To Look or Not to Look During Vaccination: A Pilot Randomized Trial

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science
Department of Pharmaceutical Sciences
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Abstract

Objective: To examine the impact of looking at the needle versus looking away from the needle on pain and fear during vaccination in adults.

Methods: This was a pilot randomized, 2-group parallel trial with adults receiving influenza vaccinations. Participants were stratified and randomly assigned to either look at versus away from the needle. Participants self-reported their pain and fear during vaccination.

Results: Of the 184 subjects who agreed to participate, 160 were enrolled; 66% were female. A 3-way ANOVA (looking allocation assignment x looking preference x sex) revealed significant main effects suggesting that being asked to look increases fear (p=0.025) and those who prefer to look away are more fearful (p<0.001). Females reported higher pain and fear scores (p=0.017 and p=0.001, respectively). There were no significant interactions.

Discussion: Advising individuals to look away from the needle reduces fear. A larger trial including a larger and diverse sample is recommended.
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Chapter 1

1 Introduction

1.1 Introduction to Study

We conducted a pilot randomized controlled trial to evaluate the impact of looking at the needle and looking away from it on ratings of vaccine injection pain and fear in adults while taking into account their individual needle-looking preferences. The goal of this pilot study was to test the feasibility of design, acceptability of study procedures, fidelity of this intervention, and treatment effect sizes. The intervention itself is simple, easy and cost-neutral, and has the potential to be more commonly used in clinical practice. The results of this pilot will be used to inform a larger clinical RCT with a different population.

1.2 Background

1.2.1 Impact of pain and/or fear on vaccine compliance

Vaccinations prevent morbidity and mortality from infectious diseases. However, the method of their administration – a needle puncture – is a painful and distressing experience. Approximately 25% of adults are afraid of needles, with anticipated needle pain being a significant source of this fear. This potential for pain and fear presents an important barrier to vaccination uptake, resulting in one out of twelve adults either delaying or refusing vaccinations entirely due to these concerns. Mitigating pain and fear may lead to increased vaccination compliance, and favorably impact long-term health outcomes, both for individuals and communities.

It is unfortunate that even though pain management is a human right, reducing unnecessary pain and/or fear during painful needle procedures has not been a priority in clinical practice. Many evidence-based recommendations have been suggested for clinicians (Section 1.2.2; Table 1) but there is a large gap between evidence and practice that translates into needless suffering for those undergoing painful needle procedures such as vaccinations. Considering ways to reduce pain and/or fear during medical procedures is essential as it can counteract the long-term effects
of unmanaged pain, including the development of needle fears, and the harmful impact on health outcomes in individuals who avoid important medical appointments due to fear and/or apprehensions about pain. These apprehensions may be based on negative experiences in prior medical appointments due to inattention to the individual’s pain and/or fear experience by health care providers. Therefore, it is important to pay attention to the patient’s pain and/or fear experiences in order to prevent this deleterious cycle from forming and repeating itself, and having long-term effects on not just the individual, but also the community in general.

1.2.2 Current evidence based recommendations for clinicians to reduce pain and/or fear in adults during vaccinations

In 2015, a Cross-Canada multidisciplinary team, Help Eliminate Pain in Kids & Adults, led by Dr. Anna Taddio, published a comprehensive clinical practice guideline on reducing pain during vaccinations across the lifespan. These strategies are presented as the ‘5Ps’ of pain management: pharmacological, physical, procedural, process, and psychological. The 5Ps include evidence-based strategies of pain reduction such as injection techniques, educational interventions, and topical anesthetics. Although many of these strategies are available to help reduce needle pain and combat noncompliance, some strategies (e.g. topical anesthetics) are often underutilized in clinical practice due to costs and perceived inconvenience.

The current evidence based recommendations for clinicians to reduce vaccination pain and/or fear in adults are summarized in Table 1.

1.2.3 Intervention

The majority of interventions are targeted towards children and the interventions that clinicians can use beyond procedural interventions with adults are very few and not well supported. There is a need to assess pain management strategies in adults, as adults report being more willing to be vaccinated if needle pain can be reduced. Thus, simple, quick and cost-effective pain reducing strategies that can be easily incorporated into clinical practice are needed.

One simple intervention used by some clinicians to reduce fear and pain involves advising individuals to ‘look away from the needle’ during injection. To our knowledge, there are no
randomized trials that have determined the effectiveness of this intervention with respect to reducing fear or pain during vaccination. In the only four non-clinical studies, and one clinical observational study performed to date, conflicting results were obtained for self-reported pain after asking healthy individuals to either look at versus look away during a painful stimulus.\textsuperscript{23,26-29} Higher pain scores during looking have been posited to be due to increasing autonomic nervous system activity in the individual.\textsuperscript{26,27} Conversely, lower pain scores during looking have been explained as possibly preventing an individual’s imagination from conjuring up a more traumatic experience than reality.\textsuperscript{23} These studies are briefly discussed in the next section (Section 1.2.4; Table 2).

Independent of clinician recommendation to look away from the needle, the pain and fear experience of an individual may be influenced by personal needle-looking preferences. In the only observational study carried out in a clinical setting, 73\% of 192 adult participants spontaneously looked away during venipuncture. These participants reported higher pain scores than those who looked at the needle (Section 1.2.4; Table 2).\textsuperscript{23} According to Vijayan et al. (2014), it is possible that those who naturally look away have higher pain scores because the propensity to look away may be a marker of low pain tolerance.\textsuperscript{23} In those who prefer to look, repeated pairings of looking at the needle during needle procedures may have a desensitizing effect. Therefore, it is important to also take into consideration an individual’s personal needle-looking preference when exploring the effects of this intervention.

It is possible that an individual’s preference to look at or look away from noxious stimuli is based on underlying coping style, and may impact an individual’s pain and fear experience. The literature on coping is complex with numerous ways to conceptualize different strategies.\textsuperscript{30-32} One conceptualization distinguishes between “sensitizers” versus “repressors”, who are characterized by approach versus avoidance behaviors, respectively. Sensitizers tend to actively seek out information concerning the nature of the stressful situation, whereas repressors avoid information or use coping strategies such as denial.\textsuperscript{31,32} In the context of needle procedures, sensitizers would prefer to watch the needle and learn about each step of the procedure, whereas, repressors would prefer to look away from the procedure, and/or focus on something else. The success of these coping strategies likely depends on what is being attended to/what sensitizers are focusing on (e.g., sensations vs. emotions).\textsuperscript{32} To date, however, no research has examined the complex interplay between clinical recommendations for looking and one’s own looking
preference as coping strategies and how this interaction may have an impact on pain and fear perception.

1.2.4 Summary of Literature

1.2.4.1 Previous Laboratory and Clinical Studies

Below is a brief overview of the findings from the laboratory and clinical studies, some of which have been briefly mentioned above (See: Section 1.2.3; also, Table 2.).

1.2.4.1.1 Laboratory Studies

Four previous laboratory-based experimental studies were identified on this topic (See: Table 2).

Two studies are consistent with recommendations to look away from the needle to reduce pain. In the study by Bufalari et al (2007) activations in the cortical areas that process affective-motivational components of pain were found when participants were shown video clips of needle pricks inflicted upon another person’s body. This activation was significantly related to pain intensity ratings by the participants. However, it is important to note that this study encompassed pain recordings of individuals rating another person’s pain. Another study by Hofle et al (2012), encompassed pain recordings of 25 individuals visually attending to their own pain experiences in which they received an electric current to their fingertip, while simultaneously observing this procedure on a screen. These individuals reported more pain when shown a sharp needle versus a Q-tip being applied to their fingertip on the screen, even though the electric current was the same in all cases. The reported pain scores were lowest when an image of a hand with no stimulus being applied (i.e. no needle or Q-tip) was shown on the screen. The study also showed that needle pricks intensified the responses of the autonomic nervous system (ANS). As per these findings, looking away from the needle (i.e. not visually attending) should, in theory, reduce pain and fear in individuals, as visual observation of painful stimuli has the effect of increasing activity in the affective-motivation components of pain and ANS activity in the observer’s brain and central nervous system.
Conversely, results that support visually attending to painful procedures to reduce pain were also presented in two research studies. In one study by Longo et al (2009; N=30), vision of the body receiving laser-induced pain, produced an analgesic effect on self-reported ratings of pain, compared to vision of a neutral object.\(^{28}\) In the other study by Mancini et al. (2011), participants (N=18) receiving a painful thermal stimulus on their hand reported less pain when looking at their hand being stimulated by a pain-inducing probe compared to those who did not look.\(^{29}\) In the same study, pain ratings were significantly reduced when showing participants magnified views of their hand. These findings support the conclusion that viewing the body undergoing painful procedures is analgesic, and this analgesic effect is enhanced when providing participants with more visual detail of the body.\(^{29}\)

### 1.2.4.1.2 Clinical Study

Only one observational study was identified that explored this phenomenon in a clinical setting. In the study by Vijayan et al. (2014), 192 adult participants undergoing a venipuncture in an outpatient phlebotomy clinic were observed for their natural propensity to either look at or look away during needle insertion. Pain ratings were recorded using the VNRS (0-10) and the VRS (‘no pain’ to ‘severe pain’). Participants who spontaneously looked away (73%) had significantly higher pain scores than those who looked at the needle during venipuncture procedures.\(^{23}\) While patients differed in their propensity to observe or avert their gaze from a needle being inserted, the reason for their behaviour was unclear, nor was it clear why the pain ratings of those who observed the procedure were lower than those who looked away. The authors proposed that experimental research investigating this phenomenon is warranted.

### 1.3 Pilot trial methodology

Using a pilot trial methodology was a suitable approach to our research question. There has been no RCT that has examined the effects of this intervention before. There were no prior data on how this intervention might be implemented in a trial and/or accepted by participants. A pilot trial methodology allowed us to evaluate the feasibility of design, acceptability of the study procedures, and fidelity of the intervention. For instance, in order to determine feasibility, we wanted to look at recruitment rates and the natural split that occurs in the population between
individuals who naturally prefer to look and those who prefer to look away. Similarly, to understand the possible acceptability of the intervention, it was important to see how many individuals would complete the trial from start to finish, the amount of time taken, and participant opinions about the intervention itself. Fidelity was explored by assessing the compliance of each individual with the intervention. These outcomes allowed us to judge whether it would make sense to conduct a trial like this on a larger scale. Therefore, it served as an early-phase developmental mechanism that has the potential to improve the possible success of a larger subsequent trial in the future. 33

1.4 Research Problem

A mismatch between personal needle-looking preference and clinician recommendation may negatively impact the person’s pain and fear experience. To date, no research has examined the complex interplay between clinical recommendations for looking and one’s own looking preference and how this interaction may have an impact on pain and fear perception. Therefore, we are interested in investigating the effectiveness of the intervention. Furthermore, we wanted to explore whether the effectiveness of this intervention was influenced by personal needle-looking preference.

1.5 Study Objective

We undertook a pilot randomized trial to explore the impact of being instructed to look at the needle to reduce pain and fear versus looking away, while accounting for needle-looking preferences of individuals. The specific objectives were to examine feasibility, acceptability, fidelity, and estimate effects to inform a larger randomized control trial.
1.6 Organization of Thesis

This thesis adheres to the alternative thesis format. Chapter 2 presents a description of the research methodology. Chapter 3 consists of the results, presented as a paper formatted for the Canadian Journal of Pain. Chapter 4 presents the discussion of the results, considering the study’s limitations, strengths, and future directions, and finally the study conclusion.

1.7 Summary

Many evidence-based strategies are available to help reduce needle pain and fear, and combat noncompliance, but they are underutilized in clinical practice. There is a need to find feasible interventions for adults undergoing vaccination. One simple intervention used by some clinicians to reduce fear and pain involves advising individuals to ‘look away from the needle’ during injection. To our knowledge, there are no randomized trials that have determined the effectiveness of this intervention with respect to reducing fear or pain during vaccination. This thesis includes a pilot randomized trial investigating the feasibility, fidelity, acceptability and estimate effects to inform a larger randomized control trial in the future.
Chapter 2

2 Methods

2.1 Introduction

In this chapter, I provide a description of the methodology used in the study. It includes a description of the population and setting, materials used, consenting process, randomization and allocation, study procedures, study outcomes, sample size calculation and statistical analysis.

2.2 Population and Setting

I conducted a pilot randomized 2-group parallel open trial. The setting was the University of Toronto (UofT) Health and Wellness Centre. Eligible participants included any student (18+ years old) enrolled in the undergraduate and graduate programs at the Leslie Dan Faculty of Pharmacy who consented to (i) receiving influenza vaccinations, and (ii) being randomized to either look at the needle or look away from it during vaccination. Study data collection was conducted between October 24, 2016 and January 5, 2017.

2.3 Materials

A questionnaire administered by a Research Assistant (RA) was used to collect demographic information (e.g., sex, age, ethnicity) and looking preference. Looking preference was ascertained using the question “When getting injections, do you usually prefer to look at or look away from the needle?”.

Post-vaccination, a RA administered two 11-point Verbal Numerical Rating Scales (VNRS)\(^8,34\) to collect pain and fear scores. The following two questions were asked: (i) “On a scale of 0 to 10, where 0 is no pain, and 10 is the most pain possible, how would you rate your pain during the needle?” (ii) On a scale of 0 to 10, where 0 is no fear, and 10 is the most fear possible, how fearful were you during the needle?” In addition, post-vaccination, participants also reported their needle-looking preferences for future vaccinations. This was based on responses of the participants to the question, “What would you prefer to do for your future vaccinations? [look,
look away, no preference]. The post-vaccination questionnaire also included a compliance checkbox whereby a RA checked off either ‘Yes’ or ‘No’ to the question: “Was the participant compliant with the study instructions?”.

2.4 Consenting Process

Posters, emails, and class announcements were used to introduce the study to all registered students (total population N = 1109). On-site recruitment was conducted for three weeks (from October 3, 2016 to October 21, 2016) on weekdays from 9am to 5pm, whereby interested individuals approached the study coordinator to enroll. Eligible participants included any student (18+ years old) enrolled in the undergraduate and graduate programs at the Leslie Dan Faculty of Pharmacy who consented to (i) receiving influenza vaccinations, and (ii) being randomized to either look at the needle or look away from it during vaccination. Written consent was obtained from all participants. As per routine practice, appointments were scheduled for vaccinations. A confirmation email reminder was sent. The study was approved by the University Research Ethics Board. The study was registered on www.clinicaltrials.gov (NCT02937428).

2.5 Randomization and Allocation Concealment

An RA not directly associated with trial execution created a randomization code using a computerized random number generator. A separate code was used according to individual needle-looking preference; that is, patients were stratified based on baseline preference to either look at or look away from the needle. Within each stratum, individuals were randomized to either look at or look away from the needle during the vaccine injection using a 1:1 allocation ratio. Thus, there were 4 study groups: 1) prefer to look away and randomized to look; 2) prefer to look away and randomized to look away; 3) prefer to look and randomized to look; and 4) prefer to look and randomized to look away (Figure 1). Sequentially Numbered Opaque Sealed Envelopes (SNOSE) were prepared for each stratum. This RA did not have any other involvement in the trial. On the day of the vaccination, a different RA opened the next envelope to reveal allocation group of the participant immediately before vaccination.
2.6 Study Procedures

Two registered nurses at the Health and Wellness Centre administered all vaccine injections. Both nurses underwent training prior to study execution to ensure understanding of the protocol and consistency in injection techniques used for vaccinations. Training included scripts for interactions with participants (described further below). Three RAs were involved in data collection; one was responsible for greeting and registering participants, the second collected baseline information (demographics and needle-looking preference) and opened the concealed envelope containing the allocation group, and finally, the third collected post vaccination data, which included pain and fear ratings, compliance with the intervention, and future needle-looking preference.

All vaccinations occurred in private rooms with separate entrances and exits. The immunizer provided standard information about the influenza vaccine and asked the participant questions in accordance to usual practice at the clinic. All participants sat upright on a chair, with their elbow resting on the armrest. The participant’s non-dominant arm was swabbed with alcohol (70% Isopropyl Alcohol, Healthcare, Medical Mart, Mississauga, Ontario, Canada). The nurse asked the participant to “relax the arm and let it go all loose and jiggly”. Then the participant was asked to “look directly at the needle” or “look away from the needle in the other direction,” according to group allocation. The nurse said, “Here I go…” right before injecting the vaccine. All participants received 0.5 mL of Fluviral (Sanofi, GlaxoSmithKline, Mississauga, Ontario, Canada) intramuscularly, without prior aspiration, using a 0.5 mm x 25 mm needle (BD Eclipse, Becton, Dickinson and Company, Rantoul, Illinois, USA). After injection, a band aid was applied and the nurse said, “We’re all done.” The RA asked participants about their level of pain and fear during the vaccination. Compliance with the intervention was also noted, and participants were asked about their future needle-looking preferences.
2.7 Study Outcomes

2.7.1 Primary Outcomes

*Pain:* Self-reported pain was assessed using an 11-point Verbal Numerical Rating Scale (VNRS)\(^8,17,34\) where 0=no pain and 10=most possible pain immediately after the vaccination (< 5 minutes).

*Fear:* Self-reported fear was assessed using an 11-point VNRS\(^8\), where 0=no fear and 10=most possible fear immediately after the vaccination (< 5 minutes).

2.7.2 Secondary Outcomes

2.7.2.1 Feasibility

The first feasibility criterion was to achieve a minimum overall recruitment rate of 15% (n=166) over a 6-8-week period (study timeline). This was based on an estimate of 30% of the eligible population (N=1109) getting vaccinated and a 50% enrollment rate. The second criterion for feasibility was an assumption of an equal split (50:50) in the number of people who preferred to look at or away from the needle at baseline (to allow for an equal number of participants in each stratum).

2.7.2.2 Acceptability

Acceptability of the intervention was based on three criteria. First, a rate of >75% of participants completing the trial. Second, a duration of appointment of <15 minutes. Third, the stated looking preference of participants for future vaccinations was based on responses of the participants to the question, “What would you prefer to do for your future vaccinations? [look, look away, no preference].”

2.7.2.3 Fidelity

Fidelity of the intervention was based on a rate of >75% of participants being compliant with the instruction to look at the needle or look away during the vaccination.
2.8 Sample Size Calculation

In the absence of any prior data to guide effect size estimates, the sample size was arbitrarily set to \( n=40 \) per group (total, \( n=80 \)), according to Herzog (2008).\(^{35}\) Since 2 strata were included, the sample size was doubled (i.e., \( n=80 \times 2 \) strata, or total, \( n=160 \)), assuming a 50:50 split.

2.9 Statistical Analysis

Demographic characteristics (i.e. age, sex, ethnicity) were compared between groups using a \( t \)-test and \( \chi^2 \)-test, as appropriate. Two 3-way ANOVAs (looking allocation assignment \( \times \) looking preference \( \times \) sex) were used to examine pain and fear scores. Looking allocation assignment included 2 levels (randomized to look at versus randomized to look away). Similarly, looking preference included 2 levels (participant preference to look at versus preference to look away), and sex included 2 levels (male versus female). Interactions were removed from the model if non-significant. Sex was included as an independent factor in the model as previous studies demonstrate sex differences in both pain and fear, with females reporting more pain than males.\(^{19-21}\) Q-Q plots were examined to rule out departure from normality in the residuals of the model. There were no observable departures from normality. The Pearson correlation coefficient was used to examine the relationship between pain and fear scores during vaccination.

2.10 Summary

This was a pilot randomized, 2-group parallel trial with university students receiving influenza vaccinations. Participants were first stratified according to their initial needle-looking preference and then randomly assigned to either look at versus away from the needle. Participants self-reported their pain and fear during vaccination using the Verbal Numerical Rating Scale (0=no pain/fear, 10=worst pain/fear possible). Fidelity, feasibility and acceptability of the intervention was also assessed.
Chapter 3

3 Results

3.1 Introduction

This chapter describes the results of the pilot clinical trial. It is written as a paper formatted for Canadian Journal of Pain. This manuscript was accepted for publication by Canadian Journal of Pain on November 28\(^{th}\), 2017.

3.2 Written Manuscript

To look or not to look during vaccination: A pilot randomized trial

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Abstract

**Background:** Clinicians commonly advise patients to look away from the needle during vaccinations; however, this recommendation is not evidence based.

**Aim:** To determine whether looking at the needle versus looking away affects pain and fear during vaccinations in adults.

**Methods:** This was a pilot randomized 2-group parallel trial with university students receiving influenza vaccinations. Participants were stratified according to their initial needle-looking preference and randomly assigned to either look at versus away from the needle. Participants self-reported their pain and fear during vaccination.

**Results:** Of the 184 subjects who agreed to participate, 160 were enrolled; 66% were female. A 3-way ANOVA (looking allocation assignment x looking preference x sex) revealed a significant main effect of looking allocation assignment on fear (p=0.025); those who were randomized to look had higher fear scores than those who were randomized to look away. There was also a significant main effect of looking preference on fear (p<0.001); those who preferred to look away had higher fear scores than those who preferred to look. There was no evidence of an effect of looking allocation assignment or looking preference on pain. There was a significant main effect of sex on fear and pain, with females reporting higher pain and fear scores than males (p=0.017 and p=0.001, respectively). There were no significant interactions.

**Conclusion:** These preliminary findings suggest that advising individuals to look away from the needle reduces fear. A larger trial including more individuals and a different population is recommended to confirm the results.

**Trial Registration #:** NCT02937428

**Key words:** vaccination, pain, fear, needle, looking preference
1. Introduction

Vaccinations prevent morbidity and mortality from infectious diseases.\textsuperscript{1} However, approximately 25\% of adults are afraid of needles, with anticipated needle pain being a significant source of this fear.\textsuperscript{2} This potential for pain and fear presents an important barrier to vaccination uptake, resulting in one out of twelve adults either delaying or refusing vaccinations entirely.\textsuperscript{3,4} Mitigating pain and fear may lead to increased vaccination compliance, and favorably impact long-term health outcomes, both for individuals and communities.\textsuperscript{5-9} Many evidence-based strategies are available to help reduce needle pain and fear, and combat noncompliance, but they are underutilized in clinical practice (e.g. topical anesthetics).\textsuperscript{8} In addition, the majority of these interventions are targeted towards children.\textsuperscript{9-12} There is a need to find feasible interventions for adults undergoing vaccination.

One simple intervention used by some clinicians to reduce fear and pain involves advising individuals to ‘look away from the needle’ during injection.\textsuperscript{10} To our knowledge, there are no randomized trials that have determined the effectiveness of this intervention with respect to reducing fear or pain during vaccination. In four non-clinical, and one clinical observational study performed to date, conflicting results were obtained for self-reported pain after asking healthy adults to either look at versus look away during a painful stimulus.\textsuperscript{10,13-16} Higher pain scores during looking have been explained as possibly due to increasing autonomic nervous system activity in the individual.\textsuperscript{13,14} Conversely, lower pain scores during looking have been explained as possibly preventing an individual’s imagination from conjuring up a more traumatic experience than reality.\textsuperscript{10} This evidence base did not include vaccinations. The non-clinical studies incorporated pain ratings from electrical, laser and thermal stimuli, whereas the clinical study examined venipuncture.\textsuperscript{10,13-16} The effects of looking at or looking away from different medical procedures involving needles may have different fear and pain inducing components.\textsuperscript{9} It is important to explore the effects of this intervention during vaccinations specifically.

The pain and fear experience may be influenced by personal needle looking preferences. In the only observational study carried out in a clinical setting, 73\% of 192 adult participants spontaneously looked away during venipuncture. These participants reported higher pain scores than those who preferred to look at the needle.\textsuperscript{10} According to the author, it is possible that those who naturally look away have higher pain scores because the propensity to look away may be a
marker of low pain tolerance. In those who prefer to look, repeated pairings of looking at the needle during needle procedures may have a desensitizing effect. A mismatch between personal preference and clinician recommendation may negatively impact the person’s pain and fear experience.

It is possible that an individual’s preference to look at or look away from noxious stimuli is based on underlying coping style, and may impact an individual’s pain and fear experience. The literature on coping is complex with numerous ways to conceptualize different strategies. One conceptualization distinguishes between “sensitizers” versus “repressors”, who are characterized by approach versus avoidance behaviors, respectively. Sensitizers tend to actively seek out information concerning the nature of the stressful situation, whereas repressors avoid information or use coping strategies such as denial. In the context of needle procedures, sensitizers would prefer to watch the needle and learn about each step of the procedure, whereas, repressors would prefer to look away from the procedure, and/or focus on something else. The success of these coping strategies likely depends on what is being attended to/what sensitizers are focusing on (e.g., sensations vs. emotions). To date, however, no research has examined the complex interplay between clinical recommendations for looking and one’s own looking preference as coping strategies and how this interaction may have an impact on pain and fear perception.

We undertook a pilot randomized trial to explore the impact of being instructed to look at the needle to reduce pain and fear versus looking away, while accounting for looking preferences of individuals. The specific objectives were to examine feasibility, acceptability, fidelity, and estimate effects to inform a larger randomized control trial.

2. Materials and Methods

2.1 Population and setting

We conducted a pilot randomized, 2-group parallel, open trial. The setting was the University of Toronto (UofT) Health and Wellness Centre. Eligible participants included any student (18+ years old) enrolled in the undergraduate and graduate programs at the Leslie Dan Faculty of Pharmacy who consented to (i) receiving influenza vaccinations, and (ii) being randomized to
either look at the needle or look away from it during vaccination. Study data collection was conducted between October 24, 2016 and January 5, 2017.

2.2 Materials

A questionnaire administered by a Research Assistant (RA) was used to collect demographic information (e.g., sex, age, ethnicity) and looking preference. Looking preference was ascertained using the question “When getting injections, do you usually prefer to look at or look away from the needle?”.

Post-vaccination, a RA administered two 11-point Verbal Numerical Rating Scales (VNRS) to collect pain and fear scores. The following two questions were asked: (i) “On a scale of 0 to 10, where 0 is no pain, and 10 is the most pain possible, how would you rate your pain during the needle?” (ii) On a scale of 0 to 10, where 0 is no fear, and 10 is the most fear possible, how fearful were you during the needle?” In addition, post-vaccination, participants also reported their needle-looking preferences for future vaccinations. This was based on responses of the participants to the question, “What would you prefer to do for your future vaccinations? [look, look away, no preference]”. The post-vaccination questionnaire also included a compliance checkbox whereby a RA checked off either ‘Yes’ or ‘No’ to the question: “Was the participant compliant with the study instructions?”.

2.3 Consenting process

Posters, emails, and class announcements were used to introduce the study to all registered students (total population N = 1109). On-site recruitment was conducted for three weeks (from October 3, 2016 to October 21, 2016) on weekdays from 9am to 5pm, whereby interested individuals approached the study coordinator to enroll. Written informed consent was obtained from all participants. As per routine practice, appointments were scheduled for vaccinations. A confirmation email reminder was sent. The study was approved by the University Research Ethics Board. The study was registered on www.clinicaltrials.gov (NCT02937428).

2.4 Randomization and allocation concealment

A RA not directly associated with trial execution created a randomization code using a computerized random number generator. A separate code was used according to individual
looking preference, that is, patients were stratified based on baseline preference to either look at or look away from the needle. Within each stratum, individuals were randomized to either look at or look away from the needle during the vaccine injection using a 1:1 allocation ratio. Thus, there were 4 study groups: 1) prefer to look away and randomized to look; 2) prefer to look away and randomized to look away; 3) prefer to look and randomized to look; and 4) prefer to look and randomized to look away. Sequentially Numbered Opaque Sealed Envelopes (SNOSE) were prepared for each stratum. This RA did not have any other involvement in the trial. On the day of the vaccination, a different RA opened the next envelope to reveal allocation group of the participant immediately before vaccination.

2.5 Study procedures

Two registered nurses at the Health and Wellness Centre administered all vaccine injections. Both nurses underwent training prior to study execution to ensure understanding of the protocol and consistency in injection techniques used for vaccinations. Training included scripts for interactions with participants (described further below). Three RAs were involved in data collection; one was responsible for greeting and registering participants, the second collected baseline information (demographics and needle-looking preference) and opened the concealed envelope containing the allocation group, and finally, the third collected post vaccination data, which included pain and fear ratings, compliance with the intervention, and future needle-looking preference.

All vaccinations occurred in private rooms with separate entrances and exits. The nurse provided standard information about the influenza vaccine and asked the participant questions in accordance to usual practice at the clinic. All participants sat upright on a chair, with their elbow resting on the armrest. The participant’s non-dominant arm was swabbed with alcohol (70% Isopropyl Alcohol, Healthcare, Medical Mart, Mississauga, Ontario, Canada). The nurse asked the participant to “relax the arm and let it go all loose and jiggly”. Then the participant was asked to “look directly at the needle” or “look away from the needle in the other direction,” according to group allocation. The nurse said, “Here I go…” right before injecting the vaccine. All participants received 0.5 mL of Fluviral (Sanofi, GlaxoSmithKline, Mississauga, Ontario, Canada) intramuscularly, without prior aspiration, using a 0.5 mm x 25 mm needle (BD Eclipse, Becton, Dickinson and Company, Rantoul, Illinois, USA). After injection, a band aid was
applied and the nurse said, “We’re all done.” The RA asked participants about their level of pain and fear during the vaccination. Compliance with the intervention was noted, and participants were asked about their future needle-looking preferences.

2.6. Study outcomes

2.6.1. Primary Outcomes:

Pain: Self-reported pain was assessed using an 11-point Verbal Numerical Rating Scale (VNRS)\textsuperscript{17}, where 0=no pain and 10=most pain possible immediately after the vaccination (< 5 minutes).

Fear: Self-reported fear was assessed using an 11-point VNRS\textsuperscript{8}, where 0=no fear and 10=most fear possible immediately after the vaccination (< 5 minutes).

2.6.2. Secondary Outcomes:

1. Feasibility: The first feasibility criterion was achieving a minimum overall recruitment rate of 15% (n=166) over a 6-8-week period (study timeline). This was based on an estimate of 30% of the eligible population (N=1109) getting vaccinated and a 50% enrollment rate. The second criteria for feasibility was an assumption of an equal split (50:50) in the number of people who preferred to look at or away from the needle at baseline (to allow for an equal number of participants in each stratum).

2. Acceptability: Acceptability of the intervention was based on three criteria. First, a rate of >75% of participants completing the trial. Second, a duration of appointment of <15 minutes. Third, the looking preference of participants for future vaccinations.

3. Fidelity: Fidelity of the intervention was based on a rate of >75% of participants being compliant with the instruction to look at the needle or look away during the vaccination.

2.7. Sample size calculation and statistical analysis

In the absence of any prior data to guide effect size estimates, the sample size was arbitrarily set to n=40 per group (total, n=80), according to Herzog (2008).\textsuperscript{21} Since 2 strata were included, the sample size was doubled (i.e., n=80 x 2 strata, or total, n=160), assuming a 50:50 split.
Demographic characteristics (i.e. age, sex, ethnicity) were compared between groups using a t-test and χ²-test, as appropriate. Two 3-way ANOVAs (looking allocation assignment x looking preference x sex) were used to examine pain and fear scores. Looking allocation assignment included 2 levels (randomized to look at versus randomized to look away). Similarly, looking preference included 2 levels (participant preference to look at versus preference to look away), and sex included 2 levels (male versus female). Interactions were removed from the model if non-significant. Sex was included as an independent factor in the model as previous studies demonstrate sex differences in both pain and fear, with females reporting more pain and fear than males. Q-Q plots were examined to rule out departure from normality in the residuals of the model. There were no observable departures from normality. The Pearson correlation coefficient was used to examine the relationship between pain and fear scores during vaccination.

3. Results

3.1 Participant flow

Data collection was conducted between October 24, 2016 and January 5, 2017. Altogether, 184 were enrolled of which 24 (13%) did not attend the appointment, leaving 160 participants. Fifty-five (34%) self-identified at baseline as preferring to look at the needle; the remainder 105 (66%) preferred to look away from the needle. Figure 1 shows the participant flow during the trial.

3.2. Participant characteristics

There were no statistically significant differences (p>0.05) in demographic characteristics among the four groups (Table 1).

3.3. Primary Outcomes

Table 2 presents the means and standard deviations of the pain ratings of males and females, immediately following the vaccination. There were no significant interactions. The analysis demonstrated no evidence of an effect of looking allocation assignment on pain: randomized to look [n=80, 3.09 (1.93)] versus randomized to look away [n=79, 2.95 (2.02); F(1,55)=0.33; p=0.567]. There was no evidence of an effect of looking preference on pain: preference to look [n=55, 2.58 (1.67)] versus preference to look away [n=104, 3.25 (2.08)]; [F(1,155)=2.57;
p=0.111]. There was, however, a significant effect of sex on pain: females [n=105, 3.42 (1.94)] versus males [n=54, mean 2.24 (1.79)]; [F(1,155)=12.08; p=0.0007].

Table 3 presents fear ratings of males and females. There were no significant interactions. There was a significant main effect of looking allocation assignment on fear: randomized to look [n=80, 2.81 (2.3)] versus randomized to look away [n=79, 2.06 (2.3)]; [F(1,155)=5.14; p=0.025]. There was a significant main effect of looking preference: preference to look [n=55, 1.55 (2.3)] versus preference to look away [n=104, 2.91 (2.3)]; [F(1,155)=11.79; p=0.0008]. There was a significant main effect of sex on fear: females [n=105, 2.79 (2.3)] versus males [n=54, 1.75 (2.3)]; [F(1,155)=5.78; p=0.017].

The Pearson correlation coefficient between pain and fear scores was 0.60 (p<0.0001).

3.4. Secondary Outcomes

1. Feasibility: Altogether, 184 participants were enrolled; the recruitment rate was 17%. The ratio of people who had a baseline preference to look at the needle versus look away from the needle was 66:34 in the sample.

2. Acceptability: All (100%) of participants who were randomized stayed in the study (i.e., none of the participants withdrew). The mean (standard deviation) time taken for the entire procedure from baseline questions, to vaccination procedure, to post-vaccination questions was 11min 28s (+/-2min 40s). Altogether, 74.4% of participants maintained their original looking/not looking preference for future vaccinations.

3. Fidelity: One participant (0.6%) was non-compliant with the intervention. The participant had a baseline preference to look away and was randomized to look at the needle. This individual looked away during injection.

4. Discussion

To our knowledge, this is the first randomized trial to examine the impact of looking at the needle versus looking away during vaccination on pain and fear in adults. Feasibility, acceptability and fidelity of the intervention were demonstrated. Looking at the needle versus looking away did not have a significant impact on pain, but did significantly impact fear, with
those who were told to look at the needle reporting significantly more fear. Similarly, those who initially preferred to look away reported significantly more fear. Females in our study reported significantly more pain and fear than males. There was no evidence of any interactions between the factors evaluated. Thus, there was no evidence that a mismatch between initial preference to look or not look and randomization group impacts pain or fear.

Assessing an individual’s fear during vaccination is important because fear can increase pain perception. Concerns about fear and pain can also negatively impact future vaccination compliance. Of note, reported pain did not vary with looking behavior in the present study, but reported fear did. It is possible that the fear experienced by participants was not limited to the fear of pain, but included apprehensions about other aspects of the procedure. It is also possible that no effect was observed for pain due to the small sample size, relatively low levels of fear and pain in our study population, and the specific procedure and vaccine used. Future studies are recommended that examine different populations, procedures, and vaccines.

Studies have shown that females report higher pain and fear than males. Differences in physiological responses to pain and fear have been observed in males and females, including, pupil dilation, brain scans and other neurological parameters. Explanations may include psychosocial factors, hormonal factors, genetic factors, or a combination of all of these. For instance, it is possible that males are conditioned to report less pain and fear due to differences in reinforcement of expressions of pain and fear in childhood. The results of this study are consistent with this literature – females reported more pain and fear during vaccination than their male counterparts.

The intervention evaluated in the present study demonstrated high feasibility, acceptability, and fidelity. The recruitment rate met our a priori criterion for demonstrating that the study was feasible as we met our recruitment rate of 15% within a three-week period (faster than the anticipated 6-8 weeks). To account for the 24 participants who did not attend their appointments, additional participants were enrolled for an additional recruitment week. This suggests that enrolling participants at the proposed rate for a similar study in the future is feasible. The ratio of people who had baseline preference to look at the needle versus look away was anticipated to be 50:50; however, the actual split was 34:66, which precluded us from reaching the desired sample size for people with a baseline preference to look at the needle. An uneven split was also
reported in a previous observational study by Vijayan et al. (2014) that assessed spontaneous behavior, whereby the ratio was 27:73. Future studies will need to account for this difference in recruitment rates if both needle-looking preferences are to be included.

The trial was deemed acceptable based on the low attrition rate (i.e., no drop outs/withdrawals once randomized), and short duration required to implement the intervention (~5-6 more minutes than usual practice, including all study procedures) per participant. The average time for vaccination including the study procedures was just over 10 minutes; approximately double the time usually taken in the clinic. This additional time can be built into a future trial. While compliant with the intervention, the majority of participants reported preferring to undergo future vaccinations using their baseline preference. This should be explored further, including asking participants about their satisfaction with the procedure.

Fidelity of the intervention was demonstrated by compliance of all but one participant with the instructions given by the nurse (i.e., >99% compliance). It was anticipated that those who had initial preference to look away and were randomized to look would find it hard to be compliant with the instructions to look. However, this was not the case in our study, at least as measured by observable behavior.

Limitations of the study include the small sample size and limited diversity in demographic of included participants (i.e. pharmacy students). Healthcare students, in general, may have a higher tolerance for pain and fear when it comes to vaccination due to a desensitization effect from undergoing more routine vaccinations than the average person. In addition, nurses, research personnel and the participants were not blinded to the study objective which could have introduced bias. Using an open design was considered acceptable because there was no evidence suggesting that one way (i.e. looking at the needle or not looking at it) is better than the other (i.e., bias was minimized by the lack of perceived benefit of one condition over the other).

There are numerous strengths of the study. First, personal needle-looking preference was taken into account prior to randomization. Second, the study used rigorous methodology, including randomization and allocation concealment. Third, the study procedures were standardized in order to reduce performance and detection bias that may have been introduced due to the open nature of this trial. Finally, there were no dropouts, minimizing attrition bias.
5. Conclusion

This pilot study suggests that regardless of initial looking preference or sex, telling adults to look away from the needle during vaccination can reduce fear. Alternatively, clinicians can go by the individual’s preference, especially accommodating those who have a strong preference to look away. The results have implications for clinical practice. Simply telling individuals to look away from the needle is an easy, free strategy that requires no training and can help to reduce fear during vaccination. However, given the preliminary-nature of the results, we recommend caution interpreting these results and repeating the study using a larger sample size and a different population to further examine the relationship between looking preference and telling individuals to look at versus away from the needle. This is particularly important for individuals who declare a preference to look away and report higher levels of fear. We also recommend further research for the effect of this intervention during other needle procedures.

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Declaration of Interest

Funding for this study was provided by miscellaneous funds by Dr. Taddio. The other authors have no conflicts of interest to declare.
References


Chapter 4

4 Discussion

4.1 Summary of Results

To our knowledge, this is the first randomized trial to examine the impact of looking at the needle versus looking away during vaccination on pain and fear in adults. Feasibility, acceptability and fidelity of the intervention were demonstrated. Looking at the needle versus looking away did not have a significant impact on pain, but did significantly impact fear, with those who were told to look at the needle reporting significantly more fear. Similarly, those who initially preferred to look away reported significantly more fear. Females in our study reported significantly more pain and fear than males. There was no evidence of any interactions between the factors evaluated. Thus, there was no evidence that a mismatch between initial preference to look or not look and randomization group impacts pain or fear.

4.2 Looking preference and looking assignment

With respect to initial preference, regardless of sex or looking assignment, individuals who naturally preferred to look away reported higher fear than individuals who naturally preferred to look at the needle but there was no effect of looking preference on pain. Furthermore, regardless of preference, those who were instructed to look at the needle experienced higher fear than those who were instructed to look away. Current literature does not allow us to explain these findings, as fear in this context has not been explored before. Vijayan et al. (2014) found that those who spontaneously looked away during venipuncture reported higher pain scores, but personal preference or clinician instructions had no impact on pain in our study. This difference might be due to the relatively small sample size, and non-diverse demographic (i.e. pharmacy students only) of our study, compared to a larger sample size, and more diverse group in the Vijayan study. For those who naturally prefer to look, it is possible that lower fear was experienced because repeated pairings of looking at the needle during injection procedures over the course of an individual’s life may have had a desensitization effect over the feared stimulus (i.e. the needle). This might not have been the case in those who were instructed to look in our study, as
this group also included individuals who naturally preferred to look away and may not have had prior desensitization to needle procedures. The results suggest that instructing a patient to observe a needle entering the skin during vaccination, regardless of their natural preference, is more distressing for the individual. Therefore, it seems that accommodating to people’s personal preferences is beneficial in reducing fear, with greater attention needed for those who naturally prefer to look away from the needle. Those who naturally prefer to look at the needle may not be as greatly impacted. Overall, instructing people to look at the needle is not recommended.

4.3 Fear and pain as primary outcomes

4.3.1 The impact of fear on vaccination experience and compliance

Negative emotions (i.e. fear) surrounding needle procedures are often ignored in clinical practice. This can pose as a problem because fear has been shown to have a bidirectional relationship with pain. For instance, greater perceived pain during needle procedures has been associated with higher levels of fear. Therefore, assessing an individual’s fear during vaccination is important because fear can increase pain perception. Reducing fear is important because even though acute pain is reduced after the delivery of a vaccination, the emotional impact from the experience can have a much longer lasting impact. Concerns about fear and pain can negatively impact future vaccination compliance. Those who experience high fear may experience more distress in future needle procedures, engaging in avoidance behaviors. It is important to also note that the fear patients may experience is not just limited to fear of pain, but possible apprehensions about other aspects of the medical procedure as well (e.g., the needle point, the needle entering the skin, seeing blood, needle hitting bone etc.) that may contribute to their distress. Higher fear was not associated with more pain in the present study, but asking patients to look away did lower fear overall. Asking patients to look away from the needle may be helpful in mitigating fear, possibly having a positive impact on their vaccination experience, as well as future compliance with needle procedures.

4.3.2 The impact of pain on vaccination experience and compliance

Improperly managed needle pain can leave unpleasant memories about pain in individuals undergoing needle procedures, that may impact their compliance and experience in future
vaccination appointments. The experience of pain during a vaccination procedure may lead to fear of pain itself, which can result in an escalating relationship between fear and pain over time. This relationship is complex and the current study does not attempt to delineate the intricate mechanisms surrounding this experience. However, reducing pain can have overall positive effects, especially for those who are already hesitant and fearful about the vaccination procedure. Asking individuals to look away from the needle did not have an impact on pain in our study even though it has been used as a common recommendation by clinicians to reduce pain and distress. It is speculated that those who prefer to look away from the needle may have lower pain tolerance. Since, asking individuals to look away in our study did reduce fear, suggesting this strategy as a way to reduce unnecessary negative feelings around the anticipated pain and overall experience of the procedure may be a good idea. However, whether this strategy actually decreases pain perception during the moment of vaccination cannot be concluded from the findings of this study. Future studies are recommended that examine different populations, procedures, and vaccines.

4.3.3 Pain and fear in different vaccinations and procedures

The painfulness of the vaccine and the type of needle procedure may also play a factor on a patient’s pain and/or fear experience. Only influenza vaccinations were used in this study, but it is possible that influenza vaccinations are less painful than other vaccinations, which may have resulted in lower impact on pain for this vaccine. In addition, different medical procedures involving needles have different fear and pain inducing components. For instance, compared to vaccinations that are relatively quick, are injected intramuscularly, and involve the insertion of a substance into the body, a venipuncture takes longer, is more complex (i.e. time taken to find a vein), and involves taking out a substance from the body (i.e. blood). Seeing blood, for instance, is a trigger for vasovagal syncope, which is more common in those with high needle fear. Conversely, having a substance injected into the body may have its own pain and fear inducing effects due to the rush of liquid into the muscle, and may elicit additional fears in patients (e.g., fear of needle hitting bone). As we did find an impact of this intervention on fear, it is possible that telling people to look away may have a similar or more enhanced impact on pain and fear during venipuncture, and/or other more complex needle procedures and further research is recommended with these procedures.
4.3.4 Long-term effects of unmanaged pain and/or fear

It seems that patient fear and/or pain can be underprioritized in the moment of the needle procedure, as it is “just a poke”, or only lasts for a few seconds. However, it is not as simple as this. Non-compliance with vaccinations due to unpleasant past pain and/or fear experiences can have deleterious effects for not just the individual, but also the community. Considering ways to reduce pain and/or fear during medical procedures is important as it can lessen the long-term consequences of unmitigated pain, including the development of needle fears, and the harmful impact on health outcomes in individuals who avoid important medical appointments such as blood tests, vaccination, and even dental care due to fear and/or apprehensions about pain. These apprehensions may be based on negative experiences in prior medical appointments due to inattention to the individual’s pain and/or fear experience by health care providers. In addition, people with chronic conditions that require frequent needle procedures may be especially vulnerable (e.g. insulin injections for diabetes, chemotherapy treatments), which can compromise health outcomes in this population as well. Avoidance of vaccinations, for instance, can increase the risk of infectious diseases. For example, if refraining from getting influenza vaccinations, a person may accidently expose oneself to an especially vulnerable group, such as, those >65 years of age. Outside of the realm of the vaccination experience, these negative effects from untreated pain and/or fear can have other far-reaching consequences. For instance, individuals may be more reluctant to donate blood. Donating blood has the potential to save so many lives, and it is unfortunate that hesitancy around needle procedures from negative pain and/or fear experiences can impede on people’s willingness to volunteer for such causes. Therefore, exploring ways to reduce unnecessary pain and/or fear during vaccinations and other needle procedures is important. It is especially important to find easy, cost-effective and manageable strategies that clinicians can access and remember. Asking individuals to look away from the needle during vaccinations is one such strategy to at least, reduce fear during the needle procedure, adding a quick strategy to reduce negative emotions surrounding such experiences in adults (Table 1).

4.4 Sex differences in pain and fear

The experience of pain has biological, psychological, social, and contextual factors. The way males and females perceive pain and/or fear is based on their own specific differences. Studies
have shown that females report higher pain and fear than males cite. Differences in physiological responses to pain and fear have been observed, including, pupil dilation, brain scans and other neurological parameters.\textsuperscript{51} Explanations may include psychosocial factors, hormonal factors, genetic factors, or a combination of all of these.\textsuperscript{49-50,52} For instance, it is possible that males are conditioned to report less pain due to differences in reinforcement of expressions of pain and fear in childhood.\textsuperscript{50,52} The results of this study are consistent with this literature – females reported more pain and fear during vaccination than their male counterparts.

4.5 Interaction effects between looking preference, assignment and sex

Overall, the lack of interaction among the three factors in this study suggests that a mismatch between initial preference or randomization or sex, does not have any impact on pain or fear. Whether a person has a personal preference to look at or look away, or is male or female, it seems that advising individuals to look away from the needle is optimal in reducing fear. Therefore, these results support the current practice used by some clinicians of asking patients to look away from the needle during vaccinations regardless of sex or preference. In particular, it seems prudent that those who strongly prefer to look away should especially be accommodated. Future research could also examine if doing something else while looking away (e.g. focusing on a distractor) would augment this effect.

4.6 First criterion - Feasibility

The recruitment rate met our a priori criterion for demonstrating that the study was feasible as we met our recruitment rate of 15\% within a three-week period (faster than the anticipated 6-8 weeks). To account for the 24 participants who did not show up, additional participants were enrolled for an additional recruitment week. This suggests that enrolling participants at the proposed rate for a similar study in the future will not present as a challenge. The ratio of people who had baseline preference to look at the needle versus look away was anticipated to be 50:50; however, the actual split was 34:66, which precluded us from reaching the desired sample size for people with a baseline preference to look at the needle. An uneven split was also reported in a
previous observational study by Vijayan et al. (2014) that assessed spontaneous behavior, whereby the ratio was 27:73. Future studies will need to account for this difference in recruitment rates if both needle-looking preferences are to be included.

4.7 Second criterion - Acceptability

The trial was deemed acceptable based on the low attrition rate (i.e., no drop outs/withdrawals once randomized), and short duration required to implement the intervention (~5-6 more minutes than usual practice, including all study procedures) per participant. The average time for vaccination including the study procedures was just over 10 minutes; approximately double the time usually taken in the clinic. This additional time can be built into a future trial. While compliant with the intervention, the majority of participants reported preferring to undergo future vaccinations using their baseline preference. This should be explored further, including asking participants about their satisfaction with the procedure.

4.8 Third criterion - Fidelity

Fidelity of the intervention was demonstrated by compliance of all but one participant with the instructions given by the nurse (i.e., >99% compliance). It was anticipated that those who had initial preference to look away and were randomized to look would find it hard to be compliant with the instructions to look. However, this was not the case in our study, at least as measured by observable behavior.

4.9 Limitations of the study

Limitations of the study include the small sample size and non-diverse demographic of included participants (i.e. pharmacy students). Healthcare students, in general, may have a higher tolerance for pain and fear when it comes to vaccination due to a desensitization effect from undergoing more routine vaccinations than the average person. In addition, the painfulness of the vaccine and the type of needle procedure may also play a factor. Only influenza vaccinations
were used in this study, but it is possible that influenza vaccinations are less painful than other vaccinations,\(^8\) which may have resulted in lower impact on pain for this vaccine. In addition, different medical procedures involving needles have different fear and pain inducing components, so it is possible that vaccinations are less painful compared to venipuncture, for instance, possibly resulting in lower impact on pain for this study procedure.\(^9\) In addition, nurses, research personnel and the participants were not blinded to the study objective which could have introduced bias. Using an open design was considered acceptable because there was no evidence suggesting that one way (i.e. looking at the needle or not looking at it) is better than the other (i.e., bias was minimized by the lack of perceived benefit of one condition over the other). In order to minimize potential for performance bias due to the open nature of this trial, the study procedures, setting, participant position and scripts were standardized for all participants. In addition, no one in the study knew which group the participant was going to be randomized to until immediately before the vaccination procedure. Finally, the sample size of participants who were randomized to look was much smaller than those randomized to look away, which may have under-powered the study to detect a difference between groups for individuals randomized to look.

### 4.10 Strengths of the study

There are numerous strengths of the study. First, we accounted for individual preferences to look at vs. look away from the needle in the determination of intervention effectiveness and included a separate randomization for each stratum. This was important because people have personal preferences, and a mismatch between preference and intervention could have had an impact on pain and fear. Second, the study used rigorous methodology, including randomization and allocation concealment. Third, the study procedures were optimally standardized in order to reduce performance bias that may have been introduced due to the open nature of this trial. Finally, there were no dropouts, minimizing attrition bias.

### 4.11 Future research

In order to minimize potential for performance bias, blinding of the study hypothesis could be incorporated into a future trial from the study participants, nurses, and research personnel.
Although a pilot study, this study adds preliminary treatment effects to literature suggesting that those who are told to look away may benefit from lower fear. Knowledge of this perceived benefit of one condition over the other could introduce unwanted bias to the study, which should be considered in the study design of a future trial. The study also had a significantly higher number of females compared to males, and therefore, the larger trial should be conducted in a sample that has an equal chance of males or females. Stratifying by sex would allow for an equal balance between men and women, and would negate the unbalance presented from the higher pain and fear experience of women in our study. In addition, the sample size of those who preferred to look was much smaller than those who preferred to look away, which may have under-powered the study to detect a difference between groups for individuals randomized to look. It is recommended that more individuals who have a preference to look be recruited in a future trial.

The population in our trial was university pharmacy students who may have characteristics that distinguish them from the general population (e.g., comfort in healthcare settings, degree of experience with needles), and so, more diversity in a future trial is suggested. The type of procedure is also important to consider. Replication of the trial with other needle procedures such as venipuncture or other vaccination types is also strongly recommended. Future research could also examine if doing something else while looking away (e.g. focusing on a distractor) would augment the effect of this intervention on patient fear and/or pain.
Chapter 5

5 Conclusion

This pilot study suggests that regardless of initial looking preference or sex, telling adults to look away from the needle during vaccination can reduce fear. Alternatively, clinicians can go by the individual’s preference, especially accommodating those who have a strong preference to look away. The results have implications for clinical practice. Simply telling individuals to look away from the needle is an easy, free strategy that requires no training and can help to reduce fear during vaccination. However, given the preliminary nature of the results, we recommend caution interpreting these results and repeating the study using a larger sample size and a different population to further examine the relationship between looking preference and telling individuals to look at versus away from the needle. This is particularly important for individuals who declare a preference to look away and report higher levels of fear. We also recommend further research for the effect of this intervention during other needle procedures.

References


Table 1. Current evidence based recommendations for clinicians to reduce vaccination pain and/or fear in adults.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recommendation</th>
<th>Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strong recommendations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Procedural Interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aspiration</td>
<td>No aspiration during intramuscular vaccine injections\textsuperscript{8,20}</td>
<td>Very low</td>
</tr>
<tr>
<td>Order of injection</td>
<td>Injecting the most painful vaccine last during vaccine injections\textsuperscript{8,19,21}</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Physical Interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positioning: sitting up</td>
<td>Sitting up during vaccination injections\textsuperscript{19}</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Process Interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education of clinicians</td>
<td>Education of clinicians administering vaccine injections about vaccine injection pain management\textsuperscript{22}</td>
<td>Low</td>
</tr>
<tr>
<td>Education of individuals</td>
<td>Education of individuals about pain management for vaccine injection the day of the vaccination\textsuperscript{22}</td>
<td>Very low</td>
</tr>
<tr>
<td>undergoing vaccination</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weak recommendations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physical Interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle tension</td>
<td>Muscle tension for vaccine injections in individuals with a history of fainting</td>
<td>Very low</td>
</tr>
<tr>
<td>Manual tactile stimulation</td>
<td>Do not use manual tactile stimulation during vaccine injections</td>
<td>Very low</td>
</tr>
<tr>
<td>Warming the vaccine</td>
<td>Do not warm the vaccine before vaccine injections</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Pharmacologic Interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical anesthetics</td>
<td>Topical anesthetics before vaccine injections</td>
<td>Very low</td>
</tr>
<tr>
<td>Vapocoolant</td>
<td>Vapocoolant spray before vaccine injections</td>
<td>Low</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Do not give acetaminophen before vaccine injections</td>
<td>Low</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Do not give ibuprofen before vaccine injections</td>
<td>Very low</td>
</tr>
<tr>
<td><strong>Psychological Interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal signal of impending</td>
<td>Give a verbal signal of impending procedure (vs. signal of impending pain)</td>
<td>Very low</td>
</tr>
<tr>
<td>procedure</td>
<td>before vaccine injections</td>
<td></td>
</tr>
<tr>
<td>Distraction</td>
<td>Do not use musical distraction during vaccine injection procedure</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>Do not use visual distraction during vaccine injection procedure</td>
<td>Very low</td>
</tr>
<tr>
<td>Breathing distraction</td>
<td>Breathing interventions (cough, hold-breath) during vaccine injection</td>
<td>Very low</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------------------------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Using suggestion</td>
<td>Do not use a false suggestion during vaccine injections</td>
<td>Low</td>
</tr>
<tr>
<td>Using reassurance</td>
<td>Do not use repeated reassurance during vaccine injections</td>
<td>Very low</td>
</tr>
</tbody>
</table>
Table 2: Summary of included studies.

(i) Laboratory Studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population and Setting</th>
<th>Study Question</th>
<th>Design</th>
<th>Procedure</th>
<th>N</th>
<th>Relevant Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Höfle, M., Hauck, M., Engel, A., &amp; Senkowski, D. (2012). Viewing a needle pricking a hand that you perceive as yours enhances unpleasantness of pain. <em>Pain, 153</em>(5), 1074-1081.</td>
<td>Adults; university lab</td>
<td>Does viewing a needle pricking a hand that is perceived as yours enhance pupil dilation response, unpleasantness and pain ratings?</td>
<td>Random; controlled</td>
<td>Electric stimulation</td>
<td>25</td>
<td>Visual Analogue Scale (0-100) for pain and unpleasantness scores</td>
<td>Viewing an instrument (needle prick or Q-tip) stimulating a hand perceived as own while receiving painful electrical stimuli, leads to enhanced pain intensity ratings ($F[2,48]=31.85, p&lt;0.001$), unpleasantness ratings ($F[2,48]=14.17, p&lt;0.001$), and enhanced PDR (ANS activity; $F[1,24]=84.61, p&lt;0.001$)</td>
</tr>
<tr>
<td>Bufalari, I., Aprile, T., Avenanti, A., Di Russo, F., &amp; Aglioti, S. (2007). Empathy for Pain and Touch in the Human Somatosensory Cortex. <em>Cerebral Cortex, 17</em>(11), 2553-2561.</td>
<td>Adults; university lab</td>
<td>How is somatosensory activity (specifically, the affective-motivational pain component) modulated by a painful stimuli?</td>
<td>Random; controlled</td>
<td>Electric stimuli</td>
<td>18</td>
<td>VAS (0-100) for pain intensity scores and unpleasantness scores</td>
<td>Activations in the cortical areas (P45) that process the affective-motivational pain component were found when participants were shown video clips of needle pricks inflicted upon another person's body. P45 modulation was significantly related to VAS pain intensity ($r=0.52, P=0.03$). The bodily sensation associated with pain was more intense ($t_{17}=7.95, p&lt;0.0001$) and unpleasant ($t_{17}=13.37, p&lt;0.0001$) than the one associated with touch.</td>
</tr>
<tr>
<td>Longo, M.R., Betti, V., Aglioti, S.M., Haggard, P. (2009).</td>
<td>Adults; university lab</td>
<td>Does viewing the body modulate pain perception?</td>
<td>Random, controlled, Cross-over</td>
<td>Infrared laser</td>
<td>30</td>
<td>VAS (0-100) for pain intensity scores and unpleasantness scores</td>
<td>Seeing the hand significantly reduced pain intensity scores ($F[1,14]=9.60, p&lt;0.01$) and unpleasantness scores ($F[1,14]=7.56$, p&lt;0.001)</td>
</tr>
</tbody>
</table>


| Adults; university lab | Does size of hand modulate the perception of pain? | Random, controlled, parallel design, participant-blind | Heat n=9, hand view condition n=9, object-view condition three different mirrors used (convex mirror with 2x reduction; a normal mirror; concave mirror with 2x magnification) The different visual sizes (reduced, actual size, and enlarged) were tested in separate blocks presented in random order. The hand-view and object-view conditions | Pain thresholds 18 | unpleasants scores p<0.02) compared to seeing a neutral object. | Viewing the hand at its actual size produced increased heat-pain thresholds (M = 44.90 °C, SE = 0.98), relative to viewing the object (M = 41.69 °C, SE = 1.07), t(16) = 2.14, p = .048. Visual size modulated pain thresholds when participants saw their hand, F(2, 16) = 10.18, p = .001, ηp² = .56. Visual enlargement of size increased the analgesic effect of viewing the body (p = .032), whereas visual reduction decreased the analgesic effect (p = .043) |
were tested in separate groups of participants.

(ii) Clinical Studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Group</th>
<th>Procedure</th>
<th>Pain</th>
<th>Pain Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vijayan, R., Scott, G., &amp; Brownlie, W. (2014). <em>EJP, 19</em>(1), 97-102.</td>
<td>Adults, Outpatient clinic</td>
<td>Venipuncture</td>
<td>Acute pain (VNRS 1-10); VRS (‘no pain’ to ‘severe pain’)</td>
<td>73% of patients looked away and for this group pain scores were significantly higher (mean VNRS 0.94, <em>p</em> =0.014; VRS 1.61, <em>p</em> = 0.002) than the 27% of individuals that looked away (mean VNRS 0.48, <em>p</em> =0.014; VRS 1.27, <em>p</em> = 0.002)</td>
</tr>
</tbody>
</table>
Table 3. Participant Characteristics (n=160)

<table>
<thead>
<tr>
<th></th>
<th>Prefer to look – look (n=28)</th>
<th>Prefer to look – not look (n=27)</th>
<th>Prefer to not look – look (n=52)</th>
<th>Prefer to not look – not look (n=53)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>23.8 (3.8)</td>
<td>23.7 (2.2)</td>
<td>23.1 (1.8)</td>
<td>23.2 (2.1)</td>
<td>0.487</td>
</tr>
<tr>
<td>Sex, female</td>
<td>14 (50)</td>
<td>17 (63)</td>
<td>38 (73)</td>
<td>37 (70)**</td>
<td>0.194</td>
</tr>
<tr>
<td>Ethnicity, Asian</td>
<td>23 (82)</td>
<td>16 (59)</td>
<td>37 (71)</td>
<td>31 (58)</td>
<td>0.086</td>
</tr>
</tbody>
</table>

Values are mean (standard deviation=SD) or frequency (%).

*Chi square test or ANOVA

**Missing data (n=1)
Table 4. Verbal Numerical Rating Scale* pain scores of males and females

### Males

<table>
<thead>
<tr>
<th></th>
<th>randomized to look</th>
<th>randomized to look away</th>
<th>Row mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>preference to look</td>
<td>(n=14)</td>
<td>(n=10)</td>
<td>(n=24) 2.15 (1.60)</td>
</tr>
<tr>
<td></td>
<td>2.25 (1.72)</td>
<td>2.0 (1.49)</td>
<td></td>
</tr>
<tr>
<td>preference to look</td>
<td>(n=14)</td>
<td>(n=16)</td>
<td>(n=30) 2.32 (1.95)</td>
</tr>
<tr>
<td>away</td>
<td>2.54 (2.10)</td>
<td>2.13 (1.86)</td>
<td></td>
</tr>
<tr>
<td><strong>Column mean (SD)</strong></td>
<td>(n=28)</td>
<td>(n=26)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.39 (1.89)</td>
<td>2.08 (1.70)</td>
<td></td>
</tr>
</tbody>
</table>

### Females

<table>
<thead>
<tr>
<th></th>
<th>randomized to look</th>
<th>randomized to look away</th>
<th>Row mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>preference to look</td>
<td>(n=14)</td>
<td>(n=17)</td>
<td>(n=31) 2.92 (1.66)</td>
</tr>
<tr>
<td></td>
<td>2.71 (1.59)</td>
<td>3.09 (1.75)</td>
<td></td>
</tr>
<tr>
<td>preference to look away</td>
<td>(n=38)</td>
<td>(n=36)</td>
<td>(n=74)</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td></td>
<td>3.75 (1.90)</td>
<td>3.51 (2.17)</td>
<td>3.64 (1.97)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Column mean (SD)</th>
<th>(n=52)</th>
<th>(n=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.47 (1.86)</td>
<td>3.38 (2.04)</td>
</tr>
</tbody>
</table>

Values are mean (standard deviation, SD)

General Linear Model procedure 3-way ANOVA results for pain:

There was a significant main effect of sex \[F(1,155)=12.08, p=0.0007\]; not strata \[F(1,155)=2.57, p=0.111\] or randomization (looking allocation assignment) \[F(1,155)=0.33, p=0.567\]; see text for details.

* Scores range from 0-10 (0=no pain, 10=most pain possible) immediately post-vaccination.
Table 5. Verbal Numerical Rating Scale* fear scores of males and females

<table>
<thead>
<tr>
<th></th>
<th>randomized to look</th>
<th>randomized to look away</th>
<th>Row mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preference to look</td>
<td>(n=14)</td>
<td>(n=10)</td>
<td>(n=24) 1.42</td>
</tr>
<tr>
<td></td>
<td>1.25 (1.01)</td>
<td>1.65 (1.25)</td>
<td>(1.11)</td>
</tr>
<tr>
<td>preference to look</td>
<td>(n=14)</td>
<td>(n=16)</td>
<td>(n=30) 2.02</td>
</tr>
<tr>
<td>away</td>
<td>2.36 (1.69)</td>
<td>1.72 (1.71)</td>
<td>(1.70)</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preference to look</td>
<td>(n=14)</td>
<td>(n=17)</td>
<td>(n=31) 1.65</td>
</tr>
<tr>
<td></td>
<td>1.64 (2.5)</td>
<td>1.65 (1.66)</td>
<td>(2.04)</td>
</tr>
</tbody>
</table>

*Verbal Numerical Rating Scale: 
- Pretest: 0 = no fear, 10 = extreme fear
- Posttest: 0 = no fear, 10 = extreme fear

Note: 'n' represents the number of participants.
<table>
<thead>
<tr>
<th>preference to look away</th>
<th>(n=38)</th>
<th>(n=36)</th>
<th>(n=74) 3.27</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.97 (2.65)</td>
<td>2.53 (2.34)</td>
<td>(2.59)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Column mean (SD)</th>
<th>(n=52)</th>
<th>(n=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.35 (2.79)</td>
<td>2.25 (2.17)</td>
</tr>
</tbody>
</table>

Values are mean (standard deviation, SD)

General Linear Model procedure 3-way ANOVA results for fear:

There was a significant main effect for sex \([F(1,155)=5.78, p=0.017]\), strata (looking preference) \([F(1,155)=11.79, p=0.0008]\) and randomization (looking allocation assignment) \([F(1,155)=5.14, p=0.025]\); see text for details.

* Scores range from 0-10 (0=no fear, 10=most fear possible) immediately post-vaccination.
Figures

**Figure 1.** CONSORT Participant Flow Diagram

1. **Enrollment**
   - Agreed to participate (n = 184)
     - Excluded (n = 24)
       - no shows, withdrawn
     - Participants included (n = 160)

2. **Initial Preference/Strata**
   - Preference to look away (n = 105)
   - Preference to look (n = 55)

3. **Allocation**
   - Look (n = 52)
   - Look away (n = 53)
   - Look (n = 28)
   - Look away (n = 27)

4. **Analysis**
   - Analysed (n = 52)
   - Analysed (n = 52)
   - Analysed (n = 28)
   - Analysed (n = 27)

   Data missing (n = 1)
Appendices

Appendix 1. Study approval letter from the University of Toronto Research Ethics Board

PROTOCOL REFERENCE # 33392

September 29, 2016

Dr. Anna Taddio
FACULTY OF PHARMACY

Ms. Priyajali Mithal
FACULTY OF PHARMACY

Dear Dr. Taddio and Ms. Priyajali Mithal,

Re: Your research protocol entitled, "To look or not to look? Pilot study of the effectiveness of a simple psychological intervention in reducing vaccination pain and fear in adults"

ETHICS APPROVAL

Original Approval Date: September 29, 2016
Expiry Date: September 28, 2017
Continuing Review Level: 1

We are writing to advise you that the Health Sciences Research Ethics Board (REB) has granted approval to the above-named research protocol under the REB's delegated review process. Your protocol has been approved for a period of one year and ongoing research under this protocol must be renewed prior to the expiry date.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events in the research should be reported to the Research Oversight and Compliance Office - Human Research Ethics Program as soon as possible.

Please ensure that you submit an Ethics Renewal Form or a Study Completion/Closure Report 15 to 30 days prior to the expiry date of your current ethics approval. Note that ethics renewals for studies cannot be accepted more than 30 days prior to the date of expiry.

If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Please note, all approved research studies are eligible for a routine Post-Approval Review (PAR) site visit. If chosen, you will receive a notification letter from our office. For information on PAR, please see http://www.research.utoronto.ca/wp-content/uploads/documents/2014/09/PAR-Program-Description_1.pdf.

Best wishes for the successful completion of your research.

Yours sincerely,

Elizabeth Peter, Ph.D.
REB Chair
Appendix 2. Study renewal approval letter from the University of Toronto Research Ethics Board

PROTOCOL REFERENCE # 33392

September 19, 2017

Dr. Anna Taddio
FACULTY OF PHARMACY

Ms. Priyanjali Mithal
FACULTY OF PHARMACY

Dear Dr. Taddio and Ms. Priyanjali Mithal,

Re: Your research protocol entitled, "To look or not to look? Pilot study of the effectiveness of a simple psychological intervention in reducing vaccination pain and fear in adults"

ETHICS APPROVAL

Original Approval Date: September 29, 2016
Expiry Date: September 28, 2018
Continuing Review Level: 1
Renewal: Data Analysis Only

We are writing to advise you that you have been granted annual renewal of ethics approval to the above-referenced research protocol through the Research Ethics Board (REB) delegated process. Please note that all protocols involving ongoing data collection or interaction with human participants are subject to re-evaluation after 5 years. Ongoing research under this protocol must be renewed prior to the expiry date.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events should be reported to the Research Oversight and Compliance - Human Research Ethics Program as soon as possible. If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Please ensure that you submit an Ethics Renewal Form or a Study Completion/Closure Report 15 to 30 days prior to the expiry date of your protocol. Note that ethics renewals for studies cannot be accepted more than 30 days prior to the date of expiry as per our guidelines.

Please note, all approved research studies are eligible for a routine Post-Approval Review (PAR) site visit. If chosen, you will receive a notification letter from our office. For information on PAR, please see http://www.research.utoronto.ca/wp-content/uploads/documents/2014/09/PAR-Program-Description-1.pdf.

Best wishes for the successful completion of your research.

Yours sincerely,

Elizabeth Peter, Ph.D.
REB Chair
Appendix 3. Case Record Form

## Appendix B: Case Record Form

To Look or Not to Look? Pilot Study of the Effectiveness of a Simple Psychological Intervention for Reducing Vaccination Pain and Fear in Adults

Subject ID: ___________ RA completing form: ___________ Date: ___________

### CASE RECORD FORM

Return form to: Dr. Anna Taddio c/o Ms. Priyanjali Mithal, Leslie Dan Faculty of Pharmacy, University of Toronto
Room: 745-144 College St, Toronto, ON M5S 3M2, Tel: 416-735-2693, E-mail: priyanjali.mithal@utoronto.ca

1) Participant Demographics

<table>
<thead>
<tr>
<th>UofT Student</th>
<th>Yes □</th>
<th>No □</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male □</td>
<td>Female □</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian</td>
<td>Origins in Europe, Middle East, North Africa (Arabic origins), Western Russia including Afghanistan and South Russia and Hispanics of European origin.</td>
</tr>
<tr>
<td>Do you have any chronic conditions involving regular needle procedures e.g. diabetes, rheumatoid arthritis?</td>
<td>Yes □</td>
<td>No □</td>
</tr>
<tr>
<td>If Yes, Explain:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How much do you agree with the statement &quot;I am a person who worries a lot&quot;, where 0 = no/strongly disagree/not like me at all; 10 = yes/strongly agree/totally like me?</td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
<td></td>
</tr>
<tr>
<td>When getting injections, do you usually prefer to look at or look away from the needle?</td>
<td>Looker □</td>
<td>Non-Looker □</td>
</tr>
<tr>
<td>When getting injections, how likely are you to look at or</td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
<td></td>
</tr>
<tr>
<td>Question</td>
<td>Response Options</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>look away from the needle, where 0=do not want to look at all; 10 = want to look for the entire procedure?</td>
<td>Looker □  Non-Looker □</td>
<td></td>
</tr>
<tr>
<td>If given only two options, to look or not look, what would you choose?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I want you to think about needles in general. How scared/afraid are you of needles on a scale of 0-10, where 0 is no fear and 10 is the most fear possible?</td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
<td></td>
</tr>
<tr>
<td>Do you have a parent with high needle fear?</td>
<td>Yes □  No □  Not sure □</td>
<td></td>
</tr>
<tr>
<td>Specify:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you taken any pain relievers (acetaminophen or ibuprofen) or sedatives in the last 24 hours?</td>
<td>Yes □  No □</td>
<td></td>
</tr>
<tr>
<td>If Yes: Name of Drug: ___________________ Dosage: ___________ Time Taken: ______</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you taken any pain relievers for today's needle?</td>
<td>Yes □  No □</td>
<td></td>
</tr>
<tr>
<td>Specify:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2) Baseline Measures

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>On a scale of 0 to 10, where 0 is no pain, and 10 is the most pain possible, how would you rate your pain now, before the needle?</td>
<td>Pain Evaluation (Verbal Numerical Rating Scale) - BEFORE Randomization NRS</td>
</tr>
<tr>
<td></td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
</tr>
<tr>
<td>On a scale of 0-10, where 0 is no fear and 10 is the most fear possible, how fearful are you about getting the needle now, before the needle?</td>
<td>Fear Evaluation (Verbal Numerical Rating Scale) - BEFORE Randomization NRS</td>
</tr>
<tr>
<td></td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
</tr>
</tbody>
</table>

3) Post-assignment Measures

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Assignment</td>
<td>Looker – Look at the Needle □  Non-Looker – Look at the Needle □</td>
</tr>
<tr>
<td>Looker – Look away from the Needle □  Non-Looker – Look away from the Needle</td>
<td></td>
</tr>
<tr>
<td>On a scale of 0 to 10, where 0 is no pain, and 10 is the most pain possible, how would you rate your pain now, before the needle?</td>
<td>Pain Evaluation (Verbal Numerical Rating Scale) - BEFORE Vaccination NRS</td>
</tr>
<tr>
<td></td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
</tr>
<tr>
<td>On a scale of 0-10, where 0 is no fear and 10 is the most fear possible, how fearful are you</td>
<td>Fear Evaluation (Verbal Numerical Rating Scale) - BEFORE Vaccination NRS</td>
</tr>
<tr>
<td></td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10</td>
</tr>
</tbody>
</table>

UT HREP – Application Form for Supervised/Sponsored Research
12 Queen's Park Crescent West – McMurrich Building, 2nd floor
Version Date: September 19, 2016
about getting the needle now, before the needle?

4) Post-vaccination Measures

<table>
<thead>
<tr>
<th>Name of Immunizer:</th>
<th>Was the participant compliant with the study instructions?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes ☐ No ☐</td>
</tr>
<tr>
<td>Explain</td>
<td></td>
</tr>
</tbody>
</table>

On a scale of 0 to 10, where 0 is no pain, and 10 is the most pain possible, how would you rate your pain during the needle?

Pain Evaluation (Verbal Numerical Rating Scale - AFTER Vaccination) NRS

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

On a scale of 0-10, where 0 is no fear and 10 is the most fear possible, how fearful were you during the needle?

Fear Evaluation (Verbal Numerical Rating Scale - AFTER Vaccination) NRS

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

Where did you look during the needle?

________________________________________________________________________________________

________________________________________________________________________________________

Describe what you focused on during the needle.

________________________________________________________________________________________

________________________________________________________________________________________

What were you thinking about during the needle?

________________________________________________________________________________________

________________________________________________________________________________________

Did you want more direction for what to do during the needle? (e.g., if you looked away, did you want the nurse to tell you what to look at or what to do?)

________________________________________________________________________________________

________________________________________________________________________________________

Did you find it difficult to do what you were asked? e.g., if you wanted to look away but weren’t allowed? If non-compliant, what were your reasons for failing to be compliant to the intervention?

________________________________________________________________________________________

________________________________________________________________________________________

What would you prefer to do for your future vaccinations?

☐ Look at the needle
☐ Look away from the needle
☐ Not sure
Do you have any other comments/feedback about the study?


Did the participant complete the study? If not, please indicate reason for non-completion/withdrawal.


Does the RA have any relevant comments/feedback about this particular participant/appointment? Please indicate.


TIME OF COMPLETION

____________________ AM / PM
Appendix 4. Consent form

Appendix C: Consent Form

To Look or Not to Look? Pilot Study of Effectiveness of a Simple Psychological Intervention in Reducing Vaccination Pain and Fear in Adults

Investigators
Ms. Priyanjali Mittal, BSc, MSc Cand, University of Toronto
Dr. Anna Taddio, PhD, University of Toronto
Dr. Rebecca Pillai Riddell, PhD, York University
Dr. Meghan McMurtry, PhD, University of Guelph
Ms. Pamela Simmons, Health & Wellness Centre, University of Toronto
Dr. Lisa Burry, BScPharm, PharmD, Mount Sinai Hospital

You are being asked to take part in a research study. Please read this explanation about the study and its risks and benefits before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish. Participation in this study is voluntary.

Background and Purpose of this Research:
It is common for people to advise individuals undergoing vaccination to “look away from the needle” to make them hurt less and be less scary. However, this advice is not backed up by research evidence. The purpose of this study is learn about how looking away vs. looking at the needle during vaccination makes people feel.

Description of the Research:
We will include University of Toronto undergraduate and graduate students in the Leslie Dan Faculty of Pharmacy who are getting vaccinated with the flu vaccine at the UofT Health and Wellness Centre. Altogether, 160 individuals will participate.

The nurse will give the injection as per usual practices. The only difference is that you will be advised to either look away from the needle or look at the needle during the injection. Whether you are asked to look away or look at the needle will be determined by chance, like flipping a coin. You will be asked questions about the amount of pain and fear you experienced during vaccination and your preferences to look away vs. look at the needle.

Potential Risks/Inconveniences:
There may be some inconvenience due to the time required to answer questions. This is estimated to add 10-15 minutes to your visit. Vaccination is associated with a risk of side effects such as local skin reactions and fever. These risks are not changed by participation in the study. There may be social risks related to knowledge of an individual’s participation in the study. This risk is being minimized by booking individual appointments and a separate entrance/treatment area for vaccination for study participants. It may be possible, however, that you will see someone you know accessing the clinic or may speak to each other about participation when signing up for the study. Participants will be asked to refrain from sharing any information about the study or study procedures.

Version Date: September 19, 2016
Potential Benefits:
The results may help us to learn about how to make vaccinations less painful and fearful. Students may benefit from a less painful flu vaccine injection. Students may benefit from learning about techniques being used by staff at the Health and Wellness Centre for giving vaccinations.

Alternatives to Participation:
The alternatives to participation are getting your flu vaccination without being asked to look at or away from the needle and not answering questions about your level of pain and fear.

Confidentiality
Personal Health Information
If you agree to participate in the study, you will be asked to provide some basic information about yourself. Personal health information is any information that could be used to identify you and includes: age, sex, ethnicity, past pain experiences including questions about chronic illnesses, exposure to needles and medication.

The study investigator will keep the information that is collected for the study in a locked and secure area for 7 years. Only the research team will be allowed to look at the records. The representatives of the University of Toronto Research Ethics Board (REB) may come to the research lab to look at the study records to ensure that the information collected for the study is correct and check that the study followed proper laws and guidelines. The REB is a group of people who oversee the ethical conduct of research studies.

All information collected during this study, including personal information, will be kept confidential and will not be shared with anyone outside the study unless required by law. You will not be named in any reports, publications, or presentations that may come from this study. If you decide to leave the study, you can request for the information that was collected about you to be removed up until the data is analyzed. After that point, your data may not be removed from the analysis. No new information will be collected about you without your permission.

Study Results
You may be informed about the results of the research study after the completion of the study upon your request. If interested, please write down your email address below:

Compensation for Injury
We do not anticipate any harm to you by participating in the study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities. You do not give up any of your legal rights to withdraw at any time by signing this consent form.

Expenses and Reimbursements
You will receive a $10 gift card as a token of our appreciation. There is no direct cost involved in participating. If you choose to withdraw from the study on the day of the appointment, please note that you will not be provided with the gift card.

Conflict of Interest
The research team members have no conflict of interest to declare.

Voluntary Participation
Your participation in research is voluntary. You may decide not to be in this study, or to be in the study now and change your mind later. If you choose not to participate, it will not impact you. If you choose to participate in this study you can withdraw from the study at any time up to the point that data is analyzed, after which you may no longer withdraw.
no way will participating or not participating impact your status as a student in the faculty. Your name will not be released to anyone. The results will be included aggregated data only.

Questions about the Study
If you have any questions, concerns or would like to speak to the study team for any reason, please call: Dr. Anna Taddio at # 416-813-6235 or anna.taddio@utoronto.ca.
If you have any questions about your rights as a research participant or have concerns about this study, call the Research Ethics office number at 416-946-3389. Everything that you discuss will be kept confidential.

Consent:
By signing this form, I agree that:
1) You have explained this study to me. You have answered all my questions.
2) You have explained the possible harms and benefits (if any) of this study.
3) I know what I could do instead of taking part in this study. I understand that I have the right not to take part in the study and the right to stop at any time. My decision about taking part in the study will not affect my health care at the UofT Health and Wellness Centre.
4) I am free now to ask questions about the study.
5) I have been told that my medical information will be kept private except as described to me.
6) I understand that no information about who I am will be given to anyone or be published without first asking my permission.
7) I have read and understood pages 1 to 3 of this consent form. I agree, or consent, to take part in this study.

__________________________  ____________________________  ______________  __________
Print Study Participant’s Name   Signature        Date           Time

__________________________  ____________________________  ______________  __________
Print Name of Person Obtaining Consent   Signature        Date           Time

I do not consent to participating in this study. However, I consent to providing information to investigators about myself (age, sex, and reason for refusal). This information is being used to ensure that the characteristics of participating individuals do not differ from non-participating individuals.

__________________________  ____________________________  ______________
Print Study Participant’s Name   Signature        Date

__________________________  ____________________________  ______________
Print Name of Person Obtaining Consent   Signature        Date
Appendix 5. Study advertisement poster

When getting needles, do you:

Look at it  OR  Look away?

Have you ever wondered if one way is better than the other?
Pain researchers at UofT have too!

If you are over 18 years old, and a UofT undergraduate or graduate student in the Leslie Dan Faculty of Pharmacy, you are eligible to participate in our study at the UofT Health and Wellness Centre. Get your flu vaccination and tell us how much it hurts.

You will receive a $10 gift card as a token of appreciation for your time (10-15 minutes)!

Information from this research study will be used to help make injections less painful.
Appendix E: Email Recruitment Script

Email script for undergraduate and graduate students:

“Do you usually look at or look away from needles when getting injections? Have you wondered if one way is better than the other? Researchers at the Leslie Dan Faculty of Pharmacy are studying this question so that immunizers can have more tools available to them to make needles hurt less. If you are over 18 years old, and a UofT undergraduate or graduate student in the Leslie Dan Faculty of Pharmacy, you are eligible to participate in our study at the UofT Health and Wellness Centre. Get your flu vaccination and tell us how much it hurts. You will receive a $10 gift card as a token of appreciation for your time (10-15 minutes)! Please contact Pri Mithal at [contact info] or by email at [email address]"
Appendix 7. Study information sheet for interested participants inquiring over e-mail

Thank you for inquiring about our study entitled: “To Look or Not to Look? Pilot Study of the Effectiveness of a Simple Psychological Intervention for Reducing Vaccination Pain and Fear in Adults”!

Below please find some Q&A about the study.

**What is the purpose of the study?**
We are testing whether looking at the needle vs. looking away from the needle affects pain and fear during flu vaccine injection.

**Why are we doing the study?**
We are trying to find ways to make needles less painful!

**What will happen?**
A nurse will be giving you your vaccine injection, as per usual methods. The only difference is that you will be asked to either look at the needle during the injection or look away from the needle during the injection. The group you are in will be determined by chance, like flipping a coin. You will be asked questions about your pain and fear experience. To thank you for your time and participation, you will be given a $10 gift card!

**Where is the study taking place?**
The study is happening at the UofT Health and Wellness Centre (where the UofT Bookstore is located). It is located at 214 College Street (2nd floor), at the northwest corner of St. George St. and College St. This is less than a 5-minute walk from the Leslie Dan Pharmacy Building.

**When will the study happen?**
Flu clinics are being scheduled for the study at the Health and Wellness Centre from October 24, 2016 to October 31, 2016 (not including Friday, October the 28th). These clinics will be open from 9-12:30 and 1-4:30pm on Monday and Thursday, [AND] 9-12:30 and 1-6:30pm on Tuesday and Wednesday.
**Please note:** If you do not get in for these time slots, additional time slots may be available at a later date and you will be put on a waiting list. You will be informed about this.**

A copy of the consent form is attached to this message. Read it over and if you are interested in participating, call/text the study coordinator at (416) 735-2693 to coordinate a meet up at the pharmacy building and/or come talk to us in person at the Leslie Dan Pharmacy Building main lobby (we will have a table set up there to answer questions and sign people up for the study). If you sign up, we will schedule your appointment time then.

We look forward to seeing you!

Yours sincerely,

Priyanjali Mithal
Study Coordinator, MSc Cand.
Leslie Dan Faculty of Pharmacy
Department of Pharmaceutical Sciences
University of Toronto
Appendix 8. Blurb posted on Leslie Dan Faculty of Pharmacy monitors in lobby
Appendix 9. Email confirmation sent out to individuals who signed up for study

Hi [Name of Participant],

Thank you for signing up for our study entitled “To Look or Not to Look? Pilot Study of the Effectiveness of a Simple Psychological Intervention for Reducing Vaccination Pain and Fear in Adults”!

We look forward to seeing you at your flu vaccination. The date and time for your flu vaccination appointment is [Appointment Date and Time] at the UofT Health and Wellness Centre (located in the Bookstore building) at 214 College St, on the 2nd floor.

Directions from Leslie Dan Faculty of Pharmacy (5 minute walk):
When you exit the Leslie Dan building, turn right on College St and walk west until you reach St. George St. Cross the street at St. George and walk north on St. George until you see a wheelchair ramp. Enter the building there and take the stairs on the left to the 2nd floor to the Health and Wellness Clinic. Alternatively, you can take the elevators located on the right after entering the building.

Tips to make your appointment go smoothly!
- If you are not already a Health and Wellness Centre member, give yourself about 30 minutes to sign up at the front desk. **Please bring your T-card, Health Card and insurance information. ** If you are already a member, please arrive 15 minutes before your appointment.
- Wear clothing which allows access to your arm for the needle (e.g., a short sleeved t-shirt).

We look forward to seeing you there!

Priyanjali Mithal
Study Coordinator

----------------------------------
MSc Cand., Taddio Lab
Leslie Dan Faculty of Pharmacy
Department of Pharmaceutical Sciences
University of Toronto