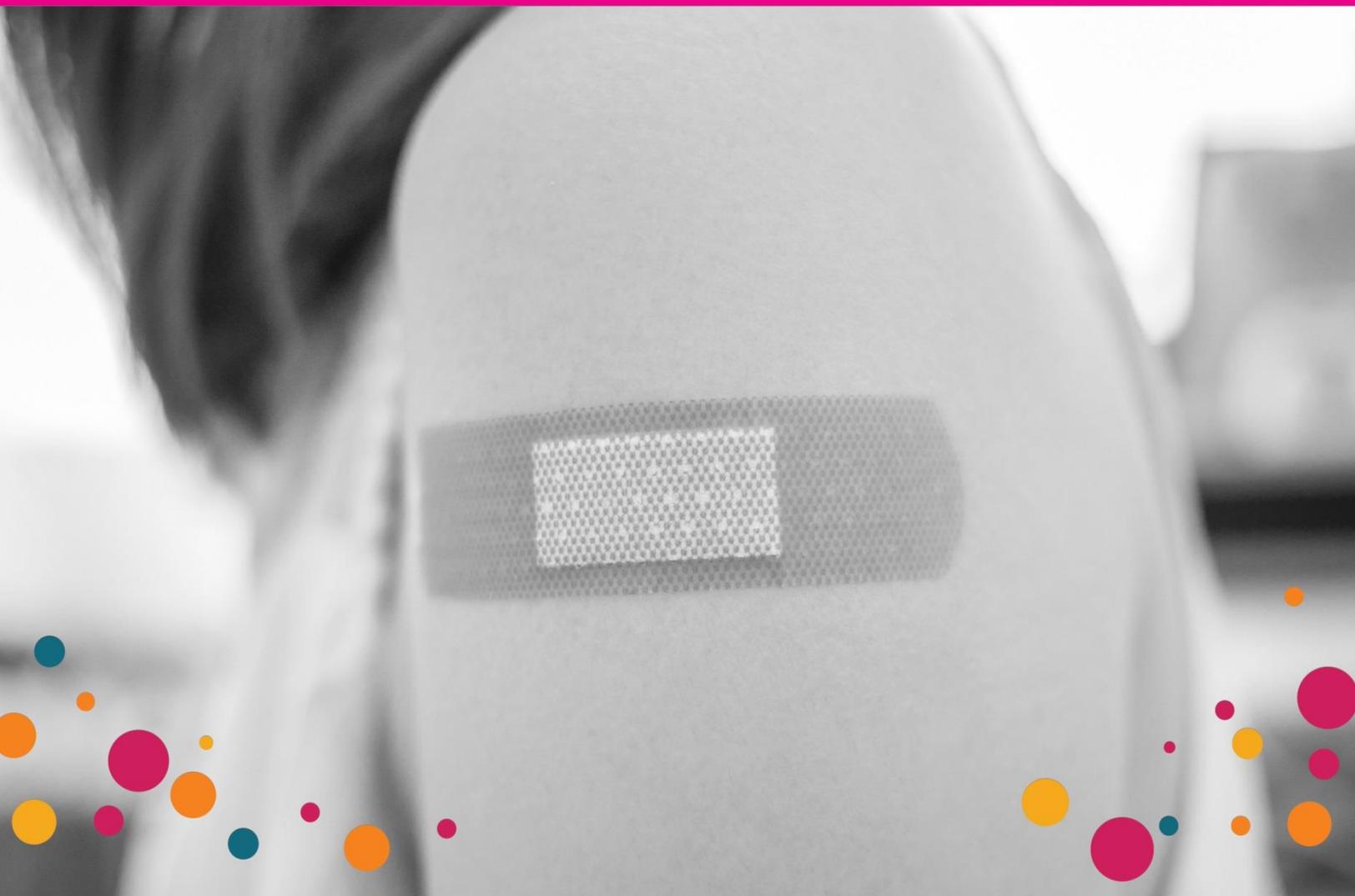


# Literature Review on Effective Strategies to Improve Vaccine Acceptance and Uptake

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*Evidence to inform research and practices*



## Building the capacity to improve vaccine acceptance and uptake

The Canadian Vaccination Evidence Resource and Exchange Centre (CANVax) is an online database of curated resources to support immunization program planning and promotional activities to improve vaccine acceptance and uptake in Canada. As an online resource centre, CANVax aims to increase access to the evidence-based products, resources, and tools to inform public health professionals in immunization program planning and promotion.

CANVax has been developed by the Canadian Public Health Association. Production of CANVax has been made possible through funding from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the view of the Public Health Agency of Canada.

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# SUMMARY

Vaccine hesitancy is receiving increasing public health attention in developed and developing countries around the world. Public health authorities can have an impact on vaccine acceptance, vaccination coverage and delay in receipt of vaccines within the general public. This review of published reviews and Canadian interventional studies aims to identify evidence-based best practices and areas for future research, to inform the development of action and research plans.

Recent reviews (n=9) and interventional studies conducted in Canada (n=10) showed that there is no strong evidence on which type of intervention to recommend to address vaccine hesitancy/refusal. Findings of this review indicate that some types of interventions showed more promising effect on vaccine acceptance and vaccine uptake (e. g. tools such as reminders and recall for patients and healthcare providers). However, it remains unclear whether educational initiatives alone alter vaccine refusal and hesitancy. Multifaceted interventions (encompassing improved access to vaccines, immunization mandates, and patient education) may increase vaccine uptake in vaccine-hesitant populations.

Some recent reviews of the literature have looked at communication strategies with parents and at the influence of these strategies on parents' decisions regarding childhood vaccination. Overall, findings showed that healthcare providers play a key role in patient/parent vaccination decision-making and are perceived as an important source of vaccination information. Poor communication or negative relationships with healthcare providers sometimes have an impact on parents' vaccination decisions. Building parental trust seems to be an important component of the provider-parent interaction.

Key principles for optimizing strategies to address vaccine hesitancy were identified. To be effective, interventions should be developed using a planning framework and should be based on a theoretical model. The use of a combination of different interventions (multiple components) appears to be more effective than single-component interventions. Interventions are most likely to succeed when they are based on empirical data and situational assessment – both to have a detailed level of understanding of the vaccine hesitancy situation (susceptible populations, key determinants of vaccination, barriers and enabling conditions, etc.) and to properly evaluate the impact of the intervention.

# RÉSUMÉ

L'hésitation vaccinale reçoit une attention croissante de la part des autorités de santé publique, tant dans les pays développés qu'en développement. Ces autorités peuvent exercer une influence sur l'acceptation des vaccins, la couverture vaccinale et le report de la vaccination dans la population. Nous avons examiné des revues de la littérature et des études interventionnelles canadiennes pour mieux cerner les pratiques exemplaires fondées sur les données probantes, ainsi que les aspects à cibler dans les études futures, pour éclairer l'élaboration de plans d'intervention et de recherche.

Selon des revues récentes (n = 9) et des études interventionnelles menées au Canada (n = 10), il n'existe pas d'indications claires sur le type d'intervention à recommander pour aborder l'hésitation vaccinale ou le refus des vaccins. Notre examen montre que certains types d'interventions ont des effets plus prometteurs que d'autres sur l'acceptation et l'adoption des vaccins (p. ex. les outils de rappel des patients et des dispensateurs de soins de santé). Il n'est toujours pas clair, cependant si les stratégies éducatives peuvent à elles seules changer le refus des vaccins et l'hésitation vaccinale. Les interventions multidimensionnelles (qui englobent l'amélioration de l'accès aux vaccins, les mandats de vaccination et l'éducation du patient) peuvent augmenter le recours aux vaccins dans les populations hésitantes.

Quelques récentes revues de la littérature ont porté sur les stratégies pour communiquer avec les parents et sur l'influence de ces stratégies sur les décisions parentales concernant la vaccination des enfants. Dans l'ensemble, il semble que les dispensateurs de soins de santé jouent un rôle clé dans les décisions des patients et des parents à l'égard de la vaccination, et que ces dispensateurs sont perçus comme une source importante d'informations à ce sujet. De mauvaises communications ou des relations négatives avec les dispensateurs de soins de santé ont parfois une incidence sur les décisions de vaccination que prennent les parents. Gagner la confiance des parents semble être un élément important de l'interaction entre les dispensateurs et les parents.

Des principes clés ont été recensés pour optimiser les stratégies à employer en cas d'hésitation vaccinale. Pour être efficaces, les interventions devraient être élaborées à l'aide d'un cadre de planification et reposer sur un modèle théorique. L'emploi d'une combinaison d'interventions (plusieurs éléments) semble être plus efficace que l'emploi d'interventions à un seul élément. Les interventions les plus susceptibles de réussir sont fondées sur des données empiriques et sur une évaluation situationnelle – à la fois pour obtenir une connaissance approfondie de la situation d'hésitation vaccinale (populations sensibles, principaux déterminants de la vaccination, conditions qui l'entravent ou qui la favorisent, etc.) et pour bien évaluer l'impact de l'intervention.

# 1. INTRODUCTION

Vaccine hesitancy is receiving increasing public health attention in developed and developing countries around the world. Vaccine hesitancy is the delay in acceptance or refusal of vaccines despite the availability of vaccine services. It is complex and context-specific varying across time, place and vaccines. It is influenced by such factors as complacency, convenience and confidence.<sup>1</sup> Recent studies suggest that in North America, Europe, and in other parts of the world, public confidence in vaccines is decreasing and anti-vaccine movements are becoming stronger.<sup>2</sup>

Public health authorities can impact on vaccine acceptance, vaccination coverage and delay in receipt of vaccines within the general public. When faced with vaccine hesitancy, public health authorities are looking for effective strategies to address it. In this report, a review of published reviews on strategies to address vaccine hesitancy and, more broadly, to enhance vaccine acceptance, is presented, and promising approaches on how to address vaccine hesitancy and its determinants are discussed. The goal of this literature review is to identify evidence-based best practices and areas for future research, to inform the development of action and research plans.

# 2. OBJECTIVE

The objective was to identify and summarize the available and recent evidence in the literature in the areas of: 1) interventions to increase vaccine acceptance and uptake, and 2) primary studies evaluating interventions to increase vaccine acceptance and uptake implemented in Canada.

# 3. METHODS

To identify relevant literature reviews or Canadian primary studies on interventions to address vaccine hesitancy and/or to enhance vaccine uptake, a search was conducted on February 28, 2018 in the following databases with the EBSCOhost search platforms: CINAHL, PsycINFO, and SocINDEX, and on the following additional databases with the OvidSP search platforms: Embase, Medline and the Cochrane database of systematic reviews. The search strategy combined relevant terms for “vaccination”, “knowledge, attitudes and behaviours” and type of possible “interventions” aimed at increasing both vaccine acceptance and uptake. Search terms were pre-defined to allow a comprehensive search strategy that included text fields (Title and Abstract) and Medical Subject Headings (MeSH terms – with an adaptation of terms for EBSCOhost). Language (English or French) and date (2015 – current) restrictions were applied.

Two different searches were run to identify: 1) literature reviews on interventions to increase vaccine acceptance and uptake, and 2) primary studies evaluating interventions to increase vaccine acceptance and uptake implemented in Canada.

Platforms search results were downloaded and combined in Endnote x5. After exclusion of duplicates, the title and abstract of all retrieved papers were screened by one researcher to exclude irrelevant papers; basic relevance appraisal was conducted by applying a set of inclusion criteria to the records based on their titles and abstracts (Box 1). The full texts of remaining papers were downloaded and were independently screened by two researchers to identify those meeting the inclusion criteria. Any disagreements were resolved by discussions.

## Box 1. Inclusion and exclusion criteria applied to articles for literature review

### Inclusion criteria

- Articles written in English or French
- Articles published between January 2015\* and February 2018 (if any)
- Articles presenting empirical data from primary studies conducted in Canada
- Literature reviews, meta-analysis or qualitative synthesis of primary studies conducted in countries comparable to Canada
- Articles or reviews focusing on vaccines currently recommended in Canada in all age groups

### Exclusion criteria

- Articles not about human vaccines
- Articles not about vaccines currently recommended in Canada (e.g. HIV vaccines)
- Articles about therapeutic vaccines
- Editorials, letters, conference abstracts or commentaries

Data was extracted using a predefined data extraction sheet developed for this purpose. Extracted information included: bibliographical information, population, purposes and settings, objectives and study design, sample sizes and response rates, and key findings. The extraction process was undertaken by one reviewer and checked by a second reviewer.

\* To update another review of a review that included reviews published between January 2010 and June 2015.

## 4. RESULTS

### 4.1 Literature reviews on interventions to increase vaccine acceptance and uptake: Main findings

Main findings for each part of the literature review are discussed in sections 4.1 and 4.2.

We have included 9 literature reviews on interventions to enhance vaccine acceptance or increased vaccine uptake published since 2015. The number of studies on vaccination included in each review ranged from 9 to 181. The included reviews are summarized in Appendix 1.

While the main interest was to include various types of interventions, the literature review was not restricted to vaccination topics solely and that is why one of the reviews included other health behaviours.<sup>3</sup> Most reviews primarily focused on childhood vaccines or influenza vaccination. The other reviews related to vaccination in general and to vaccination behaviours among healthcare workers.

Target audiences included parents, healthcare workers, children, and the general population. The main outcome of interest reported in the majority of reviews was vaccine uptake. Most reviews (7/9) reported an assessment of the quality of the studies included.

Only one review directly targeted strategies to address vaccine hesitancy.<sup>4</sup> The review included almost exclusively studies conducted in the Americas. Few strategies to address vaccine hesitancy were found to have been evaluated for the impact on either vaccination uptake and/or changes in knowledge, awareness or attitude.<sup>4</sup> The authors of this review have concluded that their review did not identify any convincing

evidence on effective interventions to address parental vaccine hesitancy and refusal, but multi-component and/or intervention having a focus on dialogue-based approaches tended to perform better than other types of interventions.<sup>4</sup>

Two reviews targeted communication about vaccines.<sup>5,6</sup> The first one investigated the influence that vaccination communication strategies can have on parents' decisions regarding childhood vaccination,<sup>5</sup> while the second one tried to identify the most effective practices to use with parents who have concerns.<sup>6</sup> Generally, findings from these reviews have shown that parents wanted more information than they were getting (mainly balanced information about benefits and harms), presented clearly and simply, and provided in good time. Healthcare workers were perceived as an important source of information, and poor communication or negative relationships with healthcare workers were shown to sometimes have a negative impact on parents' vaccination decisions. Parents also found it difficult to know which vaccination information source to trust and finding unbiased and balanced information was challenging for parents. Trialled interventions included the provision of tailored information prior to vaccination appointment, but none of the interventions that were evaluated responded to negative media stories or parental perceptions of healthcare workers motives.<sup>5</sup> Regarding the type of communication strategies that providers should employ with vaccine-hesitant parents, there is still a lack of evidence in the literature.<sup>6</sup> Building parental trust seems to be an important component of the provider-parent interaction. Vaccine providers should develop technical competence for discussing, among other things, the need for scheduled vaccinations and for identifying parents' specific concerns. Findings from this review also indicate that providers could develop specific communication approaches such as tailoring information to parents, giving a strong recommendation for vaccination, and showing respect and empathy.<sup>6</sup>

#### Parents' concerns towards vaccines

In line with findings reported by Ames et al.<sup>5</sup> and Connors et al.,<sup>6</sup> common parental concerns regarding childhood vaccines were identified in a recent literature search.<sup>7</sup> Two topics – safety and efficacy – were the most commonly shared concerns among parents. Questions about vaccination safety included concerns that vaccinations may overwhelm the immune system, cause chronic illness, and contain worrisome ingredients. In addition, parents often express concerns regarding vaccine effectiveness and whether or not contracting the disease provides a superior immune response when compared to the immune response from vaccinations. The authors noted that: *[P]roviding accurate vaccine education to parents is an important strategy to reduce vaccine hesitancy, albeit the [provider] must first establish an ideal environment, wherein the parent-nurse conversation can occur. At the very foundation of effective communication with vaccine-hesitant parents is the principle of respect. Facilitating a respectful interaction between [provider] and parents with vaccine concerns promotes trust and may ultimately help guide parents towards the decision to vaccinate.*<sup>7</sup>

#### Health literacy and informed consent

Informed consent is an important component of vaccination. Literacy and numeracy skills are required to assess the – often complex – information about vaccines. Skills to critically appraise and seek out the information to make an informed decision are also required, especially in the context of high information availability with the Internet and social media. For healthcare providers, communicating vaccine information to patients might be challenging, particularly when the patients have low health literacy.

A 2018 review has investigated the role of health literacy as a determinant of vaccine hesitancy.<sup>8</sup> Due to the heterogeneity of the 9 studies retained, the relationship between health literacy and vaccination remains unclear. The role of health literacy in predicting vaccine uptake seems to be age- and vaccine-specific, which further complicates the task of recommending interventions that could both increase

adherence with voluntary immunization and reduce vaccine hesitancy. According to the authors, conducting studies using various measurement tools (e.g., specific to vaccine literacy<sup>1</sup> and measuring general health literacy) is needed in the future to better understand the role of literacy in vaccine hesitancy and acceptance.

Two additional reviews targeted interventions to inform or educate about vaccination.<sup>9,10</sup> To some extent, reminder and recall interventions reviewed by Harvey et al. were effective, but findings were generally heterogeneous.<sup>9</sup> Subgroup analyses performed suggested that education interventions were more effective in low- and middle-income countries and when parents had a discussion with a professional (rather than receiving written information). Authors suggested that parents at high risk of non-compliance may benefit from recall strategies and/or discussion-based forums; however, further research is needed to assess the effectiveness of these strategies in this group.<sup>9</sup> Interventions applying new media (Internet and social media) to promote vaccine uptake and increase vaccination coverage were evaluated in the second review.<sup>10</sup> The authors have concluded that text messaging, accessing vaccination campaign websites, using patient-held web-based portals and computerized reminders may increase vaccine uptake, whereas there was insufficient evidence to determine the effectiveness of the use of social networks, email communication and smartphone applications.<sup>10</sup> These findings were not specific to the vaccine-hesitant population, however.

#### Other reviews on type of interventions including studies on vaccination

Other interesting reviews have been identified by our searches, but not retained due to our inclusion/exclusion criteria.<sup>11,12</sup> Badawy et al. evaluated evidence for the efficacy of text messaging and mobile phone application interventions to improve adherence to preventive behaviour among adolescents, including one study (on 19) on increasing HPV vaccination via text message reminders.<sup>11</sup> Overall findings showed that feasibility, acceptability and satisfaction regarding that type of intervention were high, but significant improvement in preventive behaviour was moderate. Crocker-Buque et al.<sup>12</sup> updated a 2009 systematic review aimed to decrease vaccine uptake inequalities in HIC. Their review highlighted some emerging evidence for text-message reminders, particularly in adolescents. Multicomponent locally designed interventions demonstrated the best evidence in children and adolescents in the short term.

<sup>1</sup> According to Ratzan, *[v]accine literacy is not simply knowledge about vaccines; but also developing a system with decreased complexity to communicate and offer vaccines as sine qua non of a functioning health system.* Ratzan, S. C. Vaccine literacy: a new shot for advancing health. *Journal of health communication* **16**, 227-229, doi:10.1080/10810730.2011.561726 (2011)

### 2018 update on patient reminders and recall interventions to improve vaccine uptake

Recently, in 2018, Jacobson Vann et al. published an update of a previously published Cochrane Review (75 studies, 28 identified during their update) aimed to evaluate and compare the effectiveness of types of patient reminders and recall interventions to improve receipt of vaccines.<sup>13</sup> The authors have concluded that patient reminder and recall systems in primary care settings were likely to be effective in increasing the proportion of the target population who receive vaccines. In their update, all types of patient reminder and recall were found to be effective; telephone reminders were the most effective single intervention type. Combinations of patient reminder or recall interventions were not observed to be as effective as telephone or letter interventions. However, some single type reminder or recall interventions used repeated contacts, which may have provided them with the same expected advantages as combination interventions. Patient reminder or recall, combined with provider reminder systems were the most effective intervention category in this review; however, the number of studies was small.

### Parents' education and information reviews

A few years ago, Sadaf et al. have examined 30 studies that evaluated interventions to increase vaccine uptake; 17 of them were parents-centred information or education about vaccination.<sup>14</sup> Although most of these studies reported a statistically significant improvement in parents' intentions to vaccinate their children, the data were conflicting and thus offered limited insights. These authors have concluded that their review did not identify any convincing evidence on effective interventions to address parental vaccine hesitancy and refusal. The conclusions of two Cochrane reviews examining interventions to inform and educate about early childhood vaccination also indicate that there is low certainty evidence that this type of intervention may increase vaccine uptake. **Discussions with the community, meetings and information campaigns may increase vaccine uptake in areas where vaccine uptake is low. There is no clear evidence for guiding face-to-face educational interventions, and the impact of such interventions is uncertain in areas where vaccine uptake is relatively high.**<sup>15,16</sup>

Another review examined the effect of mandates on the uptake of routine childhood vaccination (of note is the fact that this review included mostly studies from the United States, where the political, demographic and cultural climates are distinct from Canada).<sup>17</sup> Regardless of the vaccine, in the short-term, mandates or improved mandate enforcement were associated with higher childhood vaccination uptake. It is also suggested that improved uptake rates persist over time where mandates have been in place for many years now.<sup>17</sup>

Evidence of pharmacy students' impact on public health through their participation in vaccination efforts was assessed in one identified review.<sup>18</sup> Among the studies reviewed, all studies looking at the change in vaccination from pharmacy students' participation in vaccination programs reported increases in inpatient vaccination rates. Across studies measuring the effect of a pharmacy student intervention, all reported improvement in patient knowledge of vaccines and vaccine-preventable diseases.<sup>18</sup>

### Other reviews on pharmacy-based vaccination services

Canadian researchers have conducted a systematic review of the literature on the impact of pharmacists as educators, facilitators, and administrators of vaccines on immunization rates.<sup>19</sup> Thirty-six studies were included in the review; 22 assessed the role of pharmacists as educators and/or facilitators, and 14 assessed their role as administrators of vaccines. All studies reviewed found an increase in vaccine coverage when pharmacists were involved in the immunization process, regardless of the role (educator, facilitator, administrator) or vaccine administered (e.g., influenza, pneumococcal), when compared to vaccine provision by traditional providers without pharmacist involvement. Limitations of the results include a large number of non-randomized trials and the heterogeneity between study designs.

**In contrast, Perman et al.**<sup>20</sup> conducted a peer-reviewed study and unpublished evaluations of community pharmacy-based vaccination services implemented in the United Kingdom between 2000 and 2015 in order to assess the evidence of their impact on acceptability, uptake, cost-effectiveness and addressing inequalities. These authors have identified 28 evaluations of pharmacy immunization programs in the UK, only 3 of which were published in peer-reviewed journals. Their findings showed no evidence of increased vaccination uptake, and weak evidence of widening access to individuals who had not previously been vaccinated. There was good evidence that pharmacies were acceptable and convenient venues for vaccination. Cost-effectiveness was not assessed in any of the included studies.

Baroy et al.<sup>21</sup> conducted a review to estimate the impact that pharmacist vaccination programs have on vaccination rates. A wide variety of vaccines were provided in the 8 studies they retained, but authors concluded that this type of program could have an impact on vaccination rates, but that impact also varied.

Burson et al.<sup>22</sup> conducted a systematic review to assess the feasibility, acceptability, and effectiveness of community pharmacies as sites for adult vaccination. This type of service seemed to be widely accepted by both patients and pharmacy staff and is capable of improving access and increasing vaccination rates. However, political and organizational barriers limit the feasibility and effectiveness of vaccine delivery in pharmacies. These studies provide evidence to inform policy and organizational efforts that promote the efficacy and sustainability of pharmacy-based vaccination services.

A review investigated the effects of computer-generated reminders delivered on paper to healthcare workers (7 studies/35 included vaccination as one of their outcomes).<sup>3</sup> Findings of this review indicate that computer-generated reminders delivered on paper to healthcare workers (as a single-one intervention) may improve quality of care compared with usual care, and that adding a computer-generated reminder delivered on paper to healthcare workers to one or more co-interventions (multi-component intervention) probably improves quality of care slightly, compared with the co-interventions without the reminder component.<sup>3</sup>

Finally, evidence of interventions to improve influenza uptake among healthcare workers was reported in one identified review.<sup>23</sup> The most common interventions included educational materials and training sessions. The majority of the studies evaluating a combination of strategies showed significantly higher vaccine uptake, while the difference in vaccine uptake was rated as modest in studies where rates were compared with an intervention arm and control arm.<sup>23</sup>

### Improvement in influenza vaccine uptake in healthcare workers

Corace et al.<sup>24</sup> attempted to review the effectiveness of interventions based on psychological theories of behaviour change to improve healthcare workers' influenza vaccination rates. The review was not able to identify any intervention studies that met the inclusion criteria. A number of studies made use of a variety of behavioural frameworks to predict influenza vaccination uptake (mainly the Health Belief Model). Key constructs identified included attitudes regarding the efficacy and safety of influenza vaccination, perceptions of risk and benefit to self and others, self-efficacy, cues to action, and social-professional norms.

### Pain management during vaccination

In recent years, pain management during vaccination has attracted global attention. Fear of pain in immunization and fear of needles were identified as important drivers of hesitancy or refusal in different studies. In a Canadian cross-sectional survey, 24% of parents and 63% of children reported a fear of needles and these fears lead to vaccination non-compliance for 7% and 8%, respectively.<sup>25</sup> While some healthcare professionals might think that pain is trivial – not a problem worth addressing – early research in Canada has shown that parents are more comfortable with and more accepting of infant vaccination when pain is controlled.<sup>26</sup> In September 2015, the World Health Organization (WHO) published a position paper on pain mitigation at the time of vaccination summarizing the evidence for the reduction of pain, anxiety and fear during immunization across all age groups.<sup>27</sup> Our research strategy has identified all published reviews of the 2015 supplement issue of the *Clinical Journal of Pain* that was devoted to address the clinical care gap in vaccination pain management (<https://journals.lww.com/clinicalpain/toc/2015/10001>). It provides a knowledge synthesis of the current global research evidence on this topic. The group behind this synthesis (Help ELiminate Pain in Kids and Adults – HELPinKids&Adults) is an interdisciplinary group of clinicians, academics, and policy makers from across Canada who joined together in 2008 to undertake knowledge translation activities to improve pain management practices during childhood vaccination. They also published a practice guideline on reducing pain during childhood vaccination which includes evidence-based procedural, physical, pharmacological and psychological interventions that could help decrease pain-related hesitancy and improve vaccine acceptance.

In collaboration with the US Center for Diseases Control and Prevention, the Community Guide<sup>2</sup> has regularly published evidence-based recommendations on interventions intended to improve routine delivery of universally recommended vaccinations in the United States. This work is based on a logic framework that stratified population-based interventions to improve vaccination coverage by the outcomes that they attempted to influence and divided them into three categories: (1) interventions to increase community demand for immunizations; (2) interventions that enhance access to immunization services and (3) provider-based interventions.<sup>28</sup>

Interventions to increase community demand for vaccinations recommended by the Community Preventive Services Task Force, based on sufficient evidence of effectiveness in increasing vaccination rates in children and adults, are: client or family incentive rewards (e.g., food vouchers, gift cards, lottery prizes, baby

<sup>2</sup>The Community Guide is a website that houses the official collection of all Community Preventive Services Task Force findings and the systematic reviews on which they are based (Online: <http://www.thecommunityguide.org/>).

products, the provision of transportation or child care, administration of vaccination at no cost, etc.); reminder and recall interventions; multi-component interventions that also enhance access to vaccination services and reduce missed opportunities by vaccination providers; and vaccine requirements for daycare or school entry.

Interventions enhancing access to vaccination services recommended by the Community Preventive Services Task Force, on the basis of sufficient evidence of effectiveness, are: home visits; reducing clients out-of-pocket costs; vaccination programs in schools and organized child care centres; and vaccination programs in women, infants and children settings (WIC settings).

Provider- or system-based interventions recommended by the Community Preventive Services Task Force on the basis of sufficient evidence of effectiveness are: health-care system-based interventions implemented in combination (e.g., use of 2 or more coordinated interventions in healthcare settings); immunization information systems; assessment and feedback for vaccination providers; provider reminders; and standing orders.

According to the Community Guide, there is insufficient evidence to determine the effectiveness of client-held paper immunization records, clinic-based education when used alone, community-wide education when used alone, monetary sanction policies, and effectiveness of provider education when used alone. Effective interventions identified in the Community Guide to enhance vaccine acceptance and vaccine uptake are listed in Appendix 2.

In summary, although interventions such as reminders and recalls to patients or healthcare providers that vaccines are due/overdue are effective tools to improve vaccine uptake, there is no strong evidence to recommend any intervention to specifically address vaccine hesitancy or refusal. Multicomponent interventions were also found to be effective in enhancing vaccine uptake, but it was not possible to identify which component of the intervention had the greatest effect. Vaccination requirements or mandates for school admittance are viewed as effective to increase vaccine uptake, but these strategies might also have a negative impact on vaccine acceptance/hesitancy (backfire effect). There is mixed evidence with respect to the effectiveness of face-to-face communication interventions, large-scale communication interventions and interventions applying new media.

## **4.2 Canadian studies evaluating interventions to increase vaccine acceptance and uptake: Main findings**

Ten primary studies evaluating interventions aimed to increase vaccine acceptance and uptake, conducted in Canada, were retrieved for the 2015-2017 period. Identified studies were heterogeneous in terms of the type of interventions, study design, population target and outcomes. Interventions were mostly a single component. The included articles are summarized in Appendix 3. Four of them targeted pain management interventions.<sup>29-32</sup> The other interventions were related to:

- Uptake and use of ImmunizeCA app (now CANImmunize app)<sup>33</sup>;
- Use of an educational intervention with baccalaureate nursing students aimed to empowerment and self-efficacy for public health nursing competencies<sup>34</sup>;
- Use of a Guide (for influenza program planners) in healthcare organizations to improve influenza vaccine uptake in healthcare workers<sup>35</sup>;
- Piloting of a group health service delivery model (CenteringParenting)<sup>36</sup>;

- Education component (health promotion specialist talking to students about influenza and its interventions)<sup>37</sup>;
- Targeted education and vaccination HPV campaign<sup>38</sup>.

Due to this high level of heterogeneity, it is not possible to draw conclusions on the general effectiveness of tested interventions to improve knowledge or to promote favourable attitudes to vaccination.

### **4.3 Limits of the literature reviews and Canadian primary studies on interventions to increase vaccine acceptance and uptake**

The reviewed studies included interventions with diverse content and approaches that were implemented in different settings and targeted various populations. The number of interventions similar enough to be grouped in the literature reviews was often low and insufficient to demonstrate effectiveness using recognized validation criteria. In addition, many of the reviewed studies were conducted in the United States (such as Lee et al.<sup>17</sup>), which could limit the generalizability of the findings to the Canadian context due to differences in how vaccination services are organized. The good-quality studies that were reviewed were mostly single-component interventions (often educational interventions) that are less challenging to evaluate than multi-component interventions or interventions aiming to change determinants that are difficult to measure (such as social norms). Interventions using mass media were generally of low quality. These interventions are difficult to evaluate and are not well suited to experimental design; other types of evaluation are subject to various forms of bias due to the many potential confounding factors which limit the quality of the evidence available. When communication interventions are part of multi-component strategies, it becomes almost impossible to evaluate their direct impact on vaccine uptake.<sup>39</sup> Finally, few studies included in the literature reviews used vaccine uptake or on-time vaccination as the outcome and even fewer studies were directly targeting vaccine-hesitant individuals.

Very few interventional studies conducted in Canada were identified during the dedicated period. Most of these studies were of poor quality due to the design (e.g., experimental, a pilot study with no control group) and small sample sizes. Additionally, many studies were subject to different bias due to self-reported vaccine uptake, unrepresentative samples, limited data, and low response rates, which may limit the validity and generalizability of the results. Interventions were very specific regarding vaccines or clienteles, which also limits the generalizability of the findings.

## **5. CONCLUSIONS**

From the reviews, there is no strong evidence on which to recommend any specific intervention to address vaccine hesitancy/refusal in Canada. Findings indicate that reminders and recall for patients and health-care providers might be effective tools to improve vaccine uptake among various groups and in different settings. However, there is limited evidence on the effectiveness of reminders and recalls for vaccine-hesitant individuals.

There is mixed evidence on the effectiveness of interventions involving face-to-face communication interventions, health-care provider training, community-based actions, and communication using mass media. Overall, findings showed that healthcare providers play a key role in patient/parent vaccination decision-making and are perceived as an important source of vaccination information. Poor communication

or negative relationships with healthcare providers sometimes have an impact on parents' vaccination decisions. Building parental trust seems to be an important component of the provider-parent interaction.

Vaccination requirements or mandates for school admittance are viewed as effective in increasing vaccine uptake in high-income countries. However, the impact of potential negative consequences (e.g., distrust in the immunization program, decrease in school access) may outweigh potential benefits such as the increase in vaccination coverage in some settings.

Many traditional educational tools (e.g., information pamphlets) had little or no impact on vaccine hesitancy. This highlights the importance of carefully designed public health messages, and the fact that messages need to be tailored for the specific target group because messaging that too strongly advocates vaccination may be counterproductive, reinforcing the hesitancy of those already hesitant<sup>40</sup>.

Despite methodological limitations, the conclusion of some of the reviews indicates that mass vaccine promotion campaigns may enhance positive attitudes towards vaccination and, ultimately, increase coverage rates. In developing communication interventions to address vaccine hesitancy, the use of the Internet and social media is often recommended, but few web-based strategies have been evaluated.<sup>10,41</sup> Limitations of this type of strategy include difficulties in "attracting" vaccine-hesitant individuals and exclusion of individuals without Internet access or with low literacy levels, while advantages include low cost and high potential to adapt and personalize messages.<sup>42-44</sup> The emergence of social media as a source of online health information, combined with decreasing rates of vaccination, means that it is critical to understand how social media can influence parents' decision-making processes, and to develop communication strategies about vaccination.<sup>45</sup>

Mitigation of pain during vaccination received great attention in recent years. Evidence-based guidelines on pain mitigation during vaccination have been published, showing effective strategies for reduction of pain, such as physical intervention with proper holding, breastfeeding, needle injection techniques, etc., and psychological interventions, such as distraction, requiring only training and could be readily applied more widely. Early research in high-income countries has shown that parents are more comfortable with infant vaccination when pain is mitigated<sup>46</sup> but pain mitigation has not been specifically tested among those whose vaccine hesitancy is related to fear of pain.

Finally, key principles for optimizing the development of strategies to address vaccine hesitancy can be identified through this review. To be effective, interventions should be developed using a planning framework, such as the WHO Guide to Tailoring Immunization Programmes,<sup>47</sup> and should be based on a theoretical model. The use of a combination of different interventions (multiple components) appears to be more effective than single-component interventions. Interventions are most likely to succeed when they are based on empirical data and situational assessment – both to have level of understanding of the vaccine hesitancy situation (susceptible populations, key determinants of vaccination, barriers and enabling conditions, etc.) and to properly evaluate the impact of the intervention.<sup>47</sup> The development of culturally adapted and personalized interventions has been shown to be effective in enhancing compliance with preventive behaviours, including vaccination.<sup>48-50</sup>

In conclusion, an effective "one size fits all" intervention is unlikely ever to exist as understanding the specific concerns of the various groups of vaccine-hesitant individuals is important. Building trustful relationships with individuals might also be an important thing to do about vaccine hesitancy. Given the paucity of information on effective strategies to address vaccine hesitancy, whenever interventions are implemented, planning a rigorous evaluation of their impact on vaccine hesitancy/vaccine acceptance is essential, as is sharing of lessons learned. CANVax is a step in that direction.

APPENDIX 1

Summary of published reviews and meta-analysis of strategies to enhance vaccine acceptance and vaccine uptake

First author/ Year of publication/ Title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure			
Ames H. M. R., 2017, <i>Parents' and informal caregivers' views and experiences of communication about routine childhood vaccination: a synthesis of qualitative evidence</i>	To synthesize qualitative studies exploring the influence that vaccination communication has on parents' and informal caregivers' decisions regarding childhood vaccination	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies that utilized qualitative methods for data collection and analysis</li> <li>- Studies that focused on the views and experiences of parents and informal caregivers regarding information about vaccination for children aged up to 6 years</li> <li>- Studies from any setting globally where information about childhood vaccinations was communicated or distributed.</li> </ul> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies that collected data using qualitative methods but did not perform a qualitative analysis</li> </ul>	Parents' knowledge, attitudes and behaviour of childhood vaccination / Parents' perceptions of vaccine communication	38 (mostly from HIC)	Reported	<ul style="list-style-type: none"> <li>- Many of included studies explored mothers' perceptions of vaccine communication.</li> <li>- Generally, parents wanted more information than they were getting (high confidence in the evidence).</li> <li>- Lack of information led to worry and regret about vaccination decisions among some parents (moderate confidence).</li> <li>- Parents wanted balanced information about vaccination benefits and harms (high confidence), presented clearly and simply (moderate confidence) and tailored to their situation (low confidence in the evidence).</li> <li>- Parents wanted vaccination information to be available at a wider variety of locations, including outside health services (low confidence) and in good time before each vaccination appointment (moderate confidence).</li> <li>- Parents viewed health workers as an important source of information and had specific expectations of their interactions with them (high confidence). Poor communication and negative relationships with health workers sometimes impacted on vaccination decisions (moderate confidence).</li> <li>- Parents generally found it difficult to know which vaccination information source to trust and challenging to find information they felt was unbiased and balanced (high confidence).</li> <li>- The amount of information parents wanted and the sources they felt could be trusted appeared to be linked to acceptance of vaccination, with parents who were more hesitant to want more information (low to moderate confidence).</li> <li>- Most of the trial interventions addressed at least one or two key aspects of communication, including the provision of information prior to the vaccination appointment and tailoring information to parents' needs. None of the interventions appeared to respond to negative media stories or address parental perceptions of health worker motives.</li> </ul>
Arditi, C., 2017, <i>Computer-generated reminders delivered on paper to healthcare professionals: effects on professional practice and healthcare</i>	To examine the effects of reminders automatically generated through a computerized system (computer-generated) and delivered on paper to healthcare professionals on quality of care	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Individual- or cluster-randomized and non-randomized trials that evaluated the impact of computer-generated reminders delivered on paper to healthcare professionals</li> <li>- Delivery could be alone (single-component</li> </ul>	Quality of care endpoint (such as ordering a test or initiating a treatment)  Secondary outcomes	35 and analyzed 34 studies (40 comparisons)  (30 randomized trials and 5 non-randomized trials)	Reported	<ul style="list-style-type: none"> <li>- 29 studies took place in the USA and 6 studies took place in Canada, France, Israel, and Kenya. All studies except two took place in outpatient care. Reminders were aimed at enhancing compliance with preventive guidelines (e.g. cancer screening tests, vaccination) in half the studies and at enhancing compliance with disease management guidelines for acute or chronic conditions (e.g. annual follow-ups, laboratory tests, medication adjustment, counselling) in the other half.</li> <li>- 7 studies included vaccination as one of their outcomes.</li> <li>- In 23 comparisons, reminders targeted one type of behaviour. The behaviour was tested ordering (e.g. mammography, glycosylated hemoglobin) in 10 comparisons, vaccination in one comparison,</li> </ul>

First author/ Year of publication/ Title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure			
<i>outcomes</i>	(outcomes related to healthcare professionals' practice) and patient outcomes	<p>intervention) or in addition to one or more co-interventions (multi-component intervention), compared with usual care or the co-intervention(s) without the reminder component</p> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Expert systems for facilitating diagnosis or estimating prognosis were not considered as reminders, even if their output was printed out</li> <li>- A document listing all the drugs a patient was currently taking (e.g. drug profile) or a document summarizing the medical records, with no rules applied in the computer, were not considered as reminders, but as an organizational intervention</li> <li>- New clinical information collected directly from patients on a computer and given to the provider as a prompt was not considered as a reminder intervention, but as a patient-mediated intervention</li> </ul>	included patient outcomes (related to patients' health condition)			<p>prescribing in seven comparisons, professional-patient communication in two comparisons, and general management in three comparisons.</p> <ul style="list-style-type: none"> <li>- Computer-generated reminders delivered on paper to healthcare professionals alone (single-component intervention) probably improves quality of care compared with usual care (median improvement 11% (IQR 5.4% to 20.0%); 27 studies (27 comparisons) (moderate certainty evidence).</li> <li>- Adding computer-generated reminders delivered on paper to healthcare professionals to one or more co-interventions (multi-component intervention) probably improves quality of care slightly compared with the co-intervention(s) without the reminder component (median improvement 4% (IQR 3% to 6%); 11 studies (13 comparisons) (moderate certainty evidence).</li> <li>- There is uncertainty regarding whether reminders, alone or in addition to co-intervention(s), improve patient outcomes as the certainty of the evidence is very low (n = 6 studies (7 comparisons). None of the included studies reported outcomes related to harms or adverse effects of the intervention.</li> </ul>
Church, D., 2016, <i>A literature review of the impact of pharmacy students in immunization initiatives</i>	To review evidence of pharmacy students impact on public health through their participation in vaccination efforts	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Articles published in English</li> <li>- Published in peer-reviewed journal</li> <li>- Mentioning pharmacy students and an immunization initiative with an evaluative component or outcomes (e.g., patient screening, number of vaccines administered, patient satisfaction or knowledge)</li> </ul> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Conference abstract or gray literature</li> </ul>	Patient screening, number of vaccines administered, patient satisfaction or knowledge	18 (15 US; 3 Canada)	Not reported	<ul style="list-style-type: none"> <li>- Studies published between 2000 and 2015, 12 were conducted in the United States. Vaccines addressed in these articles included influenza (n = 10), pneumococcal (n = 5), Tdap (n = 3), hepatitis B (n = 1), herpes zoster (n = 3) and H1N1 (n = 1)</li> <li>- 8 studies reported the number of vaccine doses administered by pharmacy students. The number of vaccine doses administered by students in community-based clinics ranged from 109 to 15,000.</li> <li>- 5 studies looked at change in vaccination from pharmacy student participation in vaccination programs. All of them reported an increase in inpatient vaccination rates. Increases in vaccination rates in inpatient facilities ranged from 18.5% to 68%.</li> <li>- 5 studies measured the effect of a pharmacy student intervention on patient knowledge about vaccines and vaccine-preventable diseases. Across studies, student-led educational interventions improved patient knowledge of vaccines and vaccine-preventable diseases. Patient satisfaction with student immunization services was consistently very</li> </ul>

First author/ Year of publication/ Title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure			
		<ul style="list-style-type: none"> <li>- Studies not including evaluative outcome or studies where measures were limited to student outcomes (e.g., learning and/or confidence)</li> </ul>				high.
Connors, J. T., 2017, <i>Provider-parent communication when discussing vaccines: A systematic review</i>	To determine the most efficacious communication practices to use with parents with vaccination concerns	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Articles published in English from March 2011 to March 2016</li> <li>- Articles were limited to studies involving humans</li> <li>- Studies where the communication framework/style of the provider-parent interaction was investigated and/or communication practices were identified that may decrease parental vaccine hesitancy and increase the likelihood that vaccination will occur</li> </ul> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Manuscripts not containing any primary data (expert opinion/individual article reviews)</li> <li>- Studies where provider-parent communication was not assessed</li> <li>- Studies that were performed in developing countries where access to vaccines is a greater issue than parental concerns about vaccines (as there is a lack of vaccine availability and limited healthcare infrastructure)</li> </ul>	Parental view of vaccination / uptake of vaccine	9	Reported	<ul style="list-style-type: none"> <li>- The majority of the studies were descriptive and qualitative in nature with only one randomized controlled trial. 5 of the 9 studies utilized a descriptive cross-sectional design.</li> <li>- There is not currently enough information to definitively state the type of provider-parent interaction that should be employed.</li> <li>- The findings of this review indicated that having trust in the provider is important with regard to vaccination and also support the building of parental trust in the provider when taking into account the individual components of building trust.</li> <li>- Data from this review supports providers having technical competence under the themes: discussing the need for scheduled vaccinations with the parent and utilizing a screening tool to identify specific concerns.</li> <li>- Competence in communication is implicit in many of the themes identified from this review and include tailoring information to specific parent concerns, giving a strong recommendation for vaccination, showing respect and empathy towards parental concerns, and pursuing a vaccination recommendation in a parent that is initially resistant.</li> </ul>
Harvey, H., 2015 <i>Parental reminder, recall and educational interventions to improve early childhood immunization</i>	To evaluate available evidence on parental interventions to improve childhood (birth to 5 years) vaccine uptake	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies on interventions aimed at parents of children (<math>\leq 5</math> years old) due or overdue for one or more routine immunizations</li> <li>- Studies with outcomes</li> </ul>	Childhood vaccine uptake	28 (22 studies conducted in HIC, 6 in LMIC)	Reported	<ul style="list-style-type: none"> <li>- There is evidence to support the efficacy of postal and/or telephone reminders, parental education and parental education with postal reminders for improving child immunization uptake.</li> <li>- Receiving both postal and telephone reminders was the most effective reminder-based intervention.</li> <li>- Reminder-based interventions were significantly more effective than routine care independent of their method of delivery.</li> <li>- Postal and telephone reminders had an additive impact on uptake;</li> </ul>

First author/ Year of publication/ Title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure			
<i>uptake: A systematic review and meta-analysis</i>		<p>that measured child immunization uptake of individual or a combination of recommended vaccines</p> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies without a control group and studies that did not provide outcome data in terms of the number of children completely immunized or up-to date for their age</li> <li>- Interventions that met these criteria but for which only one study was found</li> </ul>				<p>their combined use was associated with a greater increase in immunization uptake than the use of each strategy alone. This effect could be an artefact of the most intensive recall-reminder strategies used in these trials.</p> <ul style="list-style-type: none"> <li>- Educational interventions significantly increased childhood immunization uptake. This effect was driven by two factors: 1) the study occurring in a LIMC and 2) parents having a discussion with a professional expert, rather than receiving written information.</li> </ul>
Jarrett C, 2015, <i>Strategies for addressing vaccine hesitancy – A systematic review</i>	To identify, describe and assess the potential effectiveness of strategies to respond to issues of vaccine hesitancy that have been implemented and evaluated across diverse global contexts	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies published from January 2007 to October 2013</li> <li>- Contained research on vaccine hesitancy</li> <li>- Described or evaluated an intervention addressing hesitancy and reported a measure of the primary outcome or the secondary outcome</li> <li>- Pertaining to any vaccines and vaccination programmes</li> <li>- Published in any of the six official UN languages (Arabic, Chinese, English, French, Russian and Spanish)</li> </ul>	<p>Primary outcome: Change in vaccination uptake</p> <p>Secondary outcome: Change in knowledge/awareness and/or attitudes</p>	166 (peer-review) and 15 (grey) (13 were GRADED)	Reported	<ul style="list-style-type: none"> <li>- Across the literature, few strategies to address vaccine hesitancy were found to have been evaluated for the impact on either vaccination uptake and/or changes in knowledge, awareness or attitude. The majority of evaluation studies were based in the Americas and primarily focused on influenza, human papillomavirus (HPV) and childhood vaccines.</li> <li>- Several interventions showed some positive impact on vaccination uptake, including: social mobilization, mass media, communication tool-based training for HCW, non-financial incentives, and reminder–recall activities. Interventions to increase uptake that are multi-component and/or have a focus on dialogue-based approaches tend to perform better.</li> <li>- The evidence for non-financial incentives and reminder–recall activities was also of good quality, and carries the potential to bring positive change by addressing the more practical aspects of vaccination.</li> <li>- One of the greatest drawbacks of the interventions identified is that many operate from an assumption-based rather than an evidence-based approach; appropriate evaluation is also lacking.</li> </ul>
Lee, C., 2016, <i>Systematic review of the effect of immunization mandates on short-term and long-term uptake of routine childhood immunizations</i>	To examine the effect of immunization mandates on short-term and long-term uptake of routine childhood immunizations	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies were included if they compared immunization rates in a population before and after either a new immunization mandate or improved enforcement of an existing mandate</li> <li>- Studies were included if</li> </ul>	Vaccine uptake	21 (18 from US, 1 from France, 2 from Canada)	Not reported	<ul style="list-style-type: none"> <li>- The review included 11 before-and-after studies and 10 studies comparing immunization rates in similar populations with and without immunization mandates.</li> <li>- All but two studies showed at least a trend towards increased uptake with mandates. Higher uptake was associated with a more long-standing mandate.</li> <li>- Mandates that have been in place for many years are associated with higher up-to-date immunization status, suggesting that the improved uptake rates persist over time.</li> </ul>

First author/ Year of publication/ Title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure			
		<p>they compared uptake in similar populations with and without mandate</p> <ul style="list-style-type: none"> <li>- All study designs were included</li> </ul> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies from resource-limited settings</li> <li>- Non-English articles if translation was not practical</li> </ul>				
Odone, A., 2015, <i>Effectiveness of interventions that apply new media to improve vaccine uptake and vaccine coverage</i>	To systematically collect and summarize the available evidence on the effectiveness of interventions that apply new media to promote vaccine uptake and increase vaccination coverage for children, adolescents and adults in high-income settings	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Studies conducted in countries members of the OECD<sup>3</sup></li> <li>- Interventions that applied mobile phones and Internet-based tools</li> <li>- Original studies using an observational or experimental study design</li> <li>- Published from 1 January 1999 to 30 September 2013</li> <li>- English language</li> </ul> <p><b>Exclusion:</b></p> <ul style="list-style-type: none"> <li>- Guidelines, review, letters or editorial</li> <li>- Interventions targeting vaccines recommended for people with specific medical conditions, vaccines for international travellers or health-care professionals</li> </ul>	Primary outcomes are vaccine coverage or vaccine uptake	19	Reported	<ul style="list-style-type: none"> <li>- The majority of the studies were conducted in the USA (74%, n = 14).</li> <li>- 13 (68%) of the studies were experimental, the rest having an observational study design.</li> <li>- 11 studies (58%) reported results on the primary outcome.</li> <li>- Retrieved studies explored the role of text messaging (n = 7, 37%), smartphone applications (n = 1, 5%), Youtube videos (n = 1, 5%), Facebook (n = 1, 5%), targeted websites and portals (n = 4, 21%), software for physicians and health professionals (n = 4, 21%), and email communication (n = 1, 5%).</li> <li>- There is some evidence that text messaging, accessing immunization campaign websites, using patient-held web-based portals and computerized reminders increase vaccination coverage rates.</li> <li>- Insufficient evidence is available on the use of social networks, email communication and smartphone applications.</li> <li>- Due to a high degree of heterogeneity between studies no quantitative assessment could be performed.</li> <li>- More research is needed to assess the effectiveness and cost-effectiveness of interventions applying new media and on how to successfully market constructive public health messages in the new communication era.</li> </ul>
Rashid, H., 2016, <i>Assessing interventions to improve influenza uptake among healthcare workers</i>	To understand the evidence of interventions to improve influenza vaccine uptake among healthcare workers	<p><b>Inclusion:</b></p> <ul style="list-style-type: none"> <li>- Articles published in English</li> <li>- Studies using a randomized controlled trial study design</li> <li>- Articles including personnel in paid employment, volunteering, or learning in the following settings: acute, ambulatory, chronic, or primary care; retail</li> </ul>	Influenza vaccine uptake	12 (all conducted in HIC)	Reported	<ul style="list-style-type: none"> <li>- The most common interventions were educational materials and training sessions, or “education” (in 11 studies), while lead advocates were used in 5, rewards and reminder messages in 3, making vaccines easy to access in 2 studies, and organized efforts to raise awareness or promotion in 1 study.</li> <li>- 6 studies reported a significantly higher uptake of the vaccine in the intervention arm compared to the control arm, though the difference was generally modest (5.7–26.3 percent).</li> <li>- Only one of the four studies that evaluated the effect of a single intervention in isolation demonstrated a significantly higher vaccine uptake rate in the intervention group, compared to controls.</li> </ul>

<sup>3</sup>Organisation for Economic Co-operation and Development

First author/ Year of publication/ Title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure			
		pharmacy; and diagnostic laboratory - Studies including any intervention that was tested to improve the uptake of the influenza vaccine - In comparison to one or more other interventions or no intervention at all				- 5 of the 8 studies that evaluated a combination of strategies showed significantly higher vaccine uptake. Despite the low quality of the studies identified, the data suggest that combined interventions can moderately increase vaccine uptake among healthcare workers.

## APPENDIX 2

### Effective interventions identified in the Community Guide to enhance vaccine acceptance and vaccine uptake

#### 1. Interventions increasing community demand for vaccinations

The Community Preventive Services Task Force recommends:

- Client or family incentive rewards;
- Reminder and recall interventions;
- Community-based interventions implemented in combination (to enhance access to vaccination services, increase community demand, and reduce missed opportunities by vaccination providers);
- Vaccination requirements for child care, school, and college attendance.

#### 2. Interventions enhancing access to vaccination services

The Community Preventive Services Task Force recommends:

- Home visits;
- Reducing clients out-of-pocket costs;
- Vaccination programs in schools and organized child care centres;
- Vaccination programs in WIC (women, infants and children) settings.

#### 3. Provider- or system-based interventions

The Community Preventive Services Task Force recommends:

- Health-care system-based interventions implemented in combination;
- Immunization information systems;
- Assessment and feedback for vaccination providers;
- Provider reminders;
- Standing Orders.

### APPENDIX 3

#### Summary of published Canadian studies on strategies to enhance vaccine acceptance and uptake

First author/ Year of publication/ Title	Study aims/objectives	Setting (City/Province) Year of intervention	Inclusion / Exclusion criteria	Study design / N and response rate	Main outcomes measures/ Brief description of the intervention/	Main findings	Limits
Atkinson, K.M., 2015, <i>Using mobile technologies for immunization: Predictors of uptake of a pan-Canadian immunization app (ImmunizeCA)</i>	To measure uptake and use of ImmunizeCA over a six-month period, and to assess the effectiveness of various promotional strategies in driving uptake and use of the app	Canada  2014	<b>Inclusion:</b> Baccalaureate nursing students enrolled in year three of their university nursing education program	Media monitoring (using MediaMiser SNAP)	Uptake and use of ImmunizeCA over a six-month period, and to assess the effectiveness of various promotional strategies in driving uptake and use of the application	<ul style="list-style-type: none"> <li>- During the first six months, ImmunizeCA had a total of 174,038 sessions, producing 909,257 screen views, an average of 5.22 screens per session. The average session duration was &gt;3 min (03:02 min). Information was accessed 82,126 times, and the most views occurred in March (23,242 views).</li> <li>- Across 54,610 users, 45,157 individual records were created. The most were created in March (12,347 records), followed by July (12,215 records). Of the records created, the minimum age was zero years and the maximum was 90 years of age. Fifty-five percent (24,836) of records were created for children ≤5 years of age. Of those, 52% (13,003) were zero to one year of age. The “add to calendar” feature for vaccination encounters was activated 7691 times by 5548 unique users.</li> <li>- There were two instances of a statistically significant increase in total daily downloads: during the four weeks following the launch of the application and while it was featured in the App Store, and during the two weeks following mail-out flyers. These periods were highly significant in the model (P&lt;0.0001), confirming that app downloads sharply increased during these times, whereas no other factors (social media, press releases, etc.) had any significant influence.</li> </ul>	- Not reported
Babenko-Mould, Y., 2015, <i>Influence of simulated and actual</i>	To examine students’ structural empowerment during simulated	Southwestern Ontario (Ontario)	<b>Inclusion:</b> Baccalaureate nursing students enrolled in year three of their	Non-experimental and non-comparative study where after listening to a lecture about immunizations,	Perceptions of structural empowerment and self-efficacy for PHNC	<ul style="list-style-type: none"> <li>- Students perceived themselves as structurally empowered after completing the simulated and actual community vaccination clinics.</li> <li>- Students reported a high level of self-</li> </ul>	<ul style="list-style-type: none"> <li>- Self-report bias might be a limitation to the study.</li> <li>- The findings might</li> </ul>

First author/ Year of publication/ Title	Study aims/objectives	Setting (City/Province) Year of intervention	Inclusion / Exclusion criteria	Study design / N and response rate	Main outcomes measures/ Brief description of the intervention/	Main findings	Limits
<i>community vaccination clinics on student empowerment and self-efficacy for public health nursing competencies</i> <sup>34</sup>	learning and actual nursing practice, and assess their self-efficacy for public health nursing competencies (PHNC) after involvement in a mass influenza vaccination clinic as a community practice experience	Year of study not reported	university nursing education program	students participated in a simulated learning vaccination clinic educational session and completed an online vaccine and immunization assessment to evaluate their knowledge about providing vaccinations to the public  228 students (RR 100%)		efficacy for PHNC after their actual community vaccination clinic involvement (they rated their self-efficacy at 83.96/100). - There was a significant correlation between empowerment and self-efficacy, which suggests that when students have access to empowering structures, they feel more confident to enact PHNC that aligns with practice in the clinics.	not be generalizable to programs that are not resources in a similar manner as the results here are specific to the context of a nursing program which has the resources and PHN partnerships in place to enable such a practice experience to unfold in both simulation and actual practice.
Chambers L.W., 2015, <i>A new approach to improving healthcare personnel influenza immunization programs: A randomized controlled trial</i>	This trial assessed the impact of the Guide with facilitation in improving healthcare personnel influenza immunization rates in Canadian healthcare organizations	Ottawa/Ontario  2010-2011	<b>Inclusion:</b> Eligible organizations included acute care hospitals, continuing care organizations and regional health authorities. Eligible healthcare organizations that were interested in participating in the trial were required to confirm that they: 1) regularly conducted seasonal healthcare personnel influenza immunization programs;	Randomized controlled trial  26 healthcare organizations (across six Canadian provinces (ON, MB, NS, BC, SK, NL) was randomized to Intervention (n=13) or Control groups (n=13))	The Intervention group received the Guide "Successful Influenza Immunization Programs for Healthcare Personnel: A Guide for Program Planners", facilitation support through workshops for managers and ongoing support. The Control groups conducted programs as usual. The Groups were compared using their reported influenza	- The median rate of influenza immunization among healthcare personnel for the Intervention group was 43%, 44%, and 51% at three points in time respectively, and in the Control group: 62%, 57%, and 55% respectively. - No significant differences were observed between the groups at the three points in time. However, there was a 7% increase in the median rates between the Baseline Year and Year Two in the Intervention group, and a 6% decrease in the Control group over the same time period, which was statistically significant. - Use of the Guide by organizations was not able to improve immunization uptake to the level that is now shown in programs in which influenza immunization is a condition of service.	- The 46 organizations were not recruited as estimated in the trial protocol sample size calculation. - Information characterizing the 46 organizations that did not participate in the Trial was not collected. - Facilitation may be an important intervention component, but the design of this trial did not allow for the exploration of this as a

First author/ Year of publication/ Title	Study aims/objectives	Setting (City/Province) Year of intervention	Inclusion / Exclusion criteria	Study design / N and response rate	Main outcomes measures/ Brief description of the intervention/	Main findings	Limits
			<p>2) used a systematic approach to measuring immunization rates;  3) could provide immunization rates for the Baseline Year plus two intervention years;  4) agreed to be randomized to receive the Guide or no intervention (the control organizations were promised the Guide when the trial ended);  5) would complete all questionnaires during the trial; and  6) if randomized to receive the Guide, would commit to adhering to the steps in the Guide: to plan, implement, monitor, and evaluate their program</p>		<p>healthcare personnel influenza immunization rates and scores from a program assessment questionnaire</p> <p>*Measured outcome was the immunization rate of the organization.</p>		<p>separate effect.</p>
<p>Harrison, D. 2016, <i>Using YouTube to disseminate effective vaccination</i></p>	<p>To evaluate the reach and impact of a consumer-targeted YouTube video</p>	<p>Canada 2013-2014</p>	<p>N/A</p>	<p>Descriptive cross-sectional study (survey completion)  156 viewers completed the survey; based on</p>	<p>Brief consumer-targeted video showing two infants being vaccinated was posted onto</p>	<p>- Twelve months after posting, the video had 65,478 views, 68 comments, 245 likes, 17 dislikes, and 90 shares. The average duration of viewer time was 65% of the video. The video was viewed in 175 countries, with the top five</p>	<p>- Key limitations include extremely low response rate to the linked online survey, and the</p>

First author/ Year of publication/ Title	Study aims/objectives	Setting (City/Province) Year of intervention	Inclusion / Exclusion criteria	Study design / N and response rate	Main outcomes measures/ Brief description of the intervention/	Main findings	Limits
<i>pain treatment for babies</i>	demonstrating use of effective pain reduction strategies during infant vaccinations			the number of views (65,478), this was a response rate of 0.24%	YouTube; one infant was breastfed and another infant received sucrose by mouth before and during the injection. Included a knowledge dissemination strategy using the media, social media and messages to professional organizations to promote the video  * Measured outcomes included use and intention of using pain management strategies	viewing countries being USA (24%), Canada (16%), Saudi Arabia (6%), United Kingdom (4%), and India (4%). - The viewer survey was completed by 156 (0.24%) viewers; 90 (58%) answered as HCPs and 66 (42%) as parents. - Survey results showed that the video was persuasive; intent to use or support breastfeeding or sucrose was high in both parents and HCPs after viewing the video. 25 parent respondents (38%) had breastfed their infants during vaccinations. After seeing the video, 56 (86%) parents answered they would breastfeed during their infant's subsequent immunizations. Only nine (14%) parents had used sweet solutions previously; however, after seeing the video, 47 (73%) answered they would use sweet solutions during their infants' subsequent immunizations. - Comments posted were often emotional in nature, and were related to anti- vaccination (n = 26, 38%); effectiveness or positive personal experiences (n = 21, 32%); research team comments or promotion (n = 12, 18%); pro- vaccination (n = 6, 8%) and barriers to using breastfeeding or sucrose during vaccinations (n = 3, 4%).	lack of ability to draw associations between the YouTube video and clinical outcomes.
Johnston, J. C., 2017, <i>Piloting CenteringParenting in two Alberta public health well- child clinics</i>	To pilot a group health service delivery model, CenteringParenting (CP), for new parents, to assess its feasibility and impact on maternal and infant outcomes	Calgary Zone / Alberta  2013-2014	<b>Inclusion:</b> First-time parents with full-term newborns who received post- partum visits from PHN in two Calgary area Public Health clinics were eligible and invited to participate in CP	Quasi-experimental pilot study  26 families consented to participate; of these, 24 families attended at least one session with two families withdrawing from the program prior to completion	CP model provides facilitated, women-centred prenatal care for pregnant women in a group setting that includes assessment, discussion, and socialization facilitated by two prenatal care	- Parents reported improvements in parenting experiences following the program. - At 4 months, all CP babies were vaccinated compared to 95% of babies in the comparison Group - At 12 months, all CP infants received appropriate vaccinations while just over 50% received their immunizations in the AOB cohort by 12 months.	- The small sample size of the CP study limits the - conclusions that can be drawn from this pilot

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			format for their well-child visits		providers; Families attended six, 2-hour group sessions in their child's first year of life with three to seven other families. Health assessments, parent-led discussions, and vaccinations occurred within the group  *Measured outcomes included infants' vaccination.		
Karimi, E., 2016, <i>Using the health belief model to examine the effect of educational programs on individual protective behaviours towards seasonal influenza</i>	To study the impact of education on individuals towards developing preventive behaviours against the health threat (influenza), based on the Health Belief Model (HBM) constructs	Montreal/Québec  2012	<b>Inclusion:</b> The target population of this study was the engineering undergraduate students at Concordia University	Descriptive cross- sectional study  240 students responded to the survey	Firstly, a descriptive cross- sectional questionnaire including influenza intervention history and questions based on the Health Belief Model (HBM) was used to assess students' perceptions both in control and treatment group. The second survey administered involved a treatment consisting of a health promotion	<ul style="list-style-type: none"> <li>- The results indicated significant difference at the 0.05 confidence level (<math>\alpha=0.05</math>) for the perceived susceptibility of influenza mean, the perceived barrier of vaccination mean, the perceived benefit of physical distancing mean, and the perceived barriers of self-isolation mean after the treatment.</li> <li>- Results of regression for the survey's treatment group (with the influenza awareness session) indicate that vaccination is highly correlated with all the HBM variables but particularly; between vaccination and the perceived benefits of this behaviour (OR = 2.254).</li> <li>- Results of regression for the control indicate that all of HBM variables are correlated with vaccination, but perceived benefits of vaccination is not statistically significant. Results of multivariate regression for the treatment group indicate that vaccination is highly correlated with all the HBM variables except perceived</li> </ul>	<ul style="list-style-type: none"> <li>- The retrospective self-reports of students were collected and analyzed without the verification of these reports; the results might be subject to recall biases.</li> <li>- This study was developed on the Health Belief Model and is subjected to limitations associated with this model (lack of consideration of emotional factors).</li> <li>- Lack of</li> </ul>

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					<p>specialist talking to students about influenza and its interventions for 20 min. The talk focused on the core HBM variables: susceptibility of people to influenza virus; severity of influenza; benefits and barriers of vaccination and benefits and barriers of social distancing</p> <p>* Measured outcomes include students' perceptions, impact of HBM variables on intention to develop protective behaviours against influenza</p>	severity of disease.	randomization for participant assignments to control and treatment group.
Piedimonte, S., 2017, <i>Impact of HPV education and vaccination campaign among Canadian university students</i>	To determine the level of knowledge and awareness of HPV/cervical cancer among university students and to evaluate the success of a subsequent education	Montreal/Québec 2015-2016	<b>Inclusion:</b> Not reported; university students from two targeted universities	Two-phase study Phase I: 56 participants; 29 vaccinated Phase II: 151 students approached; 64 vaccinated	Phase I was a pilot project in which participants were recruited as part of Cervical Cancer Awareness Week 2015 (one site offered vaccination, one not) where self-administered	<ul style="list-style-type: none"> <li>- In Phase I, 56 participants responded to the questionnaire and among these, 29 students were vaccinated in a 2-day resident-run clinic. There was a 50% 3-dose completion rate in Phase I.</li> <li>- A total of 151 students were approached for individual solicitation and education in Phase II. Among these, 64 students were vaccinated on site. There were 18 walk in resulting directly from the education initiatives and person-to-person solicitation. In 2016, 957</li> </ul>	<ul style="list-style-type: none"> <li>- Low participation and inability to provide continuous services from residents and medical students.</li> <li>- The present numbers do not account for</li> </ul>

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	<i>campaign on the rates of vaccination in the context of a dedicated resident-run vaccination clinic</i>				questionnaires were used. In Phase II, a targeted education and vaccination campaign was designed based on lessons learned from Phase I  * Measured outcome was vaccination uptake	students were vaccinated in both universities.	students who may have received information from the education campaign and vaccinated in another clinic (lower the impact of the intervention; difficult to calculate a vaccination rate).
Pillai Riddell, R., 2017, <i>The ABCDs of pain management: A double-blind randomized controlled trial examining the impact of a brief educational video on infants' and toddlers' pain scores and parent soothing behaviour</i>	To test the efficacy of a brief behavioural pain management strategy, delivered via video, on infants' and toddlers' pain scores and on parental soothing behaviour	Toronto/Ontario  2013-2014	<b>Exclusion:</b> Young children were excluded if they had a suspected developmental delay or chronic illness, if they had been admitted to a neonatal intensive care unit, if they were born more than three weeks premature, and/or if they had a sibling who had already participated in the present study	Multicentre, stratified (6 months and 18 months), with balanced randomization (1:1), double-blind, placebo-controlled, parallel-group study	5 min active treatment video that coached parents on how to soothe their young child during the vaccination (ABCDs - (Assess anxiety, Belly breathe, Calm Close Cuddle, Distraction) or a 5 min placebo video that was identical to that of the active video except that no specific instructions regarding how to soothe their young child during the vaccination were provided	<ul style="list-style-type: none"> <li>- The multivariate analysis on pain scores showed an interesting effect of the treatment video on the two age groups over the course of the vaccination appointment. Results indicated significant treatment effects of the video on the toddler group but only during the first two regulatory pain scores (i.e., about 1 min and 2 min after the vaccination).</li> <li>- Secondary analyses found differences in parental rocking and physical comforting between treatment conditions and between age groups (<math>d's \approx 0.37-0.54</math>)</li> </ul>	<ul style="list-style-type: none"> <li>- Generalizability of the present study's findings in a less motivated population is unclear (they were already motivated parents to learn strategies to help improve their young child's vaccination pain).</li> <li>- Generalizability may also be affected by the high education level or the generally "integrated" acculturation status of this sample.</li> <li>- Parents were</li> </ul>

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					<p>* The primary outcome was the Modified Behaviour Pain Scale coded during four epochs after the last vaccination needle</p> <p>Secondary outcomes were distraction, rocking, and physical comforting 1 min, 2 min, and 3 min after last vaccination needle</p>		<p>not given specific instructions in the treatment video about how to assess their anxiety, or detailed instruction regarding distraction.</p> <ul style="list-style-type: none"> <li>- Authors did not follow them up at another vaccination to see if parents receiving the ABCD intervention used the same techniques.</li> </ul>
Taddio, A., 2015, <i>Impact of parent-directed education on parental use of pain treatments during routine infant vaccinations: A cluster randomized trial</i>	To evaluate the effect of a parent-directed prenatal education teaching module about vaccination pain management on analgesic utilization at future infant vaccinations	Toronto/Ontario 2012-2013	<b>Inclusion:</b> Expectant mothers attending the weekend series prenatal educational program, with or without a partner, and planning to immunize their unborn child. An additional inclusion criterion applied after delivery included birth of a healthy infant(s) > 35 weeks gestational age	Partially blinded cluster –randomized trial at a perinatal teaching hospital  197 expectant mothers from 28 prenatal classes participated; follow-up was obtained in 174 (88%)	20-30-minute interactive presentation about vaccination pain management (experimental group) or general vaccination information (control group). Both presentations included a PowerPoint and video presentation, take-home pamphlet, and “Question and Answer” period	<ul style="list-style-type: none"> <li>- Significantly more participants in the pain education group reported utilizing one or more pain interventions compared to the control group (34% vs 17%, respectively; P = 0.01).</li> <li>- The percentage of participants that attempted and were unsuccessful at utilizing at least one intervention was higher (P = 0.001) in the pain education group.</li> <li>- The percentage of participants responding correctly to knowledge questions was higher in the experimental group. There was less satisfaction (P = 0.05) with pain management interventions during infant vaccination in the experimental group (0.6 [0.9] vs 0.3 [0.7], respectively); this difference was not significant (P = 0.18) when success utilizing interventions was taken into account. Maternal-reported infant pain was lower (P = 0.05) for the</li> </ul>	<ul style="list-style-type: none"> <li>- Even if both the education and script were standardized, one educator in one institution delivered the education.</li> <li>- Prenatal classes are attended by expectant women who may be more likely to implement pain interventions due to their characteristics.</li> <li>- Contamination of community healthcare providers and participants was</li> </ul>

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					* Measured outcomes were self-reported utilization of breastfeeding, sugar water, or topical anaesthetics at routine 2-month infant vaccinations	experimental group (6.1 [2.0] vs 6.6 [2.1]) after correcting for successful utilization, but not before correction (P = 0.11).	possible.
Taddio, A., 2017, <i>Relative effectiveness of additive pain interventions during vaccination in infants</i>	To compare the relative effectiveness of 3 levels of pain interventions with a placebo control on infant distress levels over time during routine vaccinations	Toronto/Ontario  2012-2016	<b>Inclusion:</b> Healthy infants receiving vaccinations in 3 pediatric outpatient clinics, including 7 physician practices in Toronto were eligible <b>Exclusion:</b> Infants born before 36 weeks' gestation, infants who stayed in hospital outside of postnatal care, and infants who were allergic to amide anaesthetics or vaccines and for whom mothers planned to use topical anaesthetics, sucrose or breastfeeding during vaccinations	Multicentre, longitudinal, double-blind, add-on, randomized controlled trial  A double-dummy design was used; hence all parents watched a video (active psychological intervention or placebo), all infants received oral solution (24% sucrose in water or placebo), and all infants received topical cream (active lidocaine 4% or placebo) before vaccinations. The active video instructed parents in a mnemonic (ABCD, whereby A = assess distress, B = belly breathing, C = cuddle, D = distract), the placebo video provided general (nondirective) information only  838 infants met the	Healthy infants were randomly assigned to 1 of 4 levels of pain management for all vaccine injections at 2, 4, 6 and 12 months: (i) placebo control; (ii) parent-directed video education about infant soothing; (iii) the video plus sucrose administered orally or (iv) the video plus sucrose plus liposomal lidocaine applied topically  *Measured outcome was infant distress during 3 phases — preinjection (baseline), vaccine injection (needle), and 1	- Baseline scores showed no evidence of an effect of treatment group (p = 0.4), but a significant effect of time (i.e., infant age) (p < 0.001). Needle scores showed group (p = 0.003) and time differences (p < 0.001). Scores were lower for the video–sucrose–lidocaine group compared with the control (p < 0.001), video (p = 0.003), and video–sucrose (p = 0.005) groups, respectively. There were no differences between any of the other groups. The mean needle score was 6.3; SD = 0.8) in the video–sucrose–lidocaine group and 6.7 SD = 0.8) in each of the other 3 groups. The observed effect size (standardized mean difference) was 0.5.  - Results suggest the benefit derived from the lidocaine component of the regimen only. A post-hoc analysis accounting for sucrose and lidocaine implementation showed similar results.	- Lack of strict control regarding the timing of study procedures (the study was integrated within clinical practices) may have increased the variability and reduced our ability to detect differences among groups.  - Breastfeeding was not included, even though it has proven pain-relieving effects. Authors exclude it because fidelity was expected to be poor over time owing to low breastfeeding rates.

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				inclusion criteria and 352 (42%) of these infants' parents agreed to participate	minute post injection (recovery) — using the Modified Behavioural Pain Scale (range 0– 10)  Secondary outcomes of pain included dichotomized Modified Behavioural Pain Scale scores (using a cut-off of 2 for no pain/pain), cry duration and observer-rated pain (parents, physicians and researchers) during injection		

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