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Impact of the CARD (Comfort Ask Relax Distract) system on school-based vaccinations: A cluster randomized trial

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ABSTRACT

Background: The CARD (Comfort Ask Relax Distract) system is a vaccine delivery framework that integrates evidence-based interventions to reduce stress-related responses and improve the vaccination experience for children undergoing vaccinations at school. In preliminary studies, CARD was acceptable and effective. The objective was to evaluate CARD in a large, pragmatic trial to confirm its effectiveness in real-world settings.

Methods: Hybrid effectiveness-implementation cluster randomized trial in schools receiving vaccination services from Wellington-Dufferin-Guelph Public Health. Forty schools with grade 7 students (12 years old) were randomized to CARD and control (n = 20/group). Nurses in CARD schools planned clinics with principals and educated students about CARD ahead of time. Principals disseminated information to staff and parents and sent reminders. Vaccination day processes minimized fear and facilitated student self-selected coping strategies. Nurses in control schools followed usual practices, which excluded principal meetings, education, reminders, and systematic integration of fear-reducing or child-selected coping strategies. Outcomes included stress-related symptoms (fear – *primary outcome*, pain, dizziness, fainting, post-vaccination reactions), use of coping interventions, vaccination uptake, attitudes and implementation outcomes (acceptability, appropriateness, feasibility, fidelity).

Results: Altogether, 1919 students were included. Fear and pain were lower in CARD schools: OR 0.65 (95% CI 0.47–0.90) and OR 0.62 (95% CI 0.50–0.77), respectively. No students fainted in CARD schools compared to 0.8% in control (p = 0.02). Dizziness and post-vaccination reactions did not differ. Student-led coping interventions were used more frequently in CARD schools. Vaccination uptake was 76.1% in CARD schools and 72.5% in control schools (OR 1.13 (95% CI 0.85–1.50)). Staff and students had positive attitudes about CARD and implementation outcomes; however, recommendations were made to improve fidelity.

Discussion: CARD reduced stress-related responses in students undergoing vaccinations at school and was positively received by students and public health staff. CARD is recommended to improve the quality of vaccination delivery services.

Trial registration: NCT03966300.

1. Introduction

School-based (mass) vaccination clinics enable efficient vaccination of large numbers of children. The process of vaccination, however, is stressful for children as it involves getting a needle. Almost two-thirds of children report that they are afraid of needles [1], and fear of needles and associated pain can exacerbate stress-related reactions during vaccination [2–5]. Negative vaccination

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experiences contribute to negative attitudes about vaccination and future vaccination non-compliance [6]. In one large survey, 5% of parents and 8% of children reported they delayed or refused childhood vaccinations because of needle fear [1]. Despite the negative consequences of unmitigated fear and pain, vaccination delivery systems do not systematically include interventions that are proven to reduce fear, pain and associated stress-related responses [7].

We recently developed a vaccination delivery framework to address this care gap called the CARD (Comfort Ask Relax Distract) system [8]. Each letter category includes evidence-based interventions that can be used to reduce stress-related responses. CARD translates our 2015 clinical practice guideline recommendations on mitigating pain [9] to the school vaccination context [8]. All stakeholders involved in the vaccination process – immunizers, students, parents, educators – are educated about CARD ahead of time and then undertake activities (i.e., they *play* their cards) on vaccination day to minimize stress-related responses during vaccination and improve the vaccination experience for students.

Importantly, with CARD, students become active participants in the vaccination process. Engaging children as active participants promotes person-centred care [10] and is particularly relevant during the pandemic because children are experiencing higher levels of anxiety [11] and mass vaccination settings are being used for routine, 'catch-up' and COVID-19 vaccinations. CARD teaches children coping skills that can be used during vaccinations and other acutely stressful situations [12,13].

In a small controlled clustered trial involving grade 7 students (12 years old), we demonstrated a reduction in fear and dizziness with CARD, and more positive attitudes about vaccination [14]. While promising, applicability was limited by the small sample size, comprehensive implementation support, and well-established relationship with schools that included onsite (school) nurses. Variability in public health settings and practices may lead to differences in effectiveness. High-quality, yet widely applicable evidence is required to inform policy makers and providers and lead to broader systemic impact (i.e., scaling CARD). In this trial, we evaluated the impact of CARD using a rigorous yet pragmatic approach, including randomization of participating schools, and independent delivery of CARD by usual public health staff that were not immersed in schools. The results have implications for vaccination delivery broadly, as well as current efforts specifically targeted to COVID-19 vaccination in mass and school settings.

2. Methods

We undertook a clustered, randomized, partially blinded, hybrid effectiveness-implementation trial to simultaneously evaluate CARD and a pragmatic implementation strategy [15]. We used an integration mixed methods approach, whereby qualitative data was used to obtain deeper and richer understanding of the implementation context and to help validate quantitative results [16]. The Consolidated Framework for Implementation Research (CFIR) [17] was used to guide inquiry of implementation barriers and facilitators. These items were subsequently subsumed into pre-specified implementation outcomes described by Proctor [18], including acceptability, appropriateness, feasibility and fidelity.

Schools in both major school boards (Public, Catholic) receiving vaccination services in 2019–2020 from Wellington-Dufferin-Guelph Public Health were eligible. Data collection was planned for two vaccine clinics per school: fall (round 1) and spring (round 2). In the fall clinic, students were offered one dose of hepatitis B vaccine and human papillomavirus vaccine. In the spring clinic, students were offered a second dose of both vaccines plus quadrivalent conjugated meningococcal vaccine. Because of the pandemic, second clinics were cancelled, and the study was prematurely terminated. Data were therefore analyzed for the first clinic only.

As the vaccination delivery program (and CARD intervention) was delivered at a school level, all grade 7 students in participating schools were included. Random allocation of schools was performed by a statistician external to the trial using a computer program (randomize.net). To minimize differences in school characteristics between groups, schools were randomized in a 1:1 ratio to intervention (CARD) or control (usual care) after stratifying by two factors: school board and school size (small, large). Students were blinded to the study and hypothesis and public health staff in the control group were blinded to the intervention and hypothesis.

Table 1 briefly summarizes activities undertaken in CARD schools, including: implementation plan development; training implementing staff; vaccination planning meetings with school principals; student, school staff and parent education; vaccination day reminders; and vaccination clinic setup and processes aimed at reducing distress and promoting student participation and coping. Implementation occurred within allocated program staffing resources. Supplementary data 1 displays a CARD pamphlet used during students' education.

Control schools followed usual practices, which included confirmation of vaccination clinic appointment times and delivery of vaccinations on clinic day. There was no formal education of relevant groups or systematic approaches to setting up clinics or involving students. Control group staff were unaware of the intervention. Supplementary data 2 provides a detailed accounting of intervention and control procedures.

Nurses in both groups recorded preparatory and clinic day activities on process checklists. During each vaccination interaction, nurses completed a checklist (yes/no) that documented stu-

Table 1
Summary of key phases and activities of CARD intervention.

Education of staff providing vaccination services	Education about CARD; Tailoring CARD implementation to address local activities and processes; Creation of tools/resources to support local implementation
Clinic planning with principal	Review CARD, vaccination clinic spaces (including private space), education of students, parents and school staff, reminders, clinic day processes
Education of students	Student in-class lesson about CARD (including 2 videos and handout) with distribution of vaccination consent forms and consent for use of topical anesthetics; Student selection of coping interventions for clinic day
Reminders	Reminders of vaccination day and CARD (students, parents, school staff)
Clinic set-up and processes	Reduce visual and auditory cues that elicit fear (e.g., create separate waiting spaces, obscure equipment and other students getting vaccinated from view); Introduction of staff to students at start of clinic and review of CARD and clinic processes; Triage students with fear and special requests (e.g., privacy, topical anesthetics); Minimize number of students waiting
Interactions during vaccination	Assess student level of fear prior to vaccination; Invite students to use their preferred coping strategies (i.e., to choose the CARDs they want to *play*) and support them in their choices; Provide distraction kits (with items such as fidget spinner, squishy ball, bubbles) for students that prefer to use external distraction agents but are not in possession of such items

dent gender (female, male, or other) obtained from vaccine consent records, procedural data (vaccine administration details), and coping interventions used (distraction – verbal/external item, support person – peer/adult, privacy, topical anesthetic, deep breathing, muscle tension). Nurses also recorded faints and other post-vaccination stress-related responses (e.g., headache, nausea, dizziness) reported by students using a checklist (yes/no) [5]. Immediately after vaccination, students independently self-rated fear, pain, and dizziness during vaccination (0–10) and perceptions about whether they should get vaccinations (5-point Likert scale), and for CARD schools, how much CARD helped and willingness to use CARD in the future. Staff knowledge (0–10) and attitudes (5-point Likert scale) about pain and fear interventions and implementation outcomes (percent compliance with 19 pre-specified components of CARD, acceptability, appropriateness, feasibility, fidelity) were collected from surveys, checklists, and a facilitated focus group discussion held after fall clinics. These variables and measurement approaches were informed by the core outcome set and instruments included in our clinical practice guideline [9], and are consistent with our prior CARD studies [12,14,19].

Approval was granted by the Research Ethics Board (REB) at the University of Toronto and the school boards. A waiver of consent was given for data collection. Public health staff, however, provided written consent for participation in the focus group. The REB approved analysis of results for fall clinics only. The trial registration number is NCT03966300.

2.1. Sample size and analysis:

The primary outcome was student-reported fear during vaccination. Fear is students' most frequent concern about vaccination, reported by 3 out of 5 students [4]. Based on a small clustered trial with CARD [14], we estimated a delta = 1.0 and standard deviation = 3.1. Altogether, 40 schools (~35 students vaccinated/school) were included to provide 80% power of declaring significance with alpha = 0.05, 5% missing data and intra-cluster correlation coefficient = 0.1. A focus group was conducted with all 10 public health staff involved in CARD implementation.

We conducted an intent-to-treat analysis including all students. Analysis was limited to the 2019 fall clinics only due to the COVID pandemic. The skewed pattern of scores, including a large number of zero values, led to the student symptoms being dichotomized. Dichotomized symptoms are considered clinically relevant and valid and were included as outcomes in the knowledge synthesis which formed the evidence base for our clinical practice guideline [9]. The cutpoint used for fear and dizziness scores was "0" no/none or ">0" yes/any and was guided by the WHO's definition of immunization stress-related responses which describes symptoms in dichotomous terms (present or absent) [5] and was consistent with how these symptoms were recorded in our post-vaccination stress-related responses checklist. Pain was recoded as "0–2" no/mild or ">2" moderate/severe as some pain was expected to be experienced and prior work set a cutpoint of 3 for moderate levels of acute pain [20]. Groups were compared using a Generalized Estimation Equation (GEE) logistic regression, adjusted for clustering (school) and gender, consistent with our prior work [14]. Chi squared test was used if there was zero frequency of an outcome (no events) as regression could not be performed. Comparison in the incidence of fainting, and use of deep breathing and muscle tension was undertaken in this manner. Ordinal outcomes were analyzed using random effect ordinal logistic regression. Knowledge, attitudes and compliance were analyzed descriptively. There was no adjustment for multiple comparisons. Directed content analysis using CFIR [17] and subsequent organization of results by implementation domain (acceptability, appropriateness, feasibility, fidelity) [18] were used for qualitative data.

3. Results

During the study period (Sept 19-Nov 20, 2019), all 40 invited schools, representing 65% of eligible schools, participated (Fig. 1). There were 900 students in CARD schools and 1019 in control schools; characteristics are displayed in Table 2. One focus group (Nov 22, 2019) included the program manager, 6 nurses, 2 registration clerks and 1 administrative assistant.

Fewer students in CARD schools experienced fear compared to controls: OR 0.65 (95% CI 0.47–0.90) (Table 3). Similarly, pain was lower in CARD schools compared to control schools: OR 0.62 (95% CI 0.50–0.77). There were 0 (0%) vs. 6 (0.8%) – 4 female, 2 male – episodes of fainting in CARD vs. control schools ($p = 0.02$), with each faint occurring in a different school (i.e., not clustered). Dizziness and post-vaccination reactions did not differ. Female gender was associated with higher fear, pain and dizziness ($p < 0.001$ for all analyses) (Table 3). The results for gender are shown in Supplementary data 3. Intra-cluster correlation coefficients were < 0.02 for all applicable analyses, meaning that the impact of clustering was negligible.

The overall vaccination rate, although higher in the CARD schools (76.1%) compared to control (72.5%), was not statistically significant; OR 1.13 (95% CI 0.85–1.50). The rate for hepatitis B or human papillomavirus vaccine uptake specifically did not differ between groups (Table 3).

The frequency of use of coping interventions is displayed in Fig. 2. CARD school students utilized external distractions, peer support, deep breathing, muscle tension, privacy, and topical anesthetics more frequently ($p < 0.0001$ for all analyses) than control school students. Verbal distraction and adult support, however, were utilized more frequently ($p < 0.0001$ and $p < 0.001$, respectively) in control school students (Fig. 2). CARD school students trended to more positive attitudes about getting vaccinated (OR 1.3; 95% CI 1.0–1.9), perceived CARD as helpful (median score 4, range 1–5) and were willing to use CARD in the future (median score 4, range 1–5).

Public health staff demonstrated knowledge about and positive attitudes towards pain and fear interventions and CARD implementation in quantitative surveys (Table 4**)** and qualitative interviews (Supplementary data 4). Compliance with CARD components ranged from 84% to 100% across intervention schools. During the focus group, staff reported satisfaction with their expanded roles educating students and collaborating with school principals. They perceived students as better prepared and less fearful. CARD added some time to vaccination planning and documentation activities but strengthened relationships among staff. A registration clerk 'in training' was maintained by the program manager to support clinics. There was a steep learning curve, and not all interventions were consistently employed. Specific coping interventions such as privacy, peer support, and topical anesthetics were challenging to implement, and staff trialed various execution approaches. Additional guidance was requested to optimize effectiveness of execution (Supplementary data 5).

4. Discussion

Children undergoing vaccinations at school commonly experience stress-related responses, such as fear and pain [4]. While evidence-based interventions exist to mitigate these symptoms [9], they have not been systematically incorporated into the vaccination delivery process [7]. The CARD system is a vaccination delivery framework that translates this evidence into action [8]. When used for providing vaccinations at school by Wellington Dufferin Guelph Public Health, CARD reduced student fear, pain and fainting. Students used self-directed coping strategies more fre-

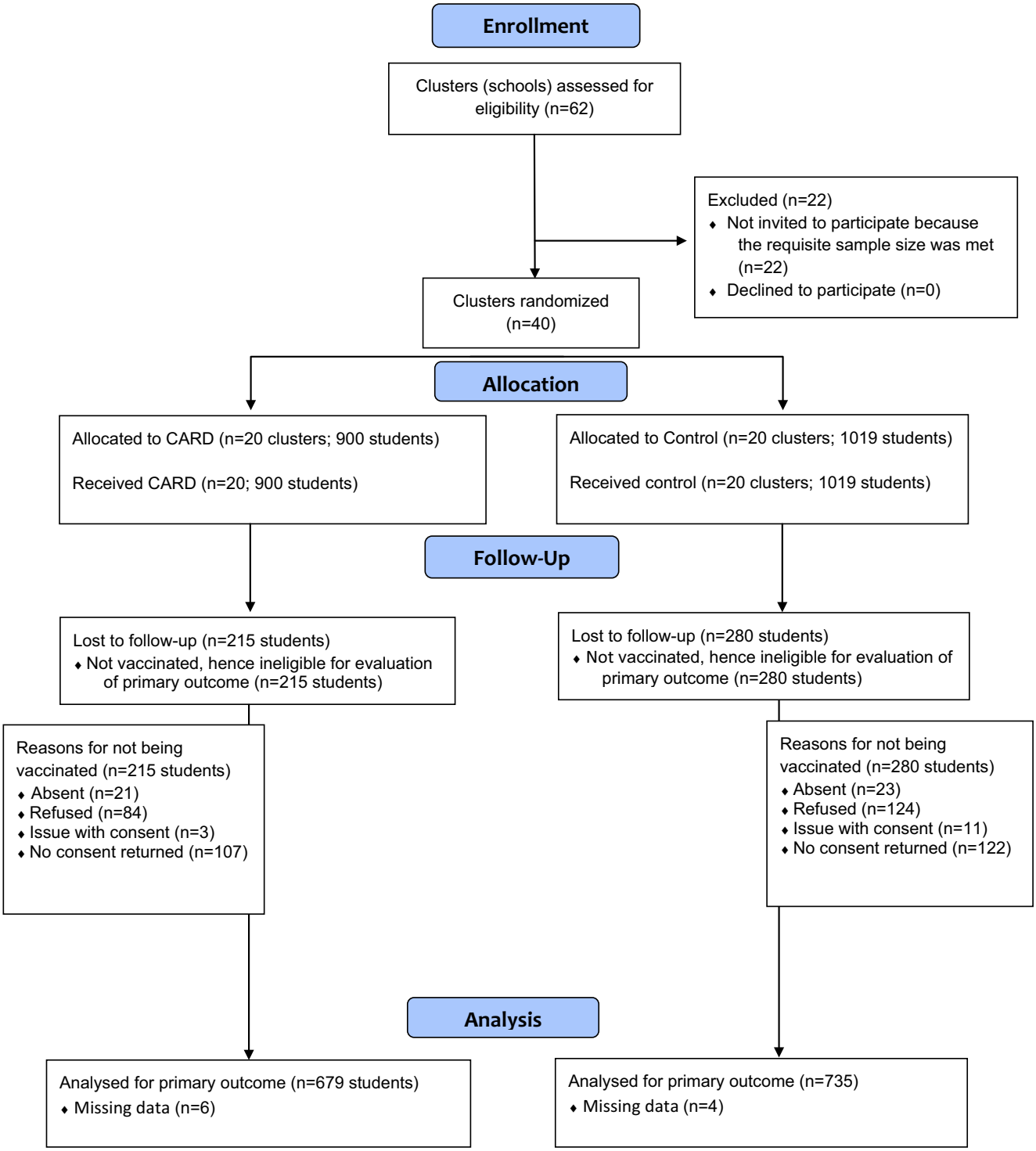

Fig. 1. CONSORT Flow diagram.

quently, including distraction items, privacy, deep breathing, peer support, topical anesthetics and muscle tension. There was no evidence of benefit on dizziness, other post-vaccination reactions or vaccination uptake. Students had positive attitudes about CARD and in using it in the future. Public health staff implementing CARD had high knowledge about and positive attitudes towards pain and fear mitigation and believed CARD was acceptable, appropriate, and feasible. While perceived as effective, some components of CARD were challenging for staff, and additional guidance was requested to optimize implementation fidelity.

Results are consistent with our prior study whereby we found a benefit on fear and dizziness; [14] however, we found added impact on pain and fainting, but not dizziness, in this study. The magnitude of the benefit was modest for fear and pain, however, the observed benefit on fainting was more impressive, particularly

Table 2
Demographics of participating schools.

	CARD (intervention) group (n = 20)	Control (standard care) group (n = 20)
Public school, no. (%)*	14 (70)	14 (70)
Median household income (CAD)**	$67,829	$72,143
Grade 7 students, mean no. per school (SD)	45 (24)	51 (27)
Sex distribution, no. male students (%)	442 (49.2)	550 (54.0)

* The remainder (n = 6 schools/group) were Catholic schools.
** Based on region of school (Census Profile, 2016 Census, Statistics Canada).

given its higher prevalence in adolescents and associated risk of hospitalization [21]. Our prior study was relatively small (10 schools, including 247 vaccinated students), with no episodes of fainting [14]. We hypothesize that student education and the higher frequency of use of evidence-based interventions during vaccination explain the observed benefits [9].

Education has been recommended for improving vaccination acceptance [22] and promoting self-efficacy and person-centredness [23]. There are other promising interventions currently under development to mitigate pain and fainting in this population [24,25], however, at present, CARD has the strongest evidence base behind it [23]. While CARD was evaluated in grade 7 students in the present trial, it was initially developed with the input of students from grades 6 to 8 [8]. It was subsequently demonstrated to be acceptable in grade 9 students [26]. The body of research on pain and fear suggest that if age-appropriate adaptations are made, it should achieve positive effects in other populations as well [27]. To this end, we recently developed a CARD web game (freely accessible via Immunize Canada at https://immunize.ca/card-game-kids) to target younger children (~6 to 12 years) for education. Playtesting results show promise with respect to learning about coping strategies and reducing needle fear for this younger age group [28].

Staff had positive attitudes about CARD and believed it improved the vaccination experience for students and themselves. They enjoyed educating students and described them as more prepared, including being more knowledgeable and wearing optimal attire. They also appreciated collaborating more closely with principals and each other. Many components of CARD were new and while training materials and checklists assisted with implementation, staff reported challenges and recommended additional guidance and staffing to improve effectiveness further. Unlike our prior study [12], debriefs held after each clinic in this study - to review what went well, did not go well, and changes for the future - did not incorporate review of student responses on the symptom survey. Thus, staff could not validate their perceptions of the effect of different processes utilized during the clinic on student symptoms. Review of student surveys is strongly recommended for future implementation tailoring to ensure that the selected implementation approaches achieve intended effects. This is particularly important for complex interventions, such as topical anesthetics, private spaces, and presence of a support person. It is important to ensure that interventions are optimally delivered. The high rate of fear and pain despite the use of CARD suggests sub-optimal fidelity of implementation. Feedback from staff identified gaps in their training and ongoing feedback that should be used to inform future training and implementation approaches.

Strengths include a randomized design, inclusion of most regional schools (65%), and collection of population level data. In addition, we used a pragmatic design with implementation in real-life practice conditions without provision of additional staffing. The public health unit accommodated training of staff and staff attendance at schools, meeting with principals, educating students, and miscellaneous items (spinners, bubbles) for students to use as distractions. We identified study outcomes from the prioritized outcome set included in our clinical practice guideline on this topic [9], providing a comprehensive evaluation of the impact of CARD. Students and parents were blinded to the hypothesis and students independently reported symptoms, reducing bias in outcome assessment. The intervention was not provided to control schools and staff educated in CARD did not deliver vaccination services to control schools or discuss the intervention with non-trained staff, minimizing contamination. In addition, there was no evidence of contamination from review of the process checklists used to track staff activities or from the pattern of coping interventions used.

There are some limitations worthy of discussion. The evaluation approach likely under-estimated the effectiveness of CARD because all data were included without a run-in or practice phase (i.e., real world). In addition, premature study termination prevented data collection in the second (spring) clinics. Our prior study demonstrated improved effectiveness of CARD on fear symptoms over time [14] and we would have therefore expected that fear would have been lower during the second clinic. The results are limited to the setting and population, which while inclusive of most neighborhoods, was limited to grade 7 students, relatively small-sized

Table 3
Student stress-related responses and vaccination uptake in CARD and Control groups.

Outcomes	Sample size CARD	Number of events (%) CARD	Sample size Control	Number of events (%) Control	Odds Ratio (95% Confidence Interval)† CARD vs Control	P-value
Primary Outcome						
Fear (>0 vs 0)*	679	555 (81.7)	735	635 (86.4)	0.65 (0.47 – 0.90)	0.01
Secondary Outcomes						
Other stress-related responses						
Pain (>2 vs <=2)*	677	456 (67.4)	734	557 (75.9)	0.62 (0.50 – 0.77)	<0.0001
Dizziness (>0 vs 0)*	680	290 (42.6)	735	344 (46.8)	0.82 (0.64 – 1.05)	0.12
Fainting (yes vs no)	685	0 (0)	739	6 (0.8)	CARD 0%, Control 0.8%	0.02
Post-vaccination symptoms (yes vs no)	684	15 (2.2)	739	15 (2.0)	1.04 (0.48 – 2.25)	0.91
Vaccination rate						
Overall vaccination (yes vs no)	899	684 (76.1)	1019	739 (72.5)	1.13 (0.85 – 1.50)	0.44
Hepatitis B (yes vs no)	899	564 (62.7)	1019	633 (62.1)	1.00 (0.83 – 1.22)	0.97
Human Papillomavirus (yes vs no)	899	632 (70.3)	1019	680 (66.7)	1.11 (0.85 – 1.45)	0.41

* Fear, pain and dizziness were scored from 0 (none) to 10 (maximum) and dichotomized for analysis.
† Derived from Generalized Estimation Equation (GEE) logistic regression adjusted for clustering and gender, or Chi squared test; see text for further details.

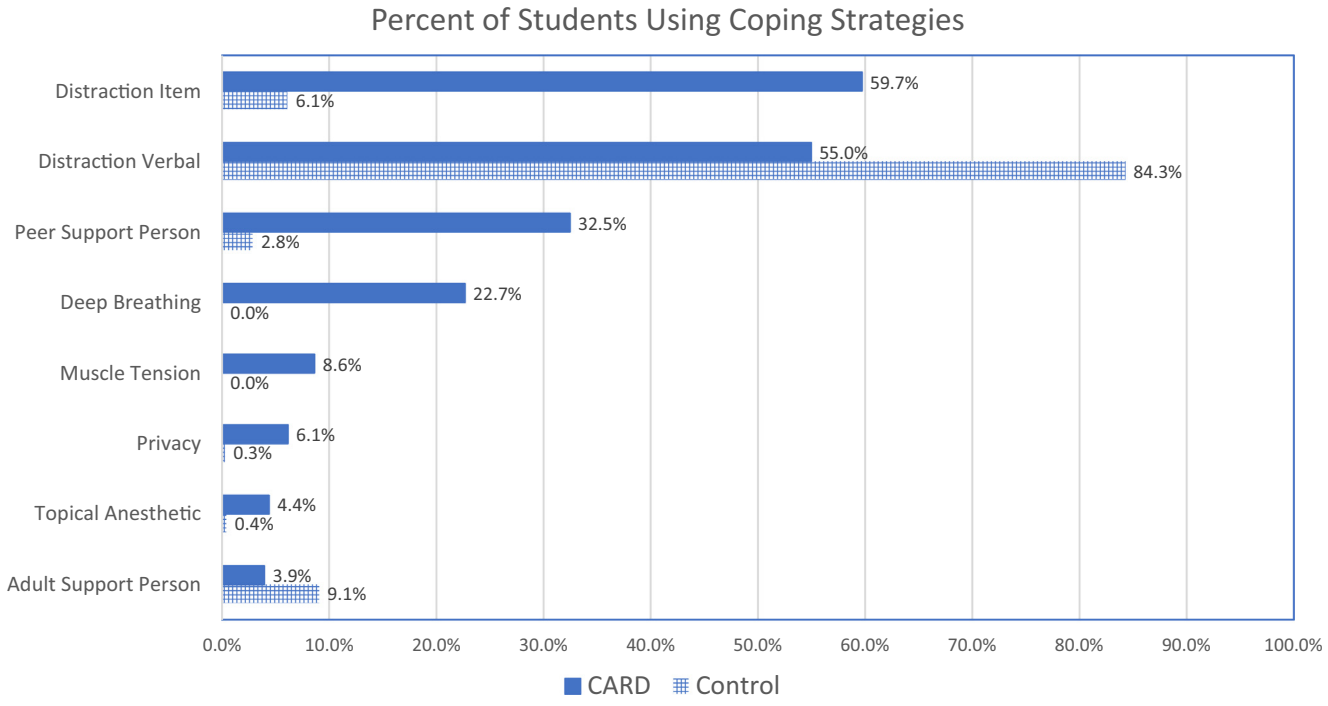

Fig. 2. Percent of students using coping strategies in CARD and Control groups. Generalized Estimation Equation (GEE) logistic regression, or Chi squared test; CARD group higher than control ($p < 0.0001$ for all analyses) for distraction with item, peer support, deep breathing, muscle tension, privacy, topical anesthetic. Control group higher than CARD for verbal distraction ($p < 0.0001$) and adult support ($p < 0.001$).

Table 4
Public health staff knowledge, beliefs and attitudes about pain and fear and CARD implementation (n = 10)*.

	Mean (SD)
Knowledge about effective pain and fear interventions, (range, 0–10)**	
Knowledge score	8.9 (1.1)
Attitudes (5-point Likert scale, range 1 = strongly disagree to 5 = strongly agree)	
Students should be given information about why vaccines are important	4.8 (0.4)
Teachers should be given information about why vaccines are important	4.8 (0.4)
Teachers should be given information about how to make vaccinations less painful and frightening	4.6 (0.7)
I believe it is important to treat students' pain and fear during vaccinations	4.5 (0.7)
Attitudes about CARD (5-point Likert scale, range 1 = strongly disagree to 5 = strongly agree)	
Acceptability	
I understand the individual components of the CARD system	4.9 (0.3)
I am willing to try all components of the CARD system	4.8 (0.4)
I would recommend the CARD system for school vaccinations	4.3 (1.1)
I am likely to continue to use the CARD system in the future	4.4 (1.1)
Appropriateness	
The CARD system is aligned with our organizational goals	4.6 (0.5)
Feasibility	
I have the support I need from other personnel to implement the CARD system	4.6 (0.5)
Management supports my daily efforts in implementing the CARD system	4.8 (0.4)
I believe the documentation involved in the CARD system is too time consuming	2.5 (1.4)
I believe that the CARD system improves collaboration between public health staff and students	4.4 (1.1)
I believe that the CARD system improves collaboration among public health staff in my unit	4.4 (1.0)
I believe that the CARD system improves collaboration between public health staff and teachers	4.8 (0.4)
I think it is realistic to continue to use the CARD system in our setting	4.3 (0.8)
Fidelity	
I am confident in my ability to use the CARD system	4.8 (0.4)
I believe the CARD system is being used in my unit	4.5 (0.7)
I believe that the CARD system improves the student experience during vaccinations	4.2 (1.0)
I believe that the CARD system improves public health staff experiences during vaccinations	4.5 (0.8)
I believe that the CARD system helps to promote vaccination	4.4 (0.7)

* These data were obtained from surveys disseminated to staff during part of the focus group discussion. They were completed independently.
** Based on sum of correct responses to 10 questions; higher values indicate greater knowledge.

schools, and one public health region in southern Ontario. Citizens of included cities and townships varied in visible minority population from 2% to 20%. This compares to an overall average of 30% for all residents of Ontario, the majority of whom live in large cities such as Toronto [29]. We did not collect information about fear level at baseline to be able to compare with prior literature values [1] or ensure that the groups were balanced. In addition, students' perspectives were limited to responses on symptom surveys. This prevented in-depth examination of factors affecting their coping strategy choices and their perceptions of the quality of care and support received by staff. At the time the study was planned, collection of these data were not considered feasible by the participating public health unit and school boards. While not statistically significant, there was a trend to higher overall vaccination rate and positive attitudes in CARD schools. The study was underpowered (40%) to detect a difference in vaccination rate. Moreover, statistical power was lost from dichotomizing variables and caution is needed when interpreting the results for secondary outcomes due to multiplicity. We recommend future studies that examine different education delivery approaches as well as the pattern of student stress-related responses over time after sustained integration of CARD.

In summary, this study demonstrated that CARD reduced student stress-related responses and was acceptable and feasible in this real-world setting. As a result of this study, the participating public health unit has implemented CARD across the region. CARD is particularly relevant now that school-based vaccination programs as well as COVID-19 and 'catch-up' vaccination programs are underway targeting children. Concerns about pain and fear of needles are common and well documented barriers to vaccination among parents and children [1], including COVID-19 vaccination [30]. Integration of pain mitigation should be a standard of care to prevent stress-related iatrogenic harms of vaccination [31]. CARD has the potential to prevent exacerbations of already elevated levels of anxiety and to promote more positive vaccination experiences and future vaccination.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: A. Taddio reports a University of Toronto Section 9 Trademark No. 924835 for CARD™. LMB reports that Immunize Canada received grants from Pfizer Inc., Merck Canada, Sanofi Pasteur, Seqiris, and Glaxo-Smith-Kline unrelated to this work. The other authors declare they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.02.069.

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