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# **The effectiveness of the Buzzy® device to reduce or prevent pain in children undergoing needle-related procedures: the results from a prospective, open-label, randomised, non-inferiority study**

## **Prevention of pain in child's vaccination: a randomised control trial**

### **Author names:**

**Katia LESCOP<sup>1</sup>**

[katia.lescop@chu-nantes.fr](mailto:katia.lescop@chu-nantes.fr)

**Isabelle JORET<sup>1</sup>**

[Isabelle.joret@chu-nantes.fr](mailto:Isabelle.joret@chu-nantes.fr)

**Paola DELBOS<sup>1</sup>**

[Paola.delbos@chu-nantes.fr](mailto:Paola.delbos@chu-nantes.fr)

**Valérie BRIEND-GODET<sup>1</sup>**

[Valerie.BRIENDGODET@chu-nantes.fr](mailto:Valerie.BRIENDGODET@chu-nantes.fr)

**Sophie BLANCHI<sup>2</sup>**

[sblanchi@ch-lemans.fr](mailto:sblanchi@ch-lemans.fr)

**Christian BRECHET<sup>3</sup>**

[christian.brechet@chd-vendee.fr](mailto:christian.brechet@chd-vendee.fr)

**Annastasia GALIVEL-VOISINE<sup>4</sup>**

[annastasia.galivelvoisine@chu-nantes.fr](mailto:annastasia.galivelvoisine@chu-nantes.fr)

**Sandrine COUDOL<sup>5</sup>**

[Sandrine.COUDOL@chu-nantes.fr](mailto:Sandrine.COUDOL@chu-nantes.fr)

**Christelle VOLTEAU<sup>6</sup>**

[christellevolteau@gmail.com](mailto:christellevolteau@gmail.com)

**Valéry-Pierre RICHE<sup>7</sup>**

[ValeryPierre.riche@chu-nantes.fr](mailto:ValeryPierre.riche@chu-nantes.fr)

Emmanuelle CARTRON<sup>4, 8</sup>

Emmanuelle.cartron@chu-nantes.fr

1. CHU de Nantes, Centre fédératif prévention dépistage, 5 allée de l'île Gloriette, 44 093 Nantes cedex 1, France.
2. CH le Mans, Centre de Prévention Vaccination et Dépistage, Service des maladies infectieuses et tropicales, 194 Avenue Rubillard, 72037 Le Mans, France.
3. CHD Vendée, Centre fédératif de prévention et de dépistage, Les Oudairies, 85 925 La Roche sur Yon cedex 9, France.
4. CHU de Nantes, Nursing and Allied Health Research Department, Department of Clinical Research, 5 allée de l'île Gloriette, 44 093 Nantes cedex 1, France.
5. CHU de Nantes, Clinique des données, 5 allée de l'île Gloriette, 44 093 Nantes cedex 1, France.
6. CHU de Nantes, Plateforme de biométrie, 5 allée de l'île Gloriette, 44 093 Nantes cedex 1, France.
7. CHU de Nantes, Service Evaluation Economique et Développement des Produits de Santé, Department of Clinical Research, 5 allée de l'île Gloriette, 44 093 Nantes cedex 1, France.
8. INSERM, SPHERE U1246 "Methods in Patients-centered Outcomes and Health Research", Nantes University, Tours University, Nantes, France.

**Corresponding author:**

Emmanuelle Cartron, RN, Ph.D

CHU de Nantes

Nursing and Allied Health Research Department, Department of Clinical Research,  
5 allée de l'île Gloriette, 44 093 Nantes cedex 1, France

Phone: +33 635 550 335

emmanuelle.cartron@chu-nantes.fr

1 **Abstract**

2 **Background**

3 Pain from needle-related procedures in children can alter pain perception, increase pain sensitivity,  
4 and generate inappropriate pain responses. Currently pain management includes the use of lidocaine-  
5 containing patches, which is complicated to manage in a busy medical setting such as a vaccination  
6 centre. We assessed the Buzzy® device, which combines vibration and cold, to manage pain in  
7 children undergoing a needle-related procedure compared to the standard lidocaine patch.

8 **Design**

9 Prospective, open-label, non-inferiority trial.

10 **Setting**

11 Conducted in the vaccination centres of three university hospitals in France

12 **Participants**

13 French speaking children aged 4-15 requiring a needle-related procedure (vaccination or  
14 venepuncture) were eligible. Principal non-inclusion criteria were allergy or sensitivity to the  
15 lidocaine patch.

16 **Methods**

17 Children were randomly allocated (1:1) to use either the Buzzy® device or the lidocaine patch during  
18 the needle-related procedure. The lidocaine patch was applied to the puncture site for the hour prior to  
19 the intervention. The Buzzy® device was applied to the puncture site for 30 seconds and then moved  
20 5 cm along the limb during the procedure. The refrigerated wings could be detached if they bothered  
21 the child. The child assessed their pain using the validated Revised Faces Pain Scale. The revised  
22 faces pain scale comprises six facial expressions from 0, normal “no pain” to 10, a screaming face  
23 “severe pain” (2 points/face). The primary endpoint was the average pain score recorded by the child.  
24 The study aimed to show the non-inferiority of Buzzy®.

25 **Results**

26 Overall 219 participants were randomised. The primary outcome was assessed in 215 children: 108 in  
27 the BUZZY group (43% did not want to use the refrigerated wings until the end of the procedure) and  
28 107 in the PATCH group. The baseline characteristics were similar study groups with an average age  
29 of 9 (range: 4.08-15.81). The average needle-related pain was 2.04 in the BUZZY group and 1.42 in  
30 the PATCH group. The average difference between the children's assessments in the groups was 0.62.  
31 Thus, not demonstrating non-inferiority. However, concerning parents' assessments, the mean  
32 difference between groups was 0.30 points, demonstrating non-inferiority of the BUZZY group  
33 compared to the PATCH group.

#### 34 **Conclusions**

35 Our study failed to show that the Buzzy® device was equivalent to the lidocaine patch in managing  
36 pain in children undergoing needle-related procedures. The Buzzy® device does seem to be more  
37 effective when the refrigerated wings are accepted by children, but the impact of temperature on the  
38 children's comfort remains unclear.

#### 39 **Tweetable abstract**

40 Pain management in children undergoing a vaccination: which efficacy for Buzzy® device as an  
41 alternative to lidocaine patch? A prospective, randomised study.

#### 42 **Trial registration**

43 NCT03220555

#### 44 **Highlights**

##### 45 What is already known?

- 47 • Effective pain management in children undergoing needle-related procedures is essential.
- 48 • Needle phobia provoked during childhood may persist into adulthood.
- 49 • Current pain management includes lidocaine-containing patches, creams and distraction  
50 techniques but is complicated to manage in a busy medical setting such as a vaccination  
51 centre.

52 What the paper adds:

- 53 • Pain relief by the Buzzy® device during needle procedure is not as effective as the lidocaine  
54 patch in a vaccination centre;
- 55 • A large proportion of children wished to remove the refrigerated wings before the end of the  
56 procedure because the cold made them feel uncomfortable;
- 57 • The incremental cost-effectiveness ratio of managing pain was lower for the Buzzy® device  
58 versus the lidocaine patch.  
59

60

61 **Key words:**

62 Vaccination, paediatric, Buzzy®, lidocaine, needle-related procedure, pain management.

63

64

## 65 **Introduction**

66

67 Needle pricks are one of the most feared medical events for both children and adults (Taddio et al.,  
68 2009). Children who often experience pain reportedly develop altered pain perception, increased pain  
69 sensitivity, and inappropriate pain responses (Buskila et al., 2003, Chen et al., 2000, Moadad et al.,  
70 2016, Valeri et al., 2015). Needle phobia in children often persists into adolescence and adulthood  
71 (Moadad et al., 2016, Valeri et al., 2015). Also, needle- phobia has been shown to reduce compliance  
72 with routine immunisation (Wright et al., 2009).

73 Management of the pain of childhood vaccination includes a large amount of both

74 nonpharmacological and pharmacological methods recommended as topical anaesthetic creams,

75 vapocoolant cold spray, parent coaching and distraction (Taddio et al., 2010). Among them, the

76 lidocaine and prilocaine-containing eutectic mixture of local anaesthetics patch is currently

77 recommended to manage pain associated with venepuncture (Shah et al., 2009). However, for the

78 patch to be effective, it must be positioned correctly for one hour before the procedure to provide

79 anaesthesia, which can be inconvenient when consultation time is very short and procedures for pain

80 management need to be quick (Rogers & Ostrow, 2004) and convenient. A new medical device,  
81 Buzzy®, combines external skin cooling with vibration. This device is a bee-shaped box with  
82 detachable, refrigerable wings. The efficacy of the Buzzy® device can be explained by the gate  
83 control theory (Melzack, 1996). This theory suggests that cold and the vibrations transmitted by  
84 unmyelinated, slowly conducting C nerve fibres may block the acute needle pain transmitted by the A  
85 fibres.

86 Several randomised clinical trials have evaluated Buzzy® during various needle-related procedures  
87 and in different age groups. A prospective study was performed in children aged between 7 and 12  
88 years, requiring a peripheral intravenous cannulation (Canbulat et al., 2015). A control study assessed  
89 Buzzy® in children of 4 to 12 years during an intravenous insertion (Moadad et al., 2016). In  
90 addition, a single-centre trial evaluated the Buzzy® device in patients aged from 4 to 18 requiring  
91 venous access (Baxter, 2011). These studies compared the Buzzy® device with a no-pain prevention  
92 measures comparator and showed that the Buzzy® was significant in reducing self-reported  
93 procedural pain. A recent meta-analysis, including seven studies which compared the Buzzy® device  
94 with a no-treatment comparator, concluded that even if the Buzzy® device showed promise in  
95 reducing needle-related pain in children, the current evidence is not enough to conclude efficacy  
96 (Ballard et al., 2019). More recently, the Buzzy® device was compared with the lidocaine patch by  
97 Potts et al. in children aged 4-18 requiring an intravenous catheter, and by Bourdier et al. in children  
98 aged between 18 months and 6 years during either a cannulation, or a blood test in the paediatric  
99 emergency department (Bourdier et al., 2019; Potts et al., 2019). The Buzzy® device allows faster  
100 analgesia than the lidocaine patch; however evidence about pain relief is conflicting in these studies.  
101 Potts reported that a vibrating cold device is equal in its effectiveness in reducing pain for children  
102 undergoing catheterisation to the lidocaine patch. However, Bourdier concluded that analgesia from  
103 the Buzzy® device is less effective than with the lidocaine patch. Moreover, to our knowledge, no  
104 previous study has compared the Buzzy® device to the lidocaine patch used in the management of  
105 pain for children undergoing vaccination. Therefore, the aim of this study was to investigate whether

106 the Buzzy® device was as efficient as the lidocaine patch in reducing or preventing the pain provoked  
107 by needles in children attending paediatric outpatient units.

## 108 **Materials and Methods**

### 109 **Study design and participants**

110

111 This study was designed as a randomised (1:1) open-label study to assess the non-inferiority of the  
112 Buzzy® device compared to the standard lidocaine patch. The study was conducted in the vaccination  
113 centres of three hospitals in France: the university hospital in Nantes and the public hospitals in La  
114 Roche sur Yon and Le Mans. The parents of potential participants were informed of the study when  
115 they made the appointment for their child's vaccination. Sometimes, children need a serology test at  
116 the time of vaccination. In this case, the venepuncture takes place before the vaccination. Children  
117 aged between 4 and 15 presenting for either a routine or travel vaccination or a serology test requiring  
118 a venepuncture were eligible for the study. Furthermore, the child needed to be registered for social  
119 security and speak French or be accompanied by an interpreter. Children with sickle cell anaemia,  
120 those presenting for a Bacillus Calmette–Guérin injection or tuberculosis test, those who were allergic  
121 or sensitive to the lidocaine patch and associated ingredients, and those who had an abrasion on the  
122 injection site were not eligible. Children with a neurological or psychological condition who might  
123 not fully understand the study were also not eligible. Each child could only participate once in the  
124 study. Furthermore, children were not permitted to participate in another study simultaneously.  
125 Parents provided informed consent before their child participated in the study. The study was  
126 performed in accordance with the French Ethical Agency (Ref. N°2017-A00177-46), the French  
127 national agency for drug safety regulations, and good clinical research practice.

### 128 **Interventions**

129 During the appointment, the study nurse explained the study and procedures to the child and the  
130 parents and study eligibility was discussed. If the child was eligible, the study nurse collected general  
131 study information and the child was randomised, using fixed blocks in a ratio of 1:1 and stratified by



132 centre. The study statistician generated the allocation list using computer-generated random numbers.  
133 Children were randomly allocated to either the PATCH or BUZZY group, using the Ennov Clinical®  
134 Software. For the children in the PATCH group, the lidocaine patch was applied to the puncture area  
135 for one hour before the procedure. After the consultation with the physician, one of the two practising  
136 nurses present removed the patch and performed the injection or venepuncture according to usual  
137 clinical practice. While the nurse was performing the injection or venepuncture, the other nurse  
138 helped the child to manage the pain. Children in the BUZZY group had the Buzzy® device applied to  
139 the puncture site for 30 seconds and then moved 5 cm further along the limb from the puncture site.  
140 The puncturing procedure was then performed. If the cold bothered the child, the refrigerated wings  
141 were detached. The parent(s) accompanied their child throughout the procedure. If desired, all  
142 children benefitted from the usual distraction procedures (playing cards, soap bubbles, soft toys, or a  
143 discussion with the child on a topic of interest). If siblings were present, the youngest was treated first  
144 and included in the study. Although the older siblings received the same pain prevention as the  
145 participating child, they were not included in the study. Following the vaccination or venepuncture  
146 procedure, both the child and parent were simultaneously asked to estimate the level of pain using the  
147 Revised Faces Pain Scale. The child looked at the scale of faces and rated the pain they felt according  
148 to the appropriate face. The parent looked at the faces and rated the pain they perceived their child had  
149 felt. The child's evaluation was performed in the presence of the parent to eliminate possible anxiety  
150 if separated. If more than one procedure had been prescribed (several vaccinations, or vaccination and  
151 venepuncture), the pain was evaluated after the first one. The following data were to be recorded:  
152 Demographic information such as child and parent age, gender, ethnicity, and whether this was the  
153 first vaccination or venepuncture experienced by the child. Also, data concerning the type of act  
154 prescribed, the administration mode (intramuscular or subcutaneous), and the anatomical zone for the  
155 puncture were collected. In the PATCH group, the number of patches used, the application time, and  
156 if the patch was applied, together with the reason if not applied. In the BUZZY group, whether the  
157 refrigerated wings were used. For both groups, data concerning other distraction methods used,

158 including the parent's involvement, the type of distraction and the number of nurses involved were  
159 collected. The child and parent Revised Faces Pain Scale scores were recorded on separate scales. The  
160 duration of the appointment and the use of other analgesics were recorded.

161

## 162 **Outcomes**

163 The primary outcome was the child's pain evaluation following the first invasive procedure. Pain was  
164 measured using the Revised Faces Pain Scale, a self-reported scale which consists of six facial  
165 expressions that correspond to a neutral expression ("no pain") up to a screaming face ("severe pain")  
166 and is scored using a numerical scale of 0 to 10 (2 points per interval),. This validated scale is  
167 commonly used to evaluate pain in children and is recommended by the French Health Authority for  
168 the evaluation of pain (Ferreira-Valente et al., 2011, Tomlinson et al., 2010, Tsze et al., 2013).

169 The secondary outcomes were the parents' perception of the child's pain following the first invasive  
170 procedure, using the Revised Faces Pain Scale, and a micro-costing analysis of the cost of preventing  
171 pain. Adverse events were not systematically recorded since neither intervention was expected to have  
172 an undesirable effect. If adverse events linked to either device did occur these events were to be  
173 reported to the appropriate pharmacovigilance service.

## 174 **Statistical analysis**

175 The non-inferiority threshold was set at 1. This threshold corresponds to the maximal average  
176 difference between the lidocaine patch and the placebo group in Cassidy's study (Cassidy et al.,  
177 2001). Assuming an error risk of 2.5%, a power of 80%, a standard deviation of 2.5 points, and an  
178 attrition rate of 10%, the study planned to randomise 220 participants. The primary analysis was the  
179 modified intent-to-treat population that consisted of all randomised participants except for those that  
180 withdrew their consent or cancelled their procedure. A sensitivity analysis was performed in the per-  
181 protocol (PP) population consisting of all participants that complied with the eligibility criteria,  
182 without any major protocol deviations, and with primary endpoint data.

183 The mean pain score was estimated in the BUZZY and PATCH groups together with the  
184 corresponding estimated 95% confidence interval (CI) of the scores. The upper limits of the CIs were  
185 to be compared to the non-inferiority threshold set at 1. Even though the Revised Faces Pain Scale  
186 consists of 6 faces incremented by 2 points from 0-10, the non-inferiority limit was set at 1 point since  
187 non-inferiority was based on the average score. The analysis was performed using a linear regression  
188 model adjusted for the centre, the stratification factor at randomisation. Missing data were imputed to  
189 the nearest integer score of the mean group value. An adjusted sensitivity analysis, considering type of  
190 act, child's age and previous experience with a puncturing intervention, was planned. A subgroup  
191 analysis was performed excluding the children in the BUZZY group who used the Buzzy® device  
192 without the refrigerated wings until the end of procedure.

193 The secondary endpoint, the average score on the Revised Faces Pain Scale, estimated by the parents,  
194 of the level of pain they perceived their child to experience was compared as for the primary endpoint,  
195 with the non-inferiority threshold set at 1. Descriptive analysis of the data collected was done in the  
196 two groups. Continuous variables were described using mean, standard deviation, and range (minimal  
197 and maximal values). Qualitative variables were described using frequencies and percentages.

198 Statistical analyses were performed with SAS® version 9.4.

199 A micro-costing analysis of the cost associated with preventing pain was planned. The nursing time  
200 was estimated for each group using the number of nurses present and the duration of each  
201 consultation. The results were to be presented as a differential cost effectiveness ratio.

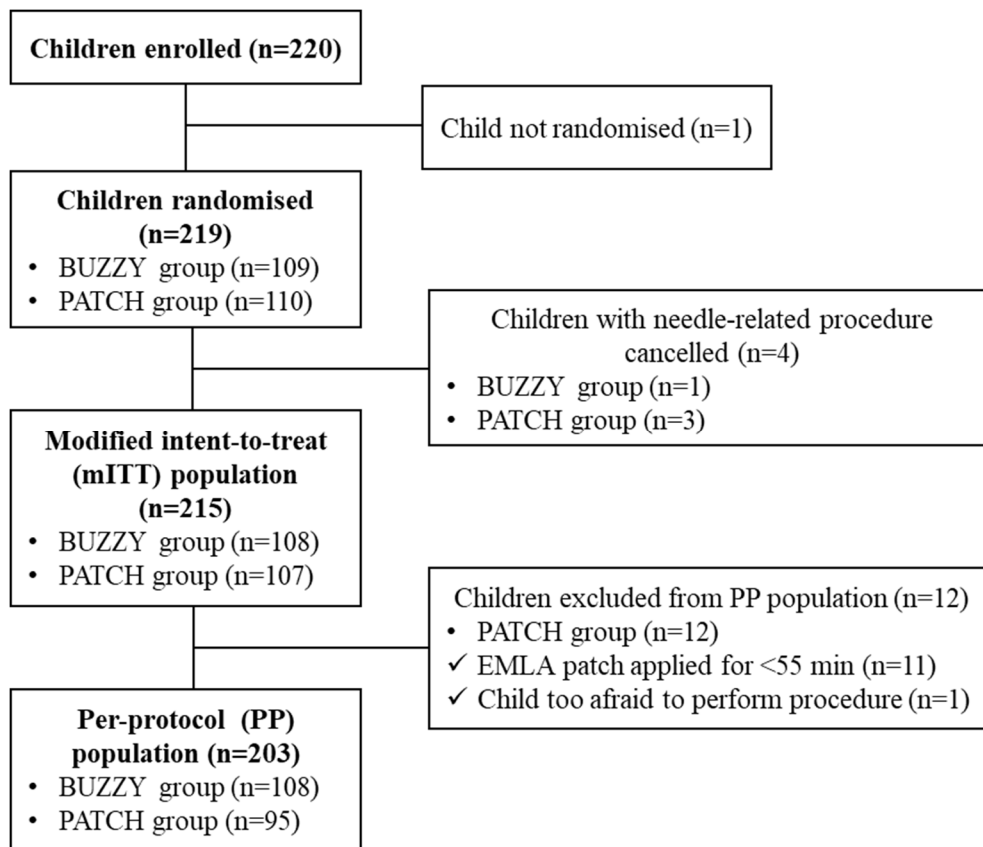
## 202 **Results**

### 203 **Participants and procedures**

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205 Between October 2017 and October 2018, 220 patients were enrolled in the study. One patient was  
206 not randomised and four withdrew their consent or cancelled their procedure after being randomised  
207 (see the flow diagram in Figure 1). Of the 215 patients in the modified intent-to-treat population, 12

208 patients (all from the PATCH group) were not included in the per-protocol population: 11 patients  
 209 because the patch was applied for less than 55 minutes and one child who was too afraid to perform  
 210 the procedure.



211  
 212 Figure 1. Flow diagram of the children in the study.

213 The participant characteristics were similar in the BUZZY and PATCH groups. Data concerning  
 214 participant's age, gender and nationality, as well as the gender of the parent who rated their child's  
 215 pain for the secondary outcome are shown in Table 1.

216  
 217  
 218

	<b>BUZZY group (n=108)</b>	<b>PATCH group (n=107)</b>	<b>mITT population (n=215)</b>
Age (years): mean	8.86 ± 3.10	9.13 ± 3.20 (4.08-	9.00 ± 3.15 (4.08-

± sd (min-max)	(4.16-15.81)	15.55)	15.81)
Female: n (%)	56 (51.9)	57 (53.3)	113 (52.6)
French: n (%)	88 (81.5)	92 (86.0)	180 (83.7)
Parent present			
Mother: n (%)	89 (82.4)	78 (72.9)	167 (77.7)
Type of needle procedure :			
venepuncture n (%)	9 (8.33)	5 (4.67)	14 (6.51)
immunisation n (%)	99 (91.67)	102 (95.33)	201 (93.49)

219

220 Table 1. Baseline characteristics of the children participating in the study.

221 mITT: Modified intent-to-treat

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		<b>BUZZY N=99</b>	<b>PATCH N=102</b>	<b>Total N=201</b>
Administration mode: n (%)	Subcutaneous	64 (64.65%)	58 (56.86%)	122 (60.70%)
	Intramuscular	35 (35.35%)	44 (43.14%)	79 (39.30%)
Anatomical zone: n (%)	Arm	84 (84.85%)	89 (87.25%)	173 (86.07%)
	Thigh	15 (15.15%)	13 (12.75%)	28 (13.93%)
Type of vaccination: n (%)	Yellow fever	60 (60.61%)	54 (52.94%)	114 (56.72%)
	Typhoid	3 (3.03%)	4 (3.92%)	7 (3.48%)
	Rabies	2 (2.02%)	7 (6.86%)	9 (4.48%)
	Diphtheria- Poliomyelitis- Pertussis Tetanus-	3 (3.03%)	0 (0.00%)	3 (1.49%)
	Measles- Mumps-Rubella	2 (2.02%)	5 (4.90%)	7 (3.48%)
	Hepatitis A	26 (26.26%)	26 (25.49%)	52 (25.87%)
	Hepatitis B	3 (3.03%)	6 (5.88%)	9 (4.48%)

235

236 Table 2 Characteristics of the type of vaccination in the two groups

237

238 On average, the children in the PATCH group waited for 84.7 minutes (range: 45.0-162.0) compared  
239 to 74.4 (range: 25.0-157.0) for those in the BUZZY group. The nurse treatment time was 5.2 minutes  
240 (range: 2.0-17.0) in the BUZZY group compared to 5.2 (range: 1.0-23.0) in the PATCH group. Most  
241 of the children in the PATCH group, 103 children (96.3%), required more than one patch. In the  
242 BUZZY group, 62 children (57.4%) used the Buzzy® device with the refrigerated wings until the end  
243 of the procedure. Most of the children presented for a vaccination, 101 (93.5%) in the BUZZY group  
244 and 104 (97.2%) in the PATCH group. Venepuncture was only performed in 9 children (8.3%) in the  
245 BUZZY group and 5 (4.7%) in the PATCH group. In both groups, 2 children (1.9%) received both a  
246 venepuncture and a vaccination injection. The puncture site was most often on the arm – 264 children  
247 (80.2%). Of the 205 children who were vaccinated, the most common vaccinations were for yellow

248 fever, in 43 children (21.0%), for hepatitis A, in 35 (17.1%), and for both yellow fever and hepatitis  
249 A, in 74 children (36.1%) (Table 2).

250 Parents actively participated in both groups, 53 of the parents (49.1%) being in the BUZZY group and  
251 44 (41.1%) in the PATCH group. Parents held their child in 18 (34.0%) cases from the BUZZY group  
252 and 21 (47.7%) from the PATCH group. Parents held and distracted their child in 14 (26.4%) cases  
253 from the BUZZY group versus 15 (34.1%) cases from the PATCH group. In the PATCH group, fewer  
254 parents distracted their child – 6 (13.6%) compared to 15 (28.3%) in the BUZZY group. Most  
255 children received some form of distraction – 105 (97.2%) in the BUZZY group and 100 (93.5%) in  
256 the PATCH group. The distraction methods employed varied widely. Most children were distracted  
257 with cards – 71 (67.6%) in the BUZZY group and 71 (71.0%) in the PATCH group. Discussions with  
258 the children were held in 17 (16.2%) cases in the BUZZY group and 19 (19.0%) in the PATCH group.  
259 Only 2 children (1.9%) in both groups received an analgesic before the procedure.

260

## 261 **Outcomes**

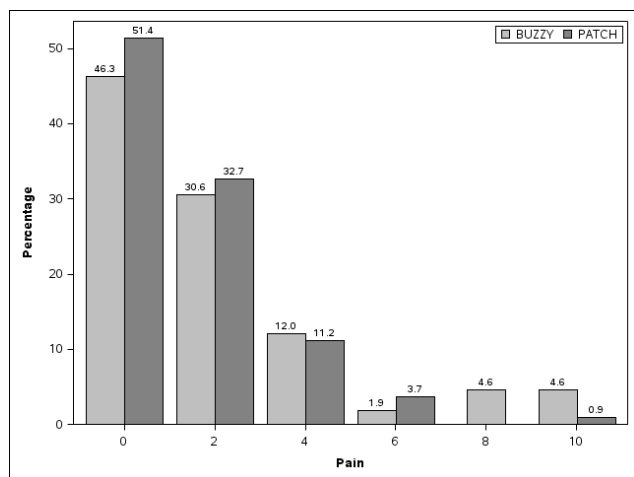
262

263 The average pain for the puncture was rated at 2.04 points (sd: 2.71; range: 0.0-10.0) by the 108  
264 children in the BUZZY group and 1.42 points (sd: 1.85; range: 0.0-10.0) by the 106 children in the  
265 PATCH group. The average difference between children's assessments in the BUZZY and PATCH  
266 groups (modified intent-to-treat population) was 0.62 points (95% CI: 0.00-1.24). This result shows  
267 non-inferiority and should be discussed (non-inferiority margin set to 1). Moreover, Figure 2 shows  
268 that moderate to severe pain was experienced by 11.1% of children with the Buzzy® device and by  
269 4.6% with the lidocaine patch. Pain scores with Buzzy® were higher compared to the lidocaine patch  
270 and “moderate to severe” pain was experienced by 11.1% of children with Buzzy® and by 4.6% with  
271 the lidocaine patch. Pain scores with Buzzy® were higher compared to the lidocaine patch. The result  
272 obtained in the modified intent-to-treat population was confirmed in the PP population. The average  
273 difference in the children's FRS-R scores in the BUZZY and PATCH groups was 0.79 points (95%

274 CI: 0.19-1.40). Only one missing datum was observed, in the PATCH group, and this was imputed to

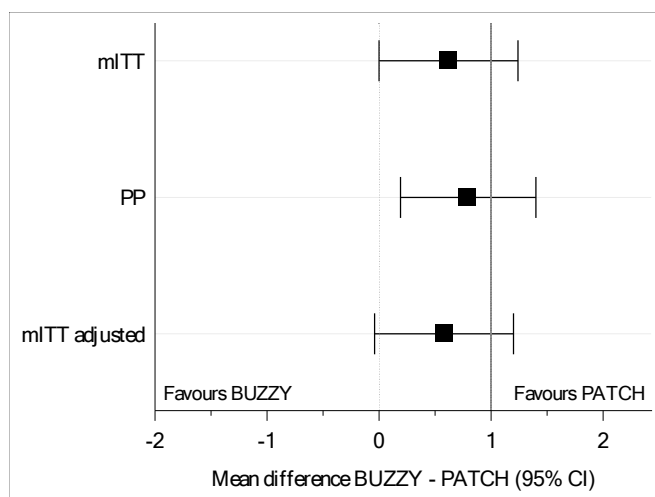
275 2, corresponding to the average pain score. The non-inferiority results are shown in Figure 3.

276



277 Figure 2. Children's Revised Faces Pain Scale scores grouped according to the score and the study  
278 group.

279



288 Figure 3. The non-inferiority analysis of the children's pain scores according to study group.

289 mITT: Modified intent-to-treat

290 PP: per-protocol

291

292



293 The adjusted analysis for the type of act performed, child's age, and previous experience with a  
294 needle-related procedure gave an adjusted mean difference of 0.58 points (95% CI: -0.04-1.20) (see  
295 Figure 3).

296 A post hoc, subgroup analysis was performed in children enrolled in the BUZZY group who used the  
297 detachable refrigerated wings until the end of the procedure. Pain in the BUZZY subgroup that used  
298 the refrigerated wings until the end seems to be equivalent to the pain in the PATCH group, with a  
299 mean difference of 0.03 points (95% CI: -0.66-0.73).

300 The secondary outcome analysis evaluated the parent's perception of their child's pain on the Revised  
301 Faces Pain Scale. The average pain score rated by the 106 parents of children in the modified intent-  
302 to-treat population was 1.51 points (sd: 1.76; range: 0.00-8.00) in the BUZZY group and 1.21 (sd:  
303 1.72; range: 0.00-6.00) in the PATCH group. Supplemental material Figure 1. The mean difference  
304 between groups was 0.30 points (95% CI: -0.17-0.77), suggesting that the pain perceived by the  
305 parent is equivalent in the BUZZY group compared to the PATCH group. This result was confirmed  
306 in the per-protocol population (see Figure 4).

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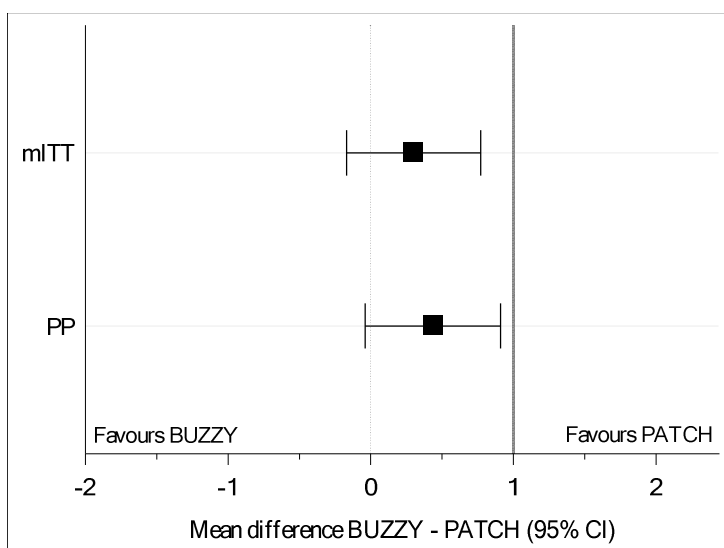
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316 Figure 4. The non-inferiority analysis of the parents' pain scores according to study group.

317 mITT: Modified intent-to-treat

318 PP: per-protocol

319

320 The micro-costing analysis of managing pain gave a mean cost per patient of EUR 6.45 (95% CI: 5.8-  
321 7.1) for children in the BUZZY group and EUR 13.49 (95% CI: 12.8-14.2) for those in the PATCH  
322 group. The incremental cost-effectiveness ratio of managing pain was EUR 11.35 per point of pain  
323 lower on the pain score for the Buzzy® device versus the lidocaine patch. No adverse events related  
324 to the devices were reported during the study.

## 325 **Discussion**

326 To the best of our knowledge, our study is the first prospective randomised controlled trial comparing  
327 the Buzzy® device to the lidocaine patch in the management of needle procedures in a vaccination  
328 centre. To allow immediate analgesia with a device combining vibration and cold was an attractive  
329 alternative to the lidocaine patch to manage pain induced by needle procedures in a busy medical  
330 setting such as a vaccination centre. However, our study failed to show that the Buzzy® device was  
331 equivalent to the lidocaine patch for preventing or reducing pain in children undergoing either a  
332 vaccination or a venepuncture, in terms of the Revised Faces Pain Scale rated by the children after the  
333 needle-related procedure. These findings are in accordance with Bourdier, who recently showed in a  
334 superiority trial that analgesia was less efficient than the lidocaine patch in the context of cannulation  
335 in a paediatric emergency department (Bourdier et al., 2019). However, another recent study indicated  
336 that the pain experienced by children undergoing IV insertion who received Buzzy® device  
337 intervention was equivalent to that experienced by children who received a lidocaine patch (Potts et  
338 al., 2019).

339 Discrepancies between designs could explain these conflicting results. First, we set a lower threshold  
340 of non-inferiority than in the Potts study. The margin in our study was set at 1, based on a previous  
341 trial which compared the lidocaine patch and a placebo, whilst Potts used a non-inferiority margin of  
342 1 face on the pain scale, equivalent to 2. Second, the Bourdier study and the Potts study took place in  
343 an emergency department so included sick children and concerned cannulation. Third, in previous

344 studies, all children received the device with the refrigerated wings (Potts et al., 2019; Bourdier et al.,  
345 2019), while our pragmatic study design followed a shared decision-making process and allowed the  
346 Buzzy® detachable refrigerated wings to be removed if the child was bothered by the cold. In the  
347 BUZZY group, 43% of the children did not use the refrigerated wings until the end of the procedure.  
348 However, the pain prevention and relief when the refrigerated wings were used to the end seems to be  
349 similar to that observed with the standard lidocaine patch. Indeed, it has been previously suggested  
350 that the combination of vibration and cold may be more effective than either component alone (Baxter  
351 et al., 2011, Inal et al., 2012). In the prospective randomised study assessing Buzzy® in children aged  
352 7 to 12 requiring venous access, all the children randomised to the Buzzy® device had the vibration  
353 and cold applied 5 cm above the planned puncture site prior to and for the duration of the procedure  
354 (Canbulat et al., 2015). Thus, in retrospect, we may have obtained better results if the refrigerated  
355 wings on the Buzzy® device had been mandatory. But our study was not empowered to analyse this  
356 hypothesis. Moreover, it is not clear if the wings should be frozen or refrigerated, nor is the impact of  
357 temperature on the children's comfort clear. Further research is required to assess the use of cold in  
358 pain management. Concerning the practice, this study highlights some points important to know for  
359 the use of Buzzy®. In order to use the Buzzy® device effectively, the site staff need to be familiar  
360 with the device and the procedure. Ideally, the child should be distracted from the Buzzy® device at  
361 the time of the injection so that the child does not see the needle that may induce anxiety. From our  
362 experience with this study, we consider that the competence of the nurses in using the device and  
363 distracting the child, as well as the communication between the nurse, doctor, parents, and child are  
364 essential for the optimum management of pain during a needle-related procedure. In addition, usually,  
365 the main limiter of the use of a lidocaine patch is the time spent waiting for it to become effective  
366 (Rogers & Ostrow, 2004), but our trial clearly shows that the waiting time of children with Buzzy®  
367 and lidocaine patch were similar (mean difference of 10 minutes). In reality, in a vaccination centre  
368 the patch is applied as soon as the child arrives in the unit.  
369

370 Our study has several limitations. It was designed to be pragmatic, thus we enrolled children  
371 presenting for various needle-related procedures offered in the vaccination centre. However, we know  
372 that certain vaccinations and procedures generate more pain than others (Taddio et al., 2010).  
373 Furthermore, we only recruited children in the vaccination centres of three French hospitals. Thus, our  
374 study population may not be representative of all children requiring needle-related procedures. In  
375 addition, adverse events were not systematically recorded in the trial, so some minor side effects such  
376 as discomfort could have been missed. Lastly, during the procedures various distractions were  
377 permitted so we cannot exclude that different techniques could have influenced the results.

378

### 379 **Conclusion**

380 Our study failed to provide evidence that the Buzzy® device was equivalent to the lidocaine patch in  
381 preventing or reducing pain in children undergoing needle-related procedures. However, the Buzzy®  
382 device tends to be more effective when the refrigerated wings are used, even if almost half of the  
383 children in our study did not like the cold. Our study provides valuable information concerning the  
384 use of the Buzzy® device. Further research is required to optimise the use of Buzzy® (influence of  
385 the duration of the cold exposure) and improve its ability to prevent and reduce pain in children  
386 undergoing needle-related procedures.

387

### 388 **Conflict of interest statement**

389 The authors have no conflict of interest to declare.

390

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394

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404 **References**

405

406 Ballard, A., Khadra, C., Adler, S., Trottier, E.D., Le May, S., 2019. Efficacy of the Buzzy  
407 Device for Pain Management During Needle-related Procedures: A Systematic Review and  
408 Meta-Analysis. *The Clinical Journal of Pain*. 35(6), 532-543.

409

410 Baxter, A.L., Cohen, L.L., McElvery, H.L., 2011. An integration of vibration and cold  
411 relieves venipuncture pain in a pediatric emergency department. *Pediatr Emer Care*. 27 (12),  
412 1151-6.

413 Blount, R.L., Loiselle, K.A., 2009. Behavioural assessment of pediatric pain. *Pain Res Manag*  
414 14 (1), 47-52.

415

416 Bourdier, S., Khelif, N., Velasquez, M., Usclade, A., Rochette, E., Pereira, B., Favard, B.,  
417 Merlin, E., Labbe, A., Sarret, C., Michaud, E., 2019. Cold Vibration (Buzzy) Versus  
418 Anesthetic Patch (EMLA) for Pain Prevention During Cannulation in Children: A  
419 Randomized Trial. *Pediatr Emerg Care*.

420 Buskila, D., Neumann, L., Zmora, E., Feldman, M., Bolotin, A., Press, J., 2003. Pain  
421 sensitivity in prematurely born adolescents. *Arch Pediatr Adolesc Med*.157 (11), 1079-1082.

422 Canbulat, N., Ayhan, F., Inal, S., 2015. Effectiveness of external cold and vibration for  
423 procedural pain relief during peripheral intravenous cannulation in pediatric patients. *Pain*  
424 *Manag Nurs*.16 (1), 33-39.

425 Canbulat Sahiner, N., Inal, S., Sevim Akbay, A., 2015. The effect of combined stimulation of  
426 external cold and vibration during immunization on pain and anxiety levels in children. *J*  
427 *Perianesth Nurs*.30 (3), 228-35.

- 428 Cassidy, K. L., Reid, G. J., McGrath, P. J., Smith, D. J., Brown, T. L., Finley, G. A., 2001. A  
 429 randomized double-blind, placebo-controlled trial of the EMLA patch for the reduction of  
 430 pain associated with intramuscular injection in four to six-year-old children. *Acta Paediatrica*.  
 431 90(11), 1329-36.
- 432 Chen, E., Zeltzer, L.K., Craske, M.G., Katz, E.R., 2000. Children's memories for painful  
 433 cancer treatment procedures: implications for distress. *Child Dev.* 71 (4), 933-947.
- 434 Ferreira-Valente, M.A., Pais-Ribeiro, J.L., Jensen, M.P., 2011. Validity of four pain intensity  
 435 rating scales. *Pain.* 152 (10), 2399-404.
- 436 Inal, S., Kelleci, M., 2012. Relief of pain during blood specimen collection in pediatric  
 437 patients. *MCN Am J Matern Child Nurs.* 37 (5), 339-45.
- 438 McMurtry, C.M., Noel, M., Chambers, C.T., McGrath, P.J., 2011. Children's fear during  
 439 procedural pain: preliminary investigation of the Children's Fear Scale. *Health Psychol.* 30  
 440 (6), 780-8.
- 441 Melzack, R., Wall, P.D., 1996. Pain mechanisms: A new theory: A gate control system  
 442 modulates sensory input from the skin before it evokes pain perception and response.  
 443 *Science.* 5 (1), 3-11.
- 444 Moadad, N., Kozman, K., Shahine, R., Ohanian, S., Badr, L.K., 2016. Distraction Using the  
 445 BUZZY for Children During an IV Insertion. *J Pediatr Nurs.* 31 (1), 64-72.
- 446 Potts, D.A., Davis, K.F., Elci, O.U., Fein, J.A., 2019. A Vibrating Cold Device to Reduce  
 447 Pain in the Pediatric Emergency Department: A Randomized Clinical Trial. *Pediatr Emerg*  
 448 *Care.* 35 (6), 419-425.
- 449 Rogers, T. L., Ostrow, C. L., 2004. The use of EMLA cream to decrease venipuncture pain in  
 450 children. *Journal of Pediatric Nursing.* 19 (1), 33-9.
- 451 Savino, F., Vagliano, L., Ceratto, S., Viviani, F., Miniero, R., Ricceri, F., 2013. Pain  
 452 assessment in children undergoing venipuncture: the Wong-Baker faces scale versus skin  
 453 conductance fluctuations. *PeerJ* .1, e37.
- 454 Shah, V., Taddio, A., Rieder, M.J., HelpinKids Team., 2009. Effectiveness and tolerability of  
 455 pharmacologic and combined interventions for reducing injection pain during routine  
 456 childhood immunizations: systematic review and meta-analyses. *Clin Ther.* 31 Suppl 2, S104-  
 457 51.
- 458 Taddio, A., Ilersich, A. L., Ipp, M., Kikuta, A., Shah, V., HelpinKids Team., 2009. Physical  
 459 interventions and injection techniques for reducing injection pain during routine childhood  
 460 immunizations: Systematic review of randomized controlled trials and quasi-randomized  
 461 controlled trials. *Clinical Therapeutics.* 31 Suppl 2, S48-76.  
 462
- 463 Taddio, A., Appleton, M., Bortolussi, R., Chambers, C., Dubey, V., Halperin, S., Hanrahan,  
 464 A., Ipp, M., Lockett, D., MacDonald, N., Midmer, D., Mousmanis, P., Palda, V., Pielak, K.,

- 465 Riddell, R. P., Rieder, M., Scott, J., Shah, V., 2010. Reducing the pain of childhood  
466 vaccination: An evidence-based clinical practice guideline (summary). *CMAJ : Canadian*  
467 *Medical Association Journal*, 182(18), 1989–95.
- 468 Taddio, A., Shah, V., McMurtry, C.M., MacDonald, N.E., Ipp, M., Riddell, R.P., Noel, M.,  
469 Chambers, C.T., HelpinKids Adults, T., 2015. Procedural and Physical Interventions for  
470 Vaccine Injections: Systematic Review of Randomized Controlled Trials and Quasi-  
471 Randomized Controlled Trials. *Clin J Pain*.31 (10 Suppl), S20-37.
- 472 Tomlinson, D., von Baeyer, C.L., Stinson, J.N., Sung, L., 2010. A systematic review of faces  
473 scales for the self-report of pain intensity in children. *Pediatrics* 126 (5), e1168-98.
- 474 Tsze, D.S., von Baeyer, C.L., Bulloch, B., Dayan, P.S., 2013. Validation of self-report pain  
475 scales in children. *Pediatrics* .132 (4), e971-e979.
- 476 Valeri, B.O., Holsti, L., Linhares, M.B., 2015. Neonatal pain and developmental outcomes in  
477 children born preterm: a systematic review. *Clin J Pain* .31 (4), 355-62.  
478
- 479 Wright, S., Yelland, M., Heathcote, K., Ng, S.-K., Wright, G., 2009. Fear of needles-Nature  
480 and prevalence in general practice. *Australian Family Physician*, 38 (3), 172-6.  
481  
482