Research Protocol

**(GREATER THAN LOW RISK (GTLR) / NON CLINICAL TRIAL)**

**Protocol Title:** Educational intervention related to nursing care of haemophilia patients

**Version number and date:** v1, 23 Aug 2023

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| **Protocol Number** |  |
| **Study Title** | Educational intervention related to nursing care of haemophilia patients |
| **Coordinating Principal Investigator** | Dr. Mark Elkins |
| **Signature:**  | Date:  |
|  | 23 Aug 2023 |
| **Protocol Authors (Co-investigators)** | Mr. Miles Kenny  |

**Ethics Statement:**

The study will be conducted in accordance with the *National Statement on Ethical Conduct in Human Research* (2007) ([Link to National Statement](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018)) , the *CPMP/ICH Note for Guidance on Good Clinical Practice* ([Link to CPMP/ICH](https://www.tga.gov.au/publication/note-guidance-good-clinical-practice-july-2000) ) and consistent with the principles that have their origin in the Declaration of Helsinki. Compliance with these standards provides assurance that the rights, safety and well-being of trial participants are respected.

# SUMMARY

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| **Protocol Title** | Educational intervention related to nursing care of haemophilia patients |
|  **Objectives** | Primary objective:* To measure the effect of an educational intervention in enhancing nursing competence when caring for patients with haemophilia

Secondary objective:* To measure the effect of an educational intervention in enhancing nursing confidence when caring for patients with haemophilia
 |
| **Study design** | Open-label, randomised controlled trial |
| **Planned sample size** | 34 participants |
| **Selection criteria** | The study will include nursing staff who are willing to engage and comply with the study procedures and have the capacity to give consent. The study will exclude nursing students and nursing staff who rate themselves as highly confident in caring for patients with haemophilia. |
| **Study Procedure** | After enrolment, participants will complete baseline assessments of competence and confidence to manage patients with haemophilia. They will then be randomised to the educational intervention group or control group (1:1). The intervention group will receive an educational intervention after randomisation, in the form of a recorded PowerPoint presentation via Microsoft Teams. The participants will have 2 weeks to review the presentation before being prompted to complete the follow-up assessments.The control group will not receive the educational intervention. All participants will then repeat the above assessments of competence and confidence.  |
| **Statistical considerations** | **Sample size calculation:**Based on the results of a previous survey of 8 nurses, a 2-point improvement on a 10-point scale was used in the calculation (smallest worthwhile effect of 2). Standard deviation calculated as 2, alpha nominated as 0.05, and beta nominated as 0.80. Sample size calculated as 34 participants (17 per group).**Analysis plan:**Change in competency questionnaire scores and Likert confidence scores at each of the two timepoints will be analysed as between-group differences with 95% confidence intervals. An intention to treat analysis will be applied, i.e., all subjects for whom outcome measures are available will be analysed in the groups to which they were originally randomised. |
| **Time Period of Data Collection** | Recruitment from 11th September to 09th October 2023. Data collection from 11th September 2023 to early November 2023. |
| **Duration of the Study** | 7 months |

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# BACKGROUND AND INTRODUCTION

## HAEMOPHILIA BACKGROUND

Haemophilia is a rare blood disorder that is typically congenital, X-linked and recessive in nature. The condition arises from a deficiency or dysfunction of clotting factor VIII (haemophilia A) or factor IX (haemophilia B) (George et al., 2017; George et al., 2021). The cardinal manifestation of haemophilia is recurrent joint bleeding (Haemarthrosis) and these bleeds either occur spontaneously or in response to trauma (George et al., 2017; George et al., 2021). Spontaneous bleeds are common in severe Haemophilia (factor VIII activity <1% of normal value), uncommon in moderate Haemophilia (factor VIII activity 1-5% of normal value), and rare in mild Haemophilia (factor VIII activity 5 to <40% of normal value) (George et al., 2021). Development of arthropathy may ensue as a result of repeated joint bleeds (George et al., 2021). The mainstay of Haemophilia treatment involves intravenous administration of exogenous factor to prevent bleeding 1-3 times a week (George at al., 2017). Factor infusions may also be required on-demand to treat bleeding episodes (George at al., 2017). Another mainstream treatment option specifically for Haemophilia A involves administration of Ecuzimab, a subcutaneous factor VIII-mimetic bispecific monoclonal antibody (George et al., 2021).

Exogenous factor replacement presents various clinical difficulties including frequent injections, difficulty accessing veins and risk of inhibitor formation ([Okaygoun](https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-021-00760-4%22%20%5Cl%20%22auth-Dide-Okaygoun) et al., 2021). These difficulties can impact adversely on treatment concordance and quality of life for those with haemophilia ([Okaygoun](https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-021-00760-4%22%20%5Cl%20%22auth-Dide-Okaygoun) et al., 2021). George et al. (2017) note that exogenous factor replacement can be problematic as it contributes to rapid increases and decreases in factor results, which can affect activities of daily living. More recently, many clinical trials have explored the effect and efficacy of adeno-associated virus (AAV) gene therapy as a treatment option for Haemophilia (George et al., 2017; George et al., 2021).

Education of patients with Haemophilia is paramount, including in Australia (Smith, 2017). This education involves a multidisciplinary approach and the nurse is a critical team member (Smith, 2017). Nurses are able to provide education on key self-management aspects such as how to prevent a bleed and advice in relation to physical activities (Smith, 2017).

In regards to nursing education, there are currently three levels of nursing registration in Australia: Enrolled Nurse (EN), Registered Nurse (RN), and Nurse Practitioner (NP) (Wang, 2016). An EN is required to complete 12-18 months of full-time study prior to registration and performs care in a range of clinical settings under the supervision of the Registered Nurse (Wang, 2016). An RN completes 3 to 3.5 years of full-time study prior to registration and is responsible for aspects such as provision of patient care, staff management, and promotion of health and wellness (Wang, 2016). An NP is an RN who has completed a relevant master’s degree (Wang, 2016). The NP works in a designated practice area and performs roles such as prescription of medications, making patient referrals to other professionals, and requesting diagnostic interventions (Wang, 2016).

## RATIONALE FOR PERFORMING THE STUDY

There is a need for an improvement in nurses’ application of evidence-based practice and research in caring for patients with haemophilia. Nurses continue to struggle in applying current research when caring for patients with haemophilia (Khair et al., 2016). Similarly, Ballmann and Ewers (2022) conclude that there is currently a lack of theory-guided, systematic and evidence-based approaches in attending to educational needs of patients with bleeding disorders. Nurses who care for patients with bleeding disorders require improved authorisation, qualification and resources in providing patient education (Ballmann & Ewers 2022). This improvement will facilitate quality haemophilia care.

# HYPOTHESIS

Haemophilia-specific education will provide a worthwhile enhancement to the competency and confidence of nursing staff when caring for patients with haemophilia.

# STUDY OBJECTIVES / AIMS

## PRIMARY OBJECTIVES

To assess nursing competence in caring for patients with haemophilia.

## SECONDARY OBJECTIVES

To measure nursing confidence in caring for patients with haemophilia.

# STUDY DESIGN

## DESIGN / STUDY TYPE

This study is an open-label, randomised controlled trial. Participants will be randomised to the educational intervention or control group (1:1).

## EXPECTED PARTICIPANT NUMBERS

Recruitment will occur from 11th September to 9th October 2023. Expected number of participants is 34 (17 per group).

## TIME PERIOD OF THE STUDY

|  |  |  |
| --- | --- | --- |
| **Task** | **Start Date** | **End Date**  |
| Ethics Submission | Start Aug 2023 | Mid Aug 2023 |
| Ethics Review and Approval | Mid Aug 2023 | Start Sep 2023 |
| Recruitment | Start Sep 2023 | Start Oct 2023 |
| Conduction of educational intervention  | Start Oct 2023 | End Oct 2023 |
| Collection of data | Start Sep 2023 | Start Nov 2023 |
| Analysis of Data | Start Nov 2023 | Start Dec 2023 |
| Publication Draft  | Start Dec 2023 | Start Feb 2024 |
| Submission of Publications and Final Reports | Start Feb 2024 | Start Mar 2024 |

## ENDPOINTS

PRIMARY ENDPOINT

The amount of change in competence scores between baseline and the post-intervention assessment will be compared between the two randomised groups and reported as a mean between-group difference with a 95% confidence interval.

SECONDARY ENDPOINT

The amount of change in confidence scores between baseline and the post-intervention assessment will be compared between the two randomised groups and reported as a mean between-group difference with a 95% confidence interval.

## CENTRES (STUDY SITES)

|  |  |
| --- | --- |
| **Site Name/s** | Royal Prince Alfred Hospital |
| **Site Contact/Investigator** | Miles Kenny |
| **Public Health Organisation (PHO)** | Yes  |
| **Study Procedures** | recruitment, data collection, data analysis  |

# STUDY PARTICIPANTS

## INCLUSION CRITERIA

1. Current nursing Australian Health Practitioner Regulation Agency (AHPRA) registration
2. Willingness to provide informed consent
3. Willingness to participate and comply with the study requirements

## EXCLUSION CRITERIA

1. Nursing students
2. Nursing staff with high confidence when caring for haemophilia patients

## KEY ELEMENTS OF RECRUITMENT (AS PER NS)

1. Who will be recruited? RPAH nursing staff
2. How will participants be identified and recruited? Study will be advertised via posters and the RPAH intranet page. Advertisements will contain a link and QR code to the REDCap consent form and Patient Information Sheet, and the Principal Investigator’s contact details. Potential participants that contact the Principal Investigator will be sent a recruitment email containing the Participant Information Sheet and link to the REDCap consent form. After completing the REDCap eConsent form, participants will be required to complete a survey assessing study eligibility. The eConsent form will terminate the ability for potential participants to enrol after 100 participants have enrolled.
3. Will the potential participants be screened? The only screening will be the REDCap survey assessing study eligibility, as discussed above.
4. What is the impact of any relationship between researchers and potential participants on recruitment? The researcher may be a work peer of the study participants but no participants will be in a subordinate role such as manager/staff.
5. How will the recruitment strategy facilitate obtaining the consent of participants? Posters and the intranet advertisement contain information about the study, link and QR code to the eConsent form, and contact details of the Principal Investigator. The use of advertisements will allow more potential participants to be aware of the study and the use of an eConsent form will make it easier for potential participants to enrol for the study.
6. How will the recruitment strategy ensure that participants can make an informed decision about participation? All information about the study is provided on the Participant Information Sheet to ensure consent is informed. Contact details of the Principal Investigator are provided in recruitment email and advertisements. Potential participants with any questions are able to contact the Principal Investigator prior to signing the eConsent form.
7. Are there any risks associated with the recruitment strategy for potential participants or for the viability of the project? No

## STUDY LIMITATIONS

The study outcome measures are nursing competence and confidence. The brief multiple-choice questionnaire may capture an indication of competence but will not provide a detailed perspective on this. It is also unknown as to whether an increase in nursing confidence will translate to improved application of evidence-based care of haemophilia patients.

# STUDY PROCEDURES

## INVESTIGATION PLAN

Participants complete eligibility survey

Participants recruited via advertisements and sign REDCap eConsent form

If eligible, participant will complete baseline characteristics survey

Participants will complete the initial confidence scale survey and competence questionnaire (participants will be given 3 weeks to complete this following signing of the eConsent form)

Intervention group

Control group

Randomised to groups

Participant informed they are in control group

Participant informed they are in the intervention group; sent educational presentation; given 2 weeks to review educational presentation

Participants will complete follow-up confidence scale survey and competence questionnaire

Participants will complete follow up confidence scale survey and competence questionnaire

Educational intervention shared with control group upon study completion

The study site is Royal Prince Alfred Hospital (RPAH). Potential participants will be invited to participate in the study via poster advertisements (displayed around RPAH) and an RPAH Intranet advertisement.

The recruitment period is 11th September to 9th October 2023. Potential participants are required to complete the REDCap Eligibility Criteria survey. If participants fit the eligibility criteria, they will be required to complete the Baseline Characteristics survey on REDCap. If they are deemed eligible, they will progress to complete the baseline competence and confidence questionnaires.

Participants will be randomised to the educational intervention or control group (1:1). Simple randomisation and concealed allocation will be achieved using a computer-generated random number system. Participants will be notified of their study group via email. Participants will have 2 weeks to complete the educational intervention.

Participants will be required to repeat the assessments 2 weeks after randomisation. Start of data collection will occur concurrently with start of recruitment as the initial assessments will be performed upon recruitment. Data collection will finish at the beginning of November 2023 after the assessments for the second timepoint have been completed.

Nursing competency will be assessed via a questionnaire consisting of 18 multiple-choice questions (appendix 1) relating to the application of evidence-based practice when caring for patients with haemophilia.

Nursing confidence will be assessed using a Likert scale (appendix 2).

The educational intervention group will be provided with a recorded 30–60 minute PowerPoint presentation via Microsoft Teams. Participants will have 2 weeks to review the presentation before completing the follow-up assessments. The educational presentation will include information, graphics and visual aids relevant to best practice nursing care of haemophilia patients. Participant access of the educational intervention will be monitored and participants will be followed up to complete the educational intervention if necessary. Additionally, participants will be sent two automated reminder emails to review the presentation, at the end of the 1st and 2nd weeks of access.

The control group will not receive any educational intervention for the duration of the study. At the end of the study, the educational intervention will be shared with the control group.

## INFORMATION AND CONSENT

Poster and RPAH Intranet advertisements will contain a link and QR code to the REDCap eConsent form and Participant Information Sheet. Contact details of Principal Investigator will be included on PIS, recruitment email, and advertisements to allow individuals to contact the Principal Investigator if any clarification or further information is required. Contact details of the SLHD Ethics Committee will also be provided on the advertisements. Consent is to be documented on the REDCap eConsent form using electronic signature. The Principal Investigator will countersign once the participant has signed the REDCap eConsent form.

# OUTCOMES

## DEFINITION OF OUTCOMES

Nursing competence measured as the result from the multiple-choice questionnaire. Nursing confidence measured as the result from the Likert scale of 0-10.

# STATISTICAL CONSIDERATIONS

## SAMPLE SIZE OR POWER CALCULATION

Based on the results of a previous survey of 8 nurses, a 2-point improvement on a 10-point scale was used in the calculation (smallest worthwhile effect of 2). Standard deviation calculated as 2, alpha nominated as 0.05, and beta nominated as 0.80. Sample size calculated as 34 participants (17 per group).

## PROVIDE A DETAILED ANALYSIS PLAN

Any differences noted in baseline characteristics that the investigator considers significant enough to influence the outcome of the results will be commented on. If the baseline characteristic is known to be prognostic of outcome, it will be adjusted for in the analysis. If at the end of the study period missing data is identified, two reminders email will be sent, a week apart.

Change in competency questionnaire scores and Likert confidence scores at each of the two timepoints will be analysed as between-group differences with 95% confidence intervals. An intention to treat analysis will be applied, i.e., all subjects for whom outcome measures are available will be analysed in the groups to which they were originally randomised.

# DATA COLLECTION AND CONFIDENTIALITY AND STORAGE AND ARCHIVING OF STUDY

## SYSTEMS

All data collected will be stored within REDCap. Personally identifiable information will be collected including names and signatures on the eConsent form. The electronic consent forms obtained via eConsent will be stored within the file repository of the REDCap project separate to the study data to ensure participant privacy. Participant email addresses are required to be collected to send out REDCap links to the assessments. Email addresses, signatures, and names are marked as an identifier within REDCap to prevent them from being exported with any data. Additionally, the hidden action tag (@HIDDEN-FORM) has been utilised to ensure that the email addresses are only visible to the system.

Data is to be stored and retained for seven years following study completion. Data will be archived in alignment with the REDCap SLHD server standard procedures. Only the Principal Investigator will have user rights to this database and information. The database information will be accessed to allow for analysis of results which will be subject to statistical procedures.

## RESEARCH DATA MANAGEMENT PLAN

Provided in a separate document. See attached.

# ETHICS AND PROTOCOL AMENDMENTS

Study activities will not commence until ethics and governance approval for Royal Prince Alfred Hospital is attained. Updated study documents will be subject to review and approval by the ethics committee before use.

# PUBLICATION & INTELLECTUAL PROPERTY

Overall study results may be published and disseminated to the clinicians by multidisciplinary meetings, hospital grand rounds, seminars and conferences. The Coordinating Principal Investigator will establish the authorship order. Participants will be informed regarding the results of the study via the contact email provided upon recruitment to the study. This is outlined in the Participant Information and Consent Form.

# REFERENCES

Ballmann, J., & Ewers, M. (2022) Nurse‐led education of people with bleeding disorders and their caregivers: A scoping review, *Haemophilia, 28*(6), 153-163. doi:10.1111/hae.14629.

George, L. A., Monahan, P. E., Eyster, M.E., Sullivan, S. K., Ragni M. V., Croteau, S. E., Rasko, J. E. J., Recht, M., Samelson-Jones, B. J., MacDougal, A., Jaworski, K., Noble, N., Curran, M., Kuranda, K., Mingozzi, F., Chang, T., Reape, K. Z., Anguela, X. M., High, K.A. (2021). Multiyear Factor VIII Expression after AAV Gene Transfer for Hemophilia A. *The New England Journal of Medicine, 385*(21), 1961-1973. doi:10.1056/NEJMoa2104205.

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Smith, J. (2017). *Development, implementation, evaluation and validation of a haemophilia nurses’ education program in South Africa Journal of Biomedical Science* (Publication No. 20103001) [Doctor of Philosophy, The University of Notre Dame Australia]. Google Scholar.

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# LIST OF ABBREVIATIONS

|  |  |
| --- | --- |
| **Abbreviation** | **Definition** |
| AHPRA | Australian Health Practitioners Regulation Agency |
| A/Prof  | Associate Professor |
| eConsent | Electronic consent |
| ICH | International Council for Harmonisation |
| LNR | Low or Negligible Risk |
| NS  | National Statement  |
| PIS | Participant Information Sheet |
| RPAH | Royal Prince Alfred Hospital |
| SLHD | Sydney Local Health District |

# APPENDICES

## Appendix 1 – Competency Questionnaire

## Appendix 2 – Confidence Scale

1) On a scale of 0-10, how confident are you in providing evidence-based nursing care for patients with Haemophilia? 0 is not confident at all 10 is extremely confident.

