

Rifampin-Ofloxacin-Minocycline (ROM) for the Treatment of Multibacillary Leprosy: A Systematic Review

Michael Klowak¹, Jahmar Hewitt², Shveta Bhasker², Raesham Mahmood¹, Arghavan Omidi², Sahar Gholzom², Andrea K. Boggild^{1,2,3,*}

¹Institute of Medical Science, University of Toronto, Toronto, ON, Canada; ²Tropical Disease Unit, Toronto General Hospital, Toronto, ON, Canada; ³Department of Medicine, University of Toronto, Toronto, ON, Canada



*Contact: andrea.boggild@utoronto.ca; boggildlab.ca; [@BoggildLab](https://twitter.com/BoggildLab)



Introduction

- From a diagnostic and management perspective, leprosy is a complex tropical infection
- Patients who are affected by leprosy are at risk of several complications associated with the disease itself and its treatment
- Standard WHO multi-drug treatment (MDT) for leprosy consists of medications that are potentially harmful and cause a range of adverse systemic effects
- Alternative options for potential treatment have emerged such as monthly dosing of Rifampin-Ofloxacin-Minocycline (ROM) combination therapy, however, there is limited synthesized evidence of efficacy
- Multibacillary leprosy, characterized by many skin lesions and a high bacillary load, may be most amenable to a fluoroquinolone-based treatment protocol
- Monthly- or single dosing of ROM has emerged as a potential treatment option for leprosy, however, a synthesis of the evidence supporting ROM does not exist

Methods

- Abstracts reporting the efficacy & safety of monthly ROM treatment in multibacillary leprosy in human patients were targeted using combinations of the search terms “ROM” & “Leprosy” from inception to May 11, 2022
- Non-English publications were included and translated using Google Translate
- During all phases of screening a tertiary arbitrator arbitrated any inclusion/exclusion discrepancies

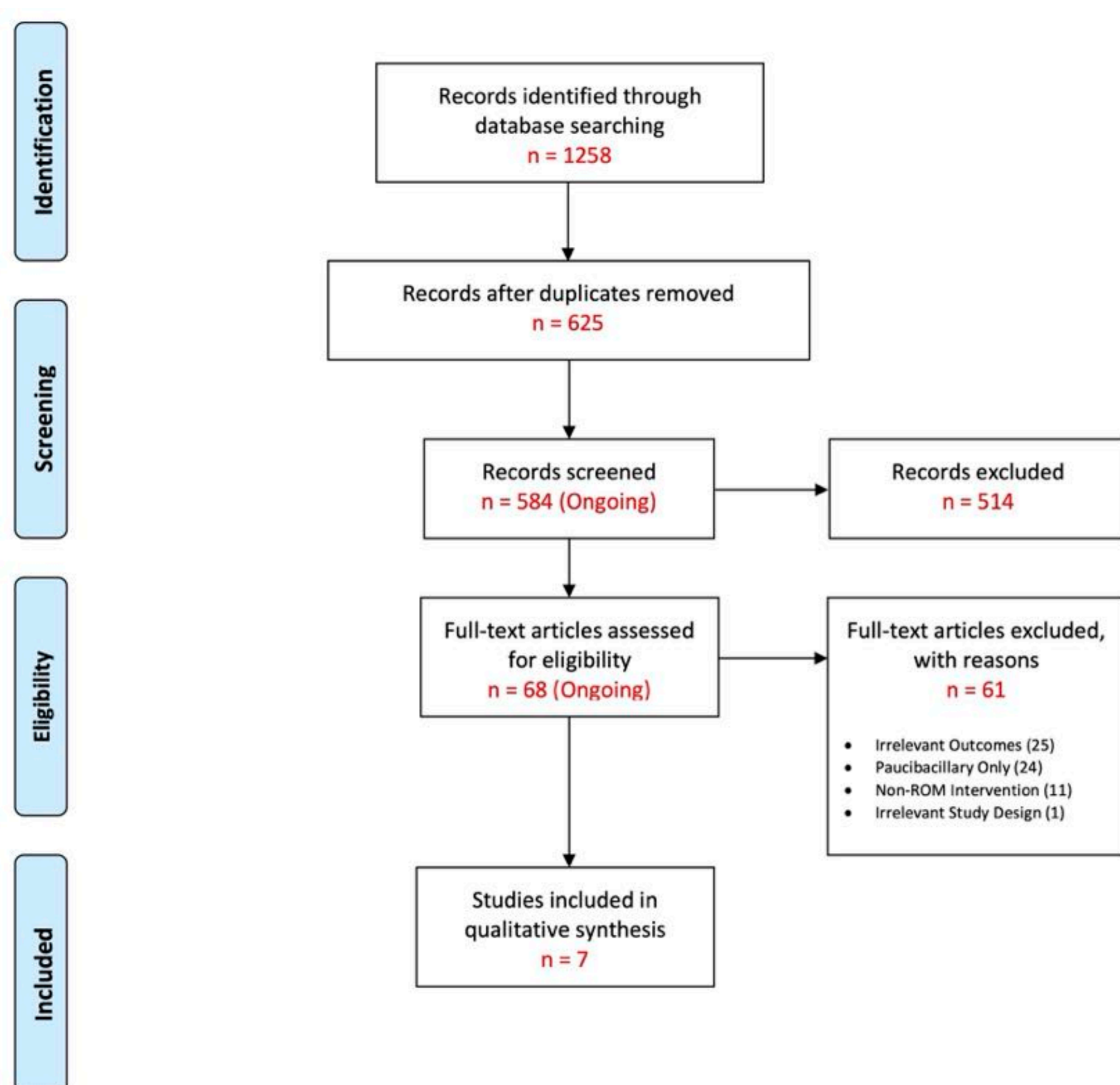


Figure 1. PRISMA Flowchart

Included	Excluded
Systematic reviews	Review articles
Randomized controlled trials	Case reports
Clinical trials	Case series (n<4)
Cohort studies	Editorials
Observational studies	Conference proceedings
Case-control studies	Animal studies
Case series (n>5)	Trial descriptions only

Table 1. Inclusion and exclusion criteria implemented during title and abstract screening

Primary Outcome Measures	Stratifiers
Lesion clearance	Social environments
Treatment failure	Education
Relapse	Socioeconomic status
Side effects	Sex / Gender
Reversal Reactions	Occupation

Table 2. Preliminary outcome measures, and stratifiers, to be assessed during full text screening

Results

Author, Year	Country	Study Design	Sample Size	Mean Age (SD), y	Male, %	Follow-Up, mo	Diagnosis of Leprosy	Treatment	Comparator
¹ Ji et al., 1998	Mali	Randomized Control Trial	20	34 (14)	80	0.25	Clinical + Histological	ROM, single dose	Ofloxacin + minocycline
² Kumar & Girdhar, 2014	India	Case Series	19	40.2 (4.0)	68.42	-	Clinical	ROM, monthly	No Comparator
³ Kumar et al., 2014	India	Cohort	289	41.6	61.8	12	Clinical	ROM, monthly	WHO-MDT
⁴ Mane et al., 1997	Senegal	Case series	220	-	60	12	Clinical + Histological	ROM, monthly	No Comparator
⁵ Shetty et al., 2011	India	Retrospective cohort	62	-	-	-	Clinical + Histological	ROM, single dose	i) WHO-MDT, ii) dapsone, iii) RO
⁶ Ura et al., 2007	Brazil	Randomized Control Trial	26	-	-	24	Clinical + Histological	ROM, monthly	WHO-MDT
⁷ Villahermosa et al., 2004	Philippines	Randomized Control Trial	21	29.4	81.5	24	Clinical + Histological	ROM, monthly	WHO-MDT

Table 3. Preliminary Baseline Characteristics of Included Studies; Rifampin + Ofloxacin (RO), Standard World Health Organization Multi-drug therapy (WHO-MDT)

Outcome	Study	ROM		Comparator		Difference
		% of patients	Proportion	% of patients	Proportion	
Treatment Failure	⁷ Villahermosa et al., 2004	0.00%	0	0%	0	0%
	Mean	4%	-	6.29%	-	-2.29%
	Median	1%	-	0.58%	-	0.42%
	Range	3%	-	18.30%	-	-15.30%
Relapse	⁷ Villahermosa et al., 2004	0%	0/6	0%	0/10	0
	Mean	1.53%	-	0.59%	-	0.94%
	Median	1.26%	-	0.35%	-	0.91%
	Range	3.60%	-	1.41%	-	2.19%
Side Effects	¹ Ji et al., 1998	40%	4/10	20%	2/10	-2/10
	⁷ Villahermosa et al., 2004	0%	0/21	100%	10/10	-100%
	Mean	8%	-	60%	-	-52%
	Median	0%	-	10%	-	-10%
Range	40%	-	100%	-	-60%	
Reversal Reactions (Type 1&2)	¹ Ji et al., 1998	0%	0/10	20%	2/10	-2/10
	Mean	13%	-	-	-	-
	Median	9%	-	-	-	-
	Range	33.33%	-	-	-	-

Table 4. Preliminary Summary of Primary Outcomes

Discussion

- Interim findings suggests that treatment failure and side effects are greater in the comparator group (+2.29% and +52% respectively), and that relapse is slightly greater in the ROM group (+0.94%). This suggests that ROM is slightly more efficacious than its comparator, however a more robust analysis is necessary
- Several determinants of health were identified qualitatively throughout this analysis including:
 - Social environments – 50% of non-adherent patients denied having leprosy due to potential loss of jobs and/or marriage prospects³
 - Patient education – 86% of respondents did not understand the concept of their disease⁸
 - Indicating a clear opportunity for bedside quality improvement
 - Gender – Women completed treatment at a rate of 65.6% and men at 79.2% (p<0.05)⁹
 - Further investigation to better understand gender- and sex-based influences on treatment and prognosis warranted
- Synthesizing the current evidence discussing the efficacy of monthly ROM, will strengthen the current body of knowledge surrounding the treatment of paucibacillary leprosy, and may allow for the development of standardized fluoroquinolone-based treatment protocols.

References

