 days.

Other Observations:

Please see the attached pdf for a recent study assessing a method to reduce the pain of immunizations for younger children: "A multifactorial strategy of pain management is associated with less pain in scheduled vaccination of children. A study realized by family practitioners in 239 children aged 4–12 years old."

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A multifactorial strategy of pain management is associated with less pain in scheduled vaccination of children. A study realized by family practitioners in 239 children aged 4–12 years old

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Boivin J-M, Poupon-Lemarquis L, Iraqi W, Fay R, Schmitt C and Rossignol P. A multifactorial strategy of pain management is associated with less pain in scheduled vaccination of children. A study realized by family practitioners in 239 children aged 4–12 years old. *Family Practice* 2008; **25**: 423–429.

Background and aims. The multiplicity of vaccine injections during childhood leads to iterative painful and stressful experiences which may lead in turn to anticipated pain and then possibly to a true needle phobia. We aimed at evaluating a multifactorial strategy of pain management combining pharmacological and non-pharmacological approaches during vaccination, as compared to usual care, in 4- to 12-year-old children.

Methods. In all, 239 children were enrolled by 25 family practitioners in an open-label study. After a pseudo-randomization, usual pain management ($n = 132$) was compared to a multifactorial strategy ($n = 107$) associating preliminary application of an anesthetic patch, preferential use of specified vaccines, child education by the parents and the doctor, parental accompaniment and child distraction with soap bubbles during the procedure. The primary outcome (i.e. child pain) was assessed with a self-report scale named visual analog scale (VAS) of pain.

Results. A significant decrease in pain was obtained using the multifactorial strategy, as assessed by self-reported VAS ($P < 0.0001$). This was confirmed by another self-report scale (the facial pain scale revised: $P = 0.005$), as well as with hetero-evaluations by GPs and parents [Children's Hospital of Eastern Ontario Pain Scale: $P = 0.0007$; GPs VAS ($P < 0.0001$), parents VAS ($P < 0.0001$)], which were secondary outcome criteria.

Conclusions. This multifactorial method significantly decreases vaccination pain in 4- to 12-year-old children. This strategy could make vaccines more acceptable to children and may improve child–doctor relationships and contribute to a decrease in child fear about health care.

Keywords. Children, family practitioner, general practitioner, pain, vaccination.

Introduction

A Child's Vaccine Programme, according to the vaccine calendar,¹ requires up to 16 possible injections by the age of 13. Vaccination can be painful and stressful. The pain is not only due to the cutaneous puncture but also to the quality of the vaccine (type).² Thus, the multiplicity of vaccinations leads to iterative painful

experiences³ and memorization by children.^{4,5} It could explain why children and some parents' have concerns about vaccinations, which could result in a bad compliance to the vaccine program, with children presenting sometimes real injection phobia.⁶ Furthermore, repeated painful acts could inhibit the relationship between the child and the doctor. Sometimes, the doctor himself increases the children awareness of pain

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during vaccination. Pre-existing painful experiences like surgery for tonsillectomy or circumcision could lead to greater pain during vaccination compared to children who have had no previous surgery.⁷

The assessment of pain in children is difficult to evaluate. However, a variety of validated pain scales are available. The French National Agency for Health Accreditation and Evaluation (ANAES) recommendations concerning Evaluation and management strategies for acute pain in the ambulatory care of children aged 1 month to 15 years old advises using the pharmacological (EMLA patch®) and non-pharmacological approaches such as recreation, relaxation, parental presence and child education.⁸ Many studies concerning those different methods show convincing results, but mainly assessed by hetero-evaluation scales, which may be less reliable than self-assessment scales.⁹ Recreation methods, combined with pharmacological methods were also proven to be effective. Therefore, if each method is individually efficient, we hypothesized that their combination may provide an optimization of pain management during vaccination. The aim of this study was to evaluate a multifactorial strategy of pain management during vaccination, as compared to usual care, in 4- to 12-year-old children, using a self-evaluation scale. We report that such a multifactorial strategy including combined pharmacological and non-pharmacological approaches decreases significantly pain.

Material and methods

This study was a prospective, open study, with pseudo-randomization.

Study population

Twenty-five investigating GPs, from the Lorraine area (East part of France), either in a teaching clinical practice at their office under the auspices of the General Medicine Department of Nancy University (48%) or being part of the research and investigating practitioners' Network of the Clinical Investigation Center (CIC)-Institut National de la Santé et de la Recherche Médicale of Nancy (52%), took part in the study. The study was held from May 1st, 2004 to October 30th, 2004 and was proposed to the first 12 children, consulting their GP for a vaccination, and meeting all the inclusion criteria and no exclusion criteria.

The inclusion criteria were as follows: 4- to 12-year-old children, of both genders, scheduled for a vaccination during the next examination at the GP's office, according to the vaccination calendar (diphtheria-tetanus-poliomyelitis-pertussis, diphtheria-tetanus-poliomyelitis, measles-mumps-rubella, Hepatitis B or vaccines for travellers). Prior parental oral consent, after having read an information form (explaining the study aims and design and mentioning that anonymous data would be analyzed was required).

The exclusion criteria were as follows: temporary or definitive vaccination contraindication, EMLA® anesthetic patch contraindication, any concomitant painful disease, mental delay and parents not willing to participate.

Pseudo-randomization procedure: the children were included in the order of booking at the office. The first six patients made up the control group whereas the six following patients formed the intervention group.

Moreover, half of the included children had to be 5–7 years old and the other 10–12 years old.

All participating doctors attended a preliminary information session in which there was a reminder of the vaccine calendar and recommended vaccine methods, a general presentation of the study aims and a reminder of Good Clinical Practices.

They read the specific protocol vaccination procedures only after having enrolled the first six control children.

Study design

Control group. Doctors vaccinated the children without changing their usual practices, including a variety of injection sites, and the use or not of an anesthetic patch or a freezing spray and distraction methods.

Intervention group. Doctors vaccinated the children following a multifactorial strategy including pharmacological and non-pharmacological approaches, associating

- Education and preparation of the parents
- Child education by the parents (a specific document was given to the parents, and another document, with images was given to the child).
- PRIORIX® vaccine to be used preferentially in case of combined vaccination against measles, mumps and rubella
- Preliminary application of an EMLA® anesthetic patch on the injection site. EMLA® use was standardized according to a written instruction letter to parents including the minimum application period (1 h before the vaccination) and the scheduled anaesthetics patch site (i.e. at the proximal arm area as shown in a picture).
- Prior education of the child by the doctor about the potentially painful aspects of the vaccination
- Presence of one of the parents maintaining a physical and reassuring contact with the child or cordial and reassuring words
- Child's distraction by blowing soap bubbles during the procedure.

Pain assessment tools

The primary study outcome (i.e. child pain) was assessed with a self-report scale named visual analog scale (VAS).

In addition, secondary outcomes were assessed, including another self-report scale: facial pain scale

revised (FPS-R) and a behavioural scale [Children's Hospital of Eastern Ontario Pain Scale (CHEOPS)] used by the GP, only in 4- to 6-year-old children. These assessment scales are recommended by the ANAES (Agence Nationale d'Accréditation et d'Evaluation des Soins)⁸ and by Stinson *et al* in a comprehensive review.¹⁰

As other secondary outcomes, the doctor and one of the parents also assessed the child's pain with VAS.

All VAS scores were assessed simultaneously and independently.

Statistical methodology

Each assessed intervention proved its efficacy on pain associated with vaccination. We made the hypothesis that their combination would demonstrate an increased efficacy.

The primary efficacy end point was self-evaluation of pain on a 0–100 mm VAS. The planned sample size of 100 children per arm was designed to provide a 80% power to detect a 10-mm difference in the primary end point at the usual 5% two-sided significance level, assuming a 25-mm SD.¹¹ We planned to enrol a total of 210 patients to adjust for 5% of expected missing values. Data presented in this paper are mean (95% confidence interval) for continuous variables and percentages and frequencies for categorical variables. Comparisons between groups were performed by Wilcoxon–Mann–Whitney and Kruskal–Wallis tests for continuous variables and chi-square or Fisher's tests for categorical variables. Correlation analyses were performed using the Spearman coefficient. All statistical analyses were performed in an intention to treat manner and carried out using the SAS V8.2 software (SAS Institute, Cary, NC). A *P* value <0.05 was considered as statistically significant.

Results

Descriptive analysis

The figure presents the study flow chart (Fig. 1), whereas child clinical information and the vaccination pattern are shown in the Table 1. Child's mean age was greater in the control group than in the intervention group, whereas other features, including the vaccines were similar. Injection sites and ways of administering vaccines differed markedly between the two groups (data not shown), as vaccination procedures were imposed by the study protocol in the intervention group only.

Pain evaluation

Children in the intervention group displayed significantly less pain as compared to the control group, using the self-report-VAS i.e. primary outcome (Table 2). Interestingly, all other secondary outcome criteria (i.e.

TABLE 1 Specifications of both studied groups

	Control group, <i>n</i> = 132	Intervention group, <i>n</i> = 107	<i>P</i> value
Mean age	8.5 (8.0–9.0)	7.7 (7.3–8.1)	0.044
4–6 years old	47 (36%)	55 (52%)	} 0.035
7–9 years old	27 (21%)	20 (19%)	
10–12 years old	57 (44%)	31 (29%)	
Not specified	1	1	
Mean number of brothers and sisters	1.6 (1.4–1.8)	1.7 (0.4–2.0)	Not significant
Pre-existing painful surgery (tonsillectomy, circumcision, appendicectomy and hernia)	24 (18.2%)	20 (18.7%)	Not significant
Pre-existing fracture	16 (12.1%)	11 (10.3%)	Not significant
Measles, Mumps and Rubella vaccine	42	36	Not significant
Diphtheria-Tetanus-Poliomyelitis	31	33	
Diphtheria-Tetanus-Poliomyelitis-Pertussis	52	40	
Hepatitis	10	4	
Other vaccines	2	4	

self-assessment with the FPS-R, behavioural assessment by GP using CHEOPS and hetero-evaluation made by the doctors and one parent using VAS) were also improved significantly within the intervention group. A *post hoc* subgroup analysis revealed that such improvements were statistically significant only in children younger than 10.

A good correlation between the different pain evaluations (child's self-report and hetero-evaluation by doctors and parents using VAS) was observed in both groups, with a correlation coefficient of 0.81 between child's self-report and doctor's evaluation, of 0.77 between child and the parent's and of 0.87 between doctor's evaluation and the parents'. There was also a strong correlation between evaluations obtained using the two self-report scales (VAS and faces pain scale revised) in both groups (Spearman correlation coefficient of 0.80).

Discussion

Our results show that a multifactorial strategy of pain management during a 4- to 12-year-old children vaccination schedule was more effective to prevent pain as compared to usual care. Such a strategy was based on the combination of pharmacological methods (anesthetic patch, selective vaccine choice, which have been individually shown effective) and non-pharmacological ones (recently shown effective according to a Cochrane meta-analysis).⁹

The French consensus agency ANAES, in its recommendations on the evaluation and strategies of

TABLE 2 Pain evaluation during vaccination in each group

		Control group		Intervention group		P value		
Self-report	VAS (0–100 mm)	4–6 years old	<i>n</i> = 43	38.3 (29.3–47.3)	<i>n</i> = 49	20.3 (13.8–26.8)	<0.0001	
		7–9 years old	<i>n</i> = 27	28.3 (19.3–37.2)	<i>n</i> = 20	12.0 (7.2–16.7)	0.011	
		10-year old +	<i>n</i> = 57	19.9 (15.4–24.5)	<i>n</i> = 31	16.7 (9.9–23.5)	0.50	
		Total	<i>n</i> = 127	27.9 (23.7–32.2)	<i>n</i> = 100	17.5 (13.6–21.4)	<0.0001	
	FPS-R (score 0–10) mean (SD)	4–6 years old	<i>n</i> = 43	3.8 (2.7–4.8)	<i>n</i> = 46	2.4 (1.6–3.3)	0.019	
		7–9 years old	<i>n</i> = 24	3.3 (2.2–4.5)	<i>n</i> = 16	1.1 (0.6–1.7)	0.011	
		10-year old +	<i>n</i> = 46	2.1 (1.5–2.8)	<i>n</i> = 25	1.4 (0.5–2.2)	0.24	
Hetero-evaluation	CHEOPS	4–6 year old	<i>n</i> = 44	7.9 (7.0–8.7)	<i>n</i> = 47	6.1 (5.4–6.9)	0.0007	
		4–6 years old	<i>n</i> = 47	28.9 (21.8–36.0)	<i>n</i> = 54	9.6 (5.9–13.3)	<0.0001	
		7–9 years old	<i>n</i> = 27	26.7 (18.2–35.3)	<i>n</i> = 20	8.9 (4.9–12.9)	0.0004	
		10-year old +	<i>n</i> = 57	15.2 (11.3–19.2)	<i>n</i> = 31	8.4 (4.4–12.5)	0.074	
		Total	<i>n</i> = 131	22.5 (18.9–26.1)	<i>n</i> = 105	9.1 (6.8–11.4)	<0.0001	
	GPs VAS (0–100 mm)	4–6 years old	<i>n</i> = 46	32.1 (23.9–40.3)	<i>n</i> = 55	12.4 (8.2–16.7)	<0.0001	
		7–9 years old	<i>n</i> = 27	30.1 (20.3–40.0)	<i>n</i> = 20	10.7 (5.5–15.8)	0.0008	
		10-year old +	<i>n</i> = 54	16.9 (12.3–21.4)	<i>n</i> = 31	11.2 (6.4–16.1)	0.20	
		Total	<i>n</i> = 127	25.2 (21.0–29.4)	<i>n</i> = 106	11.7 (9.0–14.5)	<0.0001	
		Parents VAS (0–100 mm)	4–6 years old	<i>n</i> = 44	7.9 (7.0–8.7)	<i>n</i> = 47	6.1 (5.4–6.9)	0.0007
			4–6 years old	<i>n</i> = 47	28.9 (21.8–36.0)	<i>n</i> = 54	9.6 (5.9–13.3)	<0.0001
			7–9 years old	<i>n</i> = 27	26.7 (18.2–35.3)	<i>n</i> = 20	8.9 (4.9–12.9)	0.0004
			10-year old +	<i>n</i> = 57	15.2 (11.3–19.2)	<i>n</i> = 31	8.4 (4.4–12.5)	0.074
Total	<i>n</i> = 131		22.5 (18.9–26.1)	<i>n</i> = 105	9.1 (6.8–11.4)	<0.0001		

acute ambulatory pain management in 1 month to 15-year-old children,⁸ advises the use of pharmacological and non-pharmacological approaches such as child education, parental presence and distraction. Starting from these guidelines and from other studies relating to each method, we designed a multifactorial strategy of pain management during vaccination suitable for GPs and paediatricians.

Concerning pharmacological approaches, we chose to apply an EMLA® anesthetic patch on the injection site beforehand. Various studies showed a significant efficiency on the reduction of vaccination pain,^{2,12–18} without affecting the response to antibodies.^{15,16} The PRIORIX® vaccine was preferentially selected instead of RORVAX® when the combined vaccination against measles, mumps and rubella was chosen, since it was shown less painful than RORVAX®,^{17,19–21} with an equal immunogenicity.^{20,21}

Concerning the non-pharmacological approach, we asked parents to prepare the child before the vaccination with an illustrated booklet for the youngest children²² and to accompany their child during the procedure in order to comfort him with a physical gesture or reassuring words.²³ Indeed, children usually wished their parents to be present and in the same way parents wanted to assist their child during vaccination.^{24–26} A study about parents' presence during venous puncture in children showed that parent's and child's stress was significantly less important when parents were present.²⁷ Furthermore, we decided to inform the child about the utility of the vaccination and the potential painful aspect of it. Indeed, in contrast to adults,²⁸ children prepared for a painful intervention have been shown to feel less pain than non-informed children.^{29,30} Explanations were given by the doctor in an age-adapted language. In addition, we used blowing soap bubbles as a distraction

technique. Such techniques have been shown effective to reduce stress and pain in a vaccination setting, according to the recent Cochrane meta-analysis.⁹ Other distraction techniques (such as videotapes, games and interactive books) were not chosen because of the difficulty to get a widespread use at the GP's office.^{31–34} In contrast, to blow air during the vaccination procedure as if the child was blowing out was shown to be effective in a randomized, unblinded controlled study.³⁵ We thus hypothesized that playing with a real bubble may potentialize the distraction effect, without any significant trouble. Indeed, there was no reported side effect. We, however, acknowledge that such a procedure should be compared to a sham one in a dedicated study. Anyway, blowing bubbles, although somewhat original, since only blowing out air was previously reported,^{35,36} was only one component within the overall complex intervention strategy we designed.

In summary, we found all these methods to be of interest because there are easy to use, economically acceptable and applicable to any child consulting a GP or pediatrician for a vaccination. Of note, we did not aim at demonstrating a higher efficiency of an individual method compared to another, since we wanted to assess the impact of a multifactorial approach, as compared to usual care. We do not think that a potentially more frequent use of the EMLA® patch in the intervention group influenced substantially our results, since pain decrease extent with EMLA® patch was shown lower in a randomized study,¹³ as compared to our results. Of note, in the present study, the pain levels observed were moderate and similar to other reported data.¹²

In splitting our study population into three groups to study the influence of age in a *post hoc* analysis, we observed that multiple strategy improvements were statistically significant only in children younger than

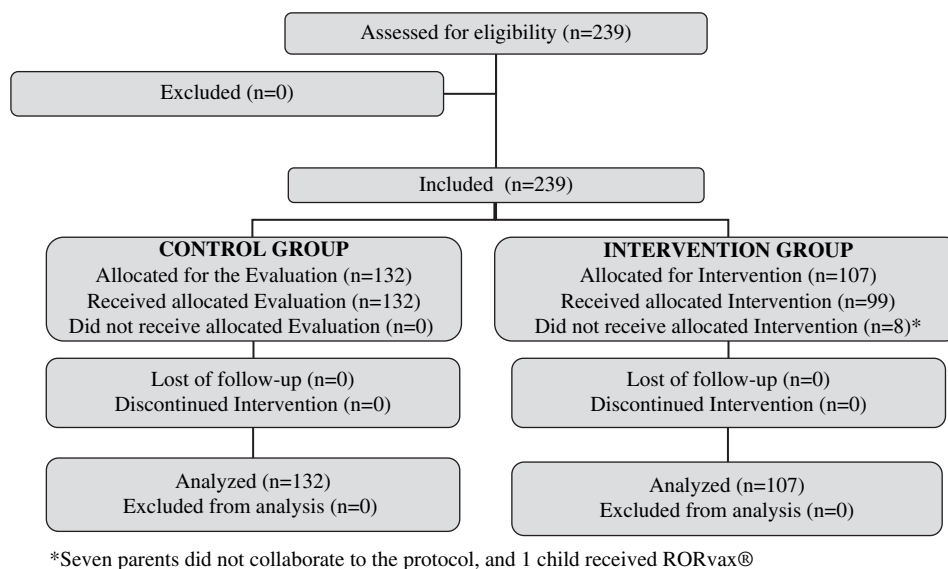


FIGURE 1 Study flow chart. *Seven parents did not collaborate to the protocol and one child received RORvax®

10. This corroborates previous data^{37,38} suggesting that child pain perception and consequences vary with age, with three different Piaget operational stages depending on age (i.e. 2–7 years: preoperational stage; 7 to 10–11 years: concrete operational stage; 10–12 years: transient formal stage).

Strengths of the current study, as compared to many previous ones, include the use of a self-report measure of pain as a primary end point, as recommended by a Cochrane collaboration review of psychological interventions for needle-treated procedural pain in children and adolescents.⁹ This review indeed highlighted the importance and utility of such methodology, as the ratings obtained via self-report were not always congruent with observer ratings or behavioural measure. In this setting, it should be emphasized that in the present study, a good agreement between the different pain evaluations was observed. Such good correlations were indeed observed between two well-established self-report scales (VAS and face pain scale revised)¹⁰ one the one hand and between VAS and hetero-evaluations on the other. That the use of different evaluation modalities lead to the same results (i.e. the superiority of the intervention strategy versus standard care) provides additional strength to our results. In addition, the study was analyzed on intention to treat basis, i.e. the children included were evaluated even if we noticed some protocol violations (e.g. no application of an anesthetic patch, wrong vaccine, parents finally not collaborating with the protocol procedure) (Fig. 1).

Our study has several limitations. This study was an open study. It was not possible to realize a double-blind study as the vaccination strategy's used needed specific management. The methodology used was the same as the one used to compare two surgical

methods. Strictly speaking, sequential allocation to treatment groups was not a randomization but a pseudo-randomization procedure. Indeed, that investigators did not encounter any refusal from the children or their parents, and the children were included in the study in an order only determined by their entry in the doctor's datebook refers to a pseudo-randomization procedure.⁹ However, a real children randomization would have been neither feasible nor ethically acceptable. Indeed, the same investigator could not be expected to act as required by the intervention protocol with a child, then with his previous usual habits. Moreover, proceeding differently among children from a same family would not have been acceptable, in case of vaccinations scheduled during the same visit. Alternatively, GP randomization in a cluster-style design would not have been feasible for practical reasons including the number of GPs needed, which would have exceeded our recruitment potential.

In conclusion, our results show that a multifactorial strategy including combined pharmacological and non-pharmacological approaches significantly decrease pain in 4- to 12-year-old children. Pain management during vaccinations not only aims at decreasing pain but also at avoiding negative psychological responses like phobia and fear during consultations. Such strategies could make vaccines more acceptable to children and improve the child–doctor relationship, also contributing to the decrease of the child's fear about health care. These strategies could even show a child his own resources. Most of the children consulting not only urban GPs and paediatricians but also infant and maternal welfare centres (Protection Maternelle et Infantile) could benefit from this multifactorial strategy, according to 'Standards Options et Recommandations' published by 'La Société Française des cancers de

l'enfant' and 'La Société Française d'étude et de traitement de la douleur'.³⁹

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Declaration

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Conflicts of interest: None.

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