Rifampicin chemoprophylaxis in preventing leprosy in contacts of patients with leprosy: a comprehensive systematic review protocol

Silvana Benevides Ferreira, RN, MPH, PhD[1,4]

Tatiana Yonekura, RN, MSC [2,4]

Juliana Takahashi[2,4]

Eliane Ignotti, RN, MPH, PhD[3]

Denise da Costa Boamorte Cortela, MSC[3]

Cássia Baldini Soares, RN, MPH, PhD[2,4]

1. University of Cuiabá, Graduate Program of Federal University of Mato Grosso, School of Nursing, University of São Paulo, Brazil

2. School of Nursing, University of São Paulo, Brazil

3. University of the State of Mato Grosso, Brazil

4. The Brazilian Centre for Evidence-based Healthcare: an Affiliate centre of The Joanna Briggs Institute

Corresponding author:

Silvana Margarida Benevides Ferreira

Silvana_benevides@hotmail.com

Review question/objective

1. What is the effectiveness of rifampicin chemoprophylaxis in preventing leprosy in contacts of patients with leprosy?
2. What are the experiences and acceptability with the use of rifampin chemoprophylaxis in the prevention of disease from contacts with patients who have leprosy, in patients with leprosy following treatment and in family and health care professionals?

Background

Leprosy is globally acknowledged as a millenary and stigmatizing disease and a condition with attributed consequences such as physical deformities and disabilities. From a multi-causal perspective, there is evidence that leprosy occurs more often in men than in women, is distributed across all age groups and occurs mainly among people living in unfavorable socioeconomic circumstances, who are also the most affected by public segregation policies.[1-4]

In 2013, a total of 215,656 new cases of leprosy were detected worldwide. Regions with the highest number of cases are Southeast Asia (72.1%) the Americas (15.3%). Whereas the countries with the highest prevalence were India (58.8%) and Brazil (14.4%). [5]

Hansen's bacillus (*Mycobacterium leprae*) is considered a microorganism of high infectivity and low pathogenicity and virulence. It is transmitted via nasal oropharyngeal secretions and breaks in the skin of infected patients. Therefore, the main form of transmissibility is inter-human and the greatest risk of contagion is cohabitation with these patients.[1-3]

It is estimated that most individuals have a natural resistance to *Mycobacterium leprae* (*M. leprae*) and that some are prone to developing a severe form of the disease, the multibacillary forms. Studies on exogenous reinfection and endogenous reactivation in chronic diseases, such as tuberculosis and leprosy, show that susceptible individuals become infected by the bacillus through contact with multibacillary patients.[1-3,6,7]

The surveillance of leprosy contacts is a priority action for control of the disease. Children are exposed to the highest risk of becoming infected by being in contact with a family member or anyone close to them who has the disease. Having a current case of leprosy in the family is associated with a 2.9 times greater risk of a healthy family member becoming infected, and that risk increases when the family has a history of the disease.[3,6-9]

Bakker et al.[7] reported that household contacts of multibacillary patients presented a four times greater risk of becoming infected with the disease compared to non-contacts. For Ximenes et al.,[10] the condition of being a contact of individuals with leprosy represented twice the risk of retreatment due to recurrence in relation to the control group. Therefore, alternative or complementary strategies, such as chemoprophylaxis, must be sought as a form of prevention of the disease.

Chemoprophylaxis is defined as the administration of drugs capable of preventing an infection or keeping infected individuals from falling ill. In leprosy, the preventive strategy consists of employing medications to prevent the infection by *M. leprae* in people with a higher risk of exposure to the disease, i.e. those in contact with the patient. Therefore, chemoprophylaxis plays an important role in the protection of individuals vulnerable to the disease. However, studies regarding its effective utilization are inconclusive.[11-15]

The first investigations of the utilization of prophylaxis in leprosy contacts in the 1960s and 1970s included dapsone and acedapsone and later in the 1980s and 1990s rifampicin. However, interest in this type of research decreased after 1982 when the World Health Organization (WHO) introduced multidrugtherapy (MDT) for the treatment of leprosy.[16-19]

Multidrugtherapy is a combination of three drugs, dapsone, rifampicin and clofazimine, to prevent the selection of resistant strains. As of 1997, the WHO adopted the alternative rifampicin, ofloxacin and minocycline (ROM) regimen, recommended for paucibacillary cases with a single lesion without the involvement of nerve stems.[19,20]

Adoption of these measures was expected to result in a reduction in the incidence of leprosy as a public health problem; however, the observed result was not significant in terms of reducing the incidence of newly detected cases. Furthermore, considering the evidence of resistance to monotherapy with dapsone, there was a rise in interest in intervention studies, particularly using rifampicin in household and community contacts.[1,2,5,11,12]

However, some studies have indicated little or no protection against the disease through the use of rifampicin. While Moet et al.[14] and Feenstra et al.[21] observed protection of two years in household contacts with a single dose of rifampicin, Bakker et al.[13] showed no difference between the experimental group and the control group with two doses of rifampicin, 600 mg for adults and 300 mg for children.

Another study of people at high risk of contracting the disease that used a single dose of ROM and rifampicin showed that there was a reduction of type immunoglobulin M antibodies among adults in both interventions.[22]

Meta-analyis of dapsone, acepdapsone and rifampicin compared with placebo showed that chemoprophlasys is an effective measure to prevent leprosy.[12]

Currently, strategies using a combination of the Bacillus Calmette-Guérin (BCG) and chemoprophylaxis with rifampicin in leprosy contacts appear to be complementary measures for protection against the disease. This strategy showed a protective effect of 80%.[23]

Studies of acceptability and experience of chemoprophylaxis to control leprosy with individuals and health professionals are scarce. In a qualitative study, Feenstra et al.[24] concluded that chemoprophylaxis for household contacts of leprosy patients is an effective and socially acceptable addition to the current leprosy control program.

A preliminary search of the Joanna Briggs Database of Systematic Reviews and Implementation Reports, the Cochrane Library, CINAHL, PubMed and PROSPERO has revealed that there are no systematic reviews (either published or underway) on this topic. In this context, it is unquestionably useful to integrate the scientific evidence from studies that evaluated the effectiveness of the rifampicin chemoprophylaxis in leprosy contacts, the experiences and acceptability of contacts of leprosy patients, patients with leprosy following treatment and family and health care professionals about this strategy for the prevention of the disease. This knowledge can support the measures adopted to reduce endemicity, which strengthens the quality of the care delivered to the population most vulnerable to becoming ill.

Operational definitions:

- Leprosy patients: individuals who present one or more of the following cardinal signs and who require multidrugtherapy: lesion(s) and/or skin areas with altered sensitivity; affected peripheral nerve(s), with or without thickening, associated with sensitive and/or motor and/or autonomic changes; and a positive skin smear bacilloscopy. Cases are classified as paucibacillary or multibacillary based on the number of lesions and/or bacilloscopy when available; cases are considered paucibacillary when patients present five or fewer skin lesions and/or negative bacilloscopy, corresponding to the undetermined and tuberculoid clinical forms; multibacillary cases are when patients present more than five skin lesions and positive bacilloscopy,corresponding to the dimorphous and Virchow's forms of the disease.[1-4,25]
- Leprosy case: term used in epidemiology to identify individuals with leprosy for purposes of monitoring the health conditions of a population.[2,26]
- Chemoprophylaxis: the administration of drugs capable of preventing the infection or keeping infected individuals from falling ill.[11,12]
- Contacts: those who cohabit or have cohabited with leprosy patients.[12,14,21]
- Index case: the first case of the disease among several similar cases that are epidemiologically related with the secondary case (index case contacts).[21]
- Recurrence: the reappearance of signs and symptoms of the disease after recuperation from a first occurrence of the disease, usually within five years.[6,10,27]

- Treatment abandonment: interrupting treatment for over twelve months.[6,10]
- Therapeutic regimen established for confirmed leprosy cases: for paucibacillary (PB) cases, six monthly supervised doses of rifampicin (RFM) 450-600mg, and daily self-administered doses of dapsone (DDS) 50-100mg, for up to nine months; for multibacillary (MB) cases, twelve supervised monthly doses of rifampicin (RFM) 450-600mg and clofazimine (CFZ) 100-300mg, associated to daily self-administered doses of dapsone (DDS) 50-100mg and CFZ 50mg, for up to 18 months. An alternative treatment for MB is 24 doses within 36 months.[1,2,19]
- Rifampicin chemoprophylaxis regimens: single-dose rifampicin of 25 mg/kg or monthly dose for six months; double-dose rifampicin or combined regimens of ROM - rifampicin (600 mg), ofloxacin (400 mg) and minocycline (100mg), according to body weight.[13-15,21]
- Efficacy/effectiveness: proof (or not) of successful intervention. Efficacy is the result of an intervention performed under ideal, well-controlled conditions, such as in randomized clinical trials. Effectiveness refers to the result of an intervention applied under usual medical practice conditions.[28]
- Operational classification: paucibacillary and multibacillary.[1,2, 25]
- Comorbidities: morbidities possibly associated with leprosy, such as tuberculosis, diabetes, HIV/AIDS, and others.[1,2]
- BCG vaccination scar: resulting from the intradermal injection of Bacillus Calmette-Guérin (BCG) vaccine on the deltoid, used to prevent tuberculosis and leprosy.[23,29]
- Adverse events: negative effects resulting from the actions of drugs.[1,2]
- Incidence rate: measures the frequency or likelihood of new cases of diseases occurring in a population.[30]
- Estimated effect of an intervention: shows the theoretical distribution of possible effects in control and treatment groups.[28,30]
- Estimated efficacy: represents the relative reduction of risk obtained with the intervention.[28.30]
- Serological response: specific immune cellular response to the presence of Mycobacterium leprae identified by serological tests.[21,22]
- Genetic status: level of kinship with the leprosy patient.[21,31]
- Endemic region (parameters): measured by the yearly detection rate of new leprosy cases per 100,000 people. Measures the power of morbidity as well as the magnitude and tendency of the endemics in a region: hyperendemic (≥40/100,000 people); very high: (20 to 39.99/100,000 people); average (10 to 19/100,000 people); low (< 2/100,000 people).[5,26]

Keywords

Leprosy; effectiveness; rifampicin; chemoprophylaxis; experiences; acceptability

Inclusion criteria

Types of participants

The quantitative and qualitative components of this evaluation will include individuals of both genders of any age who were intra-household or extra-household contacts (contacts from work, social contacts, neighbors or community) of leprosy patients diagnosed as new cases, recurring cases or abandonment of treatment who used rifampicin chemoprophylaxis. Those patients who received other chemoprophylaxis treatments such as dapsone, acedapsone or treatments not associated with rifampicin will be excluded.

The qualitative component will also include leprosy patients following treatment, family members and health care professionals who assisted those patients.

Types of intervention(s)/phenomena of interest

The quantitative component will consider studies that evaluated the effectiveness of rifampicin chemoprophylaxis at any dose, frequency, or administration and combination regimens such as single-dose, double-dose, BCG vaccine combination and ROM combination.

Comparison: placebo or chemoprophylactic regimens without rifampicin or no comparison

The qualitative component of this review will consider studies that evaluated the experiences and acceptability of contacts of leprosy patients, patients with leprosy following treatment, family and health care professionals with the use of rifampicin such as single-dose, double-dose, BCG vaccine combination and ROM combination.

Contexts that may be included but are not limited to consideration include household contact with leprosy and community and health service.

Types of outcomes

The quantitative component of the review will consider studies that have measured impact on the following outcomes using a range of measures: development of clinical leprosy in contacts of patients with leprosy (primary outcome), incidence rate, adverse effects and safety/harmful effects of rifampicin chemoprophylaxis.

The qualitative component of the review will consider studies that related to individual experiences, acceptance, compliance, treatment refusal, medication adherence and satisfaction.

Types of studies

The quantitative component of the review will consider experimental and epidemiological studies, including randomized clinical trials, non-randomized controlled studies, quasi-experimental studies, clinical community trials, before-and-after studies, prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies.

The qualitative component of the review will consider studies that focused on qualitative data, including but not limited to phenomenology, ethnography or action-research. Descriptive qualitative studies that describe the experience and acceptability or describe the effects of the experience will also be considered.

Studies on experimental animals, case reports, protocols, literature reviews, systematic or narrative reviews, meta-analyses, consensus/guidelines, reviews, program evaluations and policy, guides,

letters and editorial, studies with pregnant women, associated pathologies and research without specification of administration and dosage will be excluded.

Search strategy

Systematic review of primary studies with no restrictions as to date, language or periodical will be carried out. If necessary, translation services will be utilized for items not available in English language.

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of PubMed (MEDLINE) and CINAHL will be undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the articles. A second search using all identified keywords and index terms will then be undertaken across all included databases. Third, the reference list of all identified reports and articles will be searched for additional studies. The identified references will be managed using EndNote Web 3.0.

The search strategy will be performed with the descriptors from the international vocabulary used in the health area, MeSH - Medical Subject Headings created by the National Library of Medicine for literature indexed on MEDLINE, combined through Boolean operators.

For literature indexed on the Latin-American database, LILACS, we will use the DeCS (Health Sciences Descriptors), which consists of a translated and adapted version of MeSH. The databases to be searched include:

• PubMed

• Cochrane Library

• CINAHL- Cumulative Index to Nursing and Allied Health Literature

• WoS - Web of Science

• Scopus

• LILACS - Literatura Latino-Americana e do Caribe em Ciências da Saúde

• PsycINFO

• NICE (National Institute for Health and Clinical Excellence)

The search for unpublished studies will include:

• Google Scholar

• Proquest Dissertations and Theses

• EVIPnet (WHO)

Initial keywords to be used will be:

Contact*, Contact Tracing, Communicable Disease Control, Communicable Diseases, Chemoprevention, Prevent* Rifam*, Leprostatic Agents, Antibiotic Prophylaxis, Chemoprophylaxis; Lepr*, Mycobacterium leprae, Mycobacterium Infections.

Assessment of methodological quality

Quantitative papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Qualitative papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Qualitative Assessment and Review Instrument (JBI-QARI) (Appendix II). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Data collection

Quantitative data will be extracted from papers included in the review using the standardized data extraction tool from JBI-MAStARI (Appendix III). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

Qualitative data will be extracted from papers included in the review using the standardized data extraction tool from JBI-QARI (Appendix IV). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

The authors of primary studies will be consulted for clarification of incomplete data or doubts generated during review.

Data synthesis

Quantitative papers will, where possible, be pooled in statistical meta-analysis using JBI-MAStARI. All results will be subject to double data entry. Effect sizes expressed as odds ratios (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. Both clinical and statistical heterogeneity will be explored. In the absence of clinical and statistical heterogeneity, a fixed effect model will be applied to pooled data. In the presence of statistical heterogeneity (as estimated by the calculated Chi square statistic), a random-effects model will be applied for meta-analysis. Heterogeneity will be assessed statistically using the standard Chi-square and also explored using subgroup analyses based on the different quantitative study designs included in this review. The analysis may also be performed using additional subgroups when needed: individual, socioeconomic characteristics, clinical form of the index case, type of contact, genetic status, serological response, comorbidity, presence of BCG vaccination scar, adverse effect, chemoprophylactic dose, administration and endemic regions. Where statistical pooling is not possible, the findings will be presented in narrative form, including tables and figures to aid in data presentation where appropriate.

Qualitative research findings will, where possible, be pooled using JBI-QARI. This will involve the aggregation or synthesis of findings to generate a set of statements that represent that aggregation, through assembling the findings rated according to their quality, and categorizing these findings on the basis of similarity in meaning. These categories will then be subjected to a meta-synthesis in order to produce a single comprehensive set of synthesized findings that can be used as a basis for

evidence-based practice. Where textual pooling is not possible, the findings will be presented in narrative form.

Conflicts of interest

No conflicts of interest.

Acknowledgements

Project funded by the Brazilian Ministry of Health.

References

1. Britton WJ, Lockwood DN. Leprosy. The Lancet. 2004;363:1209-19.
2. Rodrigues LC, Lockwood DNJ. Leprosy now: epidemiology, progress, challenges, and research gaps. Lancet Infect Dis. 2011;11:464-70.
3. Santos AS, Castro DS, Falqueto A. Fatores de risco para transmissão da Hanseníase. Rev Bras Enferm. 2008;61:738-43.
4. Helene LMF, Salum MJL. A reprodução social da hanseníase: um estudo do perfil de doentes com hanseníase no Município de São Paulo. Cad. Saúde Pública. 2002; 18(1): 101-113.
5. WHO. Global leprosy: update on the 2013 situation. Weekly epidemiological record. 2014; 89(36): 389-400.
6. Ferreira SMB, Ignotti E, Gamba MA. Factors associated to relapse of leprosy in Mato Grosso, Central Western Brazil. Rev Saúde Pública. 2011; 45(5): 756-64.
7. Bakker MI, Hatta M, Kwenang A, Mosseveld P, Faber W, Klatser P, Oskam L. Risk factors for developing leprosy--a population-based cohort study in Indonesia. Leprosy Review. 2006; 77(1): 48-61.
8. Sardinha JFJ et al. Genetic risk factors for human susceptibility to infections of relevance in dermatology. An Bras Dermatol. 2011; 86(4): 708-15.
9. Oliveira, BFA, Ignotti E, Hartwuig SV, Scatena JR, Andrade VLG. Acréscimo na detecção de casos de hanseníase como resultado da vigilância de comunicantes em 15 municípios considerados prioritários do estado do Mato Grosso, Brasil. Revista Espaço para a Saúde. 2007; 8(2): 11-19.
10. Ximenes RAA, Gallo MEN, Brito MFM. Retreatment in Leprosy: a case-control study. Rev Saúde Pública. 2007; 41(4): 632-7.
11. Smith CM, Smith WC. Chemoprophylaxis is effective in the prevention of leprosy in endemic countries: a systematic review and metaanalysis. J Infect. 2000; 41: 137-42.
12. Reveiz L, Buendía JA, Téllez D. Chemoprophylaxis in contacts of patients with leprosy: systematic review and meta-analysis. Rev Panam Salud Publica. 2009; 26(4): 341-9.
13. Bakker MI, Hatta M, Kwenang A, Van Benthem BHBV, Van Beers SM, Klatser PR, Oskam L. Prevention of leprosy using rifampicin as chemoprophylaxis**.** Am J Trop Med Hyg. 2005; 72(4): 443-448.
14. Moet FJ, Pahan D, Oskam L, Richardus JH, for the COLEP 1 Study Group. Effectiveness of single dose rifampicin in preventing leprosy in close contacts of patients with newly diagnosed leprosy: cluster randomised controlled trial. BMJ. 2008; 336: 761-4.
15. Oskam L, Bakker MI. Report of the workshop on the use of 11 chemoprophylaxis in the control of leprosy held in Amsterdam, Netherlands on 14th December 2006. Lepr Rev. 2007; 78: 173-85
16. Lew J, Kim YS. Chemoprophylaxis of leprosy contacts with D.D.S. Yonsei Med J. 1966; 7: 47–51.

17. Russell DA, Worth RM, Jano B, Fasal P, Shepard CC. Acedapsone in the prevention of leprosy: field trial in three high prevalence villages in Micronesia. Am J Trop Med Hyg. 1979;28(3):559–63.

18. Cartel JL, Chanteau S, Boutin JP, Taylor R, Plichart R, Roux J, et al. Implementation of chemoprophylaxis of leprosy in the Southern Marquesas with a single dose of 25 mg per kg rifampicin. Int J Lepr Other Mycobact Dis. 1989;57(4):810–6.

19. WHO. Chemotherapy of leprosy for control programmes. World Health Organ Tech Rep. 1982; 675: 1-33.

20. Matsuoka M. High prevalence of leprosy in the Federated States of Micronesia and special project for the elimination. Nihon Hansenbyo Gakkai Zasshi. 1997; 66(3): 199-205.

21. Feenstra SG, Pahan D, Moet FJ, Oskam L, Richardus. Patient-related factors predicting the effectiveness of rifampicin chemoprophylaxis in contacts: 6 year follow up of the COLEP cohort in Bangladesh. Lepr Rev. 2012; 83(3): 292-304.

22. Oo KN, Yin NN, Han TT, Wai KT, Myint K, Gyi MM. Serological response to chemoprophylaxis in extended contacts in leprosy?a randomized controlled trial. Nihon Hansenbyo Gakkai Zasshi. 2008; 77(1): 3-10.

23. Schuring RP, Richardus JH, Pahan D, Oskam L. Protective effect of the combination BCG vaccination and rifampicin prophylaxis in leprosy prevention. Vaccine. 2009; 27: 7125-28.

24. Feenstra SG, Nahar Q, Pahan D, Oskam L, Richardus JH. Acceptability of chemoprophylaxis for household contacts of leprosy patients in Bangladesh: a qualitative study. Lepr Rev. 2011; 82(2): 178-87

25. Ridley DS, Jopling WH. Classification of leprosy according to immunity; a Five group system. Int J Leprosy. 1966; 34: 255-273.

26. Magalhães MCC, Santos ES, Queiroz ML, Lima ML, Borges RCM, Souza MS, Ramos AN. Migração e hanseníase em Mato Grosso. Rev Bras Epidemiol. 2011; 14(3): 386-97.

27. Ferreira SMB, Ignotti E, Senigalia LM, Silva DRX, Gamba MA. Recidivas de casos de hanseníase no estado de Mato Grosso. Rev Saúde Pública. 2010; 44(4): 650-7.

28. Fletcher RH, Fletcher SW, Fletcher GS. Epidemiologia Clínica: elementos essenciais. Artmed. 2014.

29. Duppre NC, Camacho LA, da Cunha SS, et al. Effectiveness of BCG vaccination among leprosy contacts: a cohort study. Trans R Soc Trop Med Hyg. 2008; 102: 631-38.

30. Medronho RA, Carvalho DMA, Bloch KV, Luis RR, Werneck GL. Epidemiologia. Editora Atheneu.2006.28.

31. Alter A, Grant A, Abel L, Alcaïs A, Schurr E. Leprosy as a genetic disease. Mamm Genome. 2011; 22: 19-31.

Appendix I: Appraisal instruments

MAStARI appraisal instrument

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Is sample representative of patients in the population as a whole?	☐	☐	☐	☐
2. Are the patients at a similar point in the course of their condition/illness?	☐	☐	☐	☐
3. Has bias been minimised in relation to selection of cases and of controls?	☐	☐	☐	☐
4. Are confounding factors identified and strategies to deal with them stated?	☐	☐	☐	☐
5. Are outcomes assessed using objective criteria?	☐	☐	☐	☐
6. Was follow up carried out over a sufficient time period?	☐	☐	☐	☐
7. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
8. Were outcomes measured in a reliable way?	☐	☐	☐	☐
9. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

Appendix II: Appraisal instruments

QARI appraisal instrument

JBI QARI Critical Appraisal Checklist for Interpretive & Critical Research

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Is there congruity between the stated philosophical perspective and the research methodology?	☐	☐	☐	☐
2. Is there congruity between the research methodology and the research question or objectives?	☐	☐	☐	☐
3. Is there congruity between the research methodology and the methods used to collect data?	☐	☐	☐	☐
4. Is there congruity between the research methodology and the representation and analysis of data?	☐	☐	☐	☐
5. Is there congruity between the research methodology and the interpretation of results?	☐	☐	☐	☐
6. Is there a statement locating the researcher culturally or theoretically?	☐	☐	☐	☐
7. Is the influence of the researcher on the research, and vice- versa, addressed?	☐	☐	☐	☐
8. Are participants, and their voices, adequately represented?	☐	☐	☐	☐
9. Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?	☐	☐	☐	☐
10. Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?	☐	☐	☐	☐

Overall appraisal: ☐ Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

_____

_____

_____

Appendix III: Data extraction instruments

MAStARI data extraction instrument

JBI Data Extraction Form for Experimental / Observational Studies

Reviewer _____ Date _____

Author _____ Year _____

Journal _____ Record Number _____

Study Method

RCT ☐ Quasi-RCT ☐ Longitudinal ☐

Retrospective ☐ Observational ☐ Other ☐

Participants

Setting

Population

Sample size

Group A _____ Group B _____

Interventions

Intervention A

Intervention B

Authors Conclusions:

Reviewers Conclusions:

Study results

Dichotomous data

Outcome	Intervention ( ) number / total number	Intervention ( ) number / total number

Continuous data

Outcome	Intervention ( ) number / total number	Intervention ( ) number / total number

Appendix IV: Data extraction instruments

QARI data extraction instrument

JBI QARI Data Extraction Form for Interpretive & Critical Research

Reviewer _____ Date _____

Author _____ Year _____

Journal _____ Record Number _____

Study Description

Methodology

Method

Phenomena of interest

Setting

Geographical

Cultural

Participants

Data analysis

Authors Conclusions

Comments

Complete Yes ☐ No ☐

Findings	Illustration from Publication (page number)	Evidence		
		Unequivocal	Credible	Unsupported

Extraction of findings complete Yes ☐ No ☐