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Leprosy post-exposure prophylaxis with single-dose rifampicin: toolkit for implementation

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Summary

Objective: Leprosy post-exposure prophylaxis with single-dose rifampicin (SDR-PEP) has proven effective and feasible, and is recommended by WHO since 2018. This SDR-PEP toolkit was developed through the experience of the leprosy post-exposure prophylaxis (LPEP) programme. It has been designed to facilitate and standardise the implementation of contact tracing and SDR-PEP administration in regions and countries that start the intervention.

Results: Four tools were developed, incorporating the current evidence for SDR-PEP and the methods and learnings from the LPEP project in eight countries. (1) the SDR-PEP policy/advocacy PowerPoint slide deck which will help to inform policy makers about the evidence, practicalities and resources needed for SDR-PEP, (2) the SDR-PEP field implementation training PowerPoint slide deck to be used to train front line staff to implement contact tracing and PEP with SDR, (3) the SDR-PEP generic field guide which can be used as a basis to create a location specific field protocol for contact tracing and SDR-PEP serving as a reference for frontline field staff. Finally, (4) the SDR-PEP toolkit guide, summarising the different components of the toolkit and providing instructions on its optimal use.

Conclusion: In response to interest expressed by countries to implement contact tracing and leprosy PEP with SDR in the light of the WHO recommendation of SDR-PEP, this evidence-based, concrete yet flexible toolkit has been designed to serve national leprosy programme managers and support them with the practical means to

translate policy into practice. The toolkit is freely accessible on the Infolep homepages and updated as required: https://www.leprosy-information.org/keytopic/leprosy-post-exposure-prophylaxis-lpep-programme

Keywords: Leprosy, prophylaxis, rifampicin, single-dose, LPEP, toolkit

Introduction

Close contacts of newly diagnosed leprosy patients have an increased risk of developing leprosy, compared to the general population.[1] This risk can be substantially reduced through the administration of a single dose of rifampicin (SDR) to contacts who meet the eligibility criteria.[2] The efficacy of a post-exposure prophylaxis (PEP) intervention has been demonstrated in various studies,[3] most notably the cluster randomised controlled COLEP trial in Bangladesh.[4,5] The Leprosy Post-Exposure Prophylaxis (LPEP) programme has established feasibility, acceptability and impact of the intervention, under routine conditions, across different health systems, socio-cultural settings and epidemiological conditions in 8 countries in Africa, Asia and Latin America.[6,7] Of note, the LPEP programme was based on a flexible approach tailored to local conditions to maximise acceptance and impact. Central tenets were integration into the health care system in general and into the leprosy control programme routine in particular, to avoid the creation of parallel and project-specific structures and to facilitate sustainability.

Based on the current evidence, the Word Health Organization (WHO) recommends "the use of single-dose rifampicin as preventive treatment for adult and child (2 years of age and above) contacts of leprosy patients, after excluding leprosy and tuberculosis (TB) disease and in the absence of other contraindications. This intervention shall be implemented by programmes that can ensure: (i) adequate management of contacts and (ii) consent of the index case to disclose his/her disease".[8] Unfortunately, the Operational Manual of the Global Leprosy Strategy 2016–2020 does not contain detailed advice on the operationalisation of leprosy prevention through PEP with SDR.[9] However, Chapter 3.2: "Early case detection through active case-finding and contact management" provides guidance on contact tracing and screening, which is arguably the most time- and resource-intensive component of leprosy PEP with SDR interventions. The same chapter also provides detailed advice on interventions to increase detection of leprosy patients, stratified by epidemiological setting.

Several national leprosy programmes participating in the LPEP programme have embraced leprosy PEP with SDR and are in the process of integrating the activity into their national leprosy control and elimination strategies, or have already done so. Based on the WHO recommendation and growing evidence from the field, it is anticipated that additional countries will follow them over the coming years. The Global Partnership for Zero Leprosy (GPLZ, https://zeroleprosy.org/) is also taking keen interest in the approach, and both the Research Agenda and Operational Excellence working groups have dedicated subgroups focusing on various aspects of the intervention. Similarly, ILEP (https://www.ilepfederation.org/) is committed to continuously supporting leprosy PEP with SDR.

Based on the above, the LPEP Steering Committee found it timely to produce a set of tools and guidance material for the introduction, implementation and documentation of leprosy PEP with SDR. The materials are generic yet practical and form a toolkit from which users may freely select the most relevant documentation for them. The toolkit's primary focus is on the needs of the national programme managers. Below we summarise the process used

to develop and validate the toolkit, describe its individual components, and provide a link to the permanent repository where the toolkit files are stored free of charge and can be accessed and downloaded.

Materials and methods

The following components were developed and are featured in the toolkit:

1. SDR-PEP policy/advocacy PowerPoint slide deck.
2. SDR-PEP field implementation training PowerPoint slide deck.
3. SDR-PEP generic field guide.
4. SDR-PEP toolkit guide.

These toolkit components were developed based on documents established and validated during the LPEP programme implementation. The main sources were the LPEP country field guides that had been developed from the generic LPEP protocol,[6] and presentations used at the in-country launch events and for training of field-level staff. All documents were critically reviewed in the light of the practical experience gained after 3 years of implementation in 8 different countries.[7] The guiding principle, in the development of the toolkit components, was that they should be evidence-based, concrete yet flexible, to cover a range of different settings, and precise yet generic to facilitate adaptation to different needs and contexts. As a result, the documents only recommend current standard practices and follow a logical planning and temporal sequence of events.

Colour coding is used to guide the user during the adaption of the tools, as follows: Standard text is in black while colour coding is used in the toolkit to represent sections that will vary between settings (see Table 1).

Throughout the documents, generic terms are intentionally used to offer the chance to adapt to local standards (e.g. “district” might be synonymous with “province” or “county” in some settings). Similarly, the naming of health workforce functions varies between countries (e.g. community health worker, village health volunteer, paramedical worker), as does the allocation of tasks between different functions (e.g. what might be the responsibility of a nurse in one country might be that of a community health worker in another system).

The toolkit documents also feature only basic formatting and are unprotected to facilitate adaptation to national standards and integration into the corporate design of the user. Pictures and graphs may be inserted throughout the documentation to illustrate points of relevance

Table 1. Colour coding of text passages

Text colour	Adaptations to be done
Green	Represents a defined number of options among which the relevant one must be selected in accordance to the target area
Blue	Indicates that a term or number must be inserted that can only be determined with reference to the target area
Purple	Identifies optional items that are applicable only to certain situations or operational purposes and can otherwise be deleted

customised to regional activities. The toolkit components can be used in their entirety, independently or be selected as excerpts.

Experts with solid experience in the actual implementation of the LPEP programme drafted all tools. Full drafts were widely shared for additional inputs and validation, by stakeholders with links to the LPEP programme, including ILEP representatives, GPZL working group members and national programme managers not previously involved in LPEP programme implementation. The consultation was facilitated by Novartis Foundation and the GPZL. Feedback was readily integrated into the drafts before finalisation of the documents.

Results

POLICY/ADVOCACY

The *SDR-PEP policy/advocacy PowerPoint* contains standard background information targeted to ministry-level staff, policy makers and donors. The presentation covers the historic and current trends in leprosy epidemiology (globally and in the targeted country/area), highlighting the value for a new approach to reduce annual new case detection rates and new child patients. It also describes the current practice and tools used to diagnose and treat leprosy at the health facility level. Contact tracing and chemoprophylaxis are then introduced as two possible instruments to increase early case detection and reduce the risk of contacts to develop clinical leprosy, possibly contributing to transmission reduction. The basic approach of SDR-PEP is presented, as well as the general results of the LPEP programme[7] and the minimal essential data needs.[10] Aspects regarding the rifampicin supply chain are included, and available data on costs and cost-effectiveness of SDR-PEP are shared. The WHO endorsement of SDR-PEP for leprosy control is featured[8] and an outlook is given on current studies that will provide complementary evidence in the field of chemoprophylaxis.

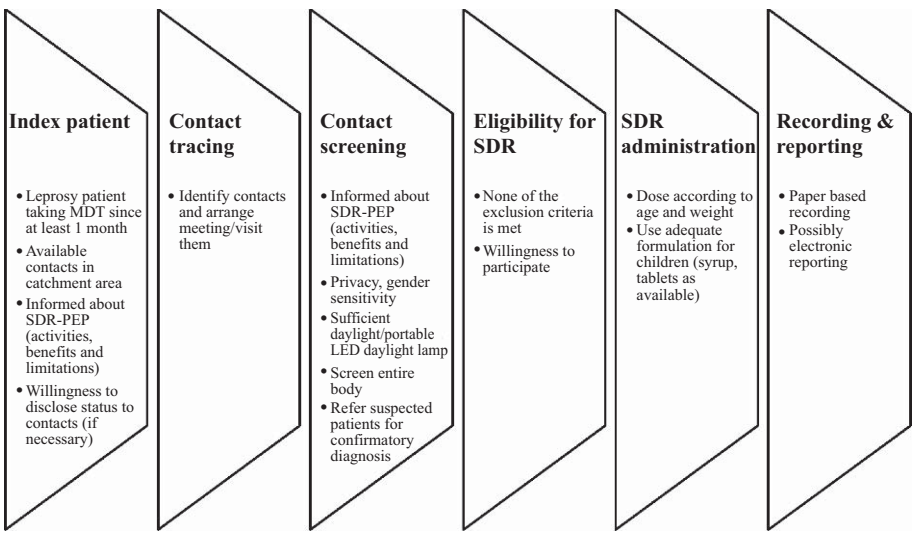

Figure 1. Activity flow of SDR-PEP.

FIELD IMPLEMENTATION TRAINING GUIDE

The *SDR-PEP field implementation training PowerPoint* provides a set of generic slides which can easily be adapted and then customised as a training module for the health staff involved in leprosy PEP field activities. It includes the following key components: First, selection criteria to facilitate the identification of intervention areas. Then, an activity flow of SDR-PEP describes the various tasks (Figure 1), from the index patient identification and inclusion/exclusion considerations, over contact tracing and inclusion/exclusion criteria, SDR administration and side effects information/monitoring, and recording and reporting, a minimal essential data form to record data on index patients and contacts are presented.[10] In addition, suggested reporting and rifampicin logistics pathways are described. Finally, a standard team composition, and the key tasks of each team member are summarised.

FIELD GUIDE

The *SDR-PEP generic field guide* offers assistance in the planning and implementation of SDR-PEP by providing a template protocol for SDR-PEP. It can also serve as a reference for frontline field staff. The guide contains a concise background on contact tracing and SDR-PEP, and lists all standard parameters, such as logistics and resources, that need to be considered in the implementation of the approach. It further summarises the roles and responsibilities of the different key personnel, and describes the key steps of index patient enrolment, contact tracing and screening for signs of leprosy, necessary referral decisions based on the suspicion for leprosy and TB, screening for SDR eligibility, and administration of SDR. Data recording and reporting are also presented.

TOOLKIT GUIDE

The *SDR-PEP toolkit guide* provides advice on the use and application of the different above mentioned toolkit instruments. It provides a more extensive summary of the current evidence on leprosy post-exposure prophylaxis (e.g. efficacy, safety and feasibility), summarises the development and validation process the tools went through, and introduces the different tools. It concludes with guidance on the adaptation of the generic documents to concrete settings on the ground where SDR-PEP is planned to be introduced.

The documents are permanently posted on the following website: https://www.leprosy-information.org/keytopic/leprosy-post-exposure-prophylaxis-lpep-programme.

For further guidance see https://zeroleprosy.org/. The documents can be freely downloaded, modified and used as required as long as users correctly acknowledge the source of the documents. Users are advised to confirm any modifications with recognized experts in the field to ensure appropriateness in the local context.

Discussion

In response to the WHO recommendation of SDR-PEP, this toolkit intends to serve national leprosy programme managers with the practical means to translate policy into practice. Available experience suggests that while contact tracing and screening represent the biggest share of work related to leprosy PEP, the SDR administration is the most contentious part of

the intervention and often requires careful and coordinated communication and training. Close supervision and continuous quality control are also important, and their collective feedback may provide further indications as to the need for guidance revision.

The introduction and implementation of SDR-PEP into the routine of national leprosy programmes will identify additional needs for tools and guidance. Together, they will form the basis for updating the toolkit components as new experiences and insights emerge. Furthermore, there are a number of studies currently ongoing or scheduled to start soon, that are exploring different aspects related to chemo- and immunoprophylaxis for leprosy prevention and *M. leprae* transmission interruption. Their common goal is to improve the effectiveness and impact of the intervention, and together they are expected to provide important further evidence that will need to be integrated into the SDR-PEP toolkit for it to remain relevant. Among these studies, we highlight the following ones: the PEOPLE trial (2018–2022) implemented on the Comoros and in Madagascar, which aims to define the optimal target population for leprosy PEP, including the deployment of a single double-dose of rifampicin (SDDR; https://clinicaltrials.gov/ct2/show/NCT03662022). The PEP4LEP trial (2018–2022) in Ethiopia, Mozambique and Tanzania evaluates different approaches for contact tracing such as community skin camps or health centre-based screening (https://nlrinternational.org/what-we-do/projects/pep4lep/). It also explores the value of the SkinApp (https://leprosyrelief.org/skinapp) to facilitate early detection and diagnosis. Furthermore, several trials assess the combination of SDR-PEP with BCG (Maltalep in Bangladesh; 2013–2019[11]), and multi-dose regimens of enhanced preventive treatment (PEP++ in Brazil, India and Indonesia; 2017–2023) for seropositive contacts while others receive standard SDR (https://nlrinternational.org/news/pep-an-enhanced-regimen-for-leprosy/). Trials of immunotherapeutic and immunoprophylactic vaccines (LepVax, MIP) are also ongoing or planned in Brazil and India.[12,13]

Corrections, suggested modifications and additions should be communicated to the corresponding author. Updated versions may be posted from time to time on the websites hosting the toolkit. Each revision will be identified by consecutive version numbers.

Review board approval

Not applicable as no approval was necessary for the elaboration of the toolkit.

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Conflicts of interest

Novartis Foundation and ILEP partners provided technical input in the design phase of the LPEP programme and ensure overall programme coordination. All authors are either staff of the Novartis Foundation, work as paid consultants for the programme described here, act as national programme coordinators or serve on the Steering Committee of the programme.

The funder had no role in the interpretation of findings or decision to publish this manuscript.

Contributorship

All co-authors are members of the LPEP Study group. TBJ drafted the manuscript. All co-authors reviewed the draft and provided comments. PST finalized the manuscript and is guarantor of the manuscript.

Patient consent statement

Not applicable as no patient consent was necessary for the elaboration of the toolkit.

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