Prospective abuse and intimate partner violence surgical evaluation (PRAISE-2 pilot): Statistical analysis plan for a pilot prospective cohort study

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ABSTRACT

Background. Intimate partner violence (IPV) is a prevalent social issue that affects the health and well-being of women globally. In orthopaedics, the prevalence of women who have experienced abuse in the past year is as high as 1 in 6. PRAISE-2 is a multi-centre pilot prospective cohort study of 250 women with musculoskeletal injuries to determine how IPV experiences affect injury-related outcomes, and how patterns of IPV change over a 12 month period of time following a musculoskeletal injury. The current report is a description of the statistical analysis plan for the PRAISE-2 pilot study.

Methods. This study is a pilot multicentre prospective cohort study to primarily assess feasibility of our recruitment, retention and data collection strategies, and to collect preliminary data on orthopaedic outcomes after experiencing IPV, as well as changes in IPV patterns following an injury. Included participants will be adult females presenting to participating fracture clinics for a fracture and/or dislocation requiring orthopaedic care. Participants will be followed for one year. The primary analysis will be descriptive. We will report recruitment, missed visits, out of window visits, participant completion data, and completed form data as counts and percentages with 95% confidence intervals. Based on the primary analyses, we will report whether the feasibility criteria have been met, and recommend modifications to the protocol for any planned definitive studies, if needed. All secondary (clinical) analyses are exploratory.

Discussion. In order for surgeons to be as effective as possible in assisting and advocating for women who have experienced abuse, we need more information on how IPV experiences are associated with musculoskeletal outcomes. Both the feasibility and clinical information gained from this pilot study will be instrumental in informing future observational and interventional IPV studies. By reporting our statistical analysis plan before the study ends, we hope to improve the transparency, integrity, and reproducibility of our study findings.

Trial registration. This study is registered on clinicaltrials.gov NCT02529267 on 20 August 2015, before the first participant was enrolled

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INTRODUCTION

Intimate partner violence (IPV) is a prevalent social issue that affects the health and well-being of women globally. In orthopaedics, the prevalence of women who have experienced abuse in the past year is as high as 1 in 6 (PRAISE Investigators, 2013). Additionally, this prevalence is higher than the prevalence in some other specialties, and is second only to addiction recovery clinics (PRAISE Investigators, 2013; PRAISE Investigators, 2011). Orthopaedic surgeons now recognize that they have an opportunity to identify and assist women in abusive relationships in hopes of preventing further abuse (COA, 2017; AAOS, 2013). In order for surgeons to be as effective as possible in assisting and advocating for women who have experienced abuse, we need more information on how IPV experiences are associated with musculoskeletal outcomes.

PRAISE-2 is a multi-centre pilot prospective cohort study of 250 women with musculoskeletal injuries to determine how IPV experiences affect injury-related outcomes, and how patterns of IPV change over a 12 month period of time following a musculoskeletal injury. The PRAISE-2 pilot study aims to evaluate the feasibility of a larger multi-national prospective cohort study of women presenting to fracture clinics with musculoskeletal injuries, and to obtain preliminary estimates of change in type/severity of IPV and cases of new abuse among injured women.

Both the feasibility and clinical information gained from this pilot study will be instrumental in informing future observational and interventional IPV studies.

METHODS

Study Design

This study is a pilot multicentre prospective cohort study to primarily assess feasibility of our recruitment, retention and data collection strategies, and to collect preliminary data on orthopaedic outcomes after experiencing IPV, as well as changes in IPV patterns following an injury. The protocol is registered on clinicaltrials.gov (NCT02529267) and the full detailed protocol is available from *Pilot and Feasibility Studies* (PRAISE-2 Investigators, 2018). We have secured approval from the Hamilton Integrated Research Ethics Board (project # 15-383) and each participating clinical site's ethics board. All participants signed a written informed consent form prior to participating.

Sample Size

Based on the statistic that 1 in 50 women present to fracture clinics because of an IPV-related injury (PRAISE Investigators, 2013), we aim to recruit 50 women at each of 5 sites (250 total). We determined *a priori* that the study will be feasible if loss to follow-up is less than 15% and adherence to study windows is 75% or greater. We believe that our loss to follow-up will be about 10%, therefore using the confidence interval approach suggested by Thabane et al. (2010) we require 214 patients to achieve a 5% margin of error (which will generate a confidence interval that excludes 15%). We believe that the adherence to study windows will be over 80%, therefore we require 214 patients to achieve a 6% margin of error (which will generate a confidence interval that excludes 75%). Therefore, 250 participants will be sufficient to assess our feasibility outcomes.

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Timing of Outcome Assessments

We will follow patients for 12 months after their injury and measure all study outcomes at 1 month, 3 months, 6 months, and 12 months post-injury. Investigators have 6 weeks to enroll a participant after her injury, so the 1-month visit is optional for participants whose injury occurred between 4 and 6 weeks before enrollment. Acceptable visit windows are defined as 0-6 weeks post-injury for baseline, 2-6 weeks for the 1 month visit, 11-15 weeks for the 3 month visit, 24-28 weeks for the 6 month visit, and 48-56 weeks for the 12 month visit.

STUDY POPULATION

Included participants will be adult females presenting to participating fracture clinics for a fracture and/or dislocation requiring orthopaedic care. Patients must be able and willing to provide written consent and they must be able to complete the questionnaires in a private location. We will collect and report the number of patients who are excluded or withdraw from the study, as well as their reasons for doing so in a CONSORT-type participant flow diagram. We will also summarize key baseline demographic and injury characteristics.

STATISTICAL PRINCIPLES

All secondary (clinical) analyses are exploratory as this is a pilot study which is insufficiently powered to definitively answer the secondary research questions. We will therefore not present p values when making comparisons. All confidence intervals that are reported will be 95% confidence intervals. We do not intend to make any adjustments for multiplicity, and we do not plan to impute for missing data in this pilot study. We do not plan to conduct any subgroup analyses.

ANALYSES

Primary Analyses

Primary Outcome

The primary outcome of the pilot study is feasibility. This includes four major components of feasibility:

1. Number of patients recruited at each site during a 12-month period
2. Percentage of missed and out of window visits
3. Percentage of included patients followed at 12 months for the primary and secondary outcomes
4. The percentage of case report forms, including patient questionnaires, completed at 12 months.

Analysis Plan – Primary

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The primary analysis will be descriptive. We will report recruitment, missed visits, out of window visits, participant completion data, and completed form data as counts and percentages with 95% confidence intervals (**Tables 1 and 2**).

Based on the primary analyses, we will report whether the feasibility criteria have been met, and recommend modifications to the protocol for any planned definitive studies, if needed.

2.4 Feasibility Criteria

We have set the following criteria for feasibility:

1. Recruitment – Each site should recruit 50 participants in 12 months or less
2. Adherence to visit windows – 75% of visits within defined windows
3. Participant retention – Loss to follow-up should remain under 15%
4. Data completeness - Questionnaire completion should remain over 80%

Table 1: Feasibility outcomes

Site	# Recruited in 12 Months	Time to Reach Target*	Missed Visits/Total Visits (%; 95% CI)	Out of Window Visits/Total Visits (%; 95% CI	Completed Participants/Total Participants (%; 95% CI
Hamilton					
Toronto					
Calgary					
Deventer					
Barcelona					
Helsinki					

*Target at each site is 50 participants except Barcelona and Helsinki (25 each)

Table 2: Percentage (and 95% CI) of completed forms at each visit

Form/ Questionnaire	Baseline	1 Month*	3 Month	6 Month	12 Month
Demographics					
IPV Status					
Return to Function					
EQ-5D					
Support Service Use					
Stages of Change					
Complications/SAEs					

*The 1-month visit is optional for participants whose injury occurred between 4 and 6 weeks before enrollment

Secondary Analyses

PRAISE-2 Secondary Outcomes

Secondary outcomes for the pilot study are the planned clinical outcomes of the definitive study including:

1. Injury-related complications

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2. Return to pre-injury function
3. Incident cases of IPV
4. Utilization and associated costs of health, legal, and social support services
5. Changes in abuse severity and type of abuse
6. Health-related quality of life (EQ-5D)
7. Stage of change (Domestic Violence Survivor Assessment)

Secondary Analyses

When referring to comparisons across groups by IPV status, the groups will be determined using the PRAISE method (PRAISE Investigators, 2013). A participant will be considered to have disclosed IPV if she answers positively to at least one of the three direct screening questions.

Injury-related complications

We will present the percentage of patients with injury-related complications descriptively (**Table 3**) by group (experienced IPV versus not). We will compare across groups using binary logistic regression. The dependent variable will be whether the participant experienced one or more injury-related complications (binary). Independent variables will include past 12 month IPV status (binary), age (continuous), type of injury (open fracture, closed fracture, dislocation), location of injury (upper extremity, lower extremity, other), and location (Canada vs. Europe). We will report odds ratios with 95% CIs (**Table 4**).

Table 3: Injury-related complications by IPV status

Complication Type	**Past 12 months**		**Lifetime**	
	IPV	**No IPV**	**IPV**	**No IPV**
Complication 1				
Complication 2				
Complication 3				
…				

Table 4: Binary logistic regression of selected demographic characteristics on injury-related complications

Factor	**Odds ratio**	**95% CI**
IPV in past 12 months		
Age (10-year increments)		
Type of injury Open fracture Closed fracture Dislocation		
Location of injury Upper extremity Lower extremity Other		
Location Canada Europe		

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Return to pre-injury function

We will report the cumulative percentage of patients achieving return to pre-injury level of function in each group at baseline, 1 month, 3 months, 6 months, and 12 months with 95% CI (**Table 5)**. Return to function will be defined as the participant reporting "I have returned to all of my responsibilities" for at least two of return to work, return to leisure, and return to home responsibilities. We will compare across groups using binary logistic regression. The dependent variable will be whether the participant achieved return to function by 12 months (binary). Independent variables will include past 12 month IPV status (binary), age (continuous), type of injury (open fracture, closed fracture, dislocation), location of injury (upper extremity, lower extremity, other), and location (Canada vs. Europe). We will report odds ratios with 95% CIs (**Table 6**).

Table 5: Cumulative return to function

Visit	**Percentage (and 95% CI) returned to function**		
	IPV in past year	**No IPV in past year**	**Total**
Baseline			
1 month*			
3 months			
6 months			
12 months			

* The 1-month visit is optional for participants whose injury occurred between 4 and 6 weeks before enrollment

Table 6: Binary logistic regression of selected demographic characteristics on return to function

Factor	**Odds ratio**	**95% CI**
IPV in past 12 months		
Age (10-year increments)		
Type of injury Open fracture Closed fracture Dislocation		
Location of injury Upper extremity Lower extremity Other		
Location Canada Europe		

Incident cases of IPV

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We will report the incidence of new IPV cases reported within the 12-month study period with 95% CI. The numerator will be the number of new IPV cases and the denominator will be the total population at risk (i.e. total sample size excluding number of non-abused women at baseline).

Utilization and associated costs of health, legal, and social support services

We will report percentages of women using each service per IPV group over 12 months and the median number of times that participants used each service with Quartiles 1 and 3 (Q1-Q3) (**Table 7**). Direct costs will be derived by assigning costs to adjudicated injury-related complications and self-reported utilization of health care services, based on provincial case costing registries and health care provider benefit schedules[6]. All remaining direct costs will be estimated by multiplying self-reported quantities of utilization (e.g., visits to social worker, use of mental health services) by the unit cost of service, based on provincial or national average charges. Indirect costs will be calculated using self-reported annual income and return to function. Costs will be presented as means with 95% CIs, and histograms. Due to the non-normality of cost data, non-parametric bootstrap estimates will be used to present the difference in mean costs between those with and without a history of IPV. Multivariable sensitivity analysis will be conducted by using 95% CI and reported cost ranges for input parameters. All costs will be inflated to 2018 Canadian dollars using the appropriate prices indices. (**Table 8**)

Table 7: Support service use

Support service type	**IPV past 12 months**		**No IPV past 12 months**	
	number using the service (%; 95% CI)	median times (Q1-Q3)	number using the service (%; 95% CI)	median times (Q1-Q3)
Primary care physician				
Emergency department				
Physiotherapist				
…				

Table 8: Economic analyses

Cost Category	**IPV past 12 months**	**No IPV past 12 months**	**Difference in 1 year mean* costs**
	Mean* cost ($)	Mean* cost ($)	($)
Direct costs			
Injury-related complications			
Utilization of health-care/services			
Indirect costs			
Time off work/loss of income			
Total			

*We will use median cost (and Q1-Q3) if the data are skewed

Changes in abuse severity and type of abuse

We will graphically present the proportion of patients who experienced no abuse, a stable level of abuse, escalating abuse, and de-escalating abuse over 12 months with 95% CI.

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Health-related quality of life (EQ-5D)

We will report the mean change in HRQL from baseline to the 1-month, 3-month, 6-month, and 12-month visits by group with 95% CI (**Table 9)**. We will also estimate utility, which will be modelled over the course of 1-year follow-up, using 3, 6 and 12 month EQ-5D scores and standard trapezoidal rules (CADTH, 2015). Utility will be presented as quality adjusted life years (QALYs) for each group, with 95% CI, where 1 represents full health and 0 represents death. The difference between each group will be presented as QALYs lost with 95% CI.

Table 9: Health related quality of life

Visit	Mean HRQL change from baseline (95% CI)		
	IPV in past year	No IPV in past year	Total
1-month*			
3-months			
6-months			
12-months			

* The 1-month visit is optional for participants whose injury occurred between 4 and 6 weeks before enrollment

Stage of change (Domestic Violence Survivor Assessment)

This analysis will only include participants who report that their current relationship is or was abusive. We will report the percentage of participants in each stage of change at each visit (**Table 10**). We will also report the percentage of participants who move forward through the stages of change, move backward, or stay at the same stage at 1-month, 3-months, 6-months, 9-months, and 12-months compared to baseline (**Table 11**).

Table 10: Percentage (95% CI) of participants at each stage of change by visit

Stage of change	Baseline	1 month*	3 months	6 months	12 months
Precontemplation					
Contemplation					
Preparation					
Action					
Maintenance					

* The 1-month visit is optional for participants whose injury occurred between 4 and 6 weeks before enrollment

Table 11: Percentage (95% CI) of participants who moved through the stages of change by visit

Visit	Stayed the same	Moved forward	Moved backward
1 month*			
3 months			
6 months			
12 months			

* The 1-month visit is optional for participants whose injury occurred between 4 and 6 weeks before enrollment

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COMPETING INTERESTS

The authors declare that they have no competing interests

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AUTHOR CONTRIBUTIONS

KM and MB designed the study. All authors provided critical refinements to the study design and/or statistical analysis plan. KM drafted the manuscript and all authors made critical revisions. All authors read and approved the final manuscript.

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