DESIGN,
ANALYZE,
COMMUNICATE DAC

Target Policy Profile

DAC Program

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Section 1: Target Policy Profile Overview

Background

In many cases, the end goal of clinical research is a change in policy, but there is often a gap between the research and policy sides, which can lead to wasted money and time. To address this, a new tool called a Target Policy Profile (TPoP) could be used prior to research to identify key research questions to support policy decisions or could be used at the point of evidence generation and dissemination. The TPoP helps researchers analyze the evidence underlying a given policy, the gaps in that evidence, and the nature of additional evidence needed to improve the policy. Furthermore, it facilitates early and ongoing communication between researchers and policymakers. Armed with this knowledge and these relationships, clinical researchers maximize the likelihood that studies meet the requirements to generate optimal policies in an efficient way.

Who should complete the TPoP?

The TPoP consists of a form for researchers to fill out, including prompts and a set of questions as a guide which can be completed by a PI or study team. The group creating a TPoP is usually the team advocating a change in policy, who wish to engage the owners of the policy to understand what evidence a policymaker or policymaking organization needs in order to act.

When should one be completed and how is it kept up to date?

A TPoP should be completed whenever a change in policy is proposed and updated whenever significant new information becomes available that may affect any of the assertions within the TPoP. A TPoP should be kept current throughout the lifecycle of the policy change.

Who is the audience for a TPoP?

The typical target audience of a TPoP is the policymaking body that decides if, when and how to change policy on how to address a health condition. It is recognized that it is not always possible to directly engage those responsible for a change in policy as a collective and in these circumstances, applying a rigorous approach to reviewing the evidence and identifying the gaps will still serve the policy objectives well. The TPoP could also serve as a tool for the academic community to agree on the current state of knowledge and research gaps. Additional audiences might include various stakeholders. These stakeholders could include research funders, other researchers, global standard organizations, organizations manufacturing, subsidizing or distributing interventions involved in the new policy, as well as technical experts that a policymaker relies on to compile evidence and make recommendations. The purpose of the TPoP document is to facilitate a discussion with all relevant stakeholders.

Section 2: Target Policy Profile Template & Instructions

Engage your target audience early and often

When ready to create your TPoP, first identify the "target audience" for the information you want to communicate. Often policymakers are the target audience. An ideal approach is to engage specific members of your target audience as well as key opinion leaders (KOLs) in early dialog that is intended to draft a "case for change". This case for change should:

- Establish arguments based on robust evidence for why the proposed policy change will save and improve lives.
- Summarize the existing approach.
- Propose the evidence requirements to justify the proposed change in policy. This will come from research and other implementations, pilots and guidelines.
- Highlight existing research and identify any gaps to be filled by further studies, serving as a tool to discuss and agree on approaches including the design of studies to address evidence gaps.

This can be done by including KOLs in a design workshop to draft the key points for your case for change and collaboratively fill in the TPoP template. The output of the initial workshop will often be required research and the planning of new studies to generate necessary evidence. The draft TPoP can be iteratively revised, based on the research and studies you complete and by working in concert with the relevant stakeholders along the way, to keep them involved in the dialog and integrate their feedback, when appropriate.

Filling out the TPoP template

The **Target Policy Profile (TPoP) Template** (**Table 1**) is a blank copy of the template for you to fill out**.** The template includes some questions (under the "Proposed Target Policy" column header) that you will need to answer to help you draft your Proposed Target Policy. These questions are for guidance only and should be removed before the template is circulated.

Once completed, the top section of the TPoP Template allows you to outline the specific "case for change story" for your proposed TPoP. If desired, this tabular structure can easily be used to draft a compelling and easy-to-read document to engage policymakers, the research community and/or other stakeholders. Such a document should include: (1) your case for change, including the list of challenges of the current policy that make the newly proposed policy attractive to public health; (2) the benefits of a new policy; (3) if it exists, an exemplar case of the how the proposed policy is performing well in current use somewhere, and (4) the proposed summary of evidence that will be presented to change the policy.

The bottom section of **TPoP Template** (Target Policy Profile "tool"), once completed, provides a side-by-side comparison of the new/proposed policy, the current policy and the pros/cons of the new policy. The completed table can be included in your TPoP document.

Table 1: Target Policy Profile Template to fill out. Proposed TPoP "case for change" outline with question prompts (in red) for the user to respond to (top section) followed by TPoP "tool" (bottom section). Question prompts are for guidance only and should be deleted prior to circulating the document.

New or Target Policy Name:	
High level Policy Currently in Place:	
Ownership of policy	
Authors and consulted parties, Date of Last Revision:	
	Proposed Target Policy
Policy Description	• What are the details of a new approach to the health problem at hand? • What are the details of the current approach to that health problem?
Existing recommendation	• What details of the current policy are you proposing to change?
Reason for the change	• What are the challenges with the current policy? • Why would a new policy be better than the current policy?
Benefits of new policy	• What are the specific health benefits of switching to a new policy? • What are the specific benefits outside public health vs the old policy?
What evidence is needed to achieve the policy change	• What questions, if answered, would call for a new policy? • What evidence is needed to answer these questions?
Existing evidence supporting a proposed policy change	• What evidence already exists to support the proposed change to the policy?
Limitations of existing evidence	• What gaps exist in the current evidence base? • Why might existing evidence not generalize to our population? • How clear & informative is research to date?
New or Forthcoming Evidence	• What new studies have completed that provide evidence, supporting the proposed change in policy? • What additional studies are currently underway or are planned to provide relevant evidence?
Additional Evidence Needed/Gap	• What research has been requested by key policymakers? • What are the residual gaps in evidence that require further research?
How will gaps be filled/plan to generate further evidence	• What is the plan to address the identified gaps? • Are there new or follow-on studies that could be completed quickly?
Qualitative Health Benefits	• What social, political, economic & quality of life benefits are expected? • What benefits exist in other populations who have the new policy?

Quantitative Health Benefits/cost effectiveness considerations	• How many lives saved or QALY benefits come from the new policy? • What cost figures must be invested to achieve those savings?
Target countries	• What geographies, regions and states would receive implementation? • What variables define what areas to target first?
Time & Costs to Implement	• How long would it take to ramp up the new policy? • What are the high & low cost estimates over what period?
Feasibility & who is Involved in generating the data	• How simple or complex is implementing the new policy? • Who has done a feasibility/practicality/acceptability analysis? • Who is addressing the gaps in the evidence?
Regulatory considerations and PQ, are relevant products eligible for PQ	• What is the regulatory path? • What regulatory issues or hurdles will need to be met? • What types of qualification have been met or need to be met?
National considerations in target countries?	• What national considerations, if any, need to be taken into account related to this proposed policy change? What current political factors might affect perception if policy changes?
Delivery and implementation considerations;	• What stakeholders, organizations or partners are involved in delivery? • Have any pilots been performed to define implementation?
Will ongoing monitoring be required	• What is the monitoring & evaluation strategy and how will it be evaluated? • Who will measure if the health benefits reach the new policy targets?
Process and timeline for policy engagement	• What specific policymakers will be solicited/communicated with? • What is the duration & roadmap for achieving policy change?
Overall risk benefit for the policy proposal	• What are the benefits, in summary? • What are the risks, in summary?
Proposed plan going forward	• What is your action plan including evidence generation, compilation, presentation to policy makers through to policy change and implementation?

Target Policy Profile Tool

	Target Policy Proposed and attributes of product(s)	Current Policy/ SOC	Pros/ Cons of New Policy
Indication, Disease, Condition			
Target Population			

Intervention/Product/Dose			
Envisioned setting for intervention (school, community etc)			
Efficacy/Effectiveness/Evidence			
Feasibility/Practicality/Achievability			
Minimum Policy Important Difference (MPID)			
Safety			
Other considerations (different populations/geographies/settings)			
Ongoing monitoring			
Guidelines/ Standard of Care (SOC)			
Policymaker Engagement			
Costs			
Implementation			
Communication & Convenings			
Political Factors			
Fairness & Acceptability			
Current Use Elsewhere			

Section 3: Appendix A - In Depth Target Policy Profile Information

Introduction

A primary goal of clinical research in global public health is to create, test, implement or monitor the best interventions and cures as soon as possible. Proactively mapping a clinical research study's outcome to public health policy is both complex and challenging. Toward this end, a new tool—a Target Policy Profile (TPoP)—could simplify, standardize, and accelerate clinical researchers' efforts to go beyond designing, analyzing and communicating research. Such a tool could be used prior to research to identify key research questions to support policy decisions or could be used at the point of evidence generation and dissemination.

While some researchers might be 'old hands' at engaging with policymakers, it is more common that researchers are not familiar or comfortable working at the policy interface. Having a tool in hand to broker or frame the dialogue is a crucial asset. The most significant value proposition of a TPoP may be not as a dissemination tool, but as a discovery tool with policymakers, to understand what is needed to change their minds.

Background, Target Product Profile

In 1997, a brand-new journal, Drug Discovery Today, published a paper by a project manager. It described an internal tool gaining momentum among drug makers. Tony Kennedy of Hoffman-LaRoche explained the tool, how it could be used, and its benefits. In his "Managing the drug discovery/development interface," the tool is proposed as a "design specification for the product."[1] It is unlikely that Tony expected his paper would be cited over 500 times in the years to follow. The tool he described has become a global standard driving decisions that touch millions of lives. His article introduced the **Target Product Profile** or TPP.

The TPP has become commonly used. It is a summary specification for a health intervention. Regulatory stakeholders have embraced the TPP as a mechanism to align, communicate and collaborate with pharmaceutical manufacturers ('pharma'). "In the United States, the target product profile is a tool to facilitate communication between the pharmaceutical industry and the FDA, as well as between stakeholders in and outside of the industry."[2] Entering their fifth decade of use (The Royal Society of Medicine once recorded Kennedy describing Smithkline Beecham's use in the late 1980's[3]), TPPs remain a commonly used tool to bring together multiple stakeholders in focused discussion. TPPs are now used in a variety of ways. TPP use cases range from summary scorecards of global interventions to Rosetta stones for understanding pharmacokinetic attributes of small-molecule drugs.

In a draft guidance to industry publication, the US Food & Drug Administration (FDA) listed seventeen attributes a drug maker ought to include in a TPP (Figure 1), and over time a common format for TPPs has emerged (Figure 2).[4,5] During the development phase, TPPs lead into prescribing information at the time of authorization (e.g. a Summary of Product Characteristics).

Figure 1. TPP attributes recommended by US FDA[4]

2007 FDA Draft Guidance, TPP Sections

- Indications and Usage
- Dosage and Administration
- Dosage Forms and Strengths
- Contraindications
- Warnings and Precautions
- Adverse Reactions
- Drug Interactions
- Use in Specific Populations
- Drug Abuse and Dependence
- Overdosage
- Description
- Clinical Pharmacology
- Nonclinical Toxicology
- Clinical Studies
- References
- How Supplied/Storage and Handling
- Patient Counseling Information

Figure 2. A common format for classical TPPs[5]

Product class:	
Product name:	*To be completed once product approaches phase 2b*
Date of TPP endorsement	
Dates of TPP revisions	

	Desired		**Minimally acceptable**		***"Insert Product Name"* profile** (Completed as product approaches phase 2b)	
	Target	**Rationale**	**Target**	**Rationale**	**Target**	**Rationale**
Indication						
Expected efficacy						
Target population(s)						
Route of administration						
Formulation & presentation						
Dosage schedule						
Safety profile						
Co-administration						
Shelf-life & storage						
Manufacturability						
Price						
Product registration and WHO prequalification						

Background, Target Policy Profile

The first print mention of a 'Target Policy Profile' is in 2017. The Bill & Melinda Gates Foundation (BMGF) introduced the term 'Target Policy Profile' as a tool for progressing from a medical innovation to a social policy or service.[6] While the TPP is a tool for agreeing on key attributes a product needs to achieve, the **Target Policy Profile** (TPoP) can be a tool for agreeing what is necessary from a particular innovation or intervention to achieve a policy goal. While the term was mentioned in 2017, no package of attributes or sections were published at the time.

TPoP Format

The actual TPoP tool must:

- be readily updated and kept current
- introduce a proposed policy in simple and succinct terms, which may include a case for change making the argument for a new approach
- show a side-by-side comparison with current and suggested policy
- include enough policy details to act as a policy specification
- be evidence-based throughout, and suggest next steps for the reader
- posit, estimate or evince the evidence necessary to achieve the policy change.

Case for Change

The TPoP will establish arguments based on robust evidence for why the proposed policy change will save and improve lives. It will summarize the existing approach as well as propose the evidence requirements to justify the proposed change in policy. This will come from research and other implementations, pilots and guidelines. It will highlight existing research and identify any gaps to be filled by further studies. It will serve as a tool to discuss and agree on approaches including the design of studies to address evidence gaps.

Innovations in implementation research, factors influencing policy changes, and capacity for policy change in low- and middle-income countries (LMIC) have emerged. New tools are being developed in the context of the ongoing need and may be helpful for preparing a TPoP.[7,8,9] One example, the Intervention Scalability Assessment Tool[8] may be immediately applicable to LMIC policy change. Another tool called CERQ-Qual helps policymakers gain a confidence level in systematic review-based evidence.[10] These tools may help decision makers feel confident in processing new scientific data and understanding potential actions, benefits and costs.

A TPoP can be defined according to primary need. In most cases, the goal will be to advocate, to 'tell the story' of the benefit of a new proposed policy, to make a case for change. The TPoP ought to start with an executive summary, followed by the benefits of a new policy, an exemplar case of the how the policy is performing well in current use somewhere else if applicable, and perhaps followed by some challenges of the current policy that make the newly proposed policy attractive to public health. The format is ideal for engaging with policymakers. Ideally the format would have been informed directly by those same policymakers, having them engaged in advance of preparing the TPoP.

The classic TPP format includes a side-by-side comparison to enable the user to understand the desired state, minimal acceptable state, current state—and can be customized to provide views into other products or product states. In a TPoP, one can imagine the comparison columns could include states such as Desired State, Current Policy, New/Proposed Policy, and others that might help critical thinking.

TPoP Use Cases

The TPoP will be helpful in several situations. Depending on the situation, certain sections of the TPoP become important. Some of the top use cases are listed here.

Use Case	When in the process	Participants	Most important section
Identifying what new evidence policymakers need generated or validated for them to feel comfortable changing to a new policy	At the beginning of a process that ends with adoption of a new policy	Researchers,implementers and policymakers	Evidence, Current Policy (i.e. the row named Evidence, and the column named Current Policy)
Post evidence-generation, going back to policymakers to make the case to act now to change policy	Late-middle in the process that ends with adoption of a new policy, when no further studies may be needed if policymakers are satisfied	Researchers and policymakers together	Evidence, New Policy (i.e. the row named Evidence, and the column named New Policy)
Post decision to adopt a new policy, planning on how to implement the new policy	After the decision has been made to implement a new policy	Policymakers, implementers, government officials, pharma or device makers, health economists	Costs, implementation, feasibility, practicality, achievability, population

Policy Details

Extending on Kennedy's description of the TPP being a specification of the product, a TPoP needs to provide plenty of detail on the new or suggested policy. **If the policy is well thought out, the breadth of details would qualify the TPoP to act as a 'policy specification'. That is the aim.** The TPoP would lay out evidentiary requirements and have technical information enabling one to envision how such an innovation would be implemented, funded, regulated, and affect citizens and patients, i.e. the likely outcome. The detail should inform clinicians establishing clinical guidance; distributors or retailers managing supply chains; public health departments administering mass drug administration, spraying or other control or testing mechanisms; pharma or device manufacturers producing interventions; and regulators imagining success of existing pharmacovigilance, quality, licensing and other programs with regards to the new policy. The policy details of the intervention would often be informed by a Health Technology Assessment (HTA).[11]

> "Health technology assessment (HTA) is a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner."[12]

While HTA includes the word 'technology', HTA's are applicable to any health intervention. It could be that a policymaker or their influencers might request the multi-dimensional diligence performed systematically with an eye toward policy that are hallmarks of an HTA. TPoP's are focused on requirements to change policy and are different from HTAs.

TPoP Focus

The TPoP tool (see bottom portion of **Section 2**, **Table 1**) may:

- be broadly applicable, or cover a specific policy, region, population or point-in-time situation
- be authored by many types of stakeholders, including global guidance bodies, researchers, policymakers, regulators, funders, industry or other procurers
- tie to one or more diseases or disease families, one or more interventions, or combinations thereof
- integrate with or feed specific instances of clinical guidance, health system policy, environmental actions, supply chain minimum standards or operating procedures, regulation, and TPPs, and
- most of all, be discussed with and agreed on with those responsible for the policy, ideally at inception of the TPoP's creation.

TPoP Attributes

A 2018 update on implementation research in global health in *The Lancet* included this:

> "Policy makers, funders, implementers, researchers, and community members each view problems differently. Wendy Graham of Aberdeen University famously characterised these differences as *'Researchers are from Venus. Policy makers are from Mars.'* …As a simple example, policy makers often do not require a confidence of $p<0{\cdot}05$ to make a decision and might hesitate to expand a sample size or the duration of a study simply to meet this threshold."[13]

Another researcher concluded on the power of research results: "the evidence of widespread, direct impact on policy…is at best patchy."[14] This may be because "health policymaking involves an uneasy balance of science, economics, and politics."[15] When researchers engage in disseminating results and attempting to participate in the 'uneasy balance', this is often called knowledge transfer and exchange (KTE). A sample of questions a policymaker or government official may want to answer during their decision-making process and KTE is listed in Table 2. These questions and related objections give a window into the thinking that may be occurring in the minds of policy stakeholders. Knowing the research results that will move 'all-impact thinking' to a policy change is a crux of the TPoP.

Table 2. All-impact Thinking by Policymakers

Type	Questions	Objections
Why	Why change policy? Why defund other programs to pay for the increased costs of this new policy?	We have a perfectly good standard of care already. This problem is not so significant. The affected population is only a fraction of our state. It will be more expensive, so the funding must be pulled from elsewhere to pay—those other programs are in place, expected by citizens.
How	How do we implement this change? How will my population feel about this change? Will it change how they vote in the next elections? How will the media cover this change? How will the risks be managed?	Such a change would be disruptive. The political climate is not ready for such disruption. If it fails, the negative media coverage will almost require a change in political leadership. It is not clear we could implement such a change as well as other countries are doing.
When	When do we need to start? When will the changeover be completed? When will the public's patience be exhausted if we don't make new medicines or policy available?	It will take years to implement. If we wait for other countries to implement the change, we will be able to see the effect, positives, drawbacks and resistance. This will be more practical to implement later.
Where	Where do we start? Is this change for all the geographies in my population?	Invariably, some region will feel disenfranchised. The indicated group is only a fraction of the population. Those affected may not have participated in convenings to date. The treated area may not include my voters.
Who	Who will be treated? Will those treated include those who vote for me? Who is receiving the funds for the new intervention? Who provides the current intervention and may lose their funding?	I don't know or trust the people who invented this new innovation. I haven't spent time with the researchers who are pushing the new policy. Our usual global partners may not co-fund this for us. With the new scheme, my voters may not receive treatment.
How Much	How much will it cost? How much benefit do we receive vs. what we have today? How much of the cost investment is received by what types of stakeholders?	This will be very expensive. It will likely cost more than is estimated. The number of lives saved is only a prediction. The global North is receiving an inordinate share of the cost investment involved.

Introduction, Case for Change

An introductory case for change TPoP could follow the format shown below and leverage the information gathered using the TPoP template (**Section 2, Table 1**):

A Case for Change: ___[name of new policy]___

Desired change in policy

- Our __ [population]___ suffers from ___[indication]___ leading to ___[health effects]___.
- We propose that ___[sovereignty]___ introduce ___[policy]___ leading to __[briefest summary benefits] ___.
- This policy could be implemented by ___[time]___, require an investment of ___[amount]___ and partnership with ___[required or proposed parties for implementation or investment___.

Current policy, current state

- Our current policy for ___[indication, condition]___ is ___[policy]___.

- This policy has been in place ___[duration]___, and has ___[insert benefits to date]___.
- Unfortunately, this policy ___[differences from proposed policy]___, and the current policy ___[negatives, costs or limitations of current policy, unrelated to proposed policy]___.

Benefits of new policy

- The new policy could lead to ___[insert number of lives saved or quantitative/numeric benefit]___ vs. our current policy.
- Further, the new policy would ___[insert new secondary health benefit vs. current policy]___.
- The new policy would ___[insert new non-health benefits vs. current policy, including financial benefits if any]___.

Approaches to achieve new policy, and tools

- This new policy's implementation could be implemented ___[summary of approach]___.
- The approach is practical due to ___[attributes of the implementation]___.
- Tools at hand include ___[mention of HTA, previous implementations elsewhere, other tools available]___.

Additional evidence needed if any

- Existing evidence is _____[insert study outcomes & evidence]__.
- Current gaps to required evidence includes _____[insert unanswered questions answerable by research]_____.
- Those gaps could be closed by conducting the following___[insert studies or other exercises if studies not appropriate]__.

This format has the benefits of an executive summary. It conveys enough information to frame discussion for those executives unlikely to study the details or read further. It would be followed by the body of the TPoP Tool (**Section 2** bottom portion of **Table 1**). Attributes or sections that need to be included in any TPoP are shown in Figure 3. Figure 3 represents a summary level TPoP and Figure 4 is a more detailed example.

If the sections of a TPoP are used on the rows, and the columns include a Target (new) Policy, Current Policy, the intersection is where details and specifics can be shown. By adding a column for notes on benefits, costs, or positive and negative attributes of a potential switch to a new policy, one can most easily compare likely impact. Figure 3 shows such a layout. However, in some cases, researchers might want attributes in the TPoP that are more product-centric and seamlessly integrate with a TPP. More often, researchers may want columns or rows that enable the summarization of current available evidence and gaps therein, or a format to help discuss evidentiary requirements.

Figure 3. Summary Target Policy Profile (TPoP) tool format: same as Section 2, bottom portion of Table 1)

New or Target Policy Name:			
Policy Currently in Place:			
Authors, Date of Last Revision:			
	Target Policy	Current Policy/ SOC	Pros/ Cons of New Policy
Indication, Disease, Condition			
Target Population			
Intervention/Product/Dose			

Envisioned setting for intervention (school, community etc)			
Efficacy/Effectiveness/Evidence			
Feasibility/Practicality/Achievability			
Safety			
Other considerations (different populations/geographies/settings)			
Ongoing monitoring			
Guidelines/ Standard of Care (SOC)			
Policymaker Engagement			
Costs			
Implementation			
Communication & Convenings			
Political Factors			
Fairness & Acceptability			
Current Use Elsewhere			

Figure 4. Detailed Target Policy Profile (TPoP) tool format

New or Target Policy Name:			
Policy Currently in Place:			
Authors, Date of Last Revision:			
	Target Policy	Current Policy/ SOC	Pros/ Cons of New Policy
Indication, Disease, Condition			
Target Population			
Intervention/Product/Dose			
Intervention and/or Product Details			
Dose, Administration			
Envisioned setting for intervention (school, community etc)			
Evidence/Efficacy/Effectiveness			
Systematic Reviews			
Key Studies Complete			
Key Studies in Progress			
Confidence Level			
Feasibility/Practicality/Achievability			
Safety			
Other considerations (different populations/geographies/settings)			
Ongoing monitoring			
Implementation			
Technique			
Facilitators			
Barriers			
Guidelines/ Standard of Care (SOC)			
Clinical Practice Guidelines			
Standard of Care			
Policymaker Engagement			
Costs			
Cost of Product			
Cost of Implementation			
Lives Saved			
Implementation Issues			
Political Factors			
Stakeholders Affected			
Public Opinion			
Fairness & Acceptability			
Current Use Elsewhere			
Countries/Regional			
Global Agendas			

The detailed TPoP format ought to be understandable by non-experts. Chinese researchers found, in a survey of 382 respondents who generate health technology assessments (HTA), that 'scientific rigor' was negatively correlated with uptake of HTA into policy.[16] They opined "It is possible that policy-makers are not so much opposed to scientific rigor in research as "alienated" by impenetrable technicalities and academic jargons in some HTA reports and most academic publications." [16] **Knowing the intended audience for the detailed TPoP is a critical success factor and should be considered before beginning the creation exercise.**

Indication, Target Population, Intervention, Product, Dose

Some number of attributes from the TPP could be included from, and overlap with, the TPoP. This might serve as a context bridge to a specification of the intervention embodied by a TPP, if appropriate. **By sharing attributes, an actor could move back and forth between the world of intervention and policy. One approach to improving the TPoP might be to have policymaker and researchers agree on what they consider the minimum acceptable and the ideal attributes that would appear on both a TPP and TPoP.** If both tools could be used 'together', common terms and definitions for the bridging attributes would be expected. The TPoP needs to be flexible enough to accommodate interventions as varied as nutrition supplements, devices and technology, vaccines and other drugs, or approaches yet to be invented.

Evidence/Efficacy/ Effectiveness/

Evidence can take many forms. Efficacy and effectiveness are particularly important. While implementation research into factors leading LMIC leaders to change policy shows the most success is early and consistent engagement with policymakers, it must be the use of evidence-based policy that is necessary to improve health. Nevertheless, a strong case must be made for the merits of the intervention, and the evidence of efficacy and effectiveness is almost always a *sine qua non* to a policy change.

Systematic reviews are at the top of the hierarchy of evidence. For policymakers, systematic reviews further de-risk a decision because they ensure there is no suspicion that the policymaker is prioritizing a single researcher, research colony or pharma. The priority given to systematic reviews has challenges. One is that the reviews may leave out key research that does not meet common criteria. All stakeholders, including study participants and funders, want their individual investments to affect the highest level of evidence. As such, designing future studies that would be included in systematic reviews is paramount.[1]

Policymakers may have technical advisors or access to subject matter experts. The support system and expert network that policymakers choose to rely on to evaluate evidence varies widely. It is likely these

[1] A contrary view could argue that some countries are sufficiently early on the maturity curve of evaluating evidence that systematic reviews could escape view. A 2006 study of Mali health officials by WHO advisor Diadié Maiga found that "no policy-makers mentioned having utilized information from systematic reviews, and most seemed unaware of their existence."[17]

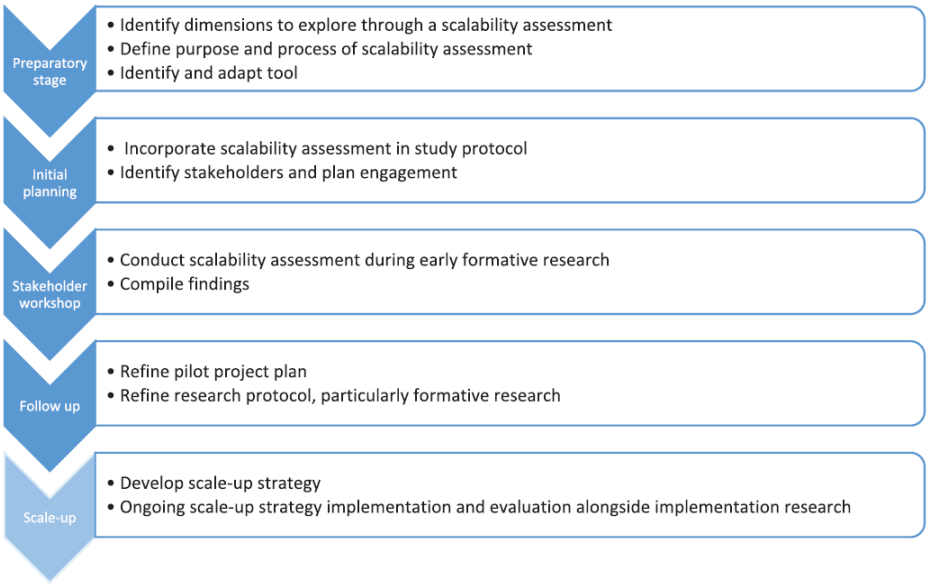
experts, and any audience, would expect the evidence section of a TPoP to include both evidence from any current, recently completed research, as well as other pertinent research, as well as understand the pipeline of future evidence and when it can be expected to arrive. Understanding the maturity of the policymakers and their advisors to absorb the evidence data, ask the best questions, and factor the evidence into decisions should not be ignored by researchers.

Feasibility/Practicality/Achievability

The clinical, social, and infrastructure context in LMICs is different than more well-developed regions. What might be practical in the global North may often not work in less-well-developed regions. Whether or not availability of trained, skilled and experienced talent, robust power, internet and supply chains, and consistent, well-managed public health programs are in place or not, the feasibility of an intervention is key. A study ranked factors that were associated with implementing the results of a health technology assessment (HTA) and changing policy in China. Beyond the factors in the category of 'acceptance of the value of an HTA', the most important factor was the "practicality of the HTA evidence".[16] Zamboni et al. evaluated frameworks of scale-up in LMIC interventions and found ten existing frameworks. Amongst the attributes these frameworks had in common, "simplicity or ease of adoption" was more frequently present than nearly all other attributes, and more frequent than key attributes such as cost and capacity.[18] Asserting practicality absolutely requires communication with, and research into, local environments in question. There is no way to properly document achievability from a lab or academic setting.

Zamboni et al. propose that a superior approach to generating data on practicality is to include a scale-up assessment as part of the clinical study itself. This would then extend into a pilot study. Their model is shown in Figure 5.

Figure 5. A scalability assessment process



From "Assessing scalability of an intervention: why, how and who?" by Zamboni et al.[18] Reproduced with permission.

Minimum Policy-Important Difference (MPID)

The impact of research on policy may be only indirectly associated with the normative inferential statistics in the study results. However, to become components of a TPoP case for change and valuable to populations for whom they are relevant, research results should provide read-outs that inform the material change that is needed to benefit a population. Readouts should also respond to justifications regarding the efficacy of existing standard-of-care or other incumbent policy and its associated funding or political support (see Table 2, "Why"). Such policy-level impact should be a formal part of study design and planning, just as defining and quantifying the clinical efficacy and safety are formal parts of proper study design.

The Target Policy Profile (TPoP) aims to facilitate formally specifying a consistent, achievable policy with an eye toward advocating what will be a beneficial change in policy for the population or community. The idea is that effective policy, and effective policy change, will be measurable. Its effectiveness should be quantitatively measurable, and the delta in effect should be "valuable enough to be worth doing" or "makes a difference" or "matters significantly to the community/society". It is like a regulatory impact statement or environmental impact statement.[19] Such statements quantitatively establish that (and set forth 'how') a proposed change will be significantly superior to the status quo or at least non-inferior to it. **That is, in a fashion much like the TPP and Minimum Clinically Important Difference (MCID) in clinical trials,[20-22] the TPoP ought to be accompanied by a statement of a Minimum Policy-Important Difference (MPID) in terms of policy impact.** Unlike the Target Product Profile (TPP) and conventional clinical trial design and clinical MCID, the TPoP encourages the investigator and other stakeholders to jointly set forth one or more MPID value-points and their rationale in the relevant dimensions, such as economic value added (EVA), DALYs averted, or employment rate improvement.

In a manner analogous to that used for MCID, we recommend that MPID is the smallest value that is judged to be both detectable and meriting policy-setting in the target population or community, in the sense that it is greater than the measurement error of a specific population exposure and it is also consequential in regard to outcomes that would eventuate for members of the population who are subject to the policy-making. A valid MPID value is premised on the rationale that a difference smaller than this is not likely to be important. Much as for MCID, the construct of interest might not be directly measured. Nonetheless, it is practical to set forth an MPID that indirectly addresses the issue of importance of a particular difference whose merits can be accounted for in fiscal or other quantifiable terms.[23] We recommend you specify your MPID and power your proposed study as you would do in order to satisfy the expectations of the HTA authority in your catchment area.

Safety

Considerations of patient and citizen safety are always important. However, policymakers may work in a context where safety concerns can be magnified or conjoined with issues of equity and/or political factors. For this reason, safety information on identified or likely adverse events (or long-term adverse events difficult to test for in a Phase III study) may be heavily considered. Transparency to all stakeholders around the specifics of safety can help prevent surprising or damaging policy results. The details of the safety data provided in policy discussions and in a TPoP, including amount, detail and types, and its effect on policymakers, needs further study.

Safety information that will be particularly pertinent relates to relative vs. absolute safety. No intervention will be perfectly, universally safe. A policymaker will make a risk-benefit comparison for the intervention/policy in isolation. Further, the policymaker will compare the intervention/policy safety to safety data or perceptions of historical interventions with which they are familiar, current standard of care, as well as perceptions of other impending interventions. Data that can make these comparisons more concrete can speed up policymaking. It is forgivable that a policymaker may want to see guarantees of absolute safety along with high efficacy and immediate availability; policymakers are charged with protecting the health of their constituents.

Clinical Guidelines/ Standard of Care (SOC)

Formal, evidence-based, 'clinical practice guidelines' enable physicians to identify consensus best practice treatments for specific conditions. The concept of clinical guidelines is less mature and prevalent in LMIC than in the global North. In fact, physicians in many regions, for many pathologies, cannot always rely on accessing guidance databases or documents. While not prevalent, and whether it is local and *de novo*, or adapted from other places, clinical guidelines exist.[23,24] More prevalent are consensus SOC that represent the incumbent approach to treatment. Standards of care could be adopted from global policy (through "policy transfer"), could form organically in health centers across a country and thus be outside of policy, or could result from existing or new policy. Like clinical guidelines, current SOC are the prospective 'before' where the intervention proposed as a result of successful research is the 'after' in the comparison. In a TPoP, documenting and presenting current, specific, precise and technical SOC, as well as the same qualities in the proposed new SOC, is a grounding way to end confusion if other areas of the TPoP are not self-explanatory. In a nutshell: there is a current SOC, new research emerges with a target policy, and if the advocacy effort is effective, the new SOC is introduced.

Policymaker Engagement

What is identified most often as the #1 factor predicting when research shapes policy change? Early, consistent engagement with policymakers before, during and after the clinical research is the most influential factor. "On whether evidence was used in policy: the quality of the relationship and collaboration between researchers and policymakers was determined to be the single most mentioned facilitator."[25] While this may be surprising, it is more dire when one considers that even the post-study exercise of KTE is often ignored by researchers. "Fewer than half of [global health] researchers were involved in KTE activities, which includes interacting with policy-makers, and fewer than half were engaging in bridging activities to facilitate the use of their research by their target audience."[26]

> "Researchers need to spend time getting to know policy and practice organizations and need to give up some control over their research. These requirements involve skills and time that researchers might not have, in part because of the challenges of budgeting and knowing how much time is needed while meeting deadlines in conventional research funding proposals. Giving up control in this way requires a greater tolerance for uncertainty, but the payoff is frequently better engagement, more immediate effects of the research, and sustained engagement.[13]

Each policymaker discussion is a key opportunity. Every discussion can move the community and policymaker forward to a go/no-go decision on policy change and should not be wasted. To that end, having a tool such as a TPoP is useful; necessary topics are discussed and documented. In theory, fewer surprises will happen later. As stated previously: while some researchers might be 'old hands' at engaging with policymakers, it is more common that researchers may not be familiar or comfortable at the policy interface: having a tool in hand to broker or frame the dialogue is even more crucial. It could be that the TPoP is used not as a dissemination tool, but as a discovery tool with policymakers to understand what is needed to change their minds.

Costs

Costs are a necessary and important consideration of deciding how to change health policy. Before estimating costs (or savings) of scaling up a new intervention resulting from a change in policy, it is necessary to identify specific costs and related factors. The more local the policymaker, the more specific certain cost questions can be. Questions arising from asset-constrained populations may touch on contextual issues that may not seem to tie to healthcare. In policy conversations with resource-constrained policymakers, embracing or accepting non-traditional cost questions is likely to be helpful. Questions identified from real-world policy cost conversations include:

- Is a donor or foreign government paying for the new intervention, and if so, for how long will that support last?
- Will our government be paying for the new intervention, and if so, what is the cost? Is it affordable and does it represent value for money? What will be the impact of spending money on this rather than something else?
- What costs will the patients/citizens/consumers bear?
- What will the scale-up, implementation and changeover costs be? Including any changes in health care delivery, will there be long term savings?
- Who is benefiting financially from the new investments (e.g. a pharma, device manufacturer, other)?
- Do these incremental costs affect our relationships with non-state actors, and if so, how?
- Are there are cost-sharing potentials or other schemes to defray costs?
- Are there unforeseen costs?

Implementation

"Evidence of the effectiveness of an intervention is not sufficient to produce better health outcomes; barriers and facilitators to its implementation must also be identified."[14] In the topic of implementation, it is common to talk about facilitators to implementation and barriers to implementation. General methods of the implementation technique are evaluated about facilitators, barriers, costs and time. A sample of often-discussed topics when LMIC stakeholders assess feasibility of scaling up an intervention includes:

- Contextual considerations
- Costs of scale-up
- Delivery system considerations
- General scale-up and implementation considerations

- Intervention adaptability
- Intervention reach & acceptability
- Monitoring & Evaluation
- Sustainability
- Workforce considerations [8]

A 2019 article[28] identified six types of pitfalls that could result when attempting to scale-up evidence-based interventions in LMIC:

- Cost effectiveness pitfall
- Health inequities pitfall
- Scaled harm pitfall
- Ethical pitfall
- Top-down pitfall
- Contextual pitfall

Implementing new policies that include an innovation has been found to be challenging. Part of the challenge may relate to cultural or contextual concerns, including inherent skepticism toward innovation being imported from the global North. A clear implementation plan can help ameliorate resistance to policies that include innovative components.

Political Factors

Lucy Gilson, one of the pioneers of health implementation research in LMIC writes: "Politics, process and power must be integrated into the study of health policies."[29] Indeed, virtually all systematic reviews of factors affecting whether research will influence or make new health policy reference politics or political factors. Quotes on the import of politics from these and relevant publications include:

- "**Political motives** have also been implicated as a strong driver that informs policy-making."[27]
- "Evidence must compete with other factors that influence decision-making, such as power, **politics**, opinions, and vested interests."[15]
- "Some frameworks have been criticized for putting emphasis on evidence, how it is disseminated and implemented with limited attention paid to the **highly political** and rapidly changing policy making context which is common in low income countries."[30]
- "Similarly, data inconsistent with beliefs, traditions, or **political agendas** may be disregarded and/or discredited to maintain cultural and social realities."[31]
- Policy decisions concerning the introduction of (new) technologies in health care are not based on the results of medical technology assessments. Rather, **'political arguments** and interest groups decide the outcomes'.[15]
- "However, competing pressures (economic, **political**, social, and cultural factors) were seen to impact on the policy process and hinder the development of evidence-based policy."[26]

A TPoP can make political context and influences transparent to all stakeholders. This lessens the relative power of political factors. It can help stakeholders craft solutions that allow intervention success to live alongside political realities. Variables affecting political factors will differ by geography, nation,

pathology being addressed, type of intervention, and whether policy is being decided at multi-national levels such as assemblies, agencies or working groups.

Communication & Convenings

Whether for solid decision-making or managing political risk, perception and consensus, policymakers will have interest in whether local experts, local researchers, members of public health services and hospitals, technical and expert advisors, specialist physicians, and academics have been able to converse and convene around the costs, benefits, opportunities and challenges of the intervention—whether any consensus has been reached or not. If a policymaker is comfortable with other aspects of a new policy, especially the evidence, cost and feasibility, a natural next question is to predict acceptance of local experts. Policymakers may need to leverage credible advocacy and support from experts known to or accepted by their populations. Toward this, convenings can be helpful. They can make a policymaker feel comfortable that opportunities for objections and assimilation of knowledge has occurred, enabling all parties to have a voice. One researcher found:

> "…organizations "vulnerable to assessment…might need to need to draw on expert knowledge to meet expectations about organizational legitimacy or appropriate policymaking…those dependent on technical appraisals will be keen to signal their expertise to underpin the legitimacy of their organization, or to substantiate decisions made." [32]

Beyond convenings, communication with policymakers themselves is as much an art as a science. From one researcher interviewing policymakers in Africa: "Policy-makers stated that research utilization is already a lengthy and time-consuming process. "Usually I do not have the time," (participant 18, male). Even if research is considered important, it still requires a significant amount of time to search, locate, access and review the relevant literature. "It demands sacrifice" (participant 11, female)."[17] Dissemination must be tailored to the individuals with influence; "Too often the experience of research is to find long reports consigned to dusty shelves in government and donor offices."[33]

How could the effort be more science than art? The effort to create standardized tools such as the TPoP is one such effort. Others could identify and adopt frameworks, models, and approaches that have been published and successfully used to change policy. Further, to the degree yet incomplete, the global health research community could define best practice communications based on empirical implementation research and exemplars, create tools, and then refine, socialize and standardize the tools. When using tools or engaging global guidance bodies, it is important relevant experts are not 'conflicted out' of participating in discussions—there are ways to ensure those convenings can use non-voting experts.

Use of expert bodies for clinical practice guidance can be helpful as new policies are being considered, as well as after adoption. Organizations like the UK's National Institute for Health and Care Excellence (NICE), the WHO Evidence-Informed Policy Network, and the WHO's Global Clinical Practice Network (GCP.Network) have global reach and influence.

Fairness & Acceptability

Also referred to as equity, fairness in this context could relate to matters of ethics, privacy, bias, racism or other social justice concepts or behaviors. Acceptability refers to matters of willingness of citizens, patients, families as well as leaders and influencers to adopt the health intervention. It could be that disparate disease burden or health outcomes in disenfranchised population segments wield power to influence policy change. Alternately, forecasting disproportionate adverse events or political scandal tied to fairness helps policy makers understand physiological and non-physiological risk. Including acceptability in the TPoP offers a channel to share potential methods of public dissemination, coordination and collaboration.

Existing Use of the Intervention

The concept of policy agendas at a wider scale (e.g. international) being adopted at country level is policy transfer. Dynamics include influence, pressure, or negotiation. Major health concerns in LMIC can be substantially supported by international governance and donor organizations. A grant by BMGF led the Oxford Policy Institute to publish a landscape analysis in 2017 on global health policy transfer. In Table 4, the relative frequency of policy transfer is shown, with the entity originating the policy, the country adopting the policy, and the genre and type of actors involved.[34] Clearly the uptake in interventions by influencing entities has influence on policymakers and may be considered a facilitator or barrier in the TPoP.

Table 4. Health policy transfer as mechanism for changing health policy[34]

Landscaping review part 3: Review of international health policy transfer literature – Learning for Action Across Health Systems

Origin countries		Recipient countries		Types and programmes of health system change		Categories of 'policy-maker'	
Global policy networks	51	Other African countries	30	HIV/AIDS	16	International agencies	53
United States	12	Other Latin American countries	16	Sexual and reproductive health	13	National elites	41
Other African countries	7	Other Asian countries	21	Efficiency and equity in health systems	10	Civic organisations	23
Other European countries	4	Other European countries	11	Access to medical care	9	NGOs	18
Other Asian countries	3	South Africa	9	Vaccination and immunisation	6	Health professionals	13
South Africa	3	India	6	Population	5	Government ministries	11
United Kingdom	2	Zambia	6	Drug enforcement	4	Private sector	10
Brazil	1	Malawi	5	Health insurance	3	Academics	8
		Kenya	4	Case management of childhood illness	2	Local communities	6
		Bangladesh	3	Disease preparedness	2	Civic leaders	5
		Brazil	3	Malaria	2	Political parties	4
		Burkina Faso	3	Mental health	2	Media	1
		Mozambique	3	Use of aid in health services	2		
		Pakistan	3	Nutrition	1		
		Thailand	3	Tuberculosis	1		
		Zimbabwe	3	Urban–rural health worker relocation	1		
		Global policy networks	1				

Policy transfer introduces the question: For any intervention, will the standard or adopted policy for any region or nation originate from the WHO? If so, should engagement with policymakers happen in Geneva? Should they happen in the LMIC country and ministry of health? If engaging with policymakers

early in the clinical study design is practiced, there will be different influencing factors than if the study only showed results to policymakers at the end of the process.

Authorship, Ownership, and Modification

Many types of stakeholders could author a TPoP. However, too many suggested policies being presented to a single policymaker could cloud decision-making. In the presence of a volume and flow of TPoP documents, policymakers might imagine there is a lack of agreement or fragmentation amongst researchers or funders. To answer the question of who ought to develop a TPoP, with what partners, and when, one could imagine a hierarchy of policies and how research impacts them**. Definition of the audience of the TPoP, including names and roles of specific individuals influencing policy decisions, is a critical success factor in the effort to change policy.** Multiple research studies have shown that early and frequent communication, *during the clinical research*, with policymakers is the more significant criterion leading to changes in policy.

Type of Policy	Owner/ provider/ guidance level	Example of a current policy	Example of New Policy
Top-level, overarching policy	Global or super-regional	Control of soil-transmitted helminths (STH), owned and provided by WHO via guidance, tied to a World Health Assembly resolution, including a number of components including mass drug administration, specific medicines, evidence of specific at-risk populations, sanitation measures, and more.	A vaccine approach to STH. Current thinking is that sanitation improvements or drug availability will reach critical mass before a vaccine could be developed and distributed. A policy introducing a vaccine would be a major change.
One part or component of the overarching policy, sub-policy	Global or super-regional	Mass drug administration today: WHO recommended medicines – albendazole (400 mg) and mebendazole (500 mg) – are effective, inexpensive, and distributable by teachers in schools. The medicine ivermectin (e.g. for *S. stercoralis*) is not yet available at affordable cost.	Identification of a new drug that has a stronger safety record than WHO recommended medicines is unlikely, but if a new medicine was found to be approaching zero cost or much more effective, one could argue to recommend a different drug.
Country-specific	Ministry of Health, Central Government	Egypt maintains regular deworming campaigns (the 3rd in 2017 with WHO and UNICEF) and has distributed 14M tablets of mebendazole.	Nigeria does not fund or mandate an ongoing teacher-based distribution of WHO-recommended medicine. Introducing such a program in Nigeria would be a new policy.

In this framework, any individual research study could provide evidence that bolsters or weakens an existing top-level or sub-policy at a global or national level*. If a research study is going to have an impact*

on policy, it is necessary—but not sufficient—that someone is making a clear link from study to policy to an addressable policy action, at the earliest possible time, ideally or in the design phase of a study or before.

Depending on a variety of circumstances, one vignette of a successful TPoP authorship team might these attributes:

- Inclusion of local community members and leaders, and local health and implementation experts
- Inclusion of those with experience both authoring TPoP's and using them to successfully influence policy
- Inclusion of authors with experience in regulatory affairs, advocacy, policy and strategy, and current or former policymakers
- Inclusion of authors with scientific expertise who are both part of as well as outside of the current study or studies providing the strongest or most current evidence for policy change.

A TPoP under consideration, to the extent possible, is helped by being widely available to the citizens it may help. Ownership of a TPoP is something to be determined and is critical. Fragmented or uncertain ownership would devalue the impact of a TPoP quickly. The modification of a TPoP is just as important. If the authors or owners of a TPoP cannot update it with the most recent evidence, its credibility will suffer. Ultimately, a non-modifiable or out-of-date TPoP will only go so far before it needs a refresh. The speed of new evidence and the breadth of topics in a TPoP make a refresh exercise a significant time investment.

Items Not Addressed Here

The TPoP template necessarily leaves several topics unanswered. Some topics that the TPoP template and this paper do not address include:

- What is policy? How far should policy reach and how customized does it need to be per country or population?
- Should there be different versions of a TPoP for varieties of interventions, such as vaccines, nutritional interventions, or unregistered products?
- Who specifically needs to contribute to a TPoP? Who needs to write it, if not researchers and public health experts? What if policymakers are not engaged before or during the writing process?
- Who specifically is the audience? Who is responsible for the policy?
- Per audience group, what is the engagement plan, and what is the rationale for that engagement plan?
- How often should it be updated? What happens if it cannot be updated when there is new evidence that materially affects the current document?

Conclusion

The TPoP is potentially a very useful tool to lay out proposed changes to policy and what is required to achieve such changes. It would serve as a tool to engage policy makers as well researchers and would act as a tool to assist in review of research proposals. This document describes a proposed approach to

develop TPoP's. With TPoP information laid out on a few pages, most policymakers can easily gauge their sense of risk and success. A full range of appropriate stakeholders can both add to the content as well as act as audience. Required thresholds for research outcomes to change policy should be identified in the TPoP-framed discussion; TPoP's may also frame discussions and present a compelling case for change after evidence generation is complete.

Assembling accurate data together across the TPoP domains is non-trivial. TPoP can act as a tool to bring together relevant disciplines and experts involved in the many facets of policymaking. To a clinical researcher specializing in narrow areas of new life-saving discoveries, and versed in designing and implementing clinical studies, the concept of collecting new data and formulating a proper TPoP might seem intimidating or unfulfilling. However, it provides an opportunity for broader engagement and input.

The global health community can play a role in making policymaker decisions more transparent, global, granular and quick. Global health community members could use a standard TPoP as one tool in that effort. Imagine if all evidence was presented to policymakers in the same format. Such cohesiveness from funder, researcher, and other 'presenting' communities would lead to a quick and necessary policymaker response: clear and explicit questions and data requests that enable new policy. This could take the form of the policymaker customizing the TPoP for the question at hand.

Funders, sponsors and stakeholders should be asking new questions. How does this research fit into an overall policy objective? Is the research designed to fulfil a specific policy or public health objective? Has engagement with policy makers taken place in designing the study? If successful, how will that change in policy be made? Does my grantee understand how to perform at the interface of research and policy? Can I fund other research groups that may be more mature or experienced at engaging with policymakers? How can I, or the grantee, or others fund additional strength in their team to collect data to populate a TPoP, develop a strategy for advocacy and dissemination, and push beyond defining new evidence? Should our researchers be engaging policymakers before a study begins? Should the policymakers' questions define the research questions be answered?

Whether a hands-on tool populated with current data, or as a method to frame discussion, a target policy profile can act as a beacon for researchers to thrive at the interface of clinical research evidence generation and policy.

Section 4: Appendix B - References & Suggested Reading

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Suggested Reading (current to February 2020)

- "The Many Meanings of Evidence: A Comparative Analysis of the Forms and Roles of Evidence Within Three Health Policy Processes in Cambodia," by Wall et al., 2018 in Evidence Use in Health Policy Making
- "On the Path to UHC–Global Evidence Must Go Local to Be Useful: Comment on" Disease Control Priorities Third Edition Is Published: A Theory of Change Is Needed for Translating Evidence to Health Policy," by Davis & Walker, 2019 in International Journal of Health Policy and Management
- "Health care must mean safe care: enshrining patient safety," by Flott et al., 2017 in The Lancet
- "Modernising vaccine surveillance systems to improve detection of rare or poorly defined adverse events," by Chandler, 2019 in BMJ
- "Apology and Unintended Harm in Global Health," by Addis and Amon, 2019 in Health & Human Rights
- "A new database of the references on international clinical practice guidelines: a facility for the evaluation of clinical research," by Eriksson et al., 2020 in Scientometrics
- "Global emergency care clinical practice guidelines: A landscape analysis," by McCaul et al., 2018 in African Journal of Emergency Medicine
- "Implementing One Health approaches to confront emerging and re-emerging zoonotic disease threats: lessons from PREDICT," by Kelly et al, 2020 in One Health Outlook
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