

**REVIEW ARTICLE** 



# Technological tools applied to leprosy: a systematic mapping

Ferramentas tecnológicas aplicadas no campo da hanseníase: um mapeamento sistemático

## Herramientas tecnológicas aplicadas a la lepra: un mapeo sistemático

Rafael Everton Assunção Ribeiro da Costa<sup>®</sup>, Fergus Tomas Rocha de Oliveira<sup>®</sup>, Vitoria Neris Rebelo Veras<sup>®</sup>, Juliana do Nascimento Sousa<sup>®</sup>, Sandra Marina Gonçalves Bezerra<sup>®</sup>, Dario Brito Calçada<sup>®</sup>

#### HOW TO CITE THIS ARTICLE:

Costa REAR, Oliveira FTR, Veras VNR, Sousa JN, Bezerra SMG, Calçada DB. Technological tools applied to leprosy: a systematic mapping. Hansen Int. 2024;49:e40288. doi: https://doi.org/10.47878/hi.2024.v49.40288.

#### CONTACT INFORMATION:

Rafael Everton Assunção Ribeiro da Costa

State University of Piauí.

e-mail: rafaelearcosta@gmail.com

EDITOR-IN-CHIEF:
Dejair Caitano do Nascimento

ASSISTANT EDITOR: Fabiana Covolo de Souza Santana

RECEIVED IN: 11/02/2024

ACCEPTED IN: 10/07/2024

PUBLISHED IN: 02/08/2024

- <sup>1</sup> State University of Piauí, Teresina, Piauí PI, Brazil. ROR
- <sup>2</sup> Federal University of Piauí, Parnaíba, Piauí PI, Brazil. ROR

#### **ABSTRACT**

**Introduction:** leprosy is an infectious disease caused by Mycobacterium leprae, remaining a significant cause of morbidity and mortality in countries such as India, Brazil, and Indonesia. **Objective:** carry out a systematic mapping of the primary research available in the literature on using technological tools in leprosy. Methods: the research question was: "What tools exist for the remote study of leprosy?". A specific search strategy was applied in the PubMed, Scopus, and Web of Science databases, including all scientific articles published in English, Portuguese, or Spanish between 2015 and 2021 that were within the scope of the research. Data were extracted using a structured questionnaire, and the bias risk of the included studies was



assessed. **Results:** the methodology used allowed the selection of 15 scientific articles. Studies in Brazil, India, and Indonesia predominated, indexed in PubMed, and published between 2020 and 2021. The studies evaluated showed the use of technological tools in leprosy on the most diverse platforms, with promising results for primary health, case management, and search; however, they were still incipient. **Conclusion:** this systematic mapping indicates the need for more studies, with greater robustness, on using technological tools to combat leprosy at the health and research level.

**Keywords:** Medical Informatics Applications. Health Technology. Leprosy. Mycobacterium leprae.

## **RESUMO**

Introdução: a hanseníase é uma doença infectocontagiosa causada pela bactéria Mycobacterium leprae, permanecendo importante causa de morbimortalidade em países como Índia, Brasil e Indonésia. **Objetivo:** realizar um mapeamento sistemático das pesquisas primárias disponíveis na literatura sobre o uso de ferramentas tecnológicas aplicadas no campo da hanseníase. Metodologia: a questão de pesquisa foi: "Quais ferramentas existem para estudo remoto da hanseníase?". Aplicou-se estratégia de busca específica nas bases PubMed, Scopus e Web of Science, tendo sido incluídos todos os artigos científicos publicados em inglês, português ou espanhol, no período entre 2015 e 2021, e que estivessem no escopo da pesquisa. Os dados foram extraídos com uso de questionário estruturado e avaliou-se o risco de viés dos estudos incluídos. Resultados: a metodologia empregada permitiu a seleção de 15 artigos científicos. Predominaram estudos realizados no Brasil, na Índia e na Indonésia, indexados no *PubMed* e publicados entre 2020 e 2021. Os estudos avaliados mostraram o uso de ferramentas tecnológicas na hanseníase nas mais diversas plataformas, com resultados promissores para a saúde primária, condução dos casos e pesquisa. Contudo, ainda de forma incipiente. Conclusão: este mapeamento sistemático indica a necessidade de mais estudos, com maior robustez, acerca do uso de ferramentas tecnológicas no enfrentamento da hanseníase em nível de saúde e pesquisa.

**Palavras-chave:** Aplicações da Informática Médica. Tecnologia em Saúde. Hanseníase. Mycobacterium leprae.



## **RESUMEN**

Introducción: la lepra es una enfermedad infecciosa causada por la bacteria Mycobacterium leprae y sique siendo una causa importante de morbilidad y mortalidad en países como India, Brasil e Indonesia. **Objetivo:** realizar un mapeo sistemático de las investigaciones primarias disponibles en la literatura sobre el uso de herramientas tecnológicas aplicadas en la lepra. Métodos: la pregunta de investigación fue: "¿Qué herramientas existen para el estudio remoto de la lepra?". Se aplicó una estrategia de búsqueda específica en las bases de datos PubMed, Scopus y Web of Science, incluyendo todos los artículos científicos publicados en inglés, portugués o español, en el período comprendido entre 2015 y 2021, que estuvieran dentro del alcance de la investigación. Los datos se extrajeron mediante un cuestionario estructurado y se evaluó el riesgo de sesgo de los estudios incluidos. Resultados: la metodología empleada permitió la selección de 15 artículos científicos. Predominaron los estudios realizados en Brasil, India e Indonesia, indexados en *PubMed* y publicados entre 2020 y 2021. Los estudios evaluados mostraron el uso de herramientas tecnológicas en lepra en una amplia variedad de plataformas, con resultados prometedores para la salud primaria, la gestión de casos y la investigatión. Sin embargo, todavía están en sus inicios. **Conclusión:** este mapeo sistemático indica la necesidad de más estudios, con mayor robustez, sobre el uso de herramientas tecnológicas en el combate a la lepra a nivel de salud y de investigación.

**Palabras clave:** Aplicaciones de la Informática Médica. Tecnología en Salud. Lepra. Mycobacterium leprae.

## INTRODUCTION

Leprosy is one of the oldest recorded diseases, with accounts dating back to the 5th century BC. However, the principal etiological agent of the disease (*Mycobacterium leprae*) was only first described in 1873 by the Norwegian physician Armauer Hansen, confirming its infectious and contagious nature<sup>1</sup>. In 2000, the World Health Organization (WHO) declared leprosy as an "eliminated" international public health problem since the global incidence of the disease had fallen to fewer than one case per 10,000 individuals. Nevertheless, leprosy cases still exist in more than 150 countries, predominantly in India, Brazil, and Indonesia, which together account for approximately 80.2% of all cases worldwide. The clinical presentation of leprosy depends on the individual's immune response to the



infection, primarily affecting the skin, the peripheral nervous system, and the reticuloendothelial system<sup>2</sup>.

The standard treatment for leprosy is carried out through multidrug therapy (MDT), which includes rifampicin, dapsone, and clofazimine. Patients with leprosy may also develop leprosy reactions: type 1 reaction (T1R), also known as reversal reaction, and type 2 reaction (T2R), also known as erythema nodosum leprosum. The WHO recommends that T1R be treated with corticosteroids and T2R with thalidomide. In pregnant and breastfeeding patients, the treatment of leprosy and leprosy reactions must consider the potential teratogenic and toxic effects of the drugs used. To date, some cases of resistance to MDT have been reported, but none involving simultaneous resistance to all three drugs, highlighting the need for ongoing surveillance regarding resistance episodes<sup>3</sup>.

The COVID-19 pandemic brought numerous challenges to healthcare, as various restrictive measures were implemented in many countries. In this context, information and communication technologies (ICTs) helped mitigate the impacts of the pandemic, highlighting the value of telehealth in patient care. ICTs are used for monitoring, screening, diagnosis, treatment, follow-up, and rehabilitation, indicating that the scope of telehealth applications offers significant potential for future research. It is worth noting that the use of wearables and devices such as pulse oximeters and digital stethoscopes enhances the value of telehealth, as innovations in equipment and systems represent essential advances in healthcare<sup>4,5</sup>.

Telehealth also addresses challenges posed by many infectious and noninfectious diseases<sup>6</sup>. Regarding infectious diseases, innovative approaches are essential for monitoring and detecting new outbreaks through the use of mobile devices, the Internet of Things (IoT), and cloud computing, for example<sup>7</sup>. Although the use of telehealth to improve population health is more prevalent in high-income countries compared to low- and middle-income countries, the findings of this study show that developing countries are the ones conducting the most research on using ICTs for leprosy control<sup>8</sup>. This can be explained by the global distribution of the disease, in which Brazil, India, and Indonesia are responsible for the highest number of new cases and the countries conducting the most research in this field<sup>2</sup>.

Since the beginning of the pandemic, there has been a tremendous increase in the use of ICTs in the healthcare field (eHealth). For example, medical and health-related applications (mHealth) have been widely adopted. The potential benefits of eHealth are numerous, including improved outcomes and lower costs in health promotion efforts, greater access to specialist physicians through telemedicine, better patient data management, and more accurate monitoring of clinical conditions, among others. However, several challenges must be addressed, such as better education on using these new technologies, changes in the interaction between professionals and patients, data security and privacy issues, interoperability, standardization of clinical data, and lower patient adherence, for example<sup>9,10</sup>.

Leprosy remains a significant cause of morbidity and mortality, especially in countries with higher prevalence, such as Brazil, India, and Indonesia. On the other hand, the growth of eHealth in recent years and its potential benefits can significantly contribute to mitigating the impact of leprosy on global health. In this context, this study's objective was to systematically map the primary research available in the literature on the use of technological tools applied to leprosy.

## **METHODS**

## **Study Design**

This systematically maps the literature on technological tools related to leprosy. Systematic mappings aim to quantify the primary research conducted in a specific knowledge field and identify gaps in the databases used. They highlight topics requiring further primary studies that have not yet been addressed in systematic reviews. Systematic mappings describe the "state of the art" of a subject, summarizing the research carried out<sup>11</sup>.

## **Guiding Research Question**

The guiding research question was: "What tools exist for the remote study of leprosy?".

## Search Strategy

A search was conducted in the PubMed, Scopus, and Web of Science databases using the following strategy: "(Computational system OR Digital health OR Mobile App OR Digital platform OR Digital technologies OR Mobile applications OR Software OR Framework) AND (Leprosy OR Mycobacterium leprae)."

## **Eligibility Criteria**

The titles and abstracts of the publications retrieved from the selected databases were reviewed. Scientific articles were included if they were primary studies that presented a technological tool related to leprosy in alignment with the scope of the research. All duplicate articles found across the databases, those published outside the period from 2015 to 2021, and those written in languages other than English, Portuguese, or Spanish were excluded.



## **Data Extraction**

The selected scientific articles were read in full. For data extraction, a three-question questionnaire was used as guidance: "Who are the tool users?"; "On which platforms does the tool operate?"; "What are the functionalities of the tool?". Two researchers conducted data collection independently and compared the results at the end of the process. In case of any doubt about a raised topic, a third researcher with more significant experience in the research area was consulted.

## Risk of Bias

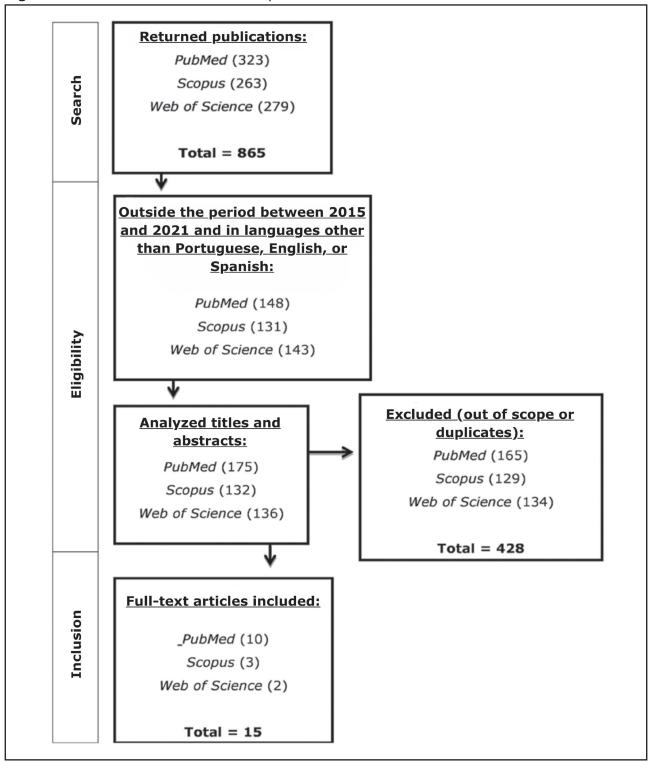
As is usually done in systematic mappings, the risk of bias was assessed generally based on the methodologies used in the selected studies. Quantitative data were evaluated for the overall risk of bias associated with each study design, and data presented qualitatively were reviewed for the coherence of the research and the usefulness of the findings<sup>11</sup>.

## **RESULTS**

As shown in the article selection flowchart (Figure 1), the search strategy in the PubMed, Scopus, and Web of Science databases returned 865 publications. Of these, 850 were excluded after applying the eligibility criteria, leaving 15 scientific articles to read in full for data extraction and analysis in the study.

Figure 2 characterizes the 15 included scientific articles by study authors, year of publication, database from which the article was retrieved, country where the research was conducted, technology platform, users and target audience of the technological tool related to leprosy presented, purpose of the technology, and results achieved.

Figure 1 - Flowchart of the selection process of included articles.



Source: Created by the authors.

Figure 2 – Characterization of the scientific articles included in the study.

Author / Year	Database	Country	Platform	Users	Objective	Results
Nisha et al. <sup>12</sup> 2018	PubMed	India	Web Servers	Researchers	Characterize the interaction of Ofloxacin (OFLX) with native and mutant GyrA forms that are complex with DNA.	Computational visualization of GyrA-DNA-OFLX interaction and a better understanding of M. leprae resistance mediated by OFLX due to mutation A91V.
Nisha et al. <sup>13</sup> 2015	PubMed	India	Web Servers	Researchers	Study molecular and structural binding mechanism of rifampicin to native and mutant rpoB.	A better understanding of molecular resistance mechanism to RMP due to mutation S425L.
Rachmani et al. <sup>14</sup> 2019	PubMed	Indonesia	SMS Notification App	Leprosy patients	Send SMS reminders about leprosy treatment to patients, families, and health professionals involved.	Optimized treatment and better disease control.
Dhane et al. <sup>15</sup> 2017	PubMed	India	Digital Camera AI	People with chronic wounds	Delineate and estimate ulcer boundary using optical images.	Wound area delineation with 91.5% accuracy.
De Souza et al. <sup>16</sup> 2021	PubMed	Brazil	Multiplatform App	Leprosy patients	Recognize leprosy lesion patterns using artificial intelligence.	The app could recognize patterns in SINAN leprosy cases and classify new paucibacillary or multibacillary patients.

Technological tools in leprosy

Author / Year	Database	Country	Platform	Users	Objective	Results
Choo et al. <sup>17</sup> 2015	PubMed	Malaysia	Web	Health professionals and researchers	Database for Mycobacterium genus, hosting genomic data of Mycobacterium species.	MycoCAP was a next- generation web comparative analysis helpful platform for the Mycobacterium research community.
Portelli et al. <sup>18</sup> 2020	PubMed	UK	Web Server	Health professionals	Prediction and visualization of missense mutation phenotypes related to M. tuberculosis, M. leprae, P. aeruginosa, and S. aureus.	The diagnostic tool SUSPECT-RIF helped explain the differences in the underlying molecular mechanisms conveyed by resistance mutations compared to susceptible ones.
Vedithi et al. <sup>19</sup> 2021	PubMed	UK	Web serves, Desktop Mobile App	Researchers	Protein modeling to understand molecular mechanisms underlying resistance mutations compared to susceptible strains.	Improved prediction of mutation impacts.
Sosa et al. <sup>20</sup> 2018	PubMed	Argentina	Web	Researchers	Integrate weighted information using protein sequences or structures or both.	Classification of proteins and pathways to prioritize promising targets for new drug development.

Author / Year	Database	Country	Platform	Users	Objective	Results
Rachmani et al. <sup>21</sup> 2020	PubMed	Indonesia	SMS Notification App	Leprosy patients and health professionals	Automatically send SMS reminders about treatment to leprosy patients.	Low-cost program to assist primary-level leprosy control programs.
Irawatia et al. <sup>22</sup> 2020	Scopus	Indonesia	Mobile App	Leprosy patients	Evaluate the reliability of Peek Acuity compared to the Snellen Chart for visual acuity screening in leprosy patients.	Peek Acuity was as accurate and repeatable as the Snellen Chart.
Mieras et al. <sup>23</sup> 2018	Scopus	Mozambique	Mobile App	Leprosy patients and health professionals	Support health professionals in recognizing early signs and symptoms of skin diseases, especially neglected tropical diseases like leprosy.	mHealth and NLR SkinApp are promising in improving the management of skin NTDs.
Canci et al. <sup>24</sup> 2021	Scopus	Brazil	Mobile App	Leprosy patients and health professionals	Assist in the early detection of leprosy and clarify doubts regarding evaluating suspected cases.	The app is expected to support health professionals in leprosy control actions.

Technological tools in leprosy



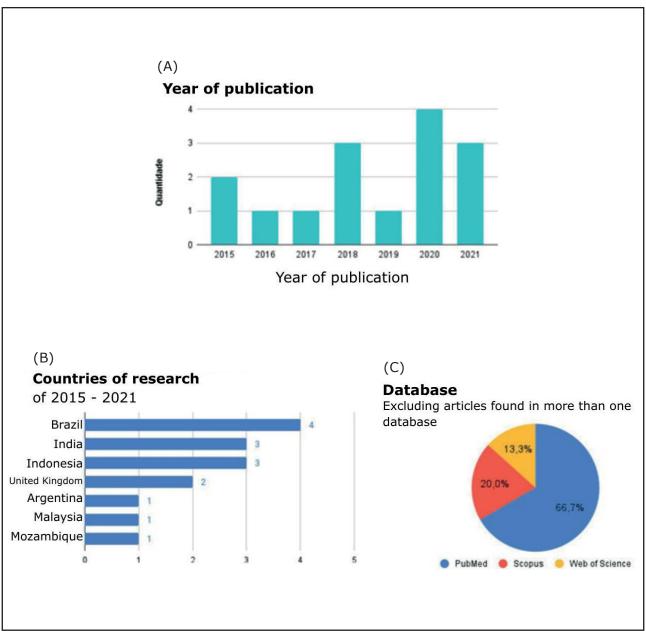
(	3	
ВҮ	⊕	

Author / Year	Database	Country	Platform	Users	Objective	Results
Cavalheiro et al. <sup>25</sup> 2016	Web of Science	Brazil	Infrared Camera & Therma CAM Software 2.9	Leprosy patients and health professionals	Assist early detection of neuropathies.	Infrared thermography detected temperature changes in the hands of leprosy patients, showing distinct behavior by clinical form and affected nerve.
Soares et al. <sup>26</sup> 2020	Web of Science	Brazil	Desktop (Metropsis software)	Leprosy patients	Analyze sensitivity to spatial luminance contrast and color discrimination.	Visual expression changes are considered biological markers to distinguish early leprosy.

Source: Created by the authors.

Seven of the 15 scientific articles included in the study were published between 2020 and 2021 (Figure 3A). Regarding the countries where the research was conducted, most studies (10) were conducted in Brazil, India, and Indonesia (Figure 3B). As for the databases analyzed, most of the scientific articles were indexed in PubMed, accounting for 66.7% of the total (Figure 3C).

**Figure 3** – Scientific articles included in the study by: (A) – Year of publication; (B) – Countries where the research was conducted; (C) – Database in which the article was indexed.



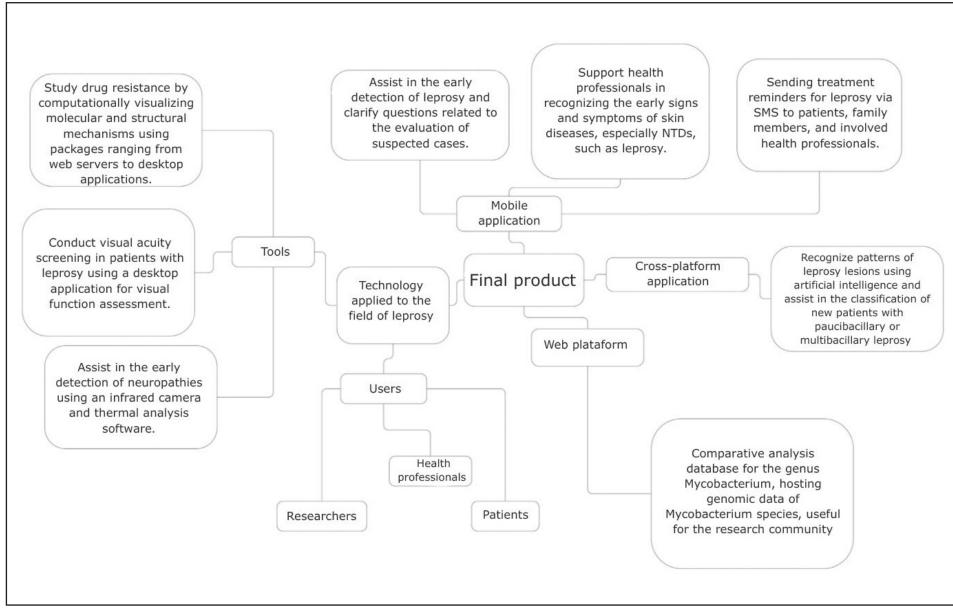
Source: Created by the authors.

Figure 4 shows the conceptual map constructed from the extracted data, highlighting the main aspects of the tools addressed by the scientific articles included in the systematic mapping.





Figure 4 - Concept map.



Source: Created by the authors.

## **DISCUSSION**

Although declared eradicated by the WHO in 2000, the incidence of new leprosy cases remains steady, and early diagnosis is essential to prevent the disabling sequelae of the disease<sup>2,27</sup>. One solution to this problem is using Artificial Intelligence (AI) in mobile applications for disease detection, as has already been implemented for COVID-19<sup>28</sup>. In this regard, Souza et al. proposed a multiplatform application using AI to recognize leprosy lesion patterns and classify patients as paucibacillary or multibacillary, contributing to early diagnosis and therapeutic guidance<sup>16</sup>. Similarly, Mieras et al. and Cancis et al. proposed mobile applications to assist healthcare professionals in identifying the early signs and symptoms of the disease, aiming to increase diagnostic suspicion for early recognition of the condition<sup>23,24</sup>.

Another essential measure to prevent sequelae is proper treatment follow-up, which is challenging due to its long duration (6 months for paucibacillary cases and 12 months for multibacillary cases). This context highlights that participatory medicine ensures better healthcare delivery to the population, as patient collaboration is essential for correct treatment adherence. To support this new paradigm, ICTs can assist patients and healthcare professionals in defining the best treatment follow-up strategy. As has been done with asthma management, Rachmani et al. proposed using a mHealth-based application to support leprosy treatment. In such cases, mobile applications notify patients about medication usage<sup>3,14,21,29</sup>.

Leprosy can primarily affect the skin, nerves, and eyes if not adequately treated. Additionally, loss of sensation and muscle strength may occur due to inflammation of Schwann cells, increasing the risk of secondary infections from trauma, which can lead to permanent disability. However, leprosy reactions are part of the natural course of the disease, even with proper treatment, meaning that healthcare professionals must always remain alert to the potential onset of these phenomena<sup>30,31</sup>. In this regard, Carvalheiro et al. used infrared thermography to detect temperature changes in patients' hands, enabling early recognition of neuropathies<sup>25</sup>; similarly, Irawatia et al. performed early lesion detection by using a mobile application to screen patients' visual acuity<sup>22</sup>.

Another consequence of poorly managed leprosy treatment is antimicrobial resistance. Although it is not as significant a problem as in tuberculosis cases, in countries like Brazil and India, resistance in the context of leprosy is becoming noteworthy, with documented cases of resistance to rifampicin and ofloxacin. In this regard, Nisha et al. studied the molecular and structural mechanism of rifampicin binding to native and mutant rpoB to understand resistance

mechanisms better. They proposed the development of a web server to share their research findings and collaborate with the scientific community<sup>12,13</sup>. This proposal aligns with that of Choo et al., who aimed to create a database for the *Mycobacterium* genus that would host genomic data of species within this genus, thereby contributing to leprosy research within the scientific community<sup>17</sup>. These initiatives are essential as they strengthen the monitoring of resistant leprosy cases and help researchers remain prepared for mutant strains<sup>32</sup>.

Innovative clinical follow-up and epidemiological surveillance methods are being developed to address infectious diseases using telemedicine, mHealth, and artificial intelligence (AI)<sup>33</sup>. Accordingly, this study aimed to gather innovations related to combating leprosy so that the scientific community can validate these strategies for efficient implementation within the healthcare system to eradicate leprosy. It is worth noting that the systematic mapping conducted revealed that there are still few primary studies on the use of technological tools in the field of leprosy, with most of the research on this topic being conducted in the three countries with the highest incidence of new cases: Brazil, India, and Indonesia.

## **CONCLUSION**

Following the global trend of increased eHealth use over the past two years, there has been a rise in research on the topic since the emergence of the COVID-19 pandemic. Nevertheless, the currently available primary studies on using technological tools in leprosy remain scarce, highlighting the need for progress in both the quantity and robustness of studies. This advancement will enable improvements in leprosy research and local health systems.

ETHICAL APPROVAL AND INFORMED CONSENT: not applicable.

**CONFLICTS OF INTEREST:** the authors declare no conflicts of interest in this article.

**AUTHOR CONTRIBUTIONS: Costa REAR**, **Oliveira FTR**, **Veras VNR**, and **Sousa JN** contributed to the conception and design of the study, analysis, and interpretation of the results, drafting, and critical revision of the manuscript content. **Bezerra SMG** and **Calçada DB** contributed to analyzing and interpreting the data and drafting and critically revising the manuscript content. All authors performed a critical review of the manuscript's writing.

**DATA AND MATERIAL AVAILABILITY:** not applicable.



**FUNDING SOURCES:** not applicable.

**PREPRINT:** not applicable.

TRANSLATION: Hansenologia Internationalis: leprosy and other infectious diseases.

## REFERENCES

- 1. Fischer M. Leprosy an overview of clinical features, diagnosis, and treatment. J Dtsch Dermatol Ges. 2017;15(8):801-27. doi: https://doi. org/10.1111/ddg.13301.
- 2. Maymone MBC, Laughter M, Venkatesh S, Dacso MM, Rao PN, Stryjewska BM, et al. Leprosy: clinical aspects and diagnostic techniques. J Am Acad Dermatol. 2020;83(1):1-14. doi: https://doi.org/10.1016/j. jaad.2019.12.080.
- 3. Maymone MBC, Venkatesh S, Laughter M, Abdat R, Hugh J, Dacso MM, et al. Leprosy: treatment and management of complications. J Am Acad Dermatol. 2020;83(1):17-30. doi: https://doi.org/10.1016/j. jaad.2019.10.138.
- 4. Doraiswamy S, Abraham A, Mamtani R, Cheema S. Use of telehealth during the COVID-19 pandemic: a scoping review. J Med Internet Res. 2020;22(12):e24087. doi: https://doi.org/10.2196/24087.
- 5. Ding X, Clifton D, Ji N, Lovell NH, Bonato P, Chen W, et al. Wearable sensing and telehealth technology with potential applications in the coronavirus pandemic. IEEE Rev Biomed Eng. 2021;14:48-70. doi: https://doi.org/10.1109/RBME.2020.2992838.
- 6. Abbott PA, Liu Y. A scoping review of telehealth. Yearb Med Inform. 2013 [cited 2023 May 23];8:51-8. Available from: https://www.thieme-connect. com/products/ejournals/pdf/10.1055/s-0038-1638832.pdf.
- 7. Huang F, Brouqui P, Boudjema S. How does innovative technology impact nursing in infectious diseases and infection control?: a scoping review. Nurs Open. 2021;8(5):2369-84. doi: https://doi.org/10.1002/nop2.863.



- 8. Scott RE, Mars M. Telehealth in the developing world: current status and future prospects. Smart Homecare Technol Telehealth. 2015;3(1):25-37. doi: https://doi.org/10.2147/SHTT.S75184.
- 9. Kernebeck S, Busse TS, Böttcher MD, Weitz J, Ehlers J, Bork U. Impact of mobile health and medical applications on clinical practice in gastroenterology. World J Gastroenterol. 2020;26(29):4182-97. doi: https://doi.org/10.3748/wjg.v26.i29.4182.
- 10. Bousquet J, Ansotegui IJ, Anto JM, Arnavielhe S, Bachert C, Basagaña X, et al. Mobile technology in allergic rhinitis: evolution in management or revolution in health and care? J Allergy Clin Immunol Pract. 2019;7(8):2511-23. doi: https://doi.org/10.1016/j.jaip.2019.07.044.
- 11. Fernandez A, Black J, Jones M, Wilson L, Salvador-Carulla L, Astell-Burt T, et al. Flooding and mental health: a systematic mapping review. PLoS One. 2015;10(4):e0119929. doi: https://doi.org/10.1371/journal.pone.0119929.
- 12. Nisha J, Shanthi V. Characterization of ofloxacin interaction with mutated (A91V) quinolone resistance determining region of DNA gyrase in *Mycobacterium leprae* through computational simulation. Cell Biochem Biophys. 2018;76(1-2):125-34. doi: https://doi.org/10.1007/s12013-017-0822-5.
- 13. Nisha J, Shanthi V. Computational simulation techniques to understand rifampicin resistance mutation (S425L) of rpoB in *M. leprae*. J Cell Biochem. 2015;116(7):1278-85. doi: https://doi.org/10.1002/jcb.25083.
- 14. Rachmani E, Hsu CY, Chang PWS, Jumanto J, Fuad A, Ningrum DNA, et al. Encouraging on-time completion of leprosy patients treatment: implementing e-leprosy framework to primary health care in Indonesia. Asia Pac J Public Health. 2019;31(4):296-305. doi: https://doi.org/10.1177/1010539519847355.
- 15. Dhane DM, Maity M, Mungle T, Bar C, Achar A, Kolekar M, et al. Fuzzy spectral clustering for automated delineation of chronic wound region using digital images. Comput Biol Med. 2017;89:551-60. doi: https://doi.org/10.1016/j.compbiomed.2017.04.004.



- 16. Souza MLM, Lopes GA, Castelo Branco A, Fairley JK, Fraga LAO. Leprosy screening based on artificial intelligence: development of a cross-platform app. JMIR mHealth uHealth. 2021;9(4):e23718. doi: https://doi.org/10.2196/23718.
- 17. Choo SW, Ang MY, Dutta A, Tan SY, Siow CC, Heydari H, et al. MycoCAP *Mycobacterium* comparative analysis platform. Sci Rep. 2015;5:18227.doi: https://doi.org/10.1038/srep18227.
- 18. Portelli S, Myung Y, Furnham N, Vedithi SC, Pires DEV, Ascher DB. Prediction of rifampicin resistance beyond the RRDR using structure-based machine learning approaches. Sci Rep. 2020;10(1):18120. doi: https://doi.org/10.1038/s41598-020-74648-y.
- 19. Vedithi SC, Malhotra S, Acebrón-García-de-Eulate M, Matusevicius M, Torres PHM, Blundell TL. Structure-guided computational approaches to unravel druggable proteomic landscape of *Mycobacterium leprae*. Front Mol Biosci. 2021;8:663301. doi: https://doi.org/10.3389/fmolb.2021.663301.
- 20. Sosa EJ, Burguener G, Lanzarotti E, Defelipe L, Radusky L, Pardo AM, et al. Target-Pathogen: a structural bioinformatic approach to prioritize Drug targets in pathogens. Nucleic Acids Res. 2018;46(D1):D413-8. doi: https://doi.org/10.1093/nar/gkx1015.
- 21. Rachmani E, Lin MC, Hsu CY, Jumanto J, Iqbal U, Shidik GF, et al. The implementation of an integrated e-leprosy framework in a leprosy control program at primary health care centers in Indonesia. Int J Med Inform. 2020;140:104155. doi: https://doi.org/10.1016/j.ijmedinf.2020.104155.
- 22. Irawatia Y, Bani AP, Gabriella K, Fitriana A, Paramita C, Susiyanti M, et al. Peek Acuity vs Snellen Chart for visual impairment screening in leprosy: a cross-sectional study. Lepr Rev. 2020;91(3):262-73. doi: https://doi.org/10.47276/lr.91.3.262.
- 23. Mieras LF, Taal AT, Post EB, Ndeve AGZ, Van Hees CLM. The development of a mobile application to support peripheral health workers to diagnose and treat people with skin diseases in resource-poor settings. Trop Med Infect Dis. 2018;3(3):102. doi: https://doi.org/10.3390/tropicalmed3030102.



- 24. Canci B, Pereira EG, Sakata-So K, Nichiata L. The development of a Portuguese mobile application for clinical support in detecting leprosy suspects. Lepr Rev. 2021;92(2):141-51. doi: https://doi.org/10.47276/lr.92.2.141.
- 25. Cavalheiro AL, Costa DT, Menezes AL, Pereira JM, Carvalho EM.

  Thermographic analysis and autonomic response in the hands of patients with leprosy. An Bras Dermatol. 2016;91(3):274-83. doi: https://doi.org/10.1590/abd1806-4841.20164612.
- 26. Soares PFC, Andrade MJO, Andrade SLE, Santos NA. Visual processing of color and shape in people with leprosy. Psicol Reflex Crit. 2020;33:14. doi: https://doi.org/10.1186/s41155-020-00153-w.
- 27. Sarode G, Sarode S, Anand R, Patil S, Jafer M, Baeshen H, et al. Epidemiological aspects of leprosy. Dis Mon. 2020;66(7):100899. doi: https://doi.org/10.1016/j.disamonth.2019.100899.
- 28. Wong CK, Ho DTY, Tam AR, Zhou M, Lau YM, Tang MOY, et al. Artificial intelligence mobile health platform for early detection of COVID-19 in quarantine subjects using a wearable biosensor: protocol for a randomised controlled trial. BMJ Open. 2020;10(7):e038555. doi: https://doi.org/10.1136/bmjopen-2020-038555.
- 29. Alonso SG, De La Torre Díez I, Zapiraín BG. Predictive, personalized, preventive and participatory (4P) medicine applied to telemedicine and eHealth in the literature. J Med Syst. 2019;43(5):140. doi: https://doi.org/10.1007/s10916-019-1279-4.
- 30. Belachew WA, Naafs B. Position statement: leprosy: diagnosis, treatment and follow-up. J Eur Acad Dermatol Venereol. 2019;33(7):1205-13. doi: https://doi.org/10.1111/jdv.15569.
- 31. Lau KHV. Neurological complications of leprosy. Semin Neurol. 2019;39(4):462-71. doi: https://doi.org/10.1055/s-0039-1687884.



- 32. Cambau E, Saunderson P, Matsuoka M, Cole ST, Kai M, Suffys P, et al. Antimicrobial resistance in leprosy: results of the first prospective open survey conducted by a WHO surveillance network for the period 2009-15. Clin Microbiol Infect. 2018;24(12):1305-10. doi: https://doi.org/10.1016/j.cmi.2018.02.022.
- 33. Carrion C, Robles N, Sola-Morales O, Aymerich M, Ruiz Postigo JA.

  Mobile health strategies to tackle skin neglected tropical diseases with
  recommendations from innovative experiences: systematic review. JMIR
  Mhealth Uhealth. 2020;8(12):e2. doi: https://doi.org/10.2196/22478.