Developing Program Logic Models and Analytic Frameworks:

Application to Neglected Tropical Diseases Research

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ABSTRACT

Program logic models and analytic frameworks can serve as essential planning and operational tools, particularly for those engaged in research. A model is a snapshot of a system, while a framework is the structure upon which the model is predicated. Both tools force situation of the problem to be addressed within its broader context, and enable one to consider how or why a pre-condition (e.g., existing program; at-risk population) will lead to outcomes following specific actions or interventions. Program logic models link resources and activities to ultimate outcomes and impacts in a step-wise manner, while analytic frameworks conceptualize how change will occur when actions are applied to a population, and necessarily embed theory of change. The literature on program logic models and analytic frameworks is voluminous and this document aims not to recapitulate or comprehensively review the work of others. Rather, this paper frames and elucidates the logic and analytic approach that I personally espouse when undertaking a body of research. In particular, I have illuminated the process to which I adhere when advancing the body of work that I lead in the neglected tropical diseases (NTDs) space. I herein provide an overview of my approach and then follow with specific illustrative case studies to assist the reader in understanding the practical utility of logic models and analytic frameworks in NTDs. Finally, I propose application of both Program Theory and Theory of Change to bench science research, and illuminate how this might be achieved.

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I. Introduction - Baseline Assumptions and Understanding

The theory, application, utility, and limitations of logic models and frameworks are fully illuminated elsewhere [1-11]. The work in this area by the United States Preventive Services Task Force (USPSTF) [1], W.K. Kellogg Foundation [5], Public Health Ontario [4], Drs. Clark and Anderson [3], and Drs. Rehfuess and Norris [8-11] is particularly useful literature elucidating the definitions, structure, theory, application, and utility of logic models and frameworks as they relate to health interventions, specifically. Many such resources are available in an open-access format, and I highly recommend familiarizing oneself with this excellent work in advance of trying to develop a model or framework.

In brief, a model is a snapshot of a system, while a framework is the structure upon which the model is predicated. Logic models enable conceptualization of interventions within their broader context, while frameworks describe the causal pathway of intervention (actions) to outcome. The original Logic Models were designed to depict program components so that activities matched outcomes. In other words, they began with a specific program in mind to evaluate or track [3]. Program Logic Models graphically illustrate components and identify outcomes, inputs, and activities. They are operational, detail- and action-oriented.

An example of a simple Program Logic Model is depicted here, in Figure 1. Note that each cell would be populated with text representing each logic model component.

Inputs	Activities	Outputs	Short-term Outcomes	Long-term Outcomes

Figure 1. Structure of a simple Program Logic Model (United Way Format) [3]

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Movement between cells in the Program Logic Model requires one to pose an "if/then" series of questions, as in "if X resources are available, then Y activities can occur, which will have Z outputs", etc (Figure 2). The overarching goal of a Program Logic Model is to *directly* link the inputs (resources) and actions (activities) to stated objectives (outcomes, impacts) through measurable deliverables (outputs). Program Logic Models facilitate tracking, accountability, efficiency, and feasibility, and by their very nature, are unidirectional.

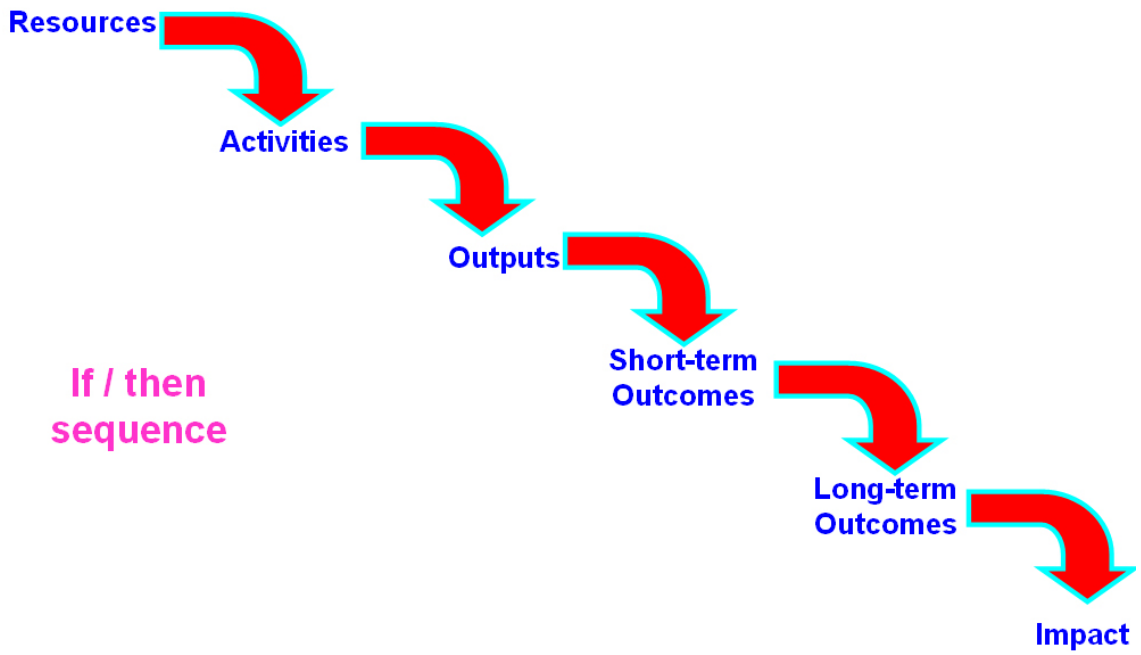

Figure 2. Program Logic Model approach to answering a research question.

Analytic frameworks, on the other hand, are conceptual, high-level, and generally represent how you think change will occur [3]. Pathways may be multidirectional. Embedded within an Analytic Framework, therefore, is at least some component of "Theory of Change", which enables diagrammatic representation of *how* and *why* you believe specific actions (e.g.,

activities, interventions) will lead to certain outcomes (e.g., changes, impacts). Thus, Logic Models add structure to a complex problem and ensure that activities match outcomes through graphical illustration, while causal Analytic Frameworks begin with a goal in mind (e.g., improved health outcome) and explain *how* and *why* the activities will link to outcomes.

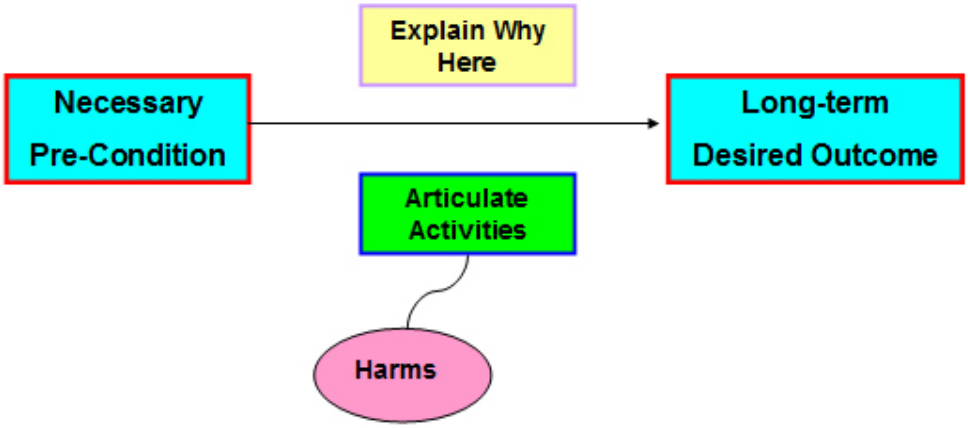

Figure 3. Basic structure of a typical Analytic Framework.

In the high-level Analytic Framework in Figure 3 above, the "Explain Why Here" box may reflect linkages between the population and outcome that are physiological, behavioural, genetic, or contextual in nature, but may also represent Intermediate outcomes (as illuminated below). Such brief explanatory notation may also be required for the user (reader) to understand the causal pathway being supported in the Analytic Framework. For simple Analytic Frameworks, such additional notation is usually unnecessary. Analytic Frameworks can be "read" from left to right with the Population on the left (#1) from which arise arrows representing actions, activities, or interventions (#2), each of which has associated harms or risks (#3), leading to ultimate outcomes (#5) in the far right and possibly through intermediate outcomes (#4) in the

middle (Figure 4). Differential weighting (i.e., thickness) of arrows can be used to denote likelihood of outcomes arising from actions when more than one such outcome could occur (e.g., as a pathway breakpoint in the Framework). Intermediate outcomes may also represent 'surrogate' outcomes, which have dotted line relationship to the long-term or ultimate outcome.

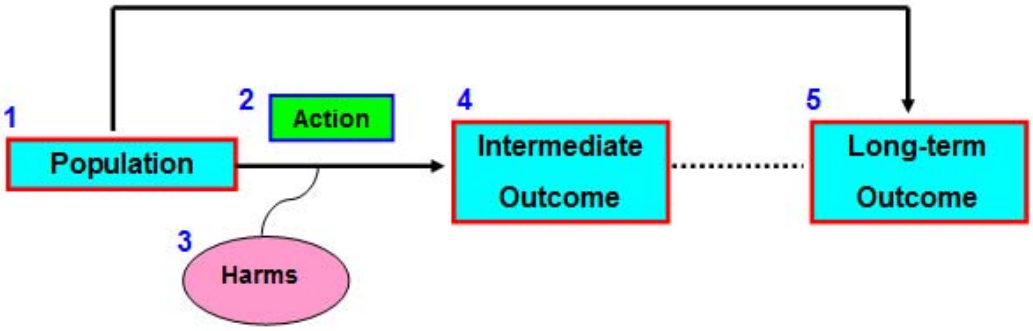

Figure 4. Flow of an Analytic Framework, with interventions applied to populations with a necessary pre-condition (i.e., state of being), leading to outcomes.

Analytic Frameworks are typically thought of as 'Testing' or 'Intervention' Frameworks. Testing Frameworks would include problems of a Screening or Diagnostic nature, while Intervention Frameworks typically focus on a particular preventive (e.g., immunization) or therapeutic (e.g., drug treatment) manoeuvre. Both types of Analytic Frameworks apply the same logic and theory, linking specific actions to outcomes, and, from a practical standpoint, differ only in nomenclature. Frameworks conceptualizing the *physiologic* mechanism of action leading to a specific health outcome are called "Physiologic Frameworks", which may also have a Testing or Intervention component, or may simply illuminate the physiologic causal pathways

leading from a state of being (e.g., impaired fasting glucose) to a health outcome (e.g., type 2 diabetes) (Figure 5).

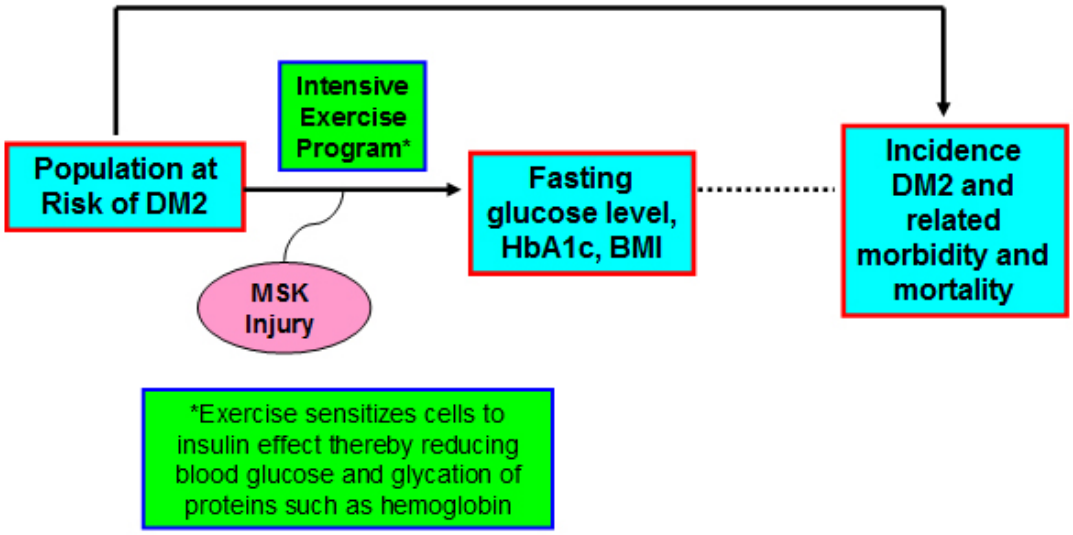

Figure 5. Sample intervention-based Analytic Framework illuminating the physiologic basis for embedded theory of change. Abbreviations: BMI, body mass index; DM2, type 2 diabetes; HBA1c, hemoglobin A1c (glycated hemoglobin); MSK, musculoskeletal.

To summarize, then, Analytic Frameworks describe the causal pathway from action (intervention) to outcome, and can be multidirectional. Logic Models, on the other hand, serve as a graphical representation of the key program components that are linked in a stepwise (usually unidirectional) manner with the overarching goal of mapping inputs (resources) to outcomes (impacts) via a set of *measurable* outputs, thereby embedding some degree of accountability into the programming.

II. Constructing a Program Logic Model and Analytic Framework: Application to NTDs Research

A. STEPS TO FOLLOW. The basic approach to constructing program logic models and analytic frameworks involves identification of: a target population; planned activities (inputs); short-term outcomes along the way (intermediate outcomes); and, ultimate end-points (goals, long-term outcomes / impacts). Table 1 provides a "quick guide" to the basic steps to follow. The very first task is to define the overarching question or theme to be answered or addressed. Resources that you will need at this stage include the published peer-reviewed literature; grey literature; consultations with colleagues, focus groups, patients, knowledge users, stakeholders, and the internal team. Next, situate the question/theme within the ethical, legal, legislative, cultural, regulatory, social, psychological, physiologic, financial, and geographical contexts of the target population. Resources at this stage will include WHO regional offices, embassies and consulates, news media, and other relevant intelligence resources.

Third, define your goals. These will differ in scope and nature depending on the problem or question for which you are developing an Analytic Framework. Should your problem of interest be of a complex nature for which you might have multiple goals, organizing these into a matrix of some sort can be helpful. However, if the goal is to produce a recommendation (guideline) for one particular type of intervention (e.g., *Varicella* immunization) for which recommendations will stem from a simple single systematic review and quality assessment, then such a matrix may not apply. Figure 6 below is just a sample matrix of multilevel goals for a new approach to coronary artery disease, for example:

Type of Goal	Self	Level of Impact		
		Patient / Individual	Population	System
Service	Fulfillment of cardiology fellowship program requirements	Reduced individual morbidity and mortality due to coronary artery disease	Increased population-level uptake of a new treatment for hypertension	Conversion of paper to electronic cardiac health records
Education	Learning a new procedural skill (cardiac catheterization)	Increased individual patient literacy around secondary prevention of coronary artery disease	Successful community KTE event regarding risk factors for coronary artery disease	Training of HCWs on use of electronic cardiac health records system

Figure 6. Sample matrix for defining and selecting goals of the program.

Resources that will be helpful at this stage include the GANTT chart as this will help refine the needed tasks and over what period of time each will be completed.

From your matrix of desired goals, choose the primary goal (highest priority goal) around which to develop your Analytic Framework. This prevents scope creep. If the problem is of a sufficiently complex nature, you may require both a Program, System, or Causal Loop Logic

Model and Analytic Framework, and possibly more than one of each. Refreshing your review of the topical and methodological scientific literature framing your problem is helpful at this stage. Think about the major outcomes that you expect to achieve (or encounter in the literature), and think about *why* and *how* you expect those outcomes to come about. Identify the mechanisms by which the outcome(s) will occur. Are they physiologic? Social? Behavioural? Economic? Climatologic? Political? Again, the scientific literature and news media will be helpful at this stage.

Next, identify how you will *measure* that outcome (or how it is traditionally measured and reported). The literature will help you here, but in general, there are many questions to consider. Are you likely to measure your outcome with a qualitative narrative? Will there be quantitative biochemical or hematological data? Will outcomes be measured as categories or proportions? Refreshing your understanding of EBM resources on measurement will be of assistance at this stage. What will define success? (at the primary and secondary goal levels). Upon what is success conditional?

If your Analytic Framework aims to conceptualize any kind of action/intervention - whether behavioural, psychological/counselling, diagnostic/screening, prevention, or therapeutic - now define your PICO. The basic approach involves:

a. Identification of a target population (the P in PICO). Population may be everyone (e.g., all persons at risk of influenza) or a subset (e.g., Andean women of reproductive age with type 2 diabetes);
b. Identification of planned interventions (inputs) (the I and C in PICO). C may include no comparator, placebo, alternate intervention, or standard of care.
c. Identification of short-term outcomes (intermediate outcomes); and,

d. Identification of the ultimate end-point (goal, long-term outcomes / impacts) (the O in PICO).

Once the PICO(s) are defined, start populating your Analytic Framework template:

a. Population goes on the far left and Outcome on the far right.
b. If there are obvious Intermediate (surrogate) Outcomes that were identified in the prior steps, put those in next just proximate to (left of) the ultimate Outcome.
c. Next, to the right of Population and denoted by arrows, add in the Intervention pathway above and Comparator pathway (if one is included) below Population.
d. At each action point (intervention, activity), a Harms/Risks/Adverse Effects pathway should exist, even if just as a placeholder in your first iteration of the model.
e. At each step along the way, the if/then question should be posed, as in: "*if* intervention X is applied to the population, *then* either Y or Z could happen". All potential contingencies should be considered (and resurrected from your exhaustive literature and peer consultation activities!), and entered into the Analytic Framework.

For Analytic Frameworks that will lead to the formulation of a guideline, recommendation, or statement suggesting a paradigm shift, there are additional considerations. After defining all the elements of the Analytic Framework and illuminating *why* and *how* you expect actions to translate into outcomes, then the influencers of your ultimate recommendation should be identified, including:

a. Acceptability;
b. Feasibility;
c. Costs, economic considerations;

d. Risk : Benefit analysis with weighting ideally pre-defined;

e. Values and Preferences (estimated or actual if literature exists) of population for whom the guideline / recommendation is intended.

Following this series of steps will enable you to both graphically represent your program components (basis of your research question), and identify all of the variables, contingencies, and relationships that will affect how your population of interest will (or is likely to) respond to your planned interventions. The Analytic Framework will account for any directionality in relationships and will enable your team to have line of sight into the Theory of Change that is embedded in your problem of interest. This latter piece is critical to understanding the "so what?" of your work and situating it within the broader context of its potential contribution to science and medicine.

B. A CASE STUDY OF DEVELOPING A PROGRAM LOGIC MODEL AND ANALYTIC FRAMEWORK FOR DIAGNOSTIC STEWARDSHIP IN AMERICAN TEGUMENTARY LEISHMANIASIS. Leishmaniasis is a vector-borne parasitic disease caused by protozoa of the genus *Leishmania*. Tegumentary leishmaniasis manifests as ulcers on the skin, and destruction of the nose, palate, and larynx, which causes ostracization of those affected from their communities. In many parts of the world, facial leishmaniasis renders women unmarriable. Peru is a top contributor to the global burden of leishmaniasis, where most cases occur in areas of extreme rural poverty. In these under-resourced areas, medical facilities are extremely basic with limited diagnostic infrastructure [12-16]. Even if medical infrastructure is available, accessing it may be difficult due to road conditions. The unpaved switchback roads that service many of these rural endemic communities further challenges the accessibility of care.

When available, highly skilled personnel procure diagnostic specimens in tegumentary leishmaniasis by either scraping, aspirating, or biopsying the unanesthetized ulcer to examine the material under a microscope, or inoculate that material into a culture tube to try to grow the parasite. Both culture and microscopy are incredibly insensitive for detection of the parasite, missing close to 75% of cases. These procedures are poorly tolerated in children. In addition to being insensitive and poorly tolerated by the patient, the diagnostic tests based on collection of invasive specimens pose a risk of sharps injury to the healthcare worker in areas devoid of safe biohazard disposal let alone occupational health infrastructure to access post-exposure HIV or hepatitis B prophylaxis.

In practice, then, given all the aforementioned challenges related to the need for expertise in specimen collection and diagnostic testing colliding with the reality of the disease as one of rural poverty, most confirmatory diagnostics are only offered in urbanized reference centres. Moreover, since leishmaniasis cannot be diagnosed clinically in endemic areas, due to its similarity to other fungal and mycobacterial infections, treatment is generally not provided empirically.

So to summarize, the traditional diagnostic approach to leishmaniasis is based on invasively collected specimens which require technical expertise to perform and are thus only available in larger urban reference centres, are painful, difficult to perform in pediatrics and in the remote endemic areas, and engender all of the risks associated with skin incision including bleeding, infection, and sharps injury [12-16]. The poor sensitivity of microscopy and culture lead to a diagnostic gap, and because empiric treatment does not occur, this diagnostic gap leads, in turn, to a treatment gap. The major challenges of access to and utility of existing traditional diagnostics culminate in thousands of patients per year in endemic areas suffering for years with

disease and disfigurement, and existing outside the cascade of care. Stemming from these limitations, then, a logical question to ask is: are there sensitive non-invasive diagnostic alternatives to current standard of care? And, as a follow-up: how do we close this treatment gap arising from a diagnostic gap?

Taking a program logic model approach to the problem of poor diagnostics in leishmaniasis, then, I began to think about how I could answer these questions, and started to map out the resources I would need to conduct certain activities (or interventions), which would have measurable outputs leading to short- and long-term outcomes with impact (Table 2). The idea being that research ultimately improves quality of care through diagnostic and management innovations, which in turn enable surveillance activities and data accrual, which inform research questions (Figure 7).

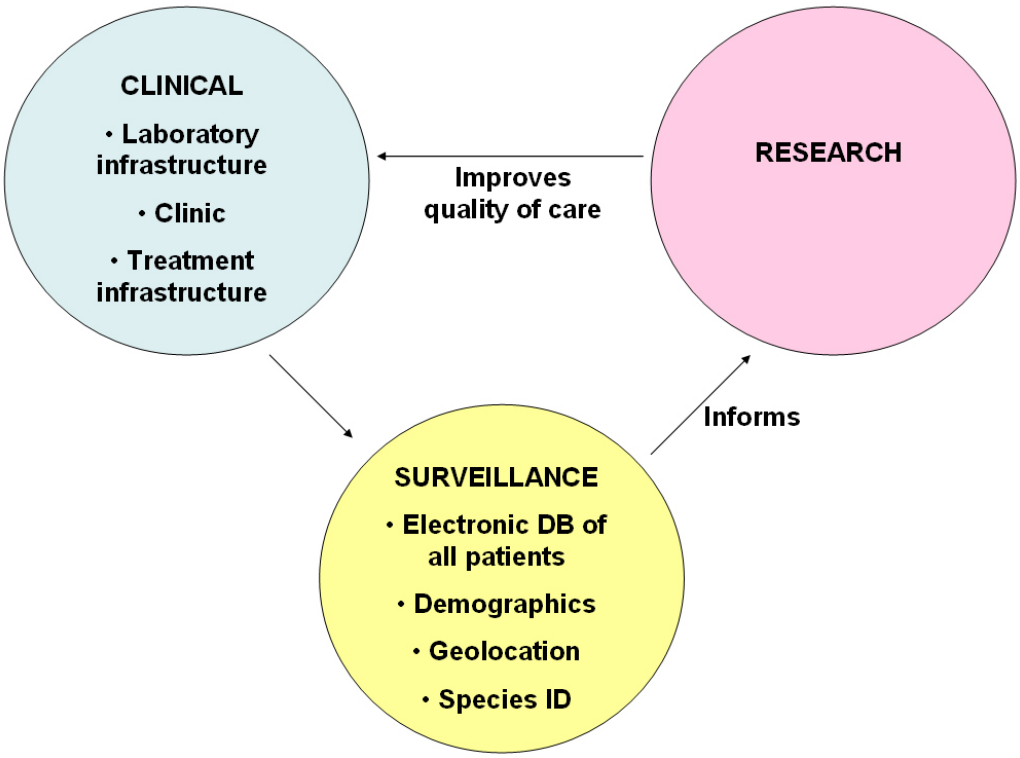

Figure 7. Sequence of contingencies and impacts of a successful research program.

Illustrated below is the program logic model linking all the resources, activities and outputs to outcomes, and ultimate impacts (Figure 8). As with any Program Logic Model, the resources and inputs are defined a priori as these will dictate the scope and scale of the activities that can occur. Similarly, the measurable outputs (quantifiable metrics) will directly relate to the planned activities, which are, again, dictated by the available resources. For example, it might make little sense to objectively measure the tolerability of a diagnostic procedure as an output if the activities within the program relate only to treatment interventions. Similarly, if the program interventions (activities) are of a diagnostic nature, then it might make little sense to objectively measure short-term drug treatment outcomes.

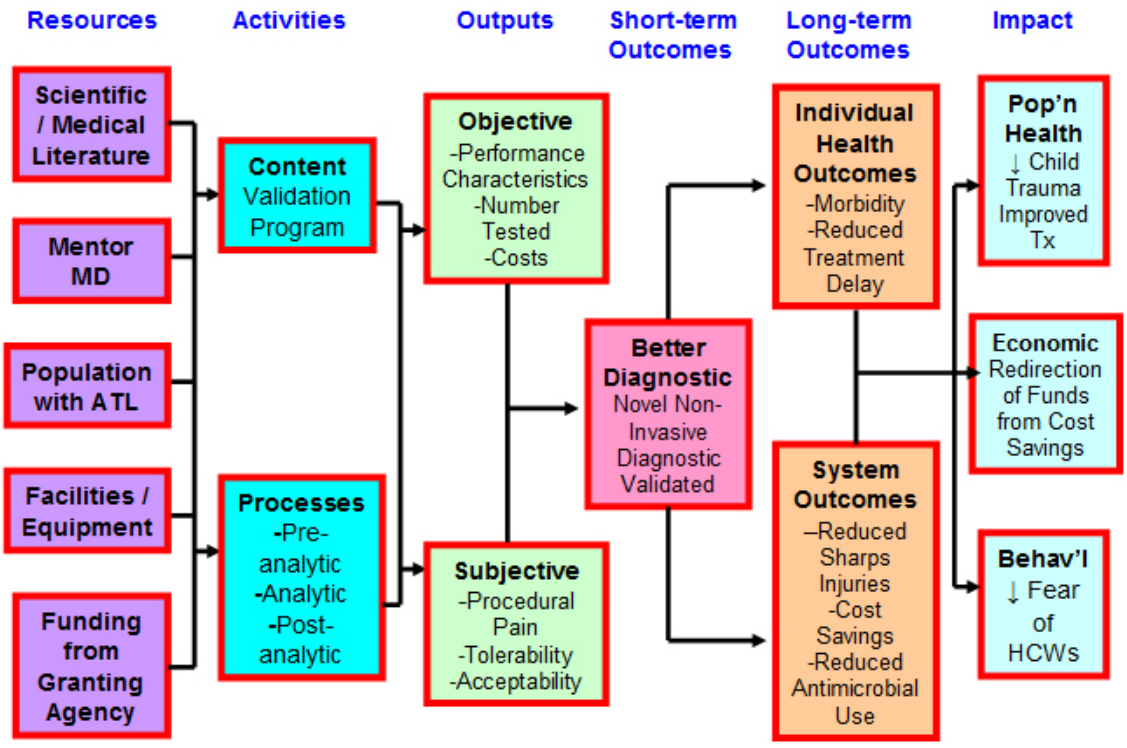

Figure 8. Program Logic Model for Non-invasive Diagnostics in American Tegumentary Leishmaniasis [12-16]. Abbreviations: HCW, healthcare worker; MD, medical doctor; Tx, treatment.

Embedded within this Program Logic model were certain hypotheses, which were amenable to construction of an Analytic Framework identifying my population of interest, actionable diagnostic Interventions and their Comparator, which would lead to both surrogate and ultimate health outcomes for American tegumentary leishmaniasis, all the while situating the PICO within the broader behavioural, economic, and long-term outcome context (Figure 9). As previously mentioned, invasive diagnostics are particularly challenging in pediatrics, and it wasn't long after I began collaborating down in Peru that I became motivated to find a more palatable solution to those invasive scrapings and aspirates. Thus was born this idea of non-invasive molecular diagnostics for American tegumentary leishmaniasis [12-16] (Figure 9).

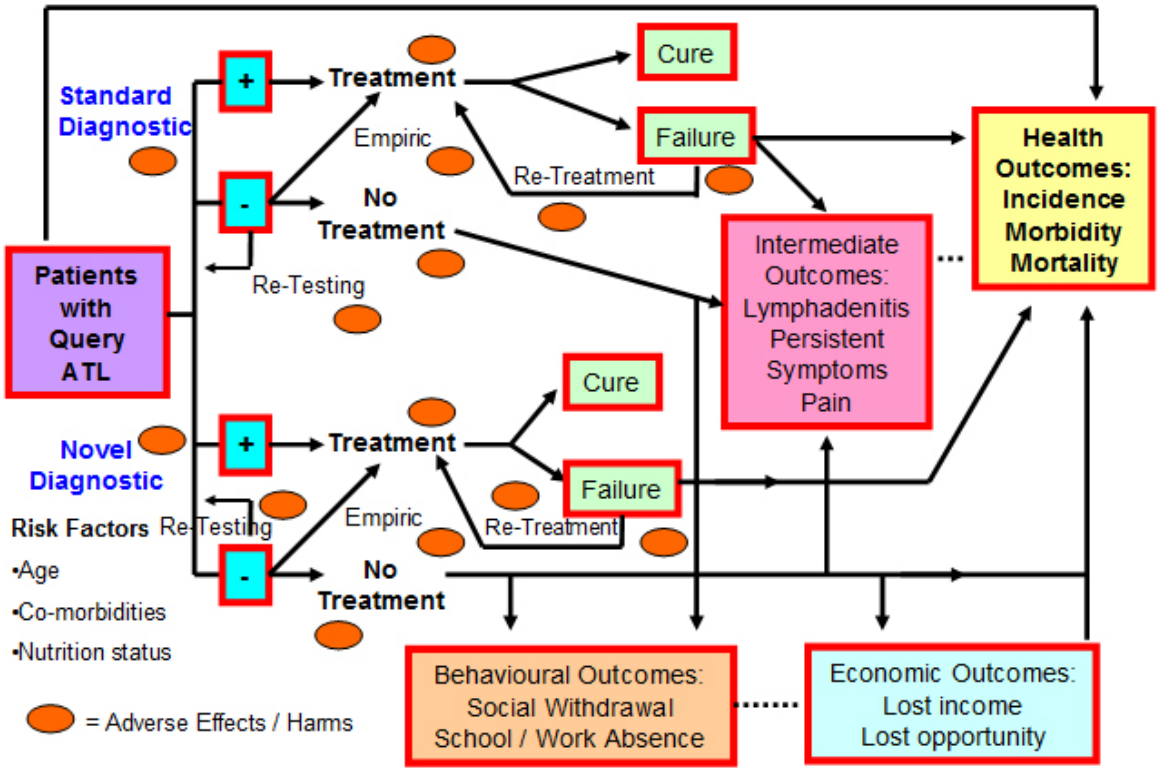

Figure 9. Analytic Framework for Non-invasive Diagnostics in American Tegumentary Leishmaniasis (ATL) [12-16].

The premise of the non-invasive approach is that one can collect lesion impressions using filter papers or absorbent brushes, which wick from the ulcer, fluid containing macrophages containing parasites [12-16]. Those parasites have many multicopy genes that are easily amplifiable once DNA is extracted from these dried papers. In addition to being highly sensitive, this strategy is portable, and reduces turnaround time, cost, and discomfort to patients. This non-invasive molecular diagnostic approach can also be used for leishmaniasis that affects the mucous membranes, manifesting as severe tissue destruction owing to a vigorous cell-mediated immune response. In several studies we compared non-invasive PCR to standard of care (scrapings, aspirates, or biopsy with histopathology) and noted substantial gains in diagnostic performance, offering essentially a four-fold improvement over standard of care [12-16]. And, importantly, the non-invasive approach portends no risk of sharps injury to the healthcare worker, nor are sharps biohazard precautions needed.

The non-invasive molecular diagnostic approach can also be adapted to field settings through deployment of handheld lithium ion battery operated PCR units, which require a fraction of the infrastructure needed for conventional histopathology and are far less operator dependent than microscopic approaches [17]. Field performance of that strategy also demonstrates a detection advantage over conventional diagnostic test methods [17].

To summarize this particular case study demonstrating the application of Program Logic Models and Analytic Frameworks to NTDs research, non-invasive molecular diagnostic approaches in leishmaniasis solve the issues of: poor diagnostic sensitivity; required technical expertise; pain, bleeding, and infection; pediatric and remote field challenges; and risks to the healthcare worker. The downstream benefits of this superior, operator-independent, and highly

sensitive approach might include impacts that are behavioural, economic, and population health-oriented, as indicated in the Model and Framework.

III. Future Directions

To date, the Program Logic Model and Analytic Framework approaches have been mostly applied to problems and issues of an economic, population health, environmental, and policy nature. As illustrated in the case study above, I have applied Program Theory and Theory of Change to questions of a diagnostic intervention nature, and my research team is also heavily involved with closing gaps in NTDs practice and research through knowledge synthesis [18,19]. As a Clinician Scientist whose research stretches from basic science to population-level disease surveillance, I have developed a keen interest in applying the same theory and logic to questions of a more bench-level and pathogenesis nature. For all the previously illuminated reasons underpinning the value of this Logic Model and Analytic Framework approach to health interventions, the same could be said for bench science, whether translational and applied, or pure basic research. Having well developed Program Logic Models and Analytic Frameworks in advance of conducting bench science research will almost certainly improve - by virtue of their a priori nature - transparency, accountability, efficiency, reproducibility, EDI (equity, diversity, and inclusion), generalizability, and measurability, and, in a commensurate fashion, reduce the influences of bias, scope creep, experimental waste, and poor contextualization. The idea is not to eliminate creativity, iteration, and innovation, but rather to establish, in a transparent manner, experimental approaches that are most likely to align with ultimate objectives (and in doing so, make an impact on science and, in my case, medicine).

In my laboratory research program, some examples of work to which a Program Logic Model and Analytic Framework approach could be applied include: the pathogenesis of New World cutaneous leishmaniasis [20-22]; the role of endosymbiotic chlamydiaceae in amoebic keratitis [23,24]; and, the presence of drug-resistant genotypes in imported isolates of *Plasmodium falciparum* [25]. In each case, the theory and logic can be easily applied by reframing the definition of a population. Historically, Program Logic Models and Analytic Frameworks have been applied to populations of *individuals*, however, there is nothing to prevent such logic and modelling from being applied at the sub-organismal (cellular or molecular) or pathogen level. Rather than the "P" in PICO representing a *population* of *individuals*, there is no reason why it cannot represent a population of genes, molecules, microorganisms, or even biological processes to which experimental interventions are applied. Outcomes and impacts, then, could be considered at the usual individual health, population, or systems-level. Alternatively, by taking the sub-organismal approach, the outcomes and impacts may also occur at a more micro level, and relate to the population of genes or cells upon which the experimenter has intervened.

Below are some graphical illustrations of this pathogen-level concept, which represent some of the work packages mentioned above. In the first graphic, a Program Logic Model for the development of a novel drug susceptibility platform for leishmaniasis is represented (Figure 10), and again, follows the same "if/then" sequence of logic illuminated previously in order to map inputs (resources and activities) to outcomes (short- and long-term) via specific measurable outputs. Conventional treatment of American tegumentary leishmaniasis relies on drugs that are toxic, expensive, mostly parenteral, and difficult to access. While some more gentle oral options exist, large scale data supporting their efficacy is limited. Thus, drug susceptibility testing of

Leishmania strains derived from actual patients has the ability allocate patients to less toxic, more economical, and more accessible therapies. However, no clinically validated or commercial laboratory test exists for this purpose. Thus, my research team and I sought to close this gap [22] (Figure 10).

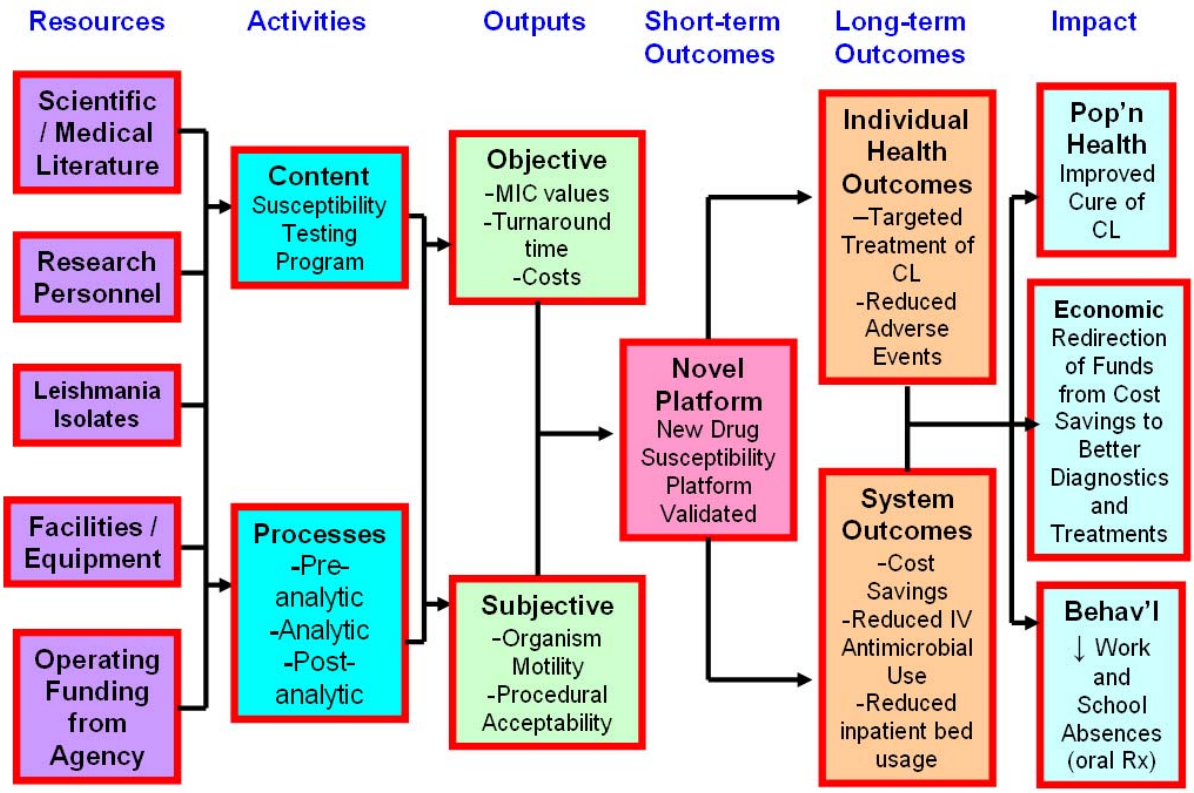

Figure 10. Program Logic Model for Novel Drug Susceptibility Testing Platform in Leishmaniasis [22]. Abbreviations: CL, cutaneous leishmaniasis; IV, intravenous; MIC, mean inhibitory concentration; Rx, therapy.

From the Program Logic Model above, an Analytic Framework can be constructed to demonstrate how new knowledge around susceptibility patterns at the organism level in leishmaniasis might translate into health outcomes for patients and populations (Figure 11).

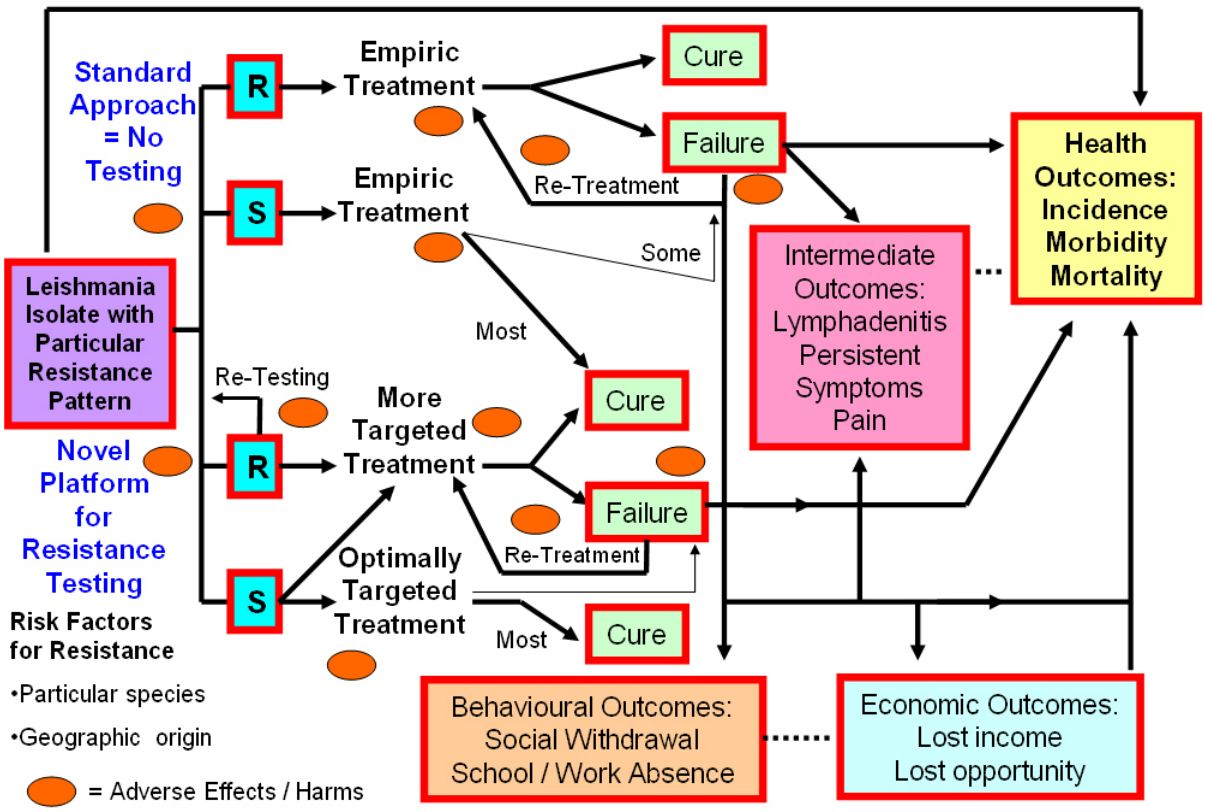

Figure 11. Analytic Framework for Novel Drug Susceptibility Testing Platform in Leishmaniasis [22]. Abbreviations: R, resistant; S, susceptible. (Note the differential weighting of arrows arising from actions, which are represented in that manner in order to convey to the user the likelihood of a given outcome, when more than one outcome is possible).

Thus, Figures 10 and 11 underscore how developing a program to generate new knowledge around drug susceptibility testing for a particular NTD requires both a Program Logic Model approach as well as construction of an Analytic Framework.

Another parasitic protozoan disease on which my team and I work is Amoebic Keratitis (AK), a potentially blinding corneal infection that predominantly affects contact lens users, and is

caused by members of the genus *Acanthamoeba*. Acanthamoebae are opportunistic organisms that are found in fresh water and the environment, and can easily contaminate contact lenses and their casings when the devices are rinsed in or exposed to tap water (e.g., when showering with contact lenses in place). Owing to the limited vascular supply and immunologic privilege of the cornea, AK is an incredibly recalcitrant infection to treat, typically requiring months to more than a year of combined topical and oral therapy. Even then, up to 10% of AK patients will require some further definitive surgical management, which, in its most drastic form, involves full orbital enucleation. Given the dismal success rate of current therapeutic approaches to AK, and the frequency of contact lens use in populations residing in upper-middle- and high-income countries, novel therapeutic approaches should be explored. Like many eukaryotes, acanthamoebae harbour endosymbiotic chlamydiaceae, mycobacteria, and rickettsiales, all of which could have theoretical effects on the pathogenesis of AK, particularly if certain species of acanthamoebae were to serve more as a vehicle by which to transport the pathogenic endosymbiont rather than elaborating truly pathogenic mechanisms themselves. Support in the literature exists for both possibilities, but there is no doubt that some acanthamoebae are clearly pathogenic on their own. In any case, one line of inquiry around which my team and I have worked relates to using a human corneal tissue model of AK to better understand the role of endosymbionts in AK pathogenesis, and whether or not such potential bacterial co-pathogens should serve as therapeutic targets [23,24].

In the next graphic below, the Analytic Framework represents how the application of different in vitro drug treatment protocols may differentially affect a *population* of acanthamoebae established in a corneal tissue model of AK, with the ultimate outcome being measured by cytopathic effect (CPE) (Figure 12). Again, note the differential weighting of arrows

signifying the likelihood of an outcome arising from a specific action (Figure 12). Also note the relationship between intermediate and ultimate outcomes.

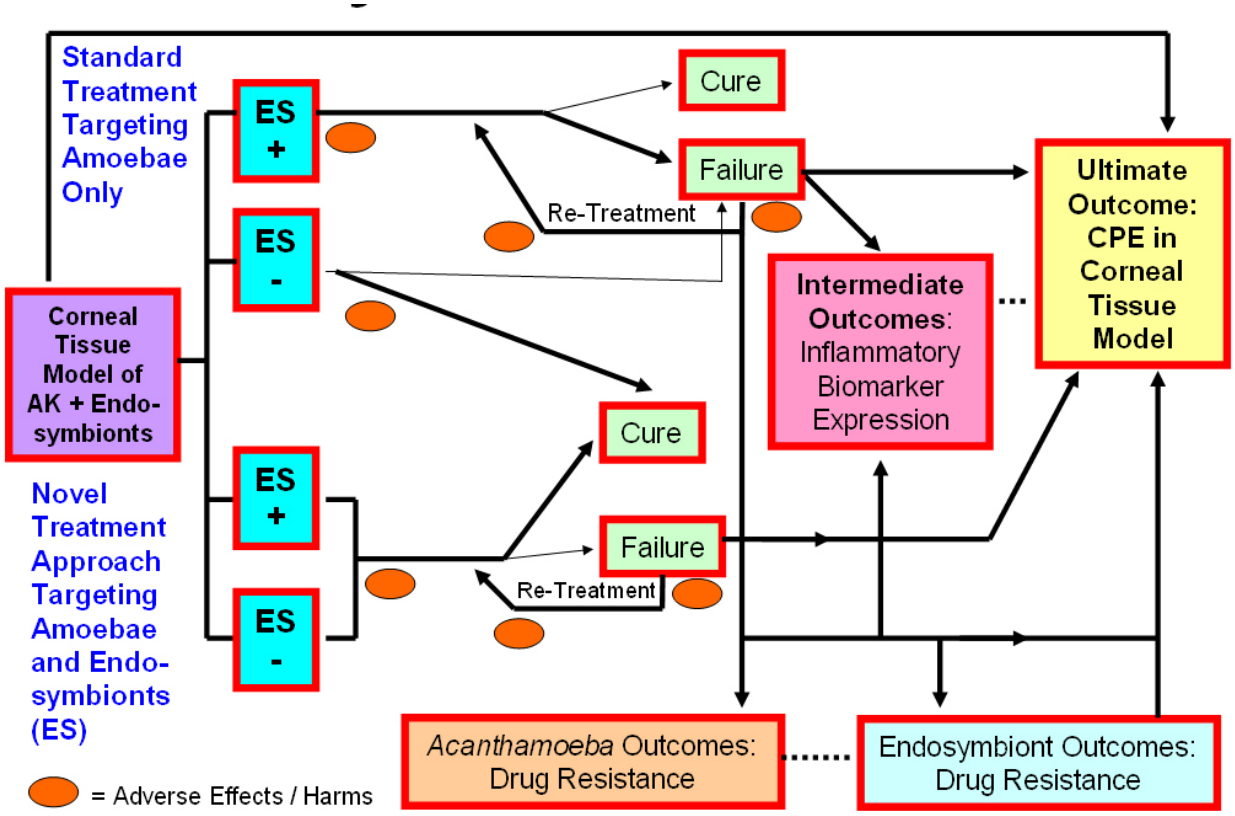

Figure 12. Analytic Framework for treatment of amoebic keratitis and the potential acanthamoebae bacterial endosymbionts using a corneal tissue model [23]. Abbreviations: AK, amoebic keratitis; CPE, cytopathic effect; ES+, endosymbiont positive; ES-, endosymbiont negative.

Unlike the previous example of drug susceptibility testing in leishmaniasis, where the "P" in PICO was a hybrid model, incorporating both individual organism and human health outcomes (Figures 10 and 11), in the AK Analytic Framework above, the work is less translational and more in the realm of basic science. Thus, the outcomes that derive specifically from our actions

applied to our population of acanthamoebae must be similarly confined to that population of interest. While a subsequent phase of the work *may* incorporate research architecture such as a randomized clinical trial with human-level interventions, the work above does not directly extend to individual people. However, given the common logic, theory, and development process, my proposed application of Program Logic Models and Analytic Frameworks to work packages and research questions of a more proximal, and less immediately translational nature, I believe is certainly worthwhile. There are many elements of bench-level and basic science research that have been adopted from the evidence-based medicine (EBM) framework, the most obvious of which being the incorporation of systematic literature review to support any foundation of theoretical work being undertaken; thus, incorporation of PICO questions, Program Logic Models (Program Theory), and Analytic Frameworks (Theory of Change) in a *formalized* manner into hypothesis-based research is likely to reap at least some of the aforementioned benefits of transparency, accountability, and efficiency.

IV. Conclusions

To conclude, both Program Theory and Theory of Change are being applied in a broad manner to questions of a public health and policy nature [1,2,4,10,11], and the logic and theory behind development of Program Logic Models and Analytic Frameworks borrow heavily from early adopters in the philanthropic space [3], which aimed to more convincingly map resources going in to impacts coming out in a data-driven (e.g., measurable) manner. Program Logic Models are operational by nature, and follow an "if/then" sequence of events that link resources and activities to both short- and long-term outcomes. Analytic Frameworks, on the other hand, are high level and embed some degree of causality into their representations, thereby explaining

how and why certain actions (interventions) applied to specific populations will generate outcomes. For comprehensive reviews and guidance around Logic Models and Analytic Frameworks in general, I would recommend familiarizing oneself with the outstanding body of literature produced by the USPSTF [1], W. K. Kellogg Foundation [5], Public Health Ontario [4], Drs. Clark and Anderson [3], and Drs. Rehfuess and Norris [8-11]. The work herein describes the development steps and application of Program Logic Models and Analytic Frameworks specifically to the NTDs research space, and is not a substitute for the domain-level literature cited above. In addition to illuminating how and why one might choose to use Program Logic Models and Analytic Frameworks in their NTDs research programming, I also describe the application of such logic and theory - in a formalized manner - to populations that exist at a sub-organismal or pathogen level. Program Logic Models and Analytic Frameworks have the potential to serve as invaluable complements to classical approaches to NTDs research as they enable one to diagrammatically conceptualize, in a formal and a priori manner, all the resources, actions, contingencies, and anticipated outcomes of a program, while situating their overarching question into the broader social, economic, political, geographic, cultural, ethical, and health context. In doing so, scientists can expect to gain transparency, accountability, reproducibility, EDI, and efficiency in their programming.

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Table 1. Quick guide to developing a Program Logic Model and Analytic Framework that will be applied to neglected tropical diseases (NTDs) research questions.

Step Number	Step Details	Stage-specific Resources
1	Define the overarching question or theme to be answered or addressed	Published peer-reviewed literature; grey literature; consultations with colleagues, focus groups, patients, knowledge users, stakeholders, and the internal team.
2	Situate the question/theme within the ethical, legal, legislative, cultural, regulatory, social, psychological, physiologic, financial, and geographical contexts of the target population	WHO regional offices, embassies and consulates, news media, and other relevant intelligence resources.
3	Define your goals	Organizing these into a matrix of some sort can be helpful GANTT chart as this will help refine the needed tasks and over what period of time each will be completed
4	From your matrix of desired goals, choose the primary goal (highest priority goal) around which to develop	Review of the topical and methodological scientific literature framing your problem is helpful at this stage

	your Analytic Framework	
5	Think about the major outcomes that you expect to achieve (or encounter in the literature), and think about *why* and *how* you expect those outcomes to come about	Scientific literature and news media will be helpful at this stage
6	identify how you will measure that outcome (or how it is traditionally measured and reported)	The literature will help you here. Refreshing your understanding of EBM resources on measurement will be of assistance at this stage
7	How will you define success?	Scientific and medical literature, internal consultation with team and stakeholders
8	Finalize defining your PICO	
9	Once the PICO(s) are defined, start populating your Analytic Framework	Analytic Framework templates (e.g., USPSTF)
10	If your Analytic Framework will lead to the formulation of a Guideline, Recommendation, or paradigm shift in standard of care, this is the stage at which you will identify the influencers of your ultimate recommendation	Literature, reports, focus group work, internal team consultations, stakeholder engagement around: acceptability; feasibility; costs and economic considerations; risk : benefit analysis; and, values and preferences

Table 2. Summary table of steps for developing a Program Logic model and Analytic Framework applicable to non-invasive diagnostics in American tegumentary leishmaniasis (ATL).

Step Number	Step Details	Inputs and Actions
1	Define the overarching question or theme to be answered or addressed	• Could a non-invasive molecular diagnostic strategy be developed for ATL?
2	Situate question / theme within ethical, legal, legislative, cultural, regulatory, social, psychological, physiologic, financial, and geographical contexts of target population	• ATL highly endemic in Latin America • Peru is a top 10 contributor • Disease of rural poverty • Endemic countries range from low-middle income countries to high income countries • Disfiguring • Drug treatment provided by PAHO • Barriers to care access in endemic areas
3	Define your goals {see table X}	Validation of a novel, non-invasive molecular diagnostic approach
4	From your matrix of desired goals,	Validation of a novel non-invasive molecular

	choose the primary goal (highest priority goal) around which to develop your LM and/or AF	diagnostic approach
5	Think about the major outcomes that you expect to achieve (or encounter in the literature), and think about *why* and *how* you expect those outcomes to come about	Outcomes: validated diagnostic, better physicians, reduced morbidity, reduced treatment delay, reduced sharps injuries, cost savings, reduced child trauma and fear of health care workers
6	Identify how you will measure that outcome (or how it is traditionally measured and reported)	Measurement: validation metrics (performance characteristics); safety (adverse event frequency and proportion); tolerability (pain on a visual analog scale); sharps injury (frequency, proportion)
7	What will define success? (at the primary and secondary goal levels). Upon what is success conditional?	Impact: • Population health level (reduced child trauma) • Economic level (cost savings from reduced blood- and body fluid exposures, disposables) • Behavioural level (reduced fear of health care workers leading to increased uptake

		of unrelated interventions like immunization)
8	If your LM / AF aims to conceptualize any kind of action/intervention - whether behavioural, psychological / counselling, diagnostic/screening, prevention, or therapeutic - now define your PICO	PICO • P: Adults and Children referred to the *Leishmania* Clinic with query ATL • I: Novel non-invasive molecular diagnostic • C: Standard of care (culture and smear of aspirates and scrapings) • O: Performance characteristics; safety; tolerability
9	Once the PICO(s) are defined, start populating your Logic Model or Analytic Framework template	At each step along the way, the if/then question should be posed, as in: "*if* intervention X is applied to the population, *then* either Y or Z could happen"
10	After defining all the elements of the Analytic Framework and illuminating *why* and *how* you expect actions to translate into outcomes, then the influencers of your ultimate recommendation should be identified	– Acceptable – Feasible – Less costly, economically advantageous – Risk : Benefit analysis – less risky to patient and health care workers – Values and Preferences