CASE REPORT

A conceptual protocol for translational research in the complex reality of leprosy

PIM KUIPERS*, P.S.S. RAO**, M.S. RAJU**, ANNAMMA S. JOHN** & LOUIS PALUKU SABUNI***
*Population and Social Health Research Program, Griffith Health Institute, Griffith University & Metro South Health, Queensland, Australia
**Research Resource Centre, The Leprosy Mission Trust India, New Delhi, India
***The Leprosy Mission, DR Congo, Kinshasa, Democratic Republic of the Congo

Accepted for publication 11 June 2013

Summary In response to an international strategy to prioritise and focus research efforts in leprosy, this conceptual protocol outlines a research plan to address key translational research priorities. The protocol describes in broad terms a five-phase psychosocial and service-related research programme to facilitate: prevention of delay in diagnosis, improvement of adherence with multi-drug therapy, the roll out of chemoprophylaxis and increased participation in community based rehabilitation. The protocol proposes a model of research utilisation and the notion of complexity to form an integrating theoretical framework for exploring and enhancing research translation. The proposed sequential research programme is characterised by traditional and participatory strategies, culminating in participatory implementation of findings. Publication of the conceptual protocol prior to operationalisation and commencement of the research aims to encourage debate, refinement of strategies, collaboration and the optimisation of resources.

Introduction

There have been considerable efforts to conduct research, build evidence,¹ review evidence,²,³ and to ensure currency of reviews for prevention, treatment and care in leprosy.⁴ Based on such work, the technical commission of the International Federation of Anti-leprosy Associations (ILEP) developed a five-year leprosy research strategy focusing on prevention, care of people affected by leprosy, and reducing the consequences of the disease.⁴ This strategy, which was
also endorsed by the WHO expert committee on leprosy, provides a framework to prioritise research, to identify the steps needed to develop and implement new tools, and to identify funding gaps. The strategy recommends action through applied research, comprising eleven investigations to evaluate effectiveness (where there is already proof of principle), and nine technology transfer initiatives (where evidence of effectiveness exists, but further translational work is required for roll out to scale).\textsuperscript{4}

The Leprosy Mission, International Research Committee has identified the technology transfer initiatives as consistent areas of unmet need, noting that few have been the focus of international collaborations, and indeed none have attracted substantial funding to date. In prioritising the technology transfer initiatives, it was noted that over half (five) require a mix of service provision, evaluation, networking, advocacy, lobbying and service development to be rolled out to scale. As such, these five are not primarily research issues, but focus on:

4a. use of monofilaments (which has the objective of testing the effectiveness of providing all people affected by leprosy and field staff, with monofilaments and education),
5a. integration of national programmes for prevention of disability (POD) (which has the objective of the integration of POD activities with the ‘Legs to Stand On’ network),
7a. implementation of stigma reduction (which has the objective of advocacy for implementing effective interventions),
7c. translation and dissemination of United Nations (UN) Guidelines on leprosy discrimination (which has the objective of advocacy for change in legislation and regulations), and
8a. integration of health and social care (which has the objective of implementing leprosy services linked with primary health care, dermatology, and other services).\textsuperscript{4}

The remaining four technology transfer priorities outlined in the ILEP Strategy however, were seen as key priorities for research. These require substantial psycho-social and service-related research in order to be addressed.\textsuperscript{4} They are:

1a. roll out of chemoprophylaxis,
2a. prevent delay in diagnosis,
3a. improve adherence with multi-drug therapy (MDT), and
6a. increase participation in community based rehabilitation (CBR).

As noted within the ILEP strategy, all four of these priorities pertain to existing effective strategies but require translational research to improve the impact of those treatments/strategies.\textsuperscript{4}

While each of these has been identified as a priority for research, they are not without some existing foundation. Some of these four priorities have been the focus of some attention, albeit without integrated support to date. For most of the above priorities there are some elements of evidence established,\textsuperscript{3,5} some research studies completed,\textsuperscript{6} and some principles that pertain.\textsuperscript{7} Likewise, there are a few studies currently underway which inform these priorities. Studies to promote voluntary early reporting of leprosy,\textsuperscript{8} and to address issues such as defaulting from MDT,\textsuperscript{9} are underway and there are also instances of potentially beneficial investigations and practices in some clinical settings.\textsuperscript{10} Further, there is much to be learned from translational research beyond the area of leprosy.\textsuperscript{11}
A key challenge for translational research in leprosy then, is to identify a research framework and conduct a multifaceted research programme which investigates psycho-social, cultural, service delivery, and systems-related barriers and enablers to the translation of evidence within the complex reality of services and care to people affected by leprosy in diverse settings. As a preliminary step, the current protocol suggests a conceptual foundation for such work drawn from a model of research utilisation, and from the area of complexity theory.

A UTILISATION FRAMEWORK FOR TRANSLATIONAL RESEARCH IN LEPROSY

Recognising that a host of barriers and enablers to effective translation of the above four priorities may be noted, an integrating framework will be required to link concepts together where possible. The current proposal suggests that an adaptation of the Ottawa Model of Research Utilisation (OMRU) may be constructive, particularly given its relevance to developing countries. The OMRU is a knowledge translation model, intended to guide the process of transferring research into practice, and specifically focuses on translating existing research to knowledge. The model has gone through some revisions since its inception. The most recent version of the OMRU includes six key elements which should be considered when seeking to ensure maximum uptake and utilisation of research into practice settings. They are:

- **Intervention related dimensions**: These relate to the attributes of the intervention itself which include quality factors, logistical aspects, as well as the means of delivery of the intervention within other services,
- **Adopter and stakeholder dimensions**: These include attitudes, concerns, knowledge and skills of potential adopters (namely, people affected by leprosy, service providers and other stakeholders).
- **Contextual and environmental dimensions**, which include structural, social, economic, cultural and social dimensions. These also include the service environment, policy, costs, funding, governance, etc.
- **Implementation factors**: These relate to the process of implementation of the intervention, how it is transferred to adopters and other stakeholders and how the process is followed up.
- **Adoption related** factors include issues related to the intended and unintended use and application of the intervention.
- **Outcome related** factors are those resulting from implementation of the innovation. These include outcomes for potential adopters and other stakeholders as well as system outcomes.

Some of these barriers may be common across all priorities, and across all leprosy situations, some may be specific to a particular priority area, and some may be specific to a particular context, culture or country. Each might be considered in the process of guiding research to implementation. While these dimensions are clearly important, the current protocol suggests that this framework may be further enhanced by inclusion of the notion of complexity as it relates to research translation in leprosy.

COMPLEXITY: A FURTHER DIMENSION OF A FRAMEWORK FOR TRANSLATIONAL RESEARCH IN LEPROSY

An important construct that has emerged in health care, and international development, which has gained substantial prominence in recent years is the notion of
It is generally recognised that health care complexity arises out of the interaction of a number of dimensions (e.g. medical, treatment-related, care-related, patient-related, situational, behavioural and systemic), and comprises ‘multiple, dynamic components interacting in non-linear, unpredictable ways’ (p. 1003).26

Complexity theorists suggest that issues which can be characterised as ‘complex’ are substantially different from non-complex issues, and that they require new understandings and a new set of approaches to address them. They observe that complex healthcare issues are often distributed across a range of stakeholders and manifest themselves in different ways at different levels.25,27 They note that complex issues are typically difficult to predict, dynamic in nature, at times paradoxical, and may involve considerable ambiguity and conflicting evidence.25 Unfortunately traditional problem solving approaches, which are based on a premise of linear causation, the neutrality of knowledge, and reductionism to identify causal elements, are mostly inadequate to address complex issues.25,27,28

While complexity has been associated with numerous diseases and conditions which are difficult to control,29 it is not necessarily a characteristic of all challenging health conditions. For example, some neglected tropical diseases, while pervasive, may be amenable to rapid impact and/or vertical control measures.30 In contrast, leprosy is far more complex and enigmatic,31,32 requiring multidimensional and systemic approaches. The complexity of leprosy is evident in the array of interacting dimensions involved, including biological, skin and nerve damage, epidemiological, the array of treatments, vaccines, prophylaxis and broader prevention and surveillance strategies and potential reactions.31 Numerous political and social dimensions also impact on the complexity of leprosy, reflected in the way concepts of prevalence, incidence and elimination have been applied, and in debates over disease-specific vs. integrated services.31 Indeed reflections of complexity are evident in organisational, health, structural, management, communication and policy dimensions of leprosy.33 Finally and importantly, complexity is evident in the impact of the disease on individuals, families and communities, through disablement, disfigurement, functional, social, cultural and economic implications, as well as stigma.34 Despite the complexity of issues in leprosy, it would appear that the application of complexity-relevant theories and methods to this issue is rare. Indeed the application of complexity-relevant approaches to health systems in low and middle income countries (LMIC) is in its infancy.28

The current protocol suggests that a complexity framework drawn from relevant literature22–25,27,28,34 will contribute to a translational research framework to further identify constraints and enablers to translation which arise from the complexity of leprosy. The framework will also assist in conceptualising the implementation of effective strategies in leprosy.

In addition to seeking and investigating the OMRU elements, the proposed study will also explore the following complexity related features and their impact on utilisation:

- Investigate processes of implementation, including pathways of implementation in settings, choices made during implementation. Explore examples of self organisation, and local adaptation,28 as well as how change has occurred.27
- Identify consequences of implementation, particularly those that may escalate or moderate change, intended or unintended. Look for weak and strong links in the causal chain,27 for example ‘vicious circles’, such as between malnutrition and infection.
- Note localised responses and actions, including local examples of change and examples of rapid changes or positive or negative tipping points in implementation,28 recognising the potential influence of spontaneous organization and small groups.28
Explore incentives for individual and group behaviours, including perverse incentives. 28 Investigate linkages and roles of key individuals and institutions. Explore focal points, hubs, institutions or individuals with multiple links, which can disproportionately influence implementation and outcomes. 28

As the framework (Table 1) emphasises translation to poor communities in endemic areas, it is titled ‘Bench to Basti & Barrio.’ It seeks to assist in translating aspects of scientific, experimental and laboratory-based research and practice (characterised as ‘bench’) to more effective implementation in the LMIC context (characterised as ‘basti’ and ‘barrio’, which are names for poor communities or slums). The framework emphasises an incremental, capacity building approach using participatory research in the context of the clinic, household, community, government department or NGO.

PHASES OF THE TRANSLATIONAL RESEARCH STRATEGY

As reflected in Table 1, the proposed framework is consistent with suggestions for complexity-relevant research and translation in LMIC settings. 11,25 It proposes activities which:

- draw evidence from multiple and diverse sources,
- are collaborative in nature, (proposing a series of five increasingly participatory phases of research),
- focus on negotiation and action, (recognising that the capacity to tackle complex problems is often distributed across a range of players and requires practical realisation), and
- are interpretive and communicative, based on negotiated understandings, (recognising that complex problems are often ambiguous, difficult to predict, with divergent perspectives).

The focus and strategies of the first two phases are consistent with traditional approaches to evidence synthesis. First, recognising that there are numerous existing reviews and published studies in this area (in both the leprosy field and in that of related conditions), the first priority is to summarise these for current purposes. In light of the considerable number of high-quality, narrative and systematic reviews and research pertaining to chemoprophylaxis, timely diagnosis, MDT and CBR, the most fundamental step is not to duplicate such work, but to provide a brief summary of their findings as it informs questions of translation to practice.

Second, in light of the potentially meaningful and applied information beyond peer-reviewed literature, and recognising that this information is not often included in traditional reviews, 35 the proposed project will prioritise and review relevant evidence from evaluation reports, grey literature and related information as it pertains to translation in the four dimensions of leprosy treatment and care. This phase seeks and sifts evidence from more diverse sources than traditional scientific studies. It will be performed concurrently with the summary, but will be considerably more time-intensive.

The third phase of the translational research strategy recognises that some relevant understanding of translation in leprosy may not be articulated in peer reviewed publications or the grey literature. It proposes formally drawing on the experience and perspectives of the global leprosy community through a survey of a variety of stakeholders. This international survey in key leprosy settings will be informed by findings of phases one and two and will
Table 1. ‘Bench to Basti & Barrio’ translational research framework for leprosy

<table>
<thead>
<tr>
<th>Table duplicated for each priority:</th>
<th>1a. Roll out of chemoprophylaxis</th>
<th>2a. Timely diagnosis</th>
<th>3a. Adherence with MDT</th>
<th>6a. Participation in CBR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. SUMMARY:</td>
<td>Summarise existing reviews &amp; findings from leprosy-specific and non-leprosy peer-reviewed research literature.</td>
<td>0–6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. REVIEW:</td>
<td>Review ‘grey’ literature &amp; evaluations from leprosy-specific and non-leprosy literature</td>
<td>0–12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. COLLABORATIVE SURVEY:</td>
<td>Survey of consumer perspective, family member &amp; staff perspective, self help group, current practice, expert opinion, current researchers</td>
<td>12–24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. PARTICIPATORY ACTION RESEARCH:</td>
<td>Identify local actions &amp; solutions, build reflection and discussion in project offices, consider findings from phases 1.2 and 3.</td>
<td>18–36 30–60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| IDENTIFY BARRIERS | Utilisation Related (OMRU): | Contextual & Environmental | Intervention related |
| Complex Related: | Implementation factors | Adoption related | Outcome factors |
| Processes of implementation | Localised responses | Incentives | Linkages and roles |

| IDENTIFY ENABLERS | Utilisation Related (OMRU): | Contextual & Environmental | Intervention related |
| Complex Related: | Implementation factors | Adoption related | Outcome factors |
| Processes of implementation | Localised responses | Incentives | Linkages and roles |
investigate the perspectives of people affected by leprosy, their family members, service providers and staff, self help groups, managers of current services, experts in the field and those engaged in current unpublished research. It is envisaged the survey will be developed, conducted, compiled and analysed within a one year period.

The project is based on the recognition that much of the understanding and lived experience of barriers to translation in leprosy is resident in LMIC settings, often with poor people, in remote settings who may have limited literacy. As such, the potential relevance of a formal survey, even if conducted in local languages, is likely to be somewhat limited. Consequently the fourth phase comprises participatory action research in a number of LMIC settings. This phase will explore translation at the service level, and will involve localised focus groups in field sites which seek to promote reflection and discussion of barriers and enablers to translation of the four priorities. It will also explore potential local solutions, with a focus on local knowledge and grass-roots experience. This phase is consistent with complexity approaches which emphasise the importance of promoting reflexive research and building the capacity of disadvantaged stakeholders to voice their opinions.25

Finally, the translational research programme will involve piloting of findings in leprosy endemic field sites. While the nature of these interventions will depend on findings of the first four phases, and may include a variety of strategies, and stakeholders, they will provide meaningful information on the translation potential of the identified strategies. One goal of this phase is to engage key actors with the results from previous phases for on-going problem-solving and adaptation.28 It seeks to link knowledge with action and foster use-oriented research,36 recognising that shared vision and collaboration are prerequisites for progress on complex issues.25

Phases four and five reflect a commitment to broad participation, linking across sectors, boundaries and stakeholders.36 These phases are highly contextualised,16 and reflect the importance of deliberation and inclusive, face-to-face fora to promote understanding and guide action.25 In light of the reported suitability of such methods for data gathering and for the identification of strategies,37 they will foster peer-to-peer learning and the active engagement of community members and community level organisations,38 ideally leading to locally informed and managed solutions.

The indicative timeline in Table 1 also reflects the substantial proportion of time investment required for more participatory phases, and the potential to overlap certain phases. The timeline indicates that with adequate resources, the programme could be completed within 5 years, after finalisation of ethics and procedural requirements.

Conclusion

This protocol describes a project in which traditional means of knowledge translation are combined with strategies identified in the complexity literature. It seeks to encompass review methods suited to medical and scientific studies, with those that are recommended for more contextualised health services research. It has a strong focus on participatory implementation with multiple stakeholders. Such focus is critical to identifying effective interventions and achieving maximum relevance where programme implementation takes place in diverse social, political and cultural contexts. It proposes an incremental and capacity-building approach.
The protocol describes a broad approach to determining evidence as a crucial resource for effective implementation. It focuses on the key concerns of preventing delay in diagnosis, improving adherence with multi-drug therapy, enhancing the roll out of chemoprophylaxis and increasing participation in community based rehabilitation, and may also inform other issues such as preventing disabilities. In order to meaningfully explore multiple domains (including, health, educational, cultural, social, economic, psychological, legal, etc), this project will require substantial engagement with grass roots services, service providers, researchers and people affected by leprosy. This will necessitate considerable coordination and networking between actions and stakeholders, which will in part depend on adequate resources, infrastructure and support.

Acknowledgements

Ethics approval was not required for this manuscript, and no funding was provided in its preparation. This manuscript was conceptualised and initially drafted by PK. All authors reviewed subsequent drafts and contributed to refinement of the manuscript.

References

8. Darlong JD, Maximus N, Kumar A, Maximus T, Kumar S, Nanda NK. Methods to enhance voluntary early reporting (EVER) at PHC and other integrated settings. Idian Council of Medical Research, Purulia, West Bengal, India, 2010.
10. Coebergh JA, Buddingh H. Non-adherence to leprosy treatment in Western Sudan; the people behind the numbers. Lepr Rev, 2004; 75: 404.


