Contents

Protocols

Impact of a Mobile App (LoAD Calc) on the Calculation of Maximum Safe Doses of Local Anesthetics: Protocol for a Randomized Controlled Trial (e53679)
Pietro Fubini, Georges Savoldelli, Tal Beckmann, Caroline Samer, Mélanie Suppan ................................................................. 2

Adaptive Intervention to Prevent Respiratory Illness in Cerebral Palsy: Protocol for a Feasibility Pilot Randomized Controlled Trial (e49705)
Alyssa Fleischman, Carlos Lerner, Heidi Kloster, Paul Chung, Thomas Kitzner, Christopher Cushing, Danielle Gerber, Barbara Katz, Gemma Warner, Kristina Singh-Verdeflor, Roxana Delgado-Martinez, Lorena Porras-Javier, Siem Il, Teresa Wagner, Mary Ehlenbach, Ryan Coller, ... 1

Epidemiology of Syphilis in Pregnancy and Congenital Syphilis in Brazil and the Risk or Associated Factors: Protocol for a Systematic Review (e50702)
Yago Pinheiro, Janmilli Dantas, Jose Holanda, Ankilma Feitosa, Richardson Augusto Rosendo da Silva ................................................................. 27

Monitoring and Evaluation of Dementia-Friendly Neighborhoods Using a Walkshed Approach: Protocol for a Scoping Review (e50548)
Mark Groulx, Shannon Freeman, Keone Gourlay, Dawn Hemingway, Emma Rossnagel, Habib Chaudhury, Mohammadjavad Nouri ........................................... 36

Overview of Retention Strategies for Medical Doctors in Low- and Middle-Income Countries and Their Effectiveness: Protocol for a Scoping Review (e52938)
Norehan Jinah, Ili Abdullah Sharin, Pangie Bakit, Izzuan Adnan, Kun Lee ............................................................................................................. 45

Corrigenda and Addenda

Correction: Mobile Phone Technology for Preventing HIV and Related Youth Health Problems, Sexual Health, Mental Health, and Substance Use Problems in Southwest Uganda (Youth Health SMS)- Protocol for a Pilot Randomized Controlled Trial (e55725)
Philip Kreniske, Olive Namuyaba, Robert Kasumba, Phionah Namatovu, Fred Ssewamala, Gina Wingood, Ying Wei, Michele Ybarra, Charlotte Oloya, Costella Tindyebwa, Christina Ntulo, Vincent Mjuune, Larry Chang, Claude Mellins, John Santelli ............................................................................................................. 34
Impact of a Mobile App (LoAD Calc) on the Calculation of Maximum Safe Doses of Local Anesthetics: Protocol for a Randomized Controlled Trial

Pietro Elias Fubini, MD; Georges Louis Savoldelli, MEd, MD; Tal Sara Beckmann, MD; Caroline Flora Samer, MAS, MD; Mélanie Suppan, MSc, MD

Division of Anesthesiology, Department of Anesthesiology, Clinical Pharmacology, Intensive Care and Emergency Medicine, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

Clinical Pharmacology and Toxicology Division, Department of Anesthesiology, Clinical Pharmacology, Intensive Care and Emergency Medicine, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

Corresponding Author:
Mélanie Suppan, MSc, MD
Division of Anesthesiology
Department of Anesthesiology, Clinical Pharmacology, Intensive Care and Emergency Medicine
Geneva University Hospitals and Faculty of Medicine
Rue Gabrielle-Perret-Gentil 4
Geneva, 1211
Switzerland
Phone: 41 223723311
Email: melanie.suppan@hcuge.ch

Abstract

Background: Local anesthetics (LAs) are regularly used to alleviate pain during medical or surgical procedures. Their use is generally considered safe, but exceeding the maximum recommended doses can lead to LA systemic toxicity, a rare but potentially lethal complication. Determining maximum safe doses is therefore mandatory before performing local anesthesia, but rules are often unclear and the factors affecting dose calculation are numerous. Mobile health apps have been shown to help clinical decision-making, but most currently available apps present significant limitations. The Local Anesthetics Dose Calculator (LoAD Calc) app was designed to overcome these limitations by taking all relevant parameters into account. Before deploying this app in a clinical setting, it should be tested to determine its effectiveness and whether clinicians would be willing to use it.

Objective: The primary objective will be to evaluate the effectiveness of the LoAD Calc app through written simulated cases. The secondary objective will be to determine whether physicians find this app easier, faster, and safer than the methods they generally use.

Methods: We describe a parallel-group randomized controlled trial protocol. Anesthesiologists working at the Geneva University Hospitals will be invited to participate. Participants will be asked to compute the maximum dose of LA in 10 simulated clinical cases using 3 different LAs. The maximum safe dose will be determined manually using the same calculation rules that were used to develop LoAD Calc, without using the app itself. An overdose will be considered any dose higher than the correct dose, rounded to the superior integer, while an underdose will be defined as the optimal calculated dose minus 20%, rounded to the inferior integer. Randomization will be stratified according to current position (resident vs registrar). The participants allocated to the LoAD Calc (experimental) group will use the LoAD Calc app to compute the maximum safe LA doses. Those allocated to the control group will be asked to use the method they generally use. The primary outcome will be the overall overdose rate. Secondary outcomes will include the overdose rate according to ideal and actual body weight and to each specific LA, the overall underdose rate, and the time taken to complete these calculations. The app’s usability will also be assessed.

Results: A sample size of 46 participants will be needed to detect a difference of 10% with a power of 90%. Thus, a target of 50 participants was set to allow for attrition and exclusion criteria. We expect recruitment to begin during the winter of 2023, data analysis in the spring of 2024, and results by the end of 2024.

Conclusions: This study should determine whether LoAD Calc, a mobile health app designed to compute maximum safe LA doses, is safer and more efficient than traditional LA calculation methods.

International Registered Report Identifier (IRRID): PRR1-10.2196/53679
Introduction

Background

Local anesthetics (LAs) are used daily by physicians to perform minor procedures. While the doses they use are generally limited, anesthesiologists often use higher doses to perform regional anesthesia techniques [1]. While the advantages of such techniques are undeniable, using high LA doses increases the risk of local anesthetic systemic toxicity (LAST), a potentially lethal complication associated with the use of these agents [2]. The actual incidence of LAST is unknown since most minor symptoms are not specific and because LAST awareness varies considerably between practitioners [3,4]. The incidence reported in scientific studies varies from 0.04 to 1.8 per 1000 regional anesthesia procedures but is probably underestimated [5,6]. The main risk factors seem to be inadvertent intravascular injections and inappropriately large doses [7,8].

Prevention of intravascular injection can be achieved by ultrasound guidance and careful aspiration during the procedure, while adequate calculation of the maximum dose of LA before administration is the best way to avoid incorrect doses.

Although different guidelines have been created to help clinicians calculate the maximum safe LA doses, quickly and reliably determining such doses often proves difficult in clinical practice [9]. Many anesthesiologists rely on mental calculation (with or without a pen and paper aid), and some use calculators. These methods are, however, often challenging and inaccurate, especially if LA mixtures are used or when patients present multiple comorbidities [10]. More advanced solutions have been developed to support LA dosage calculation, such as the nomogram created by Williams and Walker [11]. The main limitation of this solution is that the nomogram must always be at hand. Moreover, specificities such as ideal body weight (IBW) calculation and adaptation in the case of relevant comorbidities are indicated but not directly integrated into dose determination.

To facilitate the calculation of safe maximum LA doses, a mobile health (mHealth) app, Local Anesthetics Dose Calculator (LoAD Calc), was developed at the Geneva University Hospitals [12]. This app takes all relevant parameters (IBW and actual weight, height, age, medications, and comorbidities) into account and allows the use of a mixture of 2 different LAs. Since smartphones have widely replaced older paging systems and are therefore always at hand, this mHealth app could be an appropriate solution to enable anesthesiologists to efficiently compute safe maximum LA doses.

Objectives

This study protocol follows the hypothesis that LoAD Calc, an mHealth app designed to help clinicians calculate maximum safe LA doses, is safer and more effective than traditional methods. Thus, the primary objective will be to evaluate the effectiveness of the LoAD Calc app by using it to compute the maximum single doses of LA in written simulated cases. The secondary objective will be to determine whether physicians find this app easier, faster, and safer than the methods they generally use.

Methods

Ethical Considerations

A synopsis of the study protocol was presented to the regional ethics committee (Commission Cantonale d’Ethique de la Recherche [CCER]). This committee confirmed that this project does not fall within the scope of the Swiss Federal Act on Research involving Human Beings and issued a “declaration of no objection” (CCER 2022-01577) [13]. This study protocol does not fall within the scope of the Swiss Federal Act on Research involving Human Beings [13]. It will nevertheless be presented to the regional ethics committee to ascertain that no important or relevant ethical consideration was omitted.

Participants will be told that participation is entirely voluntary, that there will be no consequence if they refuse to participate, and that they will be able to withdraw at any time without explanation. All participants will be asked to sign an electronic consent form immediately after logging in. There is no compensation for participation in the study.

Study Design

This will be a monocentric, parallel-group, randomized controlled trial based on clinical vignettes. The protocol was developed according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement (Multimedia Appendix 1) [14]. Given its design, the investigators will not be blinded as to the intervention. Nevertheless, participants will not be informed that there are 2 different arms and will not be told the exact outcomes studied, even though they will be provided with general information regarding the study. In addition, the data analyst will be blinded as to participant allocation by renaming the groups before sending data for statistical analysis. Randomization will be stratified according to current position (resident vs registrar).

Results will be reported according to the CONSORT-EHEALTH (Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and onLine TeleHealth) guidelines [15]. Relevant elements of the CHERRIES (Checklist for Reporting Results of Internet E-Surveys) will be included since web-based questionnaires will be used in the course of this study [16].

Clinical Vignettes

A total of 10 clinical vignettes will be developed for the purpose of this study. These vignettes will describe clinical cases
requiring the use of LAs for regional anesthesia. We will include 3 of the most commonly used LAs in these vignettes: lidocaine, levobupivacaine, and ropivacaine. Some vignettes will ask the participant to use LA mixtures, and several will include comorbidities or medications requiring dose adaptations.

For each vignette, 3 authors will be required to determine the maximum dose of LA the simulated patient should receive according to the rules used to develop the LoAD Calc app [12], without using the app. These rules, which are derived from the scientific literature, are summarized in Textbox 1. They were reviewed and approved by clinical pharmacologists and toxicologists [12]. Any disagreement will prompt a review of the vignette. Final vignette approval will only be possible if a consensus can be reached.
Textbox 1. Dosage elements and app rules used to calculate the maximum safe dose of local anesthetics, adapted from Suppan et al [12].

<table>
<thead>
<tr>
<th>Dose limit for a single LA (local anesthetic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Levobupivacaine: 2 mg/kg (maximum 150 mg/dose)</td>
</tr>
<tr>
<td>• Lidocaine: 3 mg/kg (maximum 300 mg/dose)</td>
</tr>
<tr>
<td>• Ropivacaine: 3 mg/kg (maximum 225 mg/dose)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Influence of epinephrine on dose limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Levobupivacaine: 3 mg/kg (maximum 150 mg/dose)</td>
</tr>
<tr>
<td>• Lidocaine: 7 mg/kg (maximum 400 mg/dose)</td>
</tr>
<tr>
<td>• Ropivacaine: 3 mg/kg (maximum 225 mg/dose)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Determination of calculation weight (CW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Calculation of BMI</td>
</tr>
<tr>
<td>• Calculation of ideal body weight (IBW; Devine formula)</td>
</tr>
<tr>
<td>• Application of the following algorithm to define CW:</td>
</tr>
<tr>
<td>- weights&lt;70 kg and BMI&lt;30 and IBW &gt; weight → CW=weight</td>
</tr>
<tr>
<td>- weights&gt;70 kg and BMI≥30 and IBW ≤ weight → CW=IBW</td>
</tr>
<tr>
<td>- weights&lt;70 kg and BMI≥30 → CW=IBW</td>
</tr>
<tr>
<td>- weight&gt;70 kg and IBW&gt;70 → CW=70</td>
</tr>
<tr>
<td>- weight&gt;70 kg and IBW≤70 → CW=IBW</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose adaptation depending on health conditions and drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Conditions</td>
</tr>
<tr>
<td>- Old age (70 years or older)</td>
</tr>
<tr>
<td>- Renal dysfunction (glomerular filtration rate [GFR]&lt;50 mL/minute)</td>
</tr>
<tr>
<td>- Hepatic insufficiency (prothrombin time &lt;50%)</td>
</tr>
<tr>
<td>- Heart failure (left ventricular ejection fraction≤30%)</td>
</tr>
<tr>
<td>- Pregnancy</td>
</tr>
<tr>
<td>- Drugs decreasing LA metabolism</td>
</tr>
<tr>
<td>• List of drugs decreasing LA metabolism</td>
</tr>
<tr>
<td>- Major CYP1A2 inhibitors: ciprofloxacin, norfloxacin, and fluvoxamine</td>
</tr>
<tr>
<td>- Major CYP3A inhibitors: azole antifungals, macrolides, calcium channel blockers, HIV antiretroviral therapy, and tyrosine kinase inhibitors</td>
</tr>
<tr>
<td>• If 1 condition is present, the calculator reduces the total maximum dose by 20%</td>
</tr>
<tr>
<td>• If 2 or more conditions are present, the calculator reduces the total maximum dose by 30%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calculation rule for LA mixtures</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The app performs the following steps</td>
</tr>
<tr>
<td>- Calculation of maximum safe volume for first LA</td>
</tr>
<tr>
<td>- The user enters which volume of first LA is to be used (0–maximum volume)</td>
</tr>
<tr>
<td>- Calculation of corresponding maximum dose of first LA and determination of percentage of total maximum dose</td>
</tr>
<tr>
<td>- Calculation of maximum dose of second LA based on remaining percentage of total maximum dose</td>
</tr>
<tr>
<td>- Calculation of maximum volume of second LA</td>
</tr>
</tbody>
</table>
Groups and Randomization

There will be 2 study groups: in the control group, participants will be asked to use the method they usually use in their clinical practice to calculate the maximum safe dose of LA; in the LoAD Calc (experiment) group, participants will be required to use the LoAD Calc app, which will be preinstalled on a standard smartphone (Galaxy XCover 4s; Samsung) running on Android 11.

Stata’s (StataCorp LLC) replicable balanced randomization mechanism will be used to allocate participants to their study group. Textbox 2 contains the code that will be used.

Textbox 2. Randomization code.

```
set obs #N
egen arm = seq(), to(2)
set seed #S
gen random = uniform()
sort random
```

Wherein “1” will be the control group, and “2” will be the LoAD Calc group.

Since randomization will be stratified according to participant position (either resident or registrar), 2 seeds (#S) will be used (07022023 and 20230207).

A sample size calculation will be used to determine the total number of observations. It will be rounded up to the nearest ten to enhance the study power and take into account attrition and potential exclusions. The stratified number of observations (#N) will be computed according to the proportion of potential participants belonging to both eligible positions (residents vs registrars).

The method used by the participants allocated to the control group to calculate the maximum safe dose of LA will be recorded. There will be no teaching or introductory intervention for any of the participants before the study, and the participants allocated to the LoAD Calc group will therefore discover the app while answering the first vignette.

Web-Based Study Platform

A specific web-based platform will be developed using the Joomla! 4.3 content management system (Open Source Matters). It will be hosted on a Swiss server (Kreativmedia GmbH) and secured by the RSFirewall 3 (RSJoomla) and AdminTools 7 (Akeeba Ltd) components. To ensure participant anonymity, unique usernames and passwords will be created using Manytools’ web-based password generator [17]. These credentials will then be imported into Stata and allocated to either study group according to the randomization process described above. Finally, this data will be exported to a CSV file, which will be imported into the web-based study platform using the Import Joomla Users component (version 3.4; Lerus Ltd).

Consents, questionnaires, and vignettes will be managed using Shondalai’s Community Surveys 6 and Community Quiz 6 components (Bulasikku Technologies Pvt Ltd). All data will be stored on an encrypted MySQL-compatible database (MariaDB 10, MariaDB Foundation).

Inclusion and Exclusion Criteria

All resident physicians and registrars working in the HUG anesthesiology department will be eligible for inclusion. The only exclusion criteria will be current or previous use of the LoAD Calc app. This criterion will be assessed by a screening question asked after the completion of all study vignettes.

Recruitment

The project will first be presented to the head of the anesthesiology department and then to all consultants. After obtaining their agreement, investigators will recruit potential participants directly in the operating room. These residents and fellows in anesthesiology will be informed that the study will last at most 1 hour and that an investigator will replace them in the operating room while they participate. They will be told that participation is entirely voluntary, that there will be no consequence if they refuse to participate, and that they will be able to withdraw at any time without explanation. No incentive other than advancing scientific knowledge will be given to promote participation. They will be given a paper sheet summarizing the information regarding the study and data protection (Multimedia Appendix 2). Those who agree will be scheduled for participation on the same day. Together with the anesthesiology consultant overseeing the operating room, an investigator will organize replacements to avoid any disruption in the operating program. There will be only 1 slot, and therefore, only 1 participant per hour.

Consent and Study Sequence

Participants will be asked to set their phones to flight mode. This will enable them to access any note, calculator, or app they use to calculate LA doses while avoiding potentially disruptive interruptions. The study itself will take place in a separate, quiet room. There, an investigator will prompt them to pick up a sealed, opaque envelope containing the credentials necessary to log in.

All participants will be asked to sign an electronic consent form immediately after logging in. Those who agree will proceed to a first questionnaire designed to gather demographical data (Textbox 3) and determine whether these participants are currently using LoAD Calc or if they have used this app before (exclusion criterion). After completing this questionnaire, an introductory screen giving information regarding the vignettes they are about to see and specifying the calculation method they are to use (LoAD Calc for the experimental group vs left at the participant’s will for the control group) will be displayed. At
this stage, those allocated to the LoAD Calc group will be given the smartphone preinstalled with the LoAD Calc app.

**Textbox 3. First questionnaire.**

<table>
<thead>
<tr>
<th>Page 1: consent</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Consent to participate and to data reuse (multiple-choice questions with only 1 acceptable answer)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Page 2: exclusion criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Has heard of LoAD Calc (multiple-choice questions with only 1 acceptable answer)</td>
</tr>
<tr>
<td>• Has installed LoAD Calc (multiple-choice questions with only 1 acceptable answer; branching logic will be used to avoid displaying irrelevant questions)</td>
</tr>
<tr>
<td>• Has used LoAD Calc (multiple-choice questions with only 1 acceptable answer; branching logic will be used to avoid displaying irrelevant questions; answering “yes” to either of those questions will lead to participant exclusion)</td>
</tr>
<tr>
<td>• Context of LoAD Calc use (multiple-choice question with only 1 acceptable answer; branching logic will be used to avoid displaying irrelevant questions)</td>
</tr>
<tr>
<td>• Has LoAD Calc still installed (multiple-choice question with only 1 acceptable answer; branching logic will be used to avoid displaying irrelevant questions)</td>
</tr>
<tr>
<td>• Still uses LoAD Calc (multiple-choice questions with only 1 acceptable answer; branching logic will be used to avoid displaying irrelevant questions; answering “yes” to either of those questions will lead to participant exclusion)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Page 3: demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Gender (multiple-choice questions with only 1 acceptable answer)</td>
</tr>
<tr>
<td>• Age (free text with regular expression [regex] validation rule)</td>
</tr>
<tr>
<td>• Position (multiple-choice questions with only 1 acceptable answer; custom answer accepted)</td>
</tr>
<tr>
<td>• Years since graduation (free text with regular expression [regex] validation rule)</td>
</tr>
<tr>
<td>• Years of practice in anesthesiology (free text with regular expression [regex] validation rule)</td>
</tr>
<tr>
<td>• Specialist diplomas (custom answer accepted; multiple-answer question with more than 1 answer accepted)</td>
</tr>
</tbody>
</table>

After completing the vignettes, the participants allocated to the LoAD Calc group will be asked to complete the French version of the System Usability Scale [18], the translation of which has been validated [19]. Participants allocated to the control group will then be asked which methods they used to calculate LA doses.

Finally, both groups will have to answer a question based on a 10-point Likert scale to assess their confidence as to the method they used to carry out the maximum safe LA dose calculations, from score 1 (absolutely not confident) to score 10 (perfectly confident).

The whole study sequence is summarized in Figure 1.

**Figure 1.** Study sequence. LoAD Calc: Local Anesthetics Dose Calculator.
Outcomes

The primary outcome will be the overall overdose rate, according to the method used. To assess this outcome, the maximum acceptable dose in milligrams, or milliliters, must therefore be established. While this might seem straightforward at first sight, it is actually rather complex. Indeed, although maximum safe doses are calculated in milligrams, anesthetists administer a volume of LA (the concentration of which can vary) rather than a quantity of LA. Therefore, even though toxicity is related to the quantity (in milligrams) of LA administered, it is clinically more relevant to determine the maximum volume (in milliliters) of LA that can be used for a particular patient. Consequently, after applying the rules described in Textbox 1, a quantity in milligrams will be obtained. It will then be converted in milliliters according to the concentration of the LA used in the vignette. This volume will then be rounded to the inferior integer. To be less conservative, 1 mm will be added to this calculated volume, and the total will represent the maximum acceptable volume.

An overdose will be considered any dose higher than this maximum acceptable volume or than its corresponding LA quantity in milligrams.

The secondary outcomes will be the overall overdose rate, considering the simulated patient’s ideal weight and the simulated patient’s actual weight, the overdose rate according to each LA studied, and the overall underdose rate. An underdose will be defined as the maximum acceptable volume minus 20% (or its corresponding LA quantity in milligrams), rounded to the inferior integer. This is an empirical choice since anesthetic underdose can only be determined clinically [20,21]. Other secondary outcomes will be the time taken to complete these calculations, the app’s usability, and the physicians’ confidence in using the method they were allocated to. The app’s usability will be evaluated using the System Usability Scale [18]. Provided that the statistical assumptions are met, factors associated with a higher probability of overdose or underdose will also be assessed.

Statistical Analysis

The sample size calculation and all other statistical analyses will be carried out using Stata (version 17.0 or above). The complete data set will be exported by the webmaster, who will give the study groups codenames before sending the curated data set for statistical analysis. Descriptive statistics will be used to present demographical data. Normality will be assessed graphically, and the Kolmogorov-Smirnov test will be used in cases of doubt. Accordingly, all outcomes will then be computed using either parametric or nonparametric tests. The data acquisition mechanisms will ensure that all data are recorded after each stage. Thus, there should not be any missing data, and there shall be no need for imputation. When LA mixtures are used, participants will be told that 1 anesthetic has already been injected and the dose used has been clearly reported. Thus, they will be asked to determine the maximum safe dose for the second local anesthetic. Multivariable regression will be used to determine an association between specific clinical parameters and the probability of overdose or underdose, provided that all required assumptions are met and that the risk of overfitting is adequately limited. Double-sided P values (P<.05) will be considered significant.

Results

The 10 vignettes necessary to carry out the study were successfully created, and the maximum safe doses were determined. These vignettes and the doses were checked and approved by all authors. The 10 vignettes, as well as their English translation, were presented to peer reviewers but are not publicly available to avoid any potential bias. They will nevertheless be published along with the results paper.

The sample size calculation was performed using Stata (version 17.0). It showed that 46 participants (23 in each group) would be needed to detect a 10% difference with a power of 90%, taking into account an SD of 10%. In line with the above methods, a total of 50 anesthesiologists should therefore be recruited. Since there are 62 residents and 52 registrars in the HUG Anesthesiology Department, a participation rate of 44% (50/114) will be necessary. This participation rate seems achievable with the aforementioned recruitment procedure. If this rate cannot be achieved, other Swiss University hospitals will be contacted, and similar recruitment procedures will be carried out to obtain the required sample size.

The study platform has been successfully created and tested by all coauthors [22]. The data extraction mechanisms have also been successfully checked.

The recruitment will take place once this study protocol has been reviewed and accepted for publication to allow for any necessary adjustments before study inception. The current version of the protocol is 0.9 (October 10, 2023). The published version will be 1.0.

It should be possible to start recruitment during the winter of 2023. This would allow data analysis to take place in spring 2024, and results should be submitted for publication in an international peer-reviewed journal by the end of the same year.

Discussion

Overview

This study should allow us to determine whether LoAD Calc, an mHealth app designed to calculate maximum safe LA doses, is safer and more effective than current clinical practice. Previous studies have shown that mHealth apps can enhance dose calculation and potentially improve safety [23], decrease time to drug delivery [23], and lessen stress [24]. Assessing this latter parameter would not make much sense given the design of this study but could prove interesting in future high-fidelity or field trials.

Other solutions have already been proposed for the calculation of the maximum safe LA dose but present significant drawbacks. Some of them, such as the nomogram created by Williams and Walker [11], do not depend on technological devices. This nomogram, which represents a rapid and calculation-free way, must, however, always be within reach. In addition, IBW must first be determined, and there is no dose adaptation based on health conditions or drug interactions. Computer-based solutions
and mobile apps have also been created, such as MDCalc Local Anesthetic Dosing Calculator [25], The Podiatry Institute’s LA Toxic Dose Calculator [26], and SafeLocal by Johns Hopkins Digital [27]. All these solutions lack key elements and do not consider either IBW, comorbidities, or medications. Most allow invalid data to be entered or suggest doses exceeding the maximum safe dose, thereby presenting potential safety issues.

No study can be devoid of limitations, and the one planned according to this protocol is no exception. The first foreseeable limitation is that the LoAD Calc app will be compared to many different methods of LA dose calculation, thereby preventing us from directly comparing this app to a specific method. However, there is no gold standard to calculate the maximum safe LA doses, and the design of the proposed study can be considered pragmatic. Another limitation is that the maximum safe doses will be calculated using the same scientifically grounded rules that were used to develop LoAD Calc [12]. However, some of the calculation rules used by the app are not supported by strong scientific evidence, and there is no gold standard for comprehensive, safe calculation of maximum LA doses. Finally, the results obtained through this study will only apply to the single-dose administration of a limited number of LAs or of LA mixtures. This will not affect the validity of the study’s results nor compromise the use of the app since the 3 LAs selected (levobupivacaine, lidocaine, and ropivacaine) are commonly used in clinical practice. Nevertheless, further app developments will be needed to take other LAs and repeated doses into account. Since some LAs, such as lidocaine, are also safe for intravenous use, future versions of the app should enable practitioners to select different injection sites and routes.

Conclusions

Following this protocol should enable us to determine whether LoAD Calc, a mHealth app designed to calculate the maximum safe doses of LA, is both safe and effective. If this hypothesis proves to be true, clinical trials could be considered, and further outcomes, such as the impact of LoAD Calc on cognitive load and physiologic stress, could be considered.

Acknowledgments

The authors of this protocol would like to thank all members of the original LoAD Calc development team for their support throughout its development.

Data Availability

The data sets generated during and/or analyzed during this study will be available in an open access repository.

Conflicts of Interest

None declared.

References


22. Suppan M. Local Anesthetics Study. URL: https://local.anesth.ch/ [accessed 2023-12-13]


Abbreviations

CCER: Commission Cantonale d’Ethique de la Recherche
CHERRIES: Checklist for Reporting Results of Internet E-Surveys
CONSORT-EHEALTH: Consolidated Standards of Reporting Trials of Electronic and Mobile HEalth Applications and onLine TeleHealth
HUG: Geneva University Hospitals
IBW: ideal body weight
LA: local anesthetic
LAST: local anesthetic systemic toxicity
Edited by G Eysenbach; submitted 15.10.23; peer-reviewed by N Buckley, T Girard; comments to author 02.11.23; revised version received 04.11.23; accepted 21.11.23; published 03.01.24.

Please cite as:
Fubini PE, Savoldelli GL, Beckmann TS, Samer CF, Suppan M
Impact of a Mobile App (LoAD Calc) on the Calculation of Maximum Safe Doses of Local Anesthetics: Protocol for a Randomized Controlled Trial
JMIR Res Protoc 2024;13:e53679
URL: https://www.researchprotocols.org/2024/1/e53679
doi:10.2196/53679
PMID:38170571

©Pietro Elias Fubini, Georges Louis Savoldelli, Tal Sara Beckmann, Caroline Flora Samer, Mélanie Suppan. Originally published in JMIR Research Protocols (https://www.researchprotocols.org), 03.01.2024. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on https://www.researchprotocols.org, as well as this copyright and license information must be included.
Protocol

Adaptive Intervention to Prevent Respiratory Illness in Cerebral Palsy: Protocol for a Feasibility Pilot Randomized Controlled Trial

Alyssa Fleischman¹, MD; Carlos Lerner², MD, MPhil; Heidi Kloster¹, MD; Paul Chung³, MD, MS; Thomas Klitzner², MD, PhD; Christopher Cushing⁴, PhD; Danielle Gerber¹, BA; Barbara Katz⁵, MA; Gemma Warner¹, MSSW; Kristina Devi Singh-Verdeflor¹, MPH; Roxana Delgado-Martinez², BA; Lorena Porras-Javier², MPH; Siem Ia², CPNP-PC; Teresa Wagner⁶, RN; Mary Ehlenbach¹, MD; Ryan Coller¹, MD, MPH

¹Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States
²Department of Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles, CA, United States
³Department of Health Systems Science, Kaiser Permanente School of Medicine, Pasadena, CA, United States
⁴Clinical Child Psychology Program and Schiefelbusch Life Span Institute, University of Kansas, Kansas, KS, United States
⁵Family Voices of Wisconsin, Madison, WI, United States
⁶UW Health Kids American Family Children's Hospital, Madison, WI, United States

Corresponding Author:
Alyssa Fleischman, MD
Department of Pediatrics
University of Wisconsin School of Medicine and Public Health
H6/551 CSC
600 Highland Ave
Madison, WI, 53792
United States
Phone: 1 608 262 9150
Email: afleischman2@wisc.edu

Abstract

Background: This study will pilot-test an innovative just-in-time adaptive intervention to reduce severe respiratory illness among children with severe cerebral palsy (CP). Our intervention program, Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT), delivers timely customized action planning and rapid clinical response when hospitalization risk is elevated.

Objective: This study aims to establish RE-PACT’s feasibility, acceptability, and fidelity in up to 90 children with severe CP. An additional aim is to preliminarily estimate RE-PACT’s effect size.

Methods: The study will recruit up to 90 caregivers of children with severe CP aged 0 to 17 years who are cared for by a respiratory specialist or are receiving daily respiratory treatments. Participants will be recruited from pediatric complex care programs at the University of Wisconsin–Madison (UW) and the University of California, Los Angeles (UCLA). Study participants will be randomly assigned to receive usual care through the complex care clinical program at UW or UCLA or the study intervention, RE-PACT. The intervention involves action planning, rapid clinical response to prevent and manage respiratory illness, and weekly SMS text messaging surveillance of caregiver confidence for their child to avoid hospitalization. RE-PACT will be run through 3 successively larger 6-month trial waves, allowing ongoing protocol refinement according to prespecified definitions of success for measures of feasibility, acceptability, and fidelity. The feasibility measures include recruitment and intervention time. The acceptability measures include recruitment and completion rates as well as intervention satisfaction. The fidelity measures include observed versus expected rates of intervention and data collection activities. The primary clinical outcome is a severe respiratory illness, defined as a respiratory diagnosis requiring hospitalization. The secondary clinical outcomes include hospital days and emergency department visits, systemic steroid courses, systemic antibiotic courses, and death from severe respiratory illness.

Results: The recruitment of the first wave began on April 27, 2022. To date, we have enrolled 30 (33%) out of 90 participants, as projected. The final wave of recruitment will end by October 31, 2023, and the final participant will complete the study by April 30, 2024. We will start analyzing the complete responses by April 30, 2024, and the publication of results is expected at the end of 2024.
Conclusions: This pilot intervention, using adaptive just-in-time strategies, represents a novel approach to reducing the incidence of significant respiratory illness for children with severe CP. This protocol may be helpful to other researchers and health care providers caring for patients at high risk for acute severe illness exacerbations.

Trial Registration: ClinicalTrials.gov NCT05292365; https://clinicaltrials.gov/study/NCT05292365

International Registered Report Identifier (IRRID): DERR1-10.2196/49705

(KEYWORDS)

just-in-time adaptive intervention; respiratory illness; cerebral palsy; action planning; digital health

Introduction

Background

Children with severe cerebral palsy (CP) have spastic quadriplegia and are classified in level IV or V on the Gross Motor Function Classification System (GMFCS), often resulting in little or no independent mobility and serious respiratory consequences [1]. The mechanisms of respiratory illness in severe CP vary, paralleling those of other neuromuscular diseases [2], and include respiratory muscle weakness, recurrent infections and aspiration with inflammatory fibrosis, impaired airway clearance from altered tone, upper airway abnormalities, and poor chest wall compliance [3,4].

Respiratory illness is consistently the leading cause of death and hospitalization in severe CP [5,6]. Respiratory illness accounts for 59% of the deaths [5,7] and 25% of the hospitalizations [8-10] in severe CP. Moreover, respiratory illness strongly predicts future risk: respiratory hospitalization risk is 10-fold higher with a respiratory illness in the past year. Nevertheless, respiratory illness risk factors in severe CP are considered modifiable [11]. The prevention of these events is a significant need and a key to improving the quality of life and decreasing mortality [1,12].

Preventing hospitalization requires the opportunity for families and clinical teams to connect early enough to change trajectory [13-15]. Parents of children with CP have expressed the need for interventions focused on crisis management and self-efficacy [9,13,16]. However, respiratory illness in severe CP has broad comorbid triggers (eg, emesis, dysphagia, aspiration, and seizures). Because of this complexity, simple action plans or coaching alone may not address the breadth of respiratory illness triggers or potential responses; for example, if a parent of a child with severe CP follows an action plan directed toward bronchospasm, it would not effectively address an acute infectious lower respiratory infection. Parents of children with severe CP need comprehensive action planning and coaching; they also need an efficient direct extension to their clinical team for a just-in-time (JIT) adaptive clinical response directed specifically to acute real-time problems.

Currently, difficulty identifying when JIT care is needed is a barrier to effective illness response. Concerns may not reach clinical teams until an emergency department (ED) visit or hospitalization is inevitable. A national expert panel to identify interventions to prevent the hospitalization of children with complex diseases concluded that enhanced access, proactive crisis planning, and support for caregiver technical skills were crucial strategies to lower hospital use [17]. Prior postdischarge research has confirmed that admissions and ED visits could be better predicted by identifying when parents were not confident that their child with chronic conditions could avoid hospitalization or an ED visit than by other clinical or demographic indicators [18,19]. Preliminary work with a cohort that included children with severe CP demonstrated that parent confidence, monitored prospectively and repeatedly by SMS text message, is feasible, is acceptable, and predicts hospitalization within 2 weeks. This program of research will drive care forward by providing JIT care triggered by parents’ self-reported period of low confidence, thus matching the intervention to the immediate clinical need and preventing respiratory crisis.

Prior Work

This team developed the earlier Plans for Action and Care Transitions (PACT) intervention to prevent hospitalizations for children with complex chronic diseases, including severe CP. After integrating a systematic literature review [20], parent interviews [21], and a national expert panel [17], each focused on preventing hospitalization, the team designed PACT to leverage evidence-based strategies from different populations: asthma action planning [22-24], health coaching [25-27], and feedback from parent advisory group meetings. The PACT intervention delivered action planning and coaching activities to children with diverse complex diseases, including severe CP, and observed 40% lower hospitalization rates for intervention versus control patients [28]. Simultaneously, our prior multisite research observed that confidence to avoid hospitalization, measured through repeated SMS text messaging, predicted hospitalization over the subsequent 2 weeks. Our clinical team and family partners hypothesized that periods of low confidence might be a useful tailoring variable to prompt intervention delivery [29].

The PACT intervention has now been adapted to prevent severe respiratory illness in children with severe CP and to integrate SMS text messaging as a tailoring variable within a JIT adaptive intervention framework [29,30].

Objectives

This pilot study (ClinicalTrials.gov: NCT05292365) is designed to establish the feasibility, acceptability, and fidelity of our intervention program, Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT) in up to 90 children with severe CP and to establish a preliminary effect size of RE-PACT to inform a future efficacy study to reduce severe
respiratory illness. This intervention consists of three related parts: (1) universal action planning, (2) an ongoing assessment of hospitalization risk, and (3) an algorithm to determine when to increase clinician contacts and tailor action plans. The study period will be divided into 3 waves; after each wave, feasibility, acceptability, and fidelity data will be reviewed against predefined measures of success to adjust the protocol and overcome implementation barriers. We describe the design and protocol of this trial in the following sections.

Methods

Participants and Setting
This intervention will recruit primary caregivers of children with severe CP. Up to 90 caregivers of children with severe (GMFCS level IV or V) CP aged 0 to 17 years and cared for by a respiratory specialist or receiving daily respiratory treatments will be enrolled. Participants will be recruited from pediatric complex care programs at the University of Wisconsin–Madison (UW) and the University of California, Los Angeles (UCLA). These programs were established to deliver care to children with medical complexity. The key components of each program include pediatric clinicians, care coordinators, and extended visit lengths, which aid in delivering comprehensive care to children with CP. Both clinical programs have been described in more detail elsewhere [28,31].

Inclusion Criteria
Participants are caregivers of children with severe CP. Individuals must meet all inclusion criteria to be eligible to participate in the study. Caregiver criteria include (1) being aged at least 18 years, (2) being the primary caregiver to an eligible child, (3) ability to speak English or Spanish well enough to be interviewed, and (4) having a mobile phone capable of sending and receiving SMS text messages. Child criteria include (1) age 0 to 17 years, (2) GMFCS level IV or V CP [32], and (3) being cared for by a respiratory specialist or receiving daily respiratory treatments (oxygen, ventilation, airway clearance device, and medications).

Exclusion Criteria
During this study, participants are asked to reply to SMS text messages when received at random times during daytime hours and connect with an intervention clinical responder either at home, in person at a mutually agreeable location, by mobile phone, or over the internet. Any individual lacking the ability or willingness to engage in SMS text messaging or clinical responder interactions during the study will be excluded from participation in the study.

Recruitment and Screening
We will recruit caregivers of children with severe CP aged between 0 and 17 years. We will recruit up to 90 participants (n=45, 50% at each site) divided across 3 waves. In each wave, there is a 1- to 2-month enrollment period. We anticipate that approximately 80% of those screened will enroll, requiring approximately 110 individuals to be screened.

Using diagnostic codes for CP (International Classification of Diseases, Tenth Revision [ICD-10]: G80-83), we will identify potential participants by reviewing clinic registries and electronic health record data, which contain detailed information about children and their diagnoses. We will send an opt-out letter that alerts families that a research study is being conducted and their child may be eligible, with a contact number to call if they wish to opt out of the research or if they wish to receive additional information or have any questions. Potentially eligible caregivers will be contacted by telephone to screen for eligibility and interest.

If the research team is not notified that a family wishes to opt out of the research, the study research personnel will attempt to call the families (or meet them at an upcoming visit) to complete screening, informed consent, baseline questionnaires, and random group assignment. CP status and additional eligibility criteria will be determined with a reliable and valid parent questionnaire and screener conducted at the beginning of the initial telephone contact [32]. Individuals who do not meet the criteria for participation in this trial (screen failure) because they meet ≥1 exclusion criteria that are likely to change over time may be rescreened. Theoretical examples might include a child developing a need for respiratory treatment or families acquiring a mobile phone capable of sending and receiving SMS text messages.

All study participants will undergo informed consent, including authorization to view the child’s medical record and participate in action planning, rapid clinical response, and weekly SMS text message surveillance.

Study Design
This is a 2-site pilot randomized controlled clinical trial to establish the RE-PACT protocol’s feasibility, acceptability, and fidelity as well as an estimate of effect size. We anticipate being underpowered to assess the efficacy of the intervention in this pilot study; however, to inform future randomized controlled trial power estimates, we will test differences between the intervention and control groups in primary and secondary clinical outcomes.

Study participants will be randomly assigned to receive usual care through the complex care clinical program at UW or UCLA or the study intervention, RE-PACT. Random allocation will be concealed from the research staff conducting recruitment and will use a 1:1 allocation with random block sizes of 2 and 4. Block randomization will be achieved with a computer-generated random number list prepared by the study biostatistician without clinical involvement in the trial. Randomization will be stratified by site to account for site-specific study characteristics.

RE-PACT will be run through 3 successively larger 6-month trials (waves), allowing ongoing protocol refinement between waves, guided by prespecified definitions of success for feasibility, acceptability, and fidelity measures. Each wave has a specific protocol refinement focus (wave 1: onboarding, training, recruitment, and data collection; wave 2: randomization and intervention activities; and wave 3: rapid enrollment and the conduct of all protocol activities with high fidelity). Participants in both groups will undergo assessments of demographic, clinical, and caregiving measures using...
questionnaires and medical record review case report forms at baseline and at 6 months after enrollment. Intervention feasibility, acceptability, and fidelity data will be collected from parent reports, medical records, and research team logs using case report forms.

Description of the Intervention

RE-PACT uses a dynamic JIT adaptive intervention design [33] to deliver proactive intervention based on risk modeling and partnership between the care team, patients, and families. Although the causes of respiratory illness in severe CP are modifiable, they are also broad and require distinct responses, even for the same child, over time. RE-PACT assumes that (1) every patient with severe CP has a risk of hospitalization, (2) some risks are knowable via the ecosystem of data generated around patient care, and (3) an intervention delivered when risk is increasing can reduce hospitalizations. RE-PACT’s design addresses the changing needs of a child and family. RE-PACT involves action planning, rapid clinical response to prevent and manage respiratory illness, and weekly SMS text messaging surveillance of caregiver confidence for their child to avoid hospitalization.

Action Planning

Overview

All intervention families will receive respiratory illness action plans within 1 month of study entry. The action plan format and process are adapted from the original PACT study, and the contents include (at minimum) recognizing, describing, and managing the child’s known contributors to respiratory illness. The three main components of the action plans are (1) focus area for the action plan (eg, asthma, aspiration, and seizures); (2) severity levels corresponding to objective and subjective indicators of baseline (green), concerning (yellow), and severe (red) statuses (eg, >2 L/min of oxygen); and (3) specific actions that caregivers should take to manage each status (eg, increase vest therapy, albuterol, suction every 4 hours, and use oxygen up to 4 L/min). As needed, JIT plans are also created at times of low confidence by parent request or by clinician determination during the study period. Any plan created will be developed with families, target an issue that plausibly will recur and lead to respiratory illness–related ED or hospital visit, and, when relevant, be harmonized with prior plans and reflect pulmonologist agreement.

Mobile Health Platform

The mobile health (mHealth) platform is built from an earlier study, Assessing Confidence at Times of Increased Vulnerability (ACTIV) [29], which was designed to elicit a SMS text rating of confidence to avoid hospitalization in the next month (ratings range from 1 to 10, where 1 is lowest confidence, and 10 is highest confidence; Figure 1). The platform supports English and Spanish languages. Beginning on the Sunday after enrollment, families will start receiving weekly SMS text messages asking them to rate their confidence for their child to avoid hospitalization in the next month. SMS text messages are programmed to be sent at random days and times to caregivers, averaging once weekly (Sunday to Thursday) between 8 AM and 9 PM (local time). The Sunday-to-Thursday time frame was chosen to support a feasible response during business days and hours. After 2 hours of nonresponse, a reminder is sent, and this is repeated up to 2 times at 2-hour intervals. Clinical responders will receive an email notification in real time if a participant reports low confidence. In addition, clinical responders will receive an SMS text message notification between 9 AM and 6 PM with the report of low confidence. If a response comes outside of these hours, it will be delayed until the next day.

Figure 1. Schematic of the mobile health (mHealth) SMS text message process in which all study participants receive weekly SMS text messages asking them to rate their confidence for their child to avoid hospitalization in the next month.
Rapid Clinical Response

This response is adapted from our prior intervention (PACT) [28]. In RE-PACT, a clinical responder guides the JIT response, adapting to the current child and family situation. Triggers for the clinical responder include (1) low family-reported confidence (a confidence rating of <5) during mHealth messaging, (2) hospital discharge, and (3) family call or electronic message to the clinic owing to acute respiratory concerns (Figure 2). Clinical responders are clinicians, including medical doctors, nurse practitioners, registered nurses, and care coordinators (or equivalent). The same responder intends to work with the family throughout study enrollment.

Figure 2. Summary of the Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT) intervention. The figure illustrates low-confidence SMS text messages as the trigger of rapid clinical response. Other triggers include hospital discharge or family-expressed respiratory concerns through telephone call or electronic message to the clinic.

Rapid clinical responses include 3 interactions between family participants and clinical responders. First, a triage contact occurs within 24 hours of a trigger (during business hours). The triage contact goals are to determine the nature of the trigger, whether an action plan exists for the situation, and whether the issue is within the clinical responder’s clinical practice scope. If not within the scope, the issue is referred to the relevant support (eg, a specialty physician or clinic social worker). Second, a response planning visit occurs either as a component of the triage contact or at a mutually agreed upon time within 72 hours of the trigger. Third, at least 2 follow-up contacts occur within 2 weeks of the trigger, with additional follow-ups as indicated by ongoing need until the issue is resolved. All contacts can occur through any of the following, at the preference of the family: telephone call, clinical encounter (telehealth, clinic, and hospitalization), or a home visit. The follow-up contacts can occur through electronic communication if the clinical responder and family determine this to be appropriate. At each contact point, there are two goals: (1) ensuring that the family understands red flags, relevant medications, and whom to call and when and keeps notes about the issue; and (2) coaching and skill transfer for the family to generate solutions and lead actions, with the responder intervening if the family is stuck or if clinical needs dictate intervention. Each contact point has scripting to guide the clinical responder as well as electronic health record documentation templates. At the end of a clinical responder event, the responder determines whether the issue affects respiratory health, is likely to recur, and poses a risk for future ED or hospital visits. If all of these are true, the responder either updates existing action plans or creates a new one to address the issue. A participant is considered to have completed the study if they have completed the baseline and 6-month follow-up assessments (Table 1; Figure 3).
Figure 3. Schematic of the study design of Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT) intervention enrollment period, enrollment visit, postenrollment evaluation, and protocol refinement. The protocol is refined between each of the 3 waves of the RE-PACT study. JIT: just-in-time; mHealth: mobile health; REDCap: Research Electronic Data Capture; UCLA: University of California, Los Angeles; UW: University of Wisconsin–Madison.
Table 1. Schedule of activities of the Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT) intervention throughout the study period, with the depiction of personnel involved.

<table>
<thead>
<tr>
<th>Activities</th>
<th>Study period (personnel involved)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Enrollment visit (research coordinator)</td>
</tr>
<tr>
<td></td>
<td>0 (T₀)ᵃ</td>
</tr>
<tr>
<td>Confirm eligibility</td>
<td>✓</td>
</tr>
<tr>
<td>Informed consent</td>
<td>✓</td>
</tr>
<tr>
<td>Baseline assessment</td>
<td>✓</td>
</tr>
<tr>
<td>6-mo assessment</td>
<td></td>
</tr>
<tr>
<td>Randomization</td>
<td>✓</td>
</tr>
<tr>
<td>Participant compensation</td>
<td>✓</td>
</tr>
<tr>
<td>Usual comprehensive medical care and coordination via complex care program</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Intervention arm only</strong></td>
<td></td>
</tr>
<tr>
<td>SMS text message training</td>
<td>✓</td>
</tr>
<tr>
<td>Weekly mHealthᵇ text message and response</td>
<td>✓</td>
</tr>
<tr>
<td>Intervention overview</td>
<td>✓</td>
</tr>
<tr>
<td>Create action plan</td>
<td>✓</td>
</tr>
<tr>
<td>Action planning</td>
<td>✓</td>
</tr>
<tr>
<td>Rapid clinical response when triggered</td>
<td>✓</td>
</tr>
<tr>
<td>Monthly study assessments</td>
<td>✓</td>
</tr>
</tbody>
</table>

ᵃMonth (time point).
ᵇmHealth: mobile health.

Outcomes

**Primary Study End Points: Feasibility, Acceptability, and Fidelity**

The specific measures and prespecified definitions of success for primary study end points, including feasibility, acceptability, and fidelity, are listed in Table 2. These measures will be summarized between each of the 3 waves, with protocol adjustments made for any measures that do not meet the definition of success.
Table 2. Primary study end points to evaluate the feasibility, acceptability, and fidelity of Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT; n=90).

<table>
<thead>
<tr>
<th>Measure and measure detail</th>
<th>Success definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feasibility</strong></td>
<td></td>
</tr>
<tr>
<td>Recruitment</td>
<td>Days to enroll target, mean (SD) &lt;14 (1)</td>
</tr>
<tr>
<td>Intervention onset</td>
<td>Days between randomization and “T₀α” activity, mean (SD) &lt;7 (1)</td>
</tr>
<tr>
<td>Time to action plan</td>
<td>Days to action plan creation &lt;30</td>
</tr>
<tr>
<td>Intervention time</td>
<td>Time logged (min) for action planning and for coaching activities, mean (SD) N/A&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Intervention costs</td>
<td>Mileage and travel costs; personnel salary; training costs; and other incurred costs, total N/A</td>
</tr>
<tr>
<td>Intervention triggers</td>
<td>Number per patient (annualized), both respiratory and nonrespiratory focused N/A</td>
</tr>
<tr>
<td><strong>Acceptability</strong></td>
<td></td>
</tr>
<tr>
<td>Enrollment</td>
<td>Enrollment rate (number of patients enrolled/number approached) &gt;80%</td>
</tr>
<tr>
<td>Consent refusal</td>
<td>Categorized reasons for refusal N/A</td>
</tr>
<tr>
<td>Loss and dropouts</td>
<td>Dropout rate (active or passive) before 6 mo (number of dropouts/number enrolled) &lt;10%</td>
</tr>
<tr>
<td>Action plan, SMS text messaging and clinical responder satisfaction</td>
<td>Do caregivers use the action plan, coaching, and texting? How could it be improved? Would caregivers recommend this to another family? N/A</td>
</tr>
<tr>
<td><strong>Fidelity</strong></td>
<td></td>
</tr>
<tr>
<td>Enrollment duration</td>
<td>Time (mo) of participant enrollment in the study, mean (SD) 6 (1)</td>
</tr>
<tr>
<td>Action plan creation</td>
<td>Number of respiratory and overall action plans per patient and action plan focus areas ≥1</td>
</tr>
<tr>
<td>Rapid clinical response: home or web-based visit</td>
<td>Success rate (number of visits completed and number expected); stratify by trigger and by “respiratory” and “nonrespiratory” &gt;80%</td>
</tr>
<tr>
<td>mHealth&lt;sup&gt;c&lt;/sup&gt; texting</td>
<td>Response rates (number of SMS texts responded and number expected); “respiratory” and “nonrespiratory” &gt;90%</td>
</tr>
<tr>
<td>Crossover</td>
<td>Number of patients inappropriately receiving any intervention component 0</td>
</tr>
<tr>
<td>Data collection</td>
<td>Complete entry and exit questionnaire, monthly questionnaire, and chart review data (number of data collection events completed and number of total data collection events) &gt;95%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Enrollment visit  
<sup>b</sup>N/A: not applicable.  
<sup>c</sup>mHealth: mobile health.

**Clinical End Points**

The study’s secondary objective is to estimate the effect size of RE-PACT. The clinical end points are listed in Textbox 1. The primary clinical end point is severe respiratory illness, defined as a respiratory diagnosis requiring hospitalization. **Respiratory diagnosis** is defined as a discharge diagnosis of any of the following: asthma, pneumonia (community or hospital acquired), bronchiolitis, influenza, upper or lower respiratory tract infection, tracheitis, aspiration pneumonia and pneumonitis, chronic lung disease, and respiratory failure [34]. **Hospitalization** is defined as a nonselective, unscheduled hospital encounter (inpatient or observation status), accompanied by both an admission history and physical examination as well as a discharge summary note signed by a physician or advanced practice provider. Field-testing the assessment of this end point with trained research personnel at study sites demonstrated high interrater reliability (κ>0.9).
Clinical end points of Respiratory Exacerbation–Plans for Action and Care Transitions (RE-PACT).

**Primary clinical end point**
- Severe respiratory illness, defined as a respiratory diagnosis requiring hospitalization

**Secondary clinical end points**
- Hospital days during severe respiratory illness
- Systemic steroid courses (systemic steroids [exclude inhaled or topical steroids for the purposes of defining an illness]: hydrocortisone, prednisone, prednisolone, dexamethasone, methylprednisolone, and triamcinolone acetonide; common inhaled steroids: fluticasone, budesonide, mometasone, beclomethasone, and triamcinolone [14-16,35])
- Systemic antibiotic courses (antibiotics: amoxicillin or amoxicillin/ and clavulanate, ampicillin, ampicillin and sulbactam, azithromycin, cefdinir, cefepime, cefixime, cefpodoxime, ceftazidime, ceftriaxone or cefotaxime, cefbuten, cefuroxime, cephalixin [Keflex], clarithromycin, clindamycin, ciprofloxacin, doxycycline, erythromycin, etampenem, imipenem, levofloxacin, linezolid, meropenem, metronidazole, moxifloxacin, oseltamivir, penicillin, piperacillin and tazobactam, rifampin, and vancomycin [14-16,35])
- Respiratory emergency department visits
- Death

The secondary clinical outcomes (Textbox 1) include total hospital days during severe respiratory illness; the number of systemic steroid courses, systemic antibiotic courses, and respiratory ED visits; and death. Hospital days are calculated through resolution if admission occurs in the study time frame, even if discharge occurs after the study exit date. *Systemic corticosteroid course* is defined by oral or parenteral corticosteroids prescribed for respiratory diagnosis, including hydrocortisone, prednisone, prednisolone, methylprednisolone at least 1 mg/kg/d (or 30 mg/d) × minimum 3 days, or dexamethasone at least 0.15 mg/kg/d (or 10 mg/d) × ≥1 days. Physiologic or stress replacement doses in adrenal insufficiency are excluded. *Systemic antibiotic course* is defined by oral or parenteral antibiotics prescribed for respiratory diagnosis for a minimum of 3 days. The specific antibiotics are derived from the Infectious Diseases Society of America pediatric pneumonia guidelines [36] and published literature [35]. Respiratory ED visits are any ED visits not resulting in admission and having a discharge respiratory diagnosis.

**Exploratory Study End Points**

The objectives of the tertiary study are to explore the mediating relationships between RE-PACT and capability, opportunity, motivation, and behavior (COM-B) measures [37]. By blending our foundational research on preventing hospitalizations [17,21] with behavioral intervention theory [38], our conceptual model suggests that decisions to seek care (behaviors) are influenced by capability (family capacity), opportunity (health system and susceptibility), and motivation (confidence). A theorized mechanism of RE-PACT’s effect is that combining action planning, mHealth surveillance, and coaching will increase caregiver COM-B measures to manage respiratory illness in severe CP. The tertiary end points are listed in Textbox 2.

**Assessment Procedures**

Data about research participants (children and their families) will be collected by study research assistants on case report forms using electronic family self-administered questionnaires, structured interviews with research personnel by telephone or in person with enrolled caregivers, and abstraction of child medical record data. Family and child measures will be recorded at baseline, and end points will be recorded at study exit (6 months after the enrollment visit \(T_0\)). Caregiving measures, which may change as a result of the intervention, will be collected at baseline and study exit. Clinical responders will enter data for intervention group families into a clinical response event case report form. Feasibility, acceptability, and fidelity end point data will be collected during each of the 3 waves by research personnel reviewing study logs, conducting monthly chart reviews, and administering surveys (by telephone, in person, or sending electronic self-administered links) with caregivers randomized to the intervention. For control group participants, the feasibility
of assessments will be evaluated by completion rates at study exit. In addition, intervention and control participants will be debriefed at study exit on their experiences in the study and asked for feedback on the strengths and weaknesses, as well as any concerns about the protocol. Between each wave and after the third wave, clinical teams at each site will be debriefed on the strengths and weaknesses, as well as concerns about the protocol.

The CP GMFCS measures and all caregiving measures have been well documented as reliable in the literature [39-45]. We have separately established the reliability of identifying respiratory illnesses in our preliminary research (κ>0.9). We will ensure reliability in data collection through direct observation, data auditing, establishing clear data dictionaries and definitions, using uniform variable definitions, and use of a central data repository coordinated and maintained by UW.

Data Collection, Storage, and Protection

Clinical data (including adverse effects) and clinical laboratory data will be entered into Research Electronic Data Capture (REDCap; UW) managed by the University of Wisconsin, a 21 Code of Federal Regulation Part 11–compliant data capture system provided by the UW Institute for Clinical and Translational Research. The data system includes password protection and internal quality checks, such as automatic range checks, to identify inconsistent, incomplete, or inaccurate data. Clinical data will be entered directly from the source documents or entered directly from secure self-administered questionnaires (surveys) sent via REDCap to participants.

Sample Size Considerations

We will enroll up to 90 participants. On the basis of this team’s preliminary work, we estimate that half (45/90, 50%) of the participants will experience at least 1 respiratory illness during the enrollment period. We expect to be able to maintain contact and collect data from ≥90% (≥81/90) of the participants at the final follow-up, evenly divided between the intervention and control groups. We assume that this sample will not be powered to establish the efficacy of the intervention; however, it will provide a sufficient sample to determine feasibility and estimate effect sizes, which will be used for power calculations in the future large randomized clinical trial. Attainable power levels were calculated for detecting differences in severe respiratory illness rates (primary clinical outcome) between the study arms at the 2-tailed <.05 significance level based on a negative binomial (NB) regression model with an overdispersion parameter of φ=1.0 (Table 3). Hence, large effect sizes with relative risks ranging between 3.0 and 5.0 for comparing the severe respiratory illness rates between the study arms will be detected with 19% to 88% power at the 2-tailed <.05 significance level.

<table>
<thead>
<tr>
<th>Relative risk (control vs intervention)</th>
<th>Number of severe respiratory illnesses in the intervention arm over the 6-mo follow-up period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 (λ=0.02)², %</td>
</tr>
<tr>
<td>3.0</td>
<td>19</td>
</tr>
<tr>
<td>4.0</td>
<td>31</td>
</tr>
<tr>
<td>5.0</td>
<td>42</td>
</tr>
</tbody>
</table>

²Severe respiratory illness rate per patient-month.

Statistical Analysis Plan

The primary outcome data will assess the RE-PACT intervention’s feasibility, acceptability, and fidelity using descriptive statistics. Categorical variables will be displayed as percentages and continuous variables as means with SDs (if normally distributed) or medians with IQRs (if skewed). We will compare observed values with the prespecified definitions of success for each of our feasibility, acceptability, and fidelity measures. We will also determine overall positive, neutral, and negative reports of feasibility and acceptability using content analysis of qualitative (open-ended comments) data. We will explore any patterns if challenges emerge (eg, enrollment refusal or dropout or low reported use of the intervention activities).

We anticipate being underpowered to assess efficacy using the clinical end points of the intervention in this pilot study. Analyses will also estimate the effect size estimates of clinical end points to allow precise sample size calculations for a future large-scale efficacy trial. We will compare differences between the intervention and active control group outcomes at 6 months. The primary clinical outcome is the severe respiratory illness rate, defined as the total number of severe respiratory illnesses divided by the person-months over the 6-month follow-up period. The severe respiratory illness rate will be analyzed using an NB regression model to account for overdispersion in the count data. For the primary analysis, univariate NB regression analysis will be conducted with a study arm as a predictor variable. The study site will be included as a stratification factor in the primary analysis to account for stratified randomization. The observed effect size of the analysis will be quantified in terms of relative risk and reported along with the corresponding 95% CI. As a secondary analysis, multivariate NB regression analysis will be performed to compare the severe respiratory illness rates between the study arms. This analysis will include clinical and demographic characteristics as covariates in an initial nonparsimonious model. The least absolute shrinkage and selection operator and elastic net penalty methods for NB regression models will be used to identify a parsimonious model with independent covariates.

Longitudinal changes in the severe respiratory illnesses within and between study arms will be evaluated with a generalized linear mixed effects model with a logit link function and
participant-specific random effects. An autoregressive correlation structure will be used to account for within-participant correlations. In this analysis, the presence or absence of severe respiratory illness at the monthly assessments will be the dependent variable, the study arm will be included as a predictor variable, and the study site will be included as a stratification variable to account for the stratified randomization.

The secondary clinical outcomes include total hospital days during severe respiratory illness; the number of systemic steroid courses, systemic antibiotic courses, and respiratory ED visits; and death. The number of systemic steroid courses, systemic antibiotic courses, and respiratory ED visits over the 6-month follow-up period will be analyzed using NB regression analysis as described previously for the primary outcome. Observed effect sizes and the corresponding 95% CIs will be reported. The presence or absence of systemic steroid courses, systemic antibiotic courses, and respiratory ED visits will be documented at the monthly assessments, and longitudinal changes within and between study arms will be analyzed using generalized linear mixed effects modeling with a logit link function and patient-specific random effects. The total number of hospital days over the 6-month follow-up period will be analyzed using ANOVA with the study site as a stratification factor. In a secondary analysis, an analysis of covariance (ANCOVA) will be performed where clinical and demographic baseline characteristics will be included as covariates, and the least absolute shrinkage and selection operator method will be used to identify a parsimonious model. Longitudinal changes in the number of hospital days per hospitalization will be analyzed using a normal mixture linear mixed effects model with patient-specific random effects. The normal mixture component will be included in the model to capture the probabilities of hospitalization at the monthly follow-up. Parameter estimation will be performed using the expectation-maximization algorithm, the standard method for the parameter estimation of mixture models.

Two-tailed $P$ values of $<.05$ will be considered statistically significant. Missing values (e.g., owing to loss of follow-up and missing monthly visits) will be evaluated by conducting a sensitivity analysis comparing the results obtained from the complete case analysis with those obtained from imputation-based analyses. Specifically, multiple imputations will be used to impute the missing values of the primary and secondary clinical outcomes. For monotonic missing value data structures, we will use regression-based multiple imputation techniques. By contrast, we will use Markov Chain Monte Carlo–based imputation techniques for nonmonotonic missing value data structures.

Although we anticipate that the intervention and control groups will be similar owing to random assignment, we will adjust for any variables in our analysis that are not equal between the groups, given the small sample size. In addition, we will analyze for any effect of primary home language on the study outcomes because this may affect families’ ability to navigate the systems of care in the United States.

Finally, as a planned exploratory analysis, we will test the mediating effect of caregiver COM-B measures on the relationship between intervention and respiratory illness outcomes. The mediating effects will be evaluated by conducting a multistep analysis approach. In the initial step, NB regression analyses will be conducted to examine whether there are differences in respiratory illness outcomes (the number of severe respiratory illnesses, systemic steroid courses, systemic antibiotic courses, and respiratory ED visits) between the intervention and control arms. In the next step, we will conduct a sequence of univariate analyses by regressing each potential mediator variable (caregiver capability COM-B measures) on the binary study arm variable. If significant associations between the potential mediator variables and the study arm are detected, we will regress the respiratory illness outcomes on both the mediator variables and study arm indicator variables using ANCOVA. The mediation effect for each potential mediator variable will then be tested using the Sobel test based on the slope parameter estimates from the corresponding regression models.

**Ethical Considerations**

This study received initial approval from the UW health system’s institutional review board on January 19, 2022 (20211532). All participants will provide informed consent before taking part in the study. Informed consent materials will be provided in private spaces in both written and verbal formats and will review in detail the study design, including random assignment to the intervention and control groups, potential risks of participation, protections against risk, and the rights of human research subjects. The informed consent process will also include review and signing of the Health Insurance Portability and Accountability Act waiver, allowing researchers to review the child’s medical records. Parents will be able to decline parts of the study and still participate in other parts and can revoke their consent at any point. Any identifying information kept for the purpose of contacting participants will be kept secure, in REDCap, a locked filing cabinet or in a password-protected electronic file and will be destroyed when the study is complete. The study is monitored by the Data Monitoring Committee at the UW-Madison Institute for Clinical and Translational Research. All participants receive an incentive of US $200, divided in 2 parts: US $100 at enrollment and US $100 after the exit survey, in the form of a gift card, check, or cash.

**Results**

The recruitment of the first wave began on April 27, 2022. To date, we have enrolled 30 (33%) out of 90 participants, as projected. The final wave of recruitment will end by October 31, 2023, and the final participant will complete the study by April 30, 2024. We will start analyzing the complete responses by April 30, 2024, and the publication of results is expected at the end of 2024.

**Discussion**

**Summary**

We describe the protocol for a pilot clinical trial of RE-PACT, a JIT adaptive intervention to reduce respiratory illness in severe
CP. A recent expert consensus statement on preventing and managing respiratory disease in young people with CP highlighted the need for 4 activities: early identification of risk factors; regular assessment of risk; effective partnerships among multidisciplinary teams, families, and individuals with CP; and proactive treatment of respiratory disease [46]. The RE-PACT intervention protocol aligns with each of these 4 critical areas.

For children with severe CP, RE-PACT was designed by families and clinicians from promising earlier interventions to manage health crises with proactive action planning, simple surveillance of family confidence to avoid hospitalization through frequent SMS text messaging, and JIT adaptive rapid clinical responses. This intervention breaks down barriers to equitably connect families and clinical teams precisely when it matters most. This approach is innovative because we tailor the intensity of the response (eg, telephone call and clinic visit) and its content to family- and illness-specific needs. The adaptive nature of the intervention ensures that it meets caregiver needs for that specific instance, flexibly changing for individuals over time in response to each intervention trigger. RE-PACT is also designed to acknowledge that respiratory illness in severe CP is driven by both respiratory and nonrespiratory comorbid and social conditions [11,46] (eg, neuromuscular weakness, seizures, dysphagia, feeding intolerance, health system navigation barriers, and coordination problems).

By conducting successively larger waves of the RE-PACT protocol, we expect to produce a final high-quality protocol that has been developed sufficiently to support the implementation of a large-scale multisite clinical efficacy trial.

**Limitations**

This study has several limitations. Although we anticipate achieving a feasible, acceptable, and high-fidelity protocol by the end of the third wave, it is possible that some challenges may remain. We anticipate being underpowered to assess intervention efficacy. Despite the randomized design, allocation concealment is not possible. As randomization occurs at the level of the family, inadvertent intervention contamination to nonintervention patients in the same clinical program may occur. This risk will be minimized by having research staff (not clinical staff) manage action planning and SMS text messaging procedures. In future studies, we will consider alternative designs (such as a stepped wedge trial), randomizing at the clinic level to avoid this threat. Threats to external validity will reflect the relatively narrow population of families recruited from 2 complex care programs. Although it is a strength that the intervention will be conducted in English and Spanish, future expansion to populations of children with CP outside of complex care programs and from more geographically and culturally diverse settings will be helpful. As research continues, it will be important to examine whether this intervention design, which relies in part on the use of digital technology, addresses disparities in access to care and inequities in outcomes.

**Conclusions**

Despite the limitations, our pilot RE-PACT intervention represents an innovative and promising strategy to reduce severe respiratory illness among children with severe CP. RE-PACT operationalizes universal action planning, mobile SMS text messaging, and a JIT adaptive rapid clinical response to deliver timely customized care to families of children with severe CP. This protocol describes detailed methods to assess intervention feasibility, acceptability, and fidelity. This line of research may be relevant to other researchers and health care providers who wish to adopt a similar early intervention strategy for patients with chronic and complex conditions at high risk of future hospitalization.

**Acknowledgments**

The research reported in this publication was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health (R34HL153570). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

**Data Availability**

The data sets generated and analyzed during this study are available from the corresponding author on reasonable request.

**Authors’ Contributions**

RC, the principal investigator of this study, obtained grant funding and conceived the study. CL, HK, TK, PC, CC, DG, BK, ME, and SI participated in the design of the study. AF and RC drafted the manuscript. RC, CL, GW, KH, LP, RD, SI, and TW are responsible for recruitment and major study activities. All authors contributed to the intellectual content of the manuscript and the development of the trial protocol, and all authors have read, revised, and approved the final manuscript.

**Conflicts of Interest**

None declared.

**References**


39. Fleischman et alJMIR RESEARCH PROTOCOLS


**Abbreviations**

- **ACTIV**: Assessing Confidence at Times of Increased Vulnerability
- **ANCOVA**: analysis of covariance
- **COM-B**: capability, opportunity, motivation, and behavior
- **CP**: cerebral palsy
- **ED**: emergency department
- **GMFCS**: Gross Motor Function Classification System
- **ICD-10**: International Classification of Diseases, Tenth Revision
- **JIT**: just-in-time
- **mHealth**: mobile health
- **NB**: negative binomial
- **PACT**: Plans for Action and Care Transitions
- **RE-PACT**: Respiratory Exacerbation–Plans for Action and Care Transitions
- **REDCap**: Research Electronic Data Capture
- **UCLA**: University of California, Los Angeles
- **UW**: University of Wisconsin–Madison

©Alyssa Fleischman, Carlos Lerner, Heidi Kloster, Paul Chung, Thomas Klitzner, Christopher Cushing, Danielle Gerber, Barbara Katz, Gemma Warner, Kristina Devi Singh-Verdeflor, Roxana Delgado-Martinez, Lorena Porras-Javier, Siem Ia, Teresa Wagner, Mary Ehlenbach, Ryan Coller. Originally published in JMIR Research Protocols (https://www.researchprotocols.org), 08.01.2024. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on https://www.researchprotocols.org, as well as this copyright and license information must be included.
Epidemiology of Syphilis in Pregnancy and Congenital Syphilis in Brazil and the Risk or Associated Factors: Protocol for a Systematic Review

Yago Tavares Pinheiro¹, PhD; Janmilli da Costa Dantas¹, PhD; Jose Rebberly Rodrigo Holanda², MD; Ankilma do Nascimento Andrade Feitosa³, PhD; Richardson Augusto Rosendo da Silva¹, PhD

¹Federal University of Rio Grande do Norte, Natal, Brazil
²Federal University of Rio Grande do Norte, Caicó, Brazil
³University Center Santa Maria, Cajazeiras, Brazil

Corresponding Author:
Yago Tavares Pinheiro, PhD
Federal University of Rio Grande do Norte
Lagoa Nova
Natal, 59078-900
Brazil
Phone: 55 (83) 99664 7797
Fax: 55 (83) 99664 7797
Email: vagostavares5@gmail.com

Abstract

Background: Syphilis in pregnancy and congenital syphilis are growing public health issues worldwide. Several factors can influence their occurrence in the population. Therefore, understanding the epidemiology of this condition and the factors that influence its occurrence is fundamental for decision-making by clinicians and health managers. However, so far, no systematic review has summarized and analyzed data on the incidence, prevalence, and predictors of these diseases in Brazilian cities, considering different sociocultural, demographic, economic, sanitary, and spatial-temporal characteristics presented across locations.

Objective: We propose a systematic review protocol to gather and analyze data on the incidence, prevalence, and risk or associated factors of syphilis in pregnancy and congenital syphilis in Brazil, taking into account different local or regional contexts.

Methods: Searches will be conducted in CINAHL, MEDLINE, LILACS, Embase, and Web of Science databases. We will include observational studies (ie, cross-sectional, longitudinal, or case-control studies), analyzing the incidence, prevalence, and risk or associated factors of syphilis in pregnancy and congenital syphilis in Brazil from primary data. The diagnosed syphilis will be assessed based on direct pathogen detection tests or through immunological, treponemal or nontreponemal tests, following Brazilian protocols for diagnosing syphilis. The studies are currently undergoing screening in the databases, and after this step, 2 reviewers will perform all identified documents. The Newcastle-Ottawa Scale and the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) system will be used to assess methodological quality and quality of evidence of studies, respectively. The Kappa coefficient will assess the agreement between researchers in each study stage. Cochran Q test will assess the heterogeneity among studies. Then, a random-effects meta-analysis will be performed.

Results: Results will be discussed based on subgroup analysis, which is as follows: (1) type of syphilis (in pregnancy or congenital), (2) type of study (case-control and cross-sectional studies for analysis of associated factors and longitudinal studies for risk factors), and (3) contextual factors (ie, region of country, socioeconomic and demographic characteristics, and year of study). This systematic review is expected to be completed by December 2023, and our results will be disseminated through publication in peer-reviewed journals and scientific events.

Conclusions: This systematic review aims to assist health care managers and professionals in their decision-making to control these diseases in Brazil, considering location heterogeneity. Furthermore, countries with health systems and demographic and socioeconomic contexts similar to those of Brazil may benefit from this information.

International Registered Report Identifier (IRRID): DERR1-10.2196/50702
sexually transmitted diseases; epidemiology; prevalence; incidence; Brazil; syphilis; pregnancy; sociocultural; economic; congenital syphilis; heterogeneity; decision-making

Introduction

Syphilis is a sexually transmitted infection caused by *Treponema pallidum* and is a major public health issue worldwide [1]. Despite the efforts of health care professionals to control this infection in Brazil, cases of syphilis have increased in recent years [2-4], impacting public and private health care systems and highlighting the need to improve disease surveillance [5,6]. Globally, 2 million out of 36 million syphilis infections occur in pregnant women [7], resulting in congenital syphilis (infection of the fetus) and adverse events (eg, early fetal death, stillbirth, premature birth, low birth weight, and neonatal death) [8,9].

Recently, an outbreak of syphilis has been observed among men and women in more economically developed countries, which can be explained by changes in the sexual behavior of individuals and increased exposure to the risk of infection due to a false sense of security stemming from new treatments and an increased search for sexual partners over the internet [10].

In this context, understanding the epidemiology and control of this disease becomes more complex and difficult.

Syphilis in pregnancy and congenital syphilis can be controlled with health care measures, such as access to prevention services, early diagnosis, and treatment [4,11,12]. Conversely, these measures require the analysis of epidemiological data and predictors [4,11]. Although studies in Brazilian cities analyzed the incidence, prevalence, and predictors of syphilis in pregnancy and congenital syphilis [13-17], each city presented different sociocultural, demographic, economic, sanitary, and spatial-temporal characteristics, hindering data extrapolation to the national territory.

Summarizing and analyzing the incidence, prevalence, and risk or associated factors of syphilis in pregnancy and congenital syphilis must take into account location heterogeneity. This type of analysis enables a broader understanding of the problem, improves control strategies and equity in disease management, and establishes reference data to help disease screening efforts in Brazil. Despite the relevance of the theme, no systematic review has been conducted to date on the epidemiological data of gestational and congenital syphilis or its predictors, subgrouping and analyzing this information from different contexts.

Thus, we propose a systematic review protocol to gather and analyze data on the incidence, prevalence, and risk or associated factors of syphilis in pregnancy and congenital syphilis in Brazil, taking into account different local or regional contexts.

Methods

Study Design

This systematic review protocol was developed according to PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) [18], which will also guide the systematic review. The protocol has been registered in PROSPERO (CRD42022329329).

Eligibility Criteria

Observational studies whose sample comprised cases of syphilis in pregnant women or newborns in Brazil will be included in the systematic review. Table 1 [2,19,20] presents the eligibility criteria used in the review.
Table 1. Eligibility criteria for the systematic review.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>• Cross-sectional, longitudinal, or case-control studies conducted in Brazil</td>
<td>• Reviews, opinion articles, editorials, or publications without primary data or not peer-reviewed</td>
</tr>
<tr>
<td></td>
<td>• Studies based on primary data</td>
<td>• The most complete and recent data will be used if studies report the same data in multiple sources [19,20].</td>
</tr>
<tr>
<td>Population and location</td>
<td>• Studies in which the sample involved pregnant women or newborns with syphilis</td>
<td>• Studies with samples involving other populations (non-pregnant women or men)</td>
</tr>
<tr>
<td></td>
<td>• Studies with residents in Brazil</td>
<td>• Studies presenting the incidence or prevalence of combined infections (i.e., syphilis with other sexually transmitted infections) and not allowing isolated analysis</td>
</tr>
<tr>
<td>Outcomes</td>
<td>• Studies reporting the prevalence or incidence of Treponema pallidum (syphilis) infection or its risk or associated factors in pregnant women or neonates</td>
<td>• No restriction regarding language or year of publication</td>
</tr>
<tr>
<td></td>
<td>• Studies that diagnosed syphilis based on direct pathogen detection tests or through immunological, treponemal, or non-treponemal tests, in accordance with Brazilian protocols for diagnosing syphilis [2]</td>
<td>• No restriction regarding to year in which the study was carried out or published</td>
</tr>
</tbody>
</table>

Language —a

Time frame —

—aNot applicable.

Study Selection

Textbox 1 presents the search strategy. Searches will be conducted in the CINAHL, MEDLINE, LILACS, Embase, and Web of Science databases. Grey literature will be also searched using the reference lists of relevant studies in addition to using databases such as Open Gray and Google Scholar. Further, reports with epidemiological data on syphilis in the country will be screened in the electronic database of the Brazilian Ministry of Health.

Two researchers will independently search, identify potentially eligible studies, and remove duplicates. Then, inclusion and exclusion criteria will be applied to titles and abstracts, eligible studies will be read in full, and reasons for exclusion will be recorded. Disagreements between researchers will be resolved by discussion or with a third researcher. The flowchart of the study selection is described in Figure 1.

Textbox 1. Search strategy.

```
#1 "syphilis" [Title/Abstract] OR "congenital syphilis" [Title/Abstract] OR "treponemal infections" [Title/Abstract] OR "T. pallidum" [Title/Abstract] OR "pallidum" [Title/Abstract] OR "serosyphilis" [Title/Abstract] OR "sexually transmitted diseases" [Title/Abstract]
#2 "pregnant" [Title/Abstract] OR "women" [Title/Abstract] OR "congenital" [Title/Abstract]
#3 "incidence" [Title/Abstract] OR "prevalence" [Title/Abstract] OR "prevalence study" [Title/Abstract] OR "cross-sectional study" [Title/Abstract] OR "observational study" [Title/Abstract]
#4 "risk factors" [Title/Abstract] OR "associated factors" [Title/Abstract] OR "measures of association, exposure, risk or outcome" [Title/Abstract]
#5 "brazil" [Title/Abstract] OR "brazilian" [Title/Abstract]
#6 #1 AND #2 AND #3 OR #4 AND #5
```
Assessment of Methodological Quality and Quality of Evidence

The Newcastle-Ottawa Scale will be used to assess the methodological quality of studies [21]. This scale includes 8 items categorized into 3 domains (ie, selection, comparability, and outcome or exposure) to assess the risk of bias in nonrandomized studies. The Newcastle-Ottawa Scale has specific tools for cohort and case-control studies. Thus, adaptations will be made to allow the proper assessment of the potential sources of bias in cross-sectional studies. In addition, quality of evidence will be analyzed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) system, which classifies evidence as high, moderate, low, and very low [22,23].

Data Extraction and Synthesis

The following data will be extracted and entered into a Microsoft Excel spreadsheet: first author, year of publication, type of study (eg, longitudinal, cross-sectional, or case-control), type of syphilis (eg, in pregnancy or congenital), the diagnostic method used, study location (eg, city and state), participants (eg, sample size, age, type of population, and presence of co-infection), population setting (eg, community, health care centers, schools, neighborhoods, and the environmental context of the participants), date of data collection, sampling method, and main results (eg, incidence, prevalence, and risk or associated factors).

After summarizing the studies, results will be discussed based on subgroup analysis, as follows: (1) type of syphilis (eg, in pregnancy or congenital), (2) type of study (eg, case-control and cross-sectional for analysis of associated factors and longitudinal for risk factors), and (3) contextual factors (eg, region of country, socioeconomic and demographic characteristics, and year of study).

Statistical Planning

Kappa coefficient will assess the agreement between researchers [24]. The unadjusted incidence or prevalence and the standard error will be recalculated based on the numerator and denominator values presented in each study. Furthermore, the prevalence or incidence may be reported using the direct method of standardization, adjusted for the variables of age, study location, and presence of co-infection. If the study does not provide data for calculating adjusted incidence or prevalence, the researchers will request this information from the study authors.

Additionally, a meta-analysis will be performed using a random-effects model due to the potential heterogeneity among studies. The random-effects model is applied when the aim is to combine several studies that have similar objectives but are conducted in different ways (ie, exhibiting methodological
heterogeneity) [25]. Moreover, the Freeman-Tukey double arcsine transformation will stabilize variances to maintain the estimates of individual effects of each study [26]. Cochran Q test will assess the heterogeneity among studies [27]. $I^2$ values of 25%, 50%, and 75% will represent low, medium, and high heterogeneity, respectively [28].

Studies will undergo a subgroup analysis using clustering variables (eg, study location, study population, method of syphilis diagnosis, mean sample size, year of data collection, sampling methods, and methodological quality) to investigate possible sources of heterogeneity [20].

Analyze will be performed using the Review Manager (RevMan) software (version 5.4; Cochrane Collaboration) and the R software (R Core Team), considering a 95% CI.

**Results**

The protocol has been registered in PROSPERO (CRD42022329329). The screening of the studies in the databases has already started, and the entire systematic review is expected to be completed by December 2023. The results of the study will provide evidence that can support decision-making regarding strategies to control syphilis in Brazil and countries with similar health, demographic, and socioeconomic profiles.

Results will be disseminated through publication in peer-reviewed journals and presentation at scientific events.

**Discussion**

**Expected Results and Practical Implications**

After a preliminary search, we found studies in Brazilian cities that analyzed epidemiological data and predictors of syphilis in pregnancy and congenital syphilis [13-17,29]. However, no study has organized and summarized data to perform a broader analysis of this public health issue.

Summarizing local studies will allow the analysis and discussion of epidemiology and risk or associated factors of syphilis in pregnancy and congenital syphilis, considering sociocultural, demographic, spatial-temporal, economic, and sanitary differences in each location. Thus, this systematic review will help in the decision-making of health care managers and professionals to control these diseases in Brazil according to location heterogeneity.

**Limitations**

Some limitations that may compromise the quality of evidence can be found in the systematic review, such as heterogeneity among studies, wide CIs, and uncertainty of estimated effects.

**Acknowledgments**

The authors would like to thank Probatus Academic Services for providing scientific language translation and revision.

This study was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES), Brazil (finance code 001).

**Data Availability**

All data generated and analyzed in this study are available upon request from the corresponding author.

**Authors’ Contributions**

YTP, JCD, and ANAF designed the study and wrote the original draft; JRRH and RARS designed the study and approved the final manuscript.

**Conflicts of Interest**

None declared.

**References**


Abbreviations

GRADE: Grading of Recommendations, Assessment, Development, and Evaluations
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
Corrigenda and Addenda

Correction: Mobile Phone Technology for Preventing HIV and Related Youth Health Problems, Sexual Health, Mental Health, and Substance Use Problems in Southwest Uganda (Youth Health SMS)- Protocol for a Pilot Randomized Controlled Trial

Philip Kreniske¹, PhD; Olive Imelda Namuyaba², BA; Robert Kasumba³, MS; Phionah Namatovu²,³, MPH; Fred Ssewamala²,³, PhD; Gina Wingood⁴, SCD; Ying Wei⁵, PhD; Michele L Ybarra⁶, PhD; Charlotte Oloya⁷, LLB, LLM; Costella Tindyebwa⁷, MA; Christina Ntulo⁸, MA; Vincent Mujune⁷, MPH; Larry W Chang⁹, MPH, MD; Claude A Mellins¹⁰, PhD; John S Santelli¹¹, MPH, MD

¹Community Health and Social Sciences Department and The Institute for Implementation Science in Population Health, Graduate School of Public Health and Health Policy, City University of New York, New York, NY, United States
²International Center for Child Development, Masaka, Uganda
³Washington University in St Louis, St Louis, MO, United States
⁴Department of Sociomedical Sciences, Mailman School of Public Health, Columbia University, New York, NY, United States
⁵Department of Biostatistics, Mailman School of Public Health, Columbia University, New York, NY, United States
⁶Center for Innovative Public Health Research, San Clemente, CA, United States
⁷StrongMinds Uganda, Kampala, Uganda
⁸Malachite Center for Mental Health, Kampala, Uganda
⁹Department of Epidemiology, School of Medicine, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States
¹⁰HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute and Columbia University, New York, NY, United States
¹¹Heilbrunn Department of Population and Family Health, Mailman School of Public Health, Columbia University, New York, NY, United States

Corresponding Author:
Philip Kreniske, PhD
Community Health and Social Sciences Department and The Institute for Implementation Science in Population Health, Graduate School of Public Health and Health Policy, City University of New York
55 W 125th Street
New York, NY, 10027
United States
Phone: 1 6463649600
Email: philip.kreniske@sph.cuny.edu

Related Article:
Correction of: https://www.researchprotocols.org/2023/1/e49352
doi:10.2196/55725

(JMIR Res Protoc 2024;13:e55725) doi:10.2196/55725

In “Mobile Phone Technology for Preventing HIV and Related Youth Health Problems, Sexual Health, Mental Health, and Substance Use Problems in Southwest Uganda (Youth Health SMS): Protocol for a Pilot Randomized Controlled Trial” (JMIR Res Protoc 2023;12:e49352), the authors noted two errors:

The affiliation of author Claude A Mellins was:
Community Health and Social Sciences Department,
Graduate School of Public Health and Health Policy,
City University of New York, New York, NY, United States

It has been revised to:
HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute and Columbia University, New York, NY, United States

The affiliation of authors Charlotte Oloya, Costella Tindyebwa and Vincent Mujune was:
Malachite Center for Mental Health, Kampala, Uganda

It has been revised to:
StrongMinds Uganda, Kampala, Uganda

The correction will appear in the online version of the paper on the JMIR Publications website on January 8, 2024, together with the publication of this correction notice. Because this was
made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

Submitted 21.12.23; this is a non–peer-reviewed article; accepted 21.12.23; published 08.01.24.

Please cite as:
Correction: Mobile Phone Technology for Preventing HIV and Related Youth Health Problems, Sexual Health, Mental Health, and Substance Use Problems in Southwest Uganda (Youth Health SMS)- Protocol for a Pilot Randomized Controlled Trial
JMIR Res Protoc 2024;13:e55725
URL: https://www.researchprotocols.org/2024/1/e55725
doi: 10.2196/55725
PMID:

©Philip Kreniske, Olive Imelda Namuyaba, Robert Kasumba, Phionah Namatovu, Fred Ssewamala, Gina Wingood, Ying Wei, Michele L Ybarra, Charlotte Oloya, Costella Tindyebwa, Christina Ntulo, Vincent Mujune, Larry W Chang, Claude A Mellins, John S Santelli. Originally published in JMIR Research Protocols (https://www.researchprotocols.org), 08.01.2024. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on https://www.researchprotocols.org, as well as this copyright and license information must be included.

Mark Groulx1, PhD; Shannon Freeman2, PhD; Keone Gourlay3, BPl; Dawn Hemingway4, PhD; Emma Rossnagel1, MPH; Habib Chaudhury5, PhD; Mohammadjavad Nouri5, PhD

1University of Northern British Columbia, Prince George, BC, Canada
2School of Nursing, University of Northern British Columbia, Prince George, BC, Canada
3School of Planning and Sustainability, University of Northern British Columbia, Prince George, BC, Canada
4School of Social Work, University of Northern British Columbia, Prince George, BC, Canada
5Department of Gerontology, Simon Fraser University, Vancouver, BC, Canada

Corresponding Author:
Mark Groulx, PhD
University of Northern British Columbia
3333 University Way
Prince George, BC, V2N 4Z9
Canada
Phone: 1 250 960 5837
Email: mark.groulx@unbc.ca

Abstract

Background: The number of people in society living with dementia is growing. In Canada, most people who live with dementia live at home, often in a neighborhood setting. Neighborhood environments can be a source of independence, social engagement, and well-being. They can also contain barriers that limit physical activity, social engagement, and well-being. A dementia-friendly neighborhood includes assets that support persons living with dementia and their caregivers in multiple life domains, including those that support walking within the neighborhood environment.

Objective: The objectives for this scoping review are twofold. First, focusing on walkshed analysis, we aim to extend scholarly understandings of methodological practices used in the monitoring and evaluation of dementia-friendly neighborhoods. Second, we aim to provide clear and practical guidance for those working in planning, design, and public health fields to assess the neighborhood context in support of evidence-based action to improve the lives of persons living with dementia.

Methods: The study design follows Arksey and O’Malley’s scoping review framework and PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidelines. We will conduct a search of peer-reviewed studies in 6 electronic databases to identify the use of Geographic Information System analysis to measure the walkshed of persons living with dementia in a community setting. As age is a primary risk factor associated with dementia, we will also include studies that focus more broadly on community-dwelling older adults aged 65 years and older. Data will be extracted, analyzed, and represented according to 3 domains. This includes study details, walkshed analysis methods, and criteria and indicators used to measure dementia-friendly neighborhoods.

Results: The results of the study and the submission of a manuscript for peer review are expected in June 2024. The results of the review are expected to contribute to an understanding of methods for monitoring and evaluating dementia-friendly neighborhoods. Expected findings will include a detailed breakdown of current parameters and routines used to conduct walkshed analysis. Findings will also convey criteria that can be operationalized in a Geographic Information System as indicators to assess barriers and facilitators to walking in a neighborhood setting.

Conclusions: As far as we are aware, the proposed scoping review will be the first to provide comprehensive methodological or technical guidance for conducting walkshed analysis specific to persons living with dementia. Both the scalability and objective nature of walkshed analysis are likely to be of direct interest to public health practitioners, planners, and allied professionals. Clearly documenting methods used in walkshed analysis can spur increased collaboration across these disciplines to enable an evidence-informed approach to improving neighborhood environments for persons living with dementia.

International Registered Report Identifier (IRRID): PRR1-10.2196/50548
Introduction

Overview

Walkshed analysis identifies the extent of the community environment surrounding a central location that is accessible at a scale where walking is a competitive mode of mobility [1]. Once a walkshed is delineated in a Geographic Information System (GIS), criteria and indicators can identify barriers and enablers to walking [2]. Walkshed analysis is relevant to planning and public-health partnerships that seek to support persons living with dementia. More than 55 million people are currently living with dementia across the world. The global prevalence of dementia is projected to continue to rise by approximately 10 million new cases per year [3]. In Canada, most people experiencing dementia live at home. As of 2016, around 69% of those aged 80 years or younger were living outside of the long-term care system [4]. As an umbrella term, dementia captures the experience of progressive cognitive decline. It can impact an individual’s mood, behavior, and actions, including the performance of key activities of daily living [5]. There are many types of dementia, including Alzheimer dementia, vascular dementia, frontotemporal dementia, lewy body dementia, mixed dementia, and young-onset dementia. Alzheimer disease is the most common cause, contributing to 60% to 70% of cases of dementia [6].

Literature on dementia-friendly communities (and neighborhoods) takes a relational view [7,8]. This view acknowledges that well-being is conditioned by interrelated aspects of a person’s social, built, and ecological surroundings [8-10]. Accordingly, scholars identify dementia-friendly environments as the arrangement of supportive assets into a community fabric that promotes meaningful societal engagement for persons living with dementia and their caregivers [11]. This includes the complex social relations that persons living with dementia experience in a community setting, making the physical neighborhood part of a relational and moral context [12,13].

Scholarship on dementia-friendly communities and neighborhoods stems from calls to better support persons who are living with dementia outside of an institutional setting [11]. These calls reflect the fact that scholars have long viewed neighborhoods as a central relational context shaping individual behavior and life quality [14]. As early as the turn of the 20th century, ideas about neighborhood planning in North America drew on sociological concepts such as Charles H Cooley’s primary group. The primary group and similar concepts asserted that the neighborhood was the main setting for the social relations that informed one’s perspectives and ideals [15].

A long fascination with neighborhood environments helps explain the growing effort to understand how the neighborhood can enable or hinder self-determination for persons living with dementia. This includes aspects of identity development and one’s ability to shape life balance [10,12,16]. Remaining close to the home, or aging in place, is also “closely intertwined with (a person’s) sense of self and identity” [17]. By contrast, moving away from familiar areas can have negative effects on persons living with dementia [18]. To remain active and engaged within their environments while aging in place, persons living with dementia need special considerations and support in their neighborhoods [17].

The influence of the built environment on a sense of community and one’s place therein remains up for debate in an increasingly mobile and digital society [19,20]. At the same time, there is a convincing body of evidence demonstrating that planning and design can impact behavior. The extent to which a neighborhood setting encourages or discourages important social and health behaviors such as walking is a particular focus for planning-health partnerships [21-23]. There is also a growing body of evidence illustrating that walking outdoors boosts quality of life for those living with dementia, contributing to improved mood, quality of sleep, and sense of freedom [17,24,25].

Urban planning scholar Lawrence Frank significantly advanced the conception and measurement of walkability. He describes walkability as the extent to which an environment’s social and physical characteristics promote walking as a competitive and desirable form of mobility [26,27]. Recent work has extended the idea of walkability to a more encompassing notion of “active living environments.” Active living environments are defined as “the emergent natural, built, and social properties of neighborhoods that promote physical activity and health and allow for equitable access to health-enhancing resources” [28].

Scholars have used a wide variety of methods to study walkability and its relation to walking behavior. These include phenomenological interviews [29], cross-sectional community surveys [30], observational techniques [31], surveys [32,33], photovoice [34,35], and in-situ walking interviews [12]. Scholars have also deployed criteria and indicators that enable monitoring and evaluation of the social, built, and ecological environments that make up a city [36]. In some cases, criteria and indicators are operationalized using a geospatial approach that assesses barriers and facilitators to walking in a small area (eg, 1 km) surrounding a central location such as a residence. This approach is often referred to as walkshed analysis.

In North America, walkability is now well researched within urban settings in the context of the “general population.” By comparison, factors that shape walkability for members of equity-deserving groups, particularly persons living with dementia, are comparatively understudied. There is a need to better document (1) what walkability criteria and indicators are relevant to the lived experience of persons living with dementia, (2) how methods are operationalized to examine barriers and facilitators using a walkshed approach, and (3) where barriers and facilitators of walkability for persons living with dementia...
may align or conflict with those of other populations. Given these needs, the objectives for this scoping review are twofold:

1. Focusing on walkshed analysis, extend scholarly understandings of methodological practices used in the monitoring and evaluation of dementia-friendly neighborhoods.
2. Provide clear and practical guidance for those working in planning, design, and public health fields to assess the neighborhood context in support of evidence-based action to improve the lives of persons living with dementia.

To achieve the preceding objectives, this scoping review will address the following research question: What dimensions, criteria, and indicators can be recognized within the academic literature for measuring neighborhood walkability for persons living with dementia based on a walkshed methodology?

### Existing Reviews

This protocol was informed by an initial review of existing peer-reviewed literature. The purpose of this review was to identify possible knowledge syntheses on the use of walkshed methodology to document barriers and facilitators faced by persons living with dementia. Table 1 summarizes key aspects of 6 related knowledge syntheses. All but 1 of the identified studies were published within the past 5 years [36]. A total of 2 of the studies directly focused on persons living with dementia. Other studies focused on dementia risk factors among older adults (see Table 1).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Title</th>
<th>Objective</th>
<th>Population focus</th>
<th>Addresses aspects of walkshed methodology</th>
<th>Addresses objective criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akinci et al</td>
<td>How different are objective operationalizations of walkability for</td>
<td>Summarize and compare methods used to operationalize objective walkability</td>
<td>Older adults or general population</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>[21], 2022</td>
<td>older adults compared to the general population? a systematic review</td>
<td>for older adults and the general population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerin et al</td>
<td>The neighbourhood physical environment and active travel in older</td>
<td>Identify correlates of neighborhood physical features and active travel in</td>
<td>Older adults</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>[36], 2017</td>
<td>adults: a systematic review and meta-analysis</td>
<td>older adults and quantify the strength of associations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sturge et al</td>
<td>Features of the social and built environment that contribute to the</td>
<td>Summarize evidence from qualitative studies about how social and built</td>
<td>Persons living with dementia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>[37], 2021</td>
<td>well-being of persons with dementia who live at home: a scoping review</td>
<td>environment features influence well-being for persons living with dementia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gan et al</td>
<td>Dementia-friendly neighbourhood and the built environment: a scoping</td>
<td>Synthesize knowledge and support policy direction related to dementia-</td>
<td>Persons living with dementia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>[25], 2022</td>
<td>review</td>
<td>friendly neighborhood environments and attendant psychosocial outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peters et al</td>
<td>Measuring the association of objective and perceived neighborhood</td>
<td>Assess the correlates of neighborhood characteristics and physical activity</td>
<td>Older adults</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>[2], 2020</td>
<td>environment with physical activity in older adults: challenges and</td>
<td>in older adults to provide a body of evidence to support neighborhood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>implications from a systematic review</td>
<td>environmental interventions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chen et al</td>
<td>Neighbourhood-built environment associated with cognition and</td>
<td>Assess the state of current knowledge on the links between neighborhood</td>
<td>Older adults at risk of dementia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>[38], 2022</td>
<td>dementia risk among older adults: a systematic literature review</td>
<td>environments and cognitive health in older adults</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gan and colleagues [25] reviewed 29 studies and documented methodologies ranging from applications of virtual reality to measurements of statistical association. No use of walkshed methods was reported. The authors also assessed the psychosocial outcomes of outdoor use (eg, increased social agency, anxiety, and promotion of personhood) and built environment characteristics that facilitate use and participation (eg, land use diversity, presence of landmarks, and irregular street grids).

By contrast, Sturge and colleagues [37] focused solely on qualitative studies exploring how social and built environments contribute to the well-being of persons living with dementia at home. Under a theme examining “connection to society and supportive relationships,” the authors review 4 key areas of support. These include contact with friends and family, social networks afforded by formal events and professional services, connections available across a host of neighborhood settings (eg, pubs and cafés), and the mixed reactions persons living with dementia can experience when disclosing their diagnosis. A second theme titled “interaction with natural environments and public space” examines supports (eg, parks and sounds of children playing) and barriers (eg, complex street environments and noise from traffic).

Both Peters and colleagues [2] and Akinci and colleagues [21] review (respectively) aspects of walkshed methodology in the context of older adults or older adults and the general public. Neither focused specifically on persons living with dementia. Peters and colleagues [2] distinguish between subjective and...
objective measures and discuss the use of accelerometers, GIS, and field-based audit approaches. They document key aspects related to the use of walkshed methods with older adults. Elements include operational definitions of a neighborhood, walking times or distances used to define a walkshed, and neighborhood attributes associated with walking and other physical activity. Akinci and colleagues [21] similarly report on GIS-based methods for spatial analysis. They report on walkshed buffer types and sizes and 167 different walkability variables across 24 studies of older adults.

The identified 6 studies are each related to the aim of this proposed scoping review. None directly cover the realm we seek to document. In 4 cases, the studies do not review objective walkshed methods. The remaining 2 cases do not focus on persons living with dementia.

Methods

Study Eligibility

The primary objective of this study is to report on research relevant to the use of walkshed methodology. We are specifically interested in walkshed analysis which involves the monitoring and evaluation of barriers and facilitators to walking in a neighborhood setting. Eligible studies will include those that reveal details about how to define a walkshed in a manner that is appropriate to the walking experience of persons living with dementia (eg, walking distance used to define a walkshed).

Textbox 1. Summary of the inclusion and exclusion process and the criteria (framed as prompts) used to exclude studies.

<table>
<thead>
<tr>
<th>Review level</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| Level 1: title, abstract, and keyword review | - Does the study include a focus on geographic areas within a community setting?  
- Does the study include a focus on outdoor spaces?  
- Does the study include a focus on people’s use of the community environment by walking or other forms of non-motorized mobility? |
| Level 2: full text article review | - Did the study collect and analyze primary or secondary data following a structured methodological approach?  
- Does the study identify measurable criteria and indicators related to walkability or report on the use of walkshed methods?  
- Does the study specifically focus on environmental use by persons living with dementia or older adults? |

Population and Setting

This review will be guided by Arskey and O’Malley’s [39] 6-step scoping review process. It will include studies that involve participants recognized to be living with dementia or mild cognitive impairment and who reside in a community setting. Studies that focus on persons living in congregate care-based facilities such as assisted living homes and long-term care homes will be excluded. We expect to find few published studies that explicitly focus on this population in the context of operational aspects of walkshed methodology. As age is the primary risk factor associated with dementia, we will also include studies that focus more broadly on community-dwelling older adults aged 65 years and older [6]. We will track differences in existing evidence between these population groups.

Search Strategy

Our search strategy was developed by a project manager with experience conducting scoping reviews. It involved consultation with a research librarian and the broader research team. The latter consultation involved a workshop that iteratively identified, tested, and respesified search domains and terms. Our search strategy includes a combination of subject headings and title or abstract-focused keyword searching (Textbox 2).

These strategies target the intersection of an activity or policy domain (walking), an environmental setting domain (outdoor neighborhood setting), and a population focus domain (persons living with dementia and older adults). We will apply search
strings to 6 electronic databases known to publish high-quality research around our focus domains (PubMed, Medline, CINAHL, APA PsycINFO, Business Source, and Web of Science). Endnote will be used to manage citations, and DistillerSR (DistillerSR Inc) and Excel (Microsoft Corporation) will be used to manage the inclusion, data extraction, and charting stages of this review.

**Textbox 2. Domain areas and search terms to be used in search strings for database searches.**

<table>
<thead>
<tr>
<th>Domain areas and search terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Activity or policy - walking, walkshed, walkability, walk, wayfinding, way finding, indicator, criteria, dimension, requirement, experience, audit, measure</td>
</tr>
<tr>
<td>• Environmental setting - footpath, greenspace, green space, population density, rural population, neighbourhood characteristics, city planning, community*, neighborhood*, built environment, urban design*, urban planning, town planning, city planning, building density*, social density*, population density*</td>
</tr>
<tr>
<td>• Population focus - dementia, alzheimer*, aged</td>
</tr>
</tbody>
</table>

**Article Selection Process**

After removing duplicate sources from our initial study pool using DistillerSR, we will use DistillerSR to complete screening at 2 levels. At level 1, we will assess the title, abstract, and keywords of each potential source. This assessment will include 2 independent reviewers using the level 1 inclusion criteria in Textbox 1. Studies will be excluded if both reviewers definitively identify relevant content and answer no to any of the criteria prompts. Studies will be moved to level 2 screening if a prompt cannot be answered definitively. To promote consistency at level 2 article screening, 2 reviewers will assess the full text of all remaining sources. Studies will only be included if reviewers can definitively answer yes to all inclusion prompts. We will address discrepancies at each level at a team meeting that involves a reassessment of the source and a consensus decision made by the team.

**Data Charting and Representation**

Data charting and representation will follow 2 interrelated steps outlined by Arksey and O’Malley [39]. Common practices in scoping review methodology and existing knowledge syntheses documented above informed the creation of the data charting schema listed below. Using this schema, we will develop a data matrix in Excel. This matrix will organize data and allow for the analysis of key items of information. Following guidance from Levac and colleagues [40], we will review and iteratively update the initial schema shown in Table 2 as the final study pool is examined. A total of 2 reviewers will extract data for a subset of papers (n=5). They will compare and update the schema as they reflect on processes and outcomes. Final data extraction will be completed by a single reviewer.

**Table 2. Initial data charting schema for creation of data charting matrix.**

<table>
<thead>
<tr>
<th>Study details</th>
<th>Walkshed methods</th>
<th>Criteria and indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td>Definition of walkability</td>
<td>Measurement domains reported</td>
</tr>
<tr>
<td>Lead author</td>
<td>GIS³ operationalization of walkshed</td>
<td>Measurement criteria reported</td>
</tr>
<tr>
<td>Year of publication</td>
<td>Distance or time parameter</td>
<td>Criteria used with persons living with dementia</td>
</tr>
<tr>
<td>Journal name</td>
<td>Data sources and types</td>
<td>Criteria used with older adults</td>
</tr>
<tr>
<td>Journal discipline (if applicable)</td>
<td>GIS routines (if reported)</td>
<td>Measurement indicators reported</td>
</tr>
<tr>
<td>Country of lead author’s institution</td>
<td>Population focus</td>
<td>GIS based indicators</td>
</tr>
<tr>
<td>Study method</td>
<td>N/A⁰</td>
<td>Data sources for indicator calculation</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A⁰</td>
<td>Method for indicator measurement or representation</td>
</tr>
</tbody>
</table>

³GIS: Geographic Information System.
⁰N/A: not applicable.

Beyond tracking the breadth (eg, diversity of methods) and location (eg, countries of origin) of literature, descriptive numerical summaries will examine 2 key topics. First, we will document the tools, data, and parameters used to define a walkshed. The review will make a contribution to the existing literature by documenting implementation approaches specific to the context of persons living with dementia. We will also compare these approaches to those used in studies of an older adult population. Second, we will chart criteria and indicators used to measure aspects of dementia-friendly neighborhood and community environments. By documenting indicators that scholars have operationalized using GIS-based analyses, we will make a key contribution to the transfer of the methodology.

The final scoping review will use descriptive results (eg, diversity of methods) represented using a combination of summary tables and figures (eg, Sankey diagrams). Limited textual information will support these visual elements. We will represent comparative results related to criteria and indicators as a larger data matrix. This matrix will visualize how
researchers have operationalized indicators in GIS for the 2 populations of interest. A longer textual description will contextualize these results. Finally, using thematic analysis, we will convey synthesized themes that capture nuance lacking in the descriptive and comparative results [41-43]. We expect to highlight considerations for the use of walkshed methodology not yet documented in recent studies focused on older adults [2,21]. We also expect to identify where criteria used to assess walkability for persons living with dementia and older adults converge and diverge. The risk of bias will not be assessed. This is consistent with the broad nature of our review question and the norms identified in the development of the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) [44,45].

Results

The results of the study and the submission of a manuscript for peer review are expected in June 2024.

Discussion

Overview

Scholars from the fields of planning, public health, urban design, gerontology, and architecture have produced a wealth of evidence and guidance related to walkability. Branching out from the “general population,” studies increasingly focus on targeted population groups. These foci better recognize the social, cultural, and demographic barriers and enablers to walking that shape one’s experience of the neighborhood. The proposed scoping review will synthesize the growing evidence base with specific reference to persons living with dementia. By including relevant studies focused on an older adult population, the review will also identify where current best practice for monitoring and evaluation diverges and converges for these populations. Expected findings include a detailed breakdown of current parameters and routines used to conduct walkshed analysis. Findings will also convey criteria that can be operationalized in GIS as indicators to assess barriers and facilitators to walking in a neighborhood setting.

Studies already identified here have documented monitoring and evaluation methods relevant to walkability for persons living with dementia. Methods include interviews, community survey techniques, and field audits of the neighborhood environment. Our planned focus on GIS-based walkshed analysis will further document a highly scalable monitoring and evaluation tool and technique.

Limitations

The final scoping review will be subject to limitations, despite following accepted methodological practice [39,40]. First, as a scoping review, there will not be a quality assessment of studies, which presents a risk of bias. Second, only English studies will be included, which will overemphasize evidence and practice from western countries. Third, we expect that the use of walkshed analysis for persons living with dementia will be an offshoot of techniques and literature focused on older adults. There may therefore be limited literature specific to persons living with dementia. To mitigate the risk of making assumptions about the transfer of methodological guidance from one population to another, we will explicitly track and compare findings across groups.

Conclusions

As far as we are aware, the proposed scoping review will be the first to provide comprehensive methodological or technical guidance for conducting walkshed analysis specific to persons living with dementia. There are 3 target audiences for this scoping review. These include applied academic researchers in the fields of urban planning and design, and evidence-based practitioners across these fields. Scholars identify neighborhood environments as an upstream source of barriers and enablers that shape walking behavior and associated health and well-being cobenefits [12,17,25]. Understanding the individual and population health impacts of neighborhood environments requires the expertise of health researchers and practitioners. Understanding how neighborhood environments came to be and how to reshape them through land-use and built-form interventions requires the expertise of planners and designers. By clearly documenting methods used in walkshed analysis, our goal is to spur increased collaboration across these disciplines to enable an evidence-informed approach to improving neighborhood environments for persons living with dementia.

Acknowledgments

The authors would like to thank the DemSCAPE team for their efforts.

Data Availability

The data generated and analyzed during this study will include content extracted from published, peer-reviewed journal articles. Full details about parameters, data sets, and Geographic Information System routines used in walkshed analysis, as well as a full list of associated indicators, will be reported in the scoping review publication. Additional data generated and analyzed during the study will be available from the corresponding author upon reasonable request.

Conflicts of Interest

None declared.
References


Abbreviations
- **GIS**: Geographic Information System
- **PRISMA-P**: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
Overview of Retention Strategies for Medical Doctors in Low- and Middle-Income Countries and Their Effectiveness: Protocol for a Scoping Review

Norehan Jinah1*, MD; Ili Abdullah Sharin1*, MD; Pangie Bakit1*, MBBS; Izzuan Khirman Adnan1*, MBBS; Kun Yun Lee1*, MBBC, MPH, DrPH
Centre of Leadership & Professional Development, Institute for Health Management, National Institutes of Health Malaysia, Shah Alam, Malaysia
* all authors contributed equally

Corresponding Author:
Norehan Jinah, MD
Centre of Leadership & Professional Development
Institute for Health Management
National Institutes of Health Malaysia
Blok B1, Kompleks NIH, Jalan Setia Murni U13/52
Seksyen U13, Setia Alam
Shah Alam, 40170
Malaysia
Phone: 60 33627400 ext 8306
Fax: 60 33627401
Email: norehan.j@moh.gov.my

Abstract

Background: The global shortage and maldistribution of health care workers, especially medical doctors, pose a significant threat to achieving the United Nations’ sustainable development goal 3 of ensuring well-being and healthy lives for all. Low- and middle-income countries (LMICs) are disproportionately affected by this crisis, with a high rate of brain drain from rural to urban areas, as well as to high-income countries. Various retention strategies have been implemented in different settings and organizations. However, their effectiveness remains underexplored, particularly in LMICs.

Objective: We aim to review the available retention strategies for medical doctors in LMICs and to determine the effectiveness of the various strategies. This review aims to compile relevant research findings on this issue to generate a thorough summary of all the retention strategies practiced in LMICs and, more importantly, to provide the current state of evidence of the effectiveness of these strategies in retaining medical doctors in countries with limited resources and high disease burden.

Methods: The structured framework given by Arksey and O’Malley will serve as the basis for conducting this scoping review. A comprehensive search strategy will be conducted across 4 electronic databases (PubMed, EBSCOHost, Scopus, and ScienceDirect). A systematic approach following the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines will be executed to search, screen, review, and extract data from studies that meet predefined inclusion criteria. Data encompassing bibliographical information, study location, retention strategies, influencing factors, and outcomes (effectiveness) will be obtained from the selected studies using standardized data extraction. Endnote and Microsoft Excel will be used for reference management and removal of duplicate studies. A narrative synthesis will be performed after categorizing and analyzing all the extracted data to identify recurrent themes.

Results: This ongoing review will generate a comprehensive compilation of retention strategies implemented in LMICs to prevent brain drain among medical doctors. Data extraction is currently in progress, and completion is expected by early 2024. Themes regarding the types of strategies, influencing factors, and outcomes will be synthesized. The findings will highlight effective retention strategies, gaps, and challenges in implementation for the benefits of future research. By identifying common barriers and facilitators, this review will provide insights into enhancing the policies and initiatives for doctor retention in LMICs.

Conclusions: This scoping review explores the retention strategies practiced in LMICs and attempts to identify effective strategies from existing research. By evaluating the barriers and challenges that influence the effectiveness of these strategies, policymakers and health care leaders can strive to obtain balanced and optimal health human resources in their respective organizations and countries.
The phenomenon of brain drain, with doctors from LMICs emigrating to high-income countries (HICs) due to better job offers and career progress. In some HICs, foreign-trained physicians sometimes amount to one-fifth of the total number of doctors in the workforce [9]. The movement of doctors from lower-to higher-income settings has resulted in substantial economic consequences, not solely due to the transfer of human capital, but more importantly, indirect impacts, such as increased morbidity and mortality associated with the loss of doctors [10].

Apart from brain drain to other countries, there is also a high rate of doctors’ resignations from the public health care system to join the more lucrative private sector, especially in countries with dual health care financing systems. Job dissatisfaction, including unsatisfactory work environment (lack of facilities, inflexible working hours, poor career progression, lack of professional autonomy, and ineffective management style) and unfavorable service conditions (poor salaries and funding, duplication of activities), are closely associated with high mobility, especially from the public to private sectors [11-13].

The phenomenon of HCWs resigning poses a significant obstacle to the advancement of the health care system in any given country, making it a topic of widespread concern [14]. The increasing number of resignations among HCWs, particularly in the Asia Pacific region, has been reported as the greatest threat to the development and sustainability of a resilient health care system in a recent study [15]. Despite efforts to increase supply and retain them, the workforce is still struggling to meet public health demands, as demonstrated in Spain and Brazil [16]. The same issue was also reported in India, where the vacancy rates were nearly 21% and 42% for medical officers and specialists at health centers, respectively [17].

Addressing the global health workforce crisis requires comprehensive strategies at both national and international levels. Retaining HCWs is a challenge in almost every country, be it HICs such as Canada, Australia, and Scotland or LMICs in Africa and Asia, especially in rural and remote areas [18,19]. Retention encompasses the duration between the initial engagement with a service and the eventual separation or departure from that service. It serves as a metric to gauge the length of time an individual stays within the service [20]. Retention strategies in the context of doctors encompass a range of interventions designed to attract and keep doctors in particular settings, such as remote or rural areas, with a specific focus on LMICs [21-23]. These strategies are aimed at mitigating doctor shortages and ensuring equitable health care access for underserved populations. Policy makers and health care managers must comprehend the factors that influence doctor retention and formulate targeted measures to address these factors [24,25]. Effective retention strategies contribute to the
stability and continuity of health care delivery, especially in regions with limited accessibility [21,23].

The significance of retention strategies lies in their capacity to yield various benefits, including cost savings, employee engagement, productivity, knowledge retention, competitive advantage, and organizational stability [26]. Addressing doctor shortages requires tailoring retention strategies to the unique challenges and requirements of health care professionals in each country. This is particularly critical in LMICs, where health care systems often contend with fragility, staffing shortages, limited resources, and a higher disease burden [27-29]. Furthermore, these countries grapple with brain drain challenges, issues of health care accessibility, weakened political will, and unstable governmental systems [30-33].

There are many known impediments to the retention of doctors, the most common being unfavorable working conditions, limited opportunities for career advancement, nonappealing financial incentive structures, unsupportive community environments, and the restriction of financial resources [34,35]. Other barriers include inadequate living standards, excessive workloads, insufficient equipment, lack of opportunities for skill enhancement and private practice, and unfair promotion practices [36]. In addition, stress, burnout, and insufficient work-life balance also play a role in doctors’ decision to leave [37]. Strategies aimed at addressing these barriers have been proposed and implemented at various levels and organizations, such as providing career development plans, ensuring minimum financial incentives, establishing avenues for private practice, enhancing work conditions, providing opportunities for skill improvement, and implementing transparent and equitable promotion systems.

Objective of Conducting the Scoping Review

Numerous publications have discussed the factors influencing the retention of doctors in LMICs [38-41], providing suggestions for various strategies and initiatives. However, there is limited research evaluating and summarizing the effectiveness of these strategies, particularly in LMICs. Therefore, the objective of this scoping review is to identify and delineate the available retention strategies for medical doctors in LMICs and to determine the effectiveness of these strategies.

To determine if prior research has addressed the same subject, we performed an initial exploratory literature review. Our search revealed the absence of existing or ongoing systematic reviews and scoping reviews related to our specific topic. McClain et al [42] primarily explored retention strategies and barriers concerning nurses, while Noya et al [43] concentrated on the rural and remote medical workforce, and Verma et al [22] focused on primary care doctors in general.

Conversely, our review aims to synthesize research evidence to generate an all-encompassing perspective on the effectiveness of retention strategies for doctors in LMICs. This synthesis will identify gaps in existing literature, pinpointing areas that require additional investigation within the context of doctor retention in resource-constrained countries with high disease burden. Our inclusive methodology considers a broad spectrum of studies and settings and delivers a comprehensive evaluation of these strategies.

Methods

Ethical Considerations

As the methodology for this scoping review solely entails reviewing and collecting data from existing literature without involving human participants, ethical clearance was waived by the Medical Research and Review Committee Malaysia.

Protocol Design

Overview

For this scoping review, we will use the methodological framework introduced by Arksey and O'Malley [44], who structured the review process into 5 stages. In addition, we enhanced the quality and rigor of our review based on the guidelines from the Joanna Briggs Institute Manual [45]. We will also incorporate the recommendations provided by Levac et al [46] to ensure consistency in assessing the studies during this scoping review. Transparent reporting will be ensured by using the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines [47]. We describe the protocol for this scoping review in five stages:

1. Formulating research questions
2. Identifying relevant studies
3. Selecting eligible studies
4. Charting the data
5. Collating, summarizing, and reporting the results

Stage 1: Formulating Research Questions

Following the recommendations given by Levac et al [46], we set our objective to explore strategies or interventions available for retaining doctors within health care institutions in LMICs and to identify effective measures to prevent doctor attrition. Therefore, we formulated two specific research questions for this review:

1. What are the retention strategies currently being implemented for doctors in LMICs?
2. Which strategies have been identified and evaluated as effective in retaining doctors in LMICs?

Stage 2: Identifying Relevant Studies

A meticulous search strategy plays a vital role in ensuring the inclusion of pertinent studies in scoping reviews. The research team has developed a comprehensive search strategy that encompasses various keywords and their synonyms related to the topic of interest. We selected search terms based on the research questions, including terms such as “retention,” “retain,” “maintain,” “doctor,” “physician,” and “general practitioner.” These terms have been used both individually and in combination following the iterative process inherent in the scoping review methodology.
The final search string, adhering to Boolean logic, takes the following form: (retention OR retain OR intention to leave OR intention to stay OR motivation to stay OR willingness to work) AND (doctor OR physician OR specialist OR general practitioner OR medical practitioner) AND (low- and middle-income countries OR LMIC). This meticulously designed search string aimed to gather all pertinent materials aligned with the objectives of this scoping review.

Various types of documents were screened during this stage, including journal articles, documents, or regulatory reviews, sourced from each of the 4 databases: PubMed, EBSCOHost, Scopus, and ScienceDirect. These databases were selected for their relevance to health and human resource services. During the screening process, if the available information in the title and abstract is insufficient to make an informed decision, the articles will be included for full-text screening. Adhering to the standard approach for conducting scoping reviews, we will not conduct quality appraisal of the included studies. An example of a preliminary MEDLINE (PubMed) search strategy is presented in Textbox 1.

Textbox 1. Example of MEDLINE (PubMed) search strategy.


Stage 3: Selecting Eligible Studies

The review process begins with the team convening to discuss decisions related to study inclusion and exclusion based on the principles of transparency, reproducibility, and rigor. This practice further advances a systematic and unbiased approach throughout the review process. The inclusion and exclusion criteria are presented in Textbox 2. We chose to focus primarily on studies published in English language due to their global prevalence, ensuring a comprehensive analysis, increased accessibility, and reduced language-related biases due to limited translation resources. Furthermore, the focus on studies published in English language streamlines the accessibility and application of research findings, making them readily available and applicable to a broader audience.

To maintain the scientific rigor of this review, we made a deliberate choice to exclude gray literature from our review, such as dissertations, essays, consensus, reports, theses, and government documents. However, while gray literature may provide valuable insights that supplement traditional academic
literature [48], it presents challenges in terms of systematic search and quality verification [49].

Following the PRISMA-ScR guidelines [47], the first step begins with identifying articles from various databases. Duplicates and irrelevant studies will then be removed. Abstracts or full texts will be evaluated based on predetermined inclusion and exclusion criteria to determine eligible studies. This screening process involves careful examination of both the retrieved search results and their reference lists. To ensure the most relevant search results, we will refine the literature search throughout the review process. At least 2 investigators will independently assess the eligibility of publications by reviewing their titles and abstracts. Publications deemed relevant to this scoping review are obtained in full text and reviewed against the same inclusion criteria.

In cases of disagreement during publication selection, both reviewers will revisit the full-text articles to reach a consensus. If consensus cannot be reached, an impartial third reviewer will be consulted to resolve the disagreement. Consistent meetings and discussions at different stages of the article review process are essential to maintain alignment, address challenges, refine search strategies, ensure consistency, and foster a collaborative and efficient approach. The scoping review will record and report reasons for excluding sources of evidence in the full text that do not meet the inclusion criteria. The reporting of the review will incorporate a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Figure 1), which visually presents the screening and selection process [50].

### Textbox 2. Inclusion and exclusion criteria of the study selection process.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publication year: January 2013 to February 2023</td>
</tr>
<tr>
<td>Language in publication: English</td>
</tr>
<tr>
<td>Research location: low- and middle-income countries (LMICs)</td>
</tr>
<tr>
<td>Target population: medical doctors</td>
</tr>
<tr>
<td>Types of documents: journal articles, documents, or regulatory reviews with proper references</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publication year: before January 2013 and after February 2023</td>
</tr>
<tr>
<td>Language in publication: other languages</td>
</tr>
<tr>
<td>Research location: other than LMICs</td>
</tr>
<tr>
<td>Target population: other health care professionals</td>
</tr>
<tr>
<td>Types of documents: dissertations, essays, consensus, government documents, reports, and theses that do not have any proper references</td>
</tr>
</tbody>
</table>
Stage 4: Charting the Data

The data extracted from the full-text articles will be organized into a data extraction table using Microsoft Excel (Microsoft Corporation). The data table will be structured to accommodate the characteristics of the data. The aim of charting the data is to create a descriptive summary of the results to address the objectives of the scoping review and to answer the research questions. This process facilitates the categorization of information before proceeding with further tabulation. For reference, Textbox 3 presents the categories corresponding to each characteristic in the data extraction table. In an iterative process, investigators will continually gather data and keep the data extraction table up-to-date. If significant data are found in records initially not designated for extraction, the data extraction form will be revised, and these additional data will be retrieved from the records already reviewed.
**Textbox 3. Preliminary data extraction table.**

<table>
<thead>
<tr>
<th>Basic characteristics and description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bibliographical data</td>
</tr>
<tr>
<td>- First author and year of publication of the article</td>
</tr>
<tr>
<td>Article title</td>
</tr>
<tr>
<td>- A succinct description of the content of the article</td>
</tr>
<tr>
<td>Country</td>
</tr>
<tr>
<td>- Name of the low- and middle-income countries</td>
</tr>
<tr>
<td>Aims or purpose of the study</td>
</tr>
<tr>
<td>- Expresses the intention or aspiration of the research</td>
</tr>
<tr>
<td>Type of study</td>
</tr>
<tr>
<td>- Study design or methodology</td>
</tr>
<tr>
<td>- Which type of study was conducted?</td>
</tr>
<tr>
<td>Study population</td>
</tr>
<tr>
<td>- Physician—specialty or department</td>
</tr>
<tr>
<td>- Number of people involved</td>
</tr>
<tr>
<td>- Inclusion and exclusion criteria of the study</td>
</tr>
<tr>
<td>- Demographic characteristics</td>
</tr>
<tr>
<td>- Other characteristics</td>
</tr>
<tr>
<td>Study location</td>
</tr>
<tr>
<td>- Location characteristics (urban, rural, or remote or hospital or district, state, or area)</td>
</tr>
<tr>
<td>- Institution (name)</td>
</tr>
<tr>
<td>Factors influencing retention</td>
</tr>
<tr>
<td>- Financial or career and professional or working conditions, personal, cultural, or living conditions factors</td>
</tr>
<tr>
<td>Retention strategy</td>
</tr>
<tr>
<td>- Strategy type or focus (education and regulatory or ii. monetary compensation or iii. management, and environment and social support)</td>
</tr>
<tr>
<td>- Strategy name</td>
</tr>
<tr>
<td>- Strategy characteristics, content, and description</td>
</tr>
<tr>
<td>- Strategy implementation (levels, duration, and date)</td>
</tr>
<tr>
<td>Outcomes measure</td>
</tr>
<tr>
<td>- Description of the result (effective or successful to retain)</td>
</tr>
<tr>
<td>- How were the turnover and results assessed?</td>
</tr>
<tr>
<td>Barriers and challenges</td>
</tr>
<tr>
<td>- Barriers and challenges in implementing the strategies</td>
</tr>
<tr>
<td>Study limitations</td>
</tr>
<tr>
<td>- Weaknesses within the research design that may influence the outcomes and conclusions of the research</td>
</tr>
</tbody>
</table>
Stage 5: Collating, Summarizing, and Reporting the Results

The primary goal of the scoping review is to present the narrative findings of existing literature through an analytical framework or thematic construction, without the requirement to assess the quality or significance of each study. We will use a traditional integrative review approach to compile all the identified materials. Our objective is to identify recurring themes across research and synthesize data from the selected studies. Using these themes as guidelines, we will create a literature map and present it in the form of a table, summarizing the publications and their respective characteristics.

The results of the scoping review will be organized into tables that categorize the characteristics of each publication. Accompanying these results will be narrative summaries that describe how each result relates to our research questions, including any unexpected or particularly notable findings. We will also address any gaps observed in the literature, research needs, and implications for practice. Subsequently, the outcomes of this review will be shared with relevant stakeholders, and their expertise and perspectives will be incorporated.

Results

This review will provide a comprehensive mapping of existing research and literature pertaining to the retention of medical doctors in LMICs to enhance the understanding of the complex dynamics of doctor retention. It will also assess the current knowledge and pinpoint any gaps in the literature, focusing on factors influencing doctor retention and effective retention strategies such as financial incentives, working conditions, career advancement opportunities, and personal motivations.

Furthermore, this review can offer insights into best practices and approaches for retaining doctors in LMICs to guide policy makers and health care administrators who struggle with retention challenges. They can customize the best policy recommendations based on specific needs and obstacles in local settings to improve doctor retention rates in their respective organizations and governments.

The review was initiated in May 2023, and the research protocol was finalized in July 2023. We registered the review with the Malaysian National Medical Research Register (NMRR ID-23-01994-OGW). The search, which was concluded in August 2023, yielded 9141 articles. The PRISMA flow diagram will be used to illustrate the flow of the literature search in this review [50]. The results will be presented using charts and tables, supplemented by a narrative description. Any existing literature gaps will be identified, and the significance of our findings will be emphasized in the subsequent discussion section. The review is expected to be concluded in January 2024, with the outcomes published in a journal for wider dissemination.

Discussion

Overview

Adequate investment in health care capacity is imperative to move toward the United Nations’ sustainable development goals, specifically goal 3 (ensuring good health and well-being) and goal 10 (reducing inequalities), and to achieve various global development objectives, with a robust health care workforce being the top priority. Therefore, establishing a comprehensive plan that encompasses effective retention strategies to complement medical education reforms is vital to cultivating a health care environment that is equitable and resilient at both regional and global levels. Our focus on retention strategies for medical doctors is driven by their unique challenges and critical roles in health care. Doctors hold central positions in health care delivery, not only providing medical expertise but also taking a leadership role in influencing critical patient care decision-making, and their turnover can have significant negative impacts on patient care and quality of health care services [51]. Furthermore, doctors are the most affected by the brain drain crisis, especially in LMICs, leading to a significant financial burden and experience loss. Therefore, prioritizing doctor retention is vital for mitigating brain drain, reducing productivity and financial loss, and sustaining effective health care service delivery.

The shortage of doctors in LMICs represents a pressing concern that demands immediate attention and concerted efforts on a global scale, in view of its significant impact on public health. This predicament has a direct adverse effect on the health and welfare of populations residing in LMICs, as doctor shortages can impede access to crucial medical services, ultimately resulting in preventable illnesses and higher mortality rates. Moreover, cross-border brain drain exacerbates existing health care inequalities both within and between countries. Persistent disparities in the accessibility of health care services, if they continue to exist, will disproportionately affect rural and underserved areas with limited resources, thereby perpetuating social and economic inequalities and impeding advancements toward achieving universal health care coverage.

Expected Outcomes

This scoping review will present a comprehensive overview of retention strategies that have been proposed, practiced, and evaluated in LMICs as a response to overcome the challenges faced in retaining medical doctors and preventing brain drain. These strategies may encompass a wide array of approaches, including financial incentives, opportunities for professional development, initiatives to promote work-life balance, and support for career advancement. Moreover, the focus on LMICs may shed light on distinct regional or country-specific challenges and variations in customized strategies. It may also highlight the varied effectiveness of different strategies, depending on the contextual factors at play. It is unlikely to be a one-size-fits-all solution, as certain strategies may exhibit promising outcomes in bolstering medical doctor retention, while others may demonstrate limited impact depending on the local settings.
In short, this review will present common barriers and facilitators that significantly influence the successful implementation of retention strategies for doctors in LMICs. By exploring the challenges encountered during strategy implementation, we also aim to offer a more comprehensive and nuanced understanding of the factors influencing the effectiveness of doctor retention strategies in LMICs. This, in turn, can contribute to improving the retention of medical doctors in LMICs, aligning with the Sustainable Development Goal 3 goal of promoting well-being and ensuring healthy lives for everyone. Comprehension of these elements has the potential to aid policy makers and health care administrators in developing more relevant interventions and prioritizing effective strategies.

Since it is likely that different contexts play a critical role in the outcomes of various retention strategies, we will also attempt to address this connection in our review. Certain strategies, if proven successful, can also be modified and embedded within a broader health care ecosystem to benefit a wider group of health care professionals. Common factors contributing to brain drain among HCWs include financial rewards, career development, hospital infrastructure, political issues, and family issues [52]. While we focus on the dynamics surrounding medical doctors and the customized retention approach for them in this review, as the challenges faced by doctors may be unique and differ significantly from those of other groups, the comparison and extrapolation of various retention strategies for different health care professionals is a worthy topic for future research or review.

Review Limitations
This review has several limitations that deserve further discussion. First, the language restriction used in the search strategy may have unintentionally excluded relevant studies published in languages other than English. This is a significant concern because many LMICs have diverse linguistic landscapes with numerous languages. The decision to focus primarily on English was necessitated by practical considerations, such as the broader availability and accessibility of English-language research. Furthermore, we believe that the exclusion of non–English-language studies would minimize language-related biases in the review process, given the limited access to translation resources in our setting.

Another limitation of this review is the exclusion of gray literature. This decision is influenced by the difficulties associated with accessing gray literature, which encompasses issues of limited availability, inconsistent indexing, variable accessibility, and challenges in assessing the quality and reliability of information. By excluding gray literature, there is a risk of missing important findings and diverse perspectives not found in peer-reviewed academic sources. Nevertheless, although gray literature can offer valuable insights as a complement to conventional academic literature [48], it introduces difficulties in systematic retrieval and quality assessment [49], thus making it difficult to maintain the scientific rigor of this review.

In addition, this review is likely to include studies with different levels of methodological rigor and quality, and this could potentially affect the overall reliability of its conclusions and may introduce heterogeneity into our analysis. Moreover, this review aims to provide a comprehensive overview of existing literature regarding effective retention strategies for doctors in LMICs; thus, the analysis results are likely to be less in depth compared with systematic reviews that follow a more rigorous and narrowly focused methodology. Nonetheless, this broad approach is valuable for summarizing the diversity of strategies and findings in the field of doctor retention in LMICs, allowing for a holistic understanding of the subject.

Conclusions
This scoping review is fundamental in providing a better understanding of the practical implications of various retention strategies for doctors in LMICs and in drawing valuable lessons from effective strategies in existing literature. Furthermore, by highlighting emerging trends and identifying implementation challenges within LMICs, this review will pave the way for more precisely targeted policies and interventions to strengthen doctor retention in the most needed regions. It also offers valuable guidance to policy makers and health care administrators by showcasing best practices with positive outcomes, thereby refining their approach to addressing attrition and brain drain.

Acknowledgments
The authors would like to thank the Director General of Health, Malaysia for the permission to publish this paper.

Data Availability
Data sharing is not applicable to this paper, as no data sets were generated or analyzed in this review.

Conflicts of Interest
None declared.

References

https://www.researchprotocols.org/2024/1/e52938 JMIR Res Protoc 2024 | vol. 13 | e52938 | p.53 (page number not for citation purposes)


6. Health workforce. World Health Organization. URL: https://www.who.int/health-topics/health-workforce#tab=tab_1 [accessed 2023-08-12]


18. Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations. World Health Organization. 2010. URL: https://iris.who.int/handle/10665/44369 [accessed 2023-08-12]


50. PRISMA flow diagram. PRISMA. URL: http://prisma-statement.org/prismastatement/flowdiagram.aspx [accessed 2023-08-12]


Abbreviations
- GNI: gross national income
- HCW: health care worker
- HICs: high-income countries
- LMICs: low- and middle-income countries
- PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
- PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

©Norehan Jinah, Ili Abdullah Sharin, Pangie Bakit, Izzuan Khirman Adnan, Kun Yun Lee. Originally published in JMIR Research Protocols (https://www.researchprotocols.org), 08.01.2024. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on https://www.researchprotocols.org, as well as this copyright and license information must be included.