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The NeuroAdvocacy Toolkit: A Knowledge Translation Strategy to Strengthen Food Fortification Policies to Prevent Neural Tube Defects in Latin American Countries. A Mixed-Method Study

Kemel A. Ghotme
George Washington University, kghotme@gwu.edu

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The NeuroAdvocacy Toolkit: A Knowledge Translation Strategy to Strengthen Food Fortification Policies to Prevent Neural Tube Defects in Latin American Countries.

A Mixed-Method Study

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Kemel A. Ghotme, MD

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COMMITTEE MEMBERS

Committee Chair: Joseph Bocchino, BA, MBA, EdD

Associate Professor of Clinical Research and Leadership

The School of Medicine and Health Sciences

The George Washington University

Committee Member: Phillip Van der Wees, PT, PhD

Adjunct Professor of Clinical Research and Leadership

The School of Medicine and Health Sciences

The George Washington University

Professor of Allied Health Sciences

Radboud Institute of Health Sciences

Committee Member: Gail L. Rosseau, MD, FACS, FAANS

Clinical Professor of Neurosurgery

Department of Neurosurgery

The School of Medicine and Health Sciences

The George Washington University

READERS

Helena Pachon, PhD

Instructor, Center for the Study of Human Health

Senior Nutrition Scientist, Food Fortification Initiative

Research Professor, Hubert Department of Global Health

Rollins School of Public Health, Emory University

Vijaya Kancherla, PhD

Assistant Professor, Department of Epidemiology

Deputy Director, Center for Spina Bifida Prevention

Associate Track Director, Applied Epidemiology, Executive MPH Program

Rollins School of Public Health, Emory University

ABSTRACT

Background. Neural tube defects are one of the leading congenital malformations that affect children in Latin America and worldwide, leading to pregnancy terminations, morbidity, mortality, and long-term disability. The most cost-effective and equitable way to prevent them is by implementing public health policies for food fortification with folic acid. However, a lack of knowledge translation strategies partly accounts for the incomplete enactment, enforcement, and scaling-up of mandatory fortification. There is no evidence in the scientific literature of studies attempting to identify the factors contributing to the development and implementation of knowledge translation strategies aiming to influence policymakers' decisions regarding mandatory food fortification to prevent neural tube defects in Latin American countries.

Objectives. The study's overall purpose was to describe the factors contributing to developing and implementing a knowledge translation strategy, named the NeuroAdvocacy Toolkit, aiming to influence policymakers in Latin American countries regarding mandatory food fortification policies to prevent neural tube defects.

Methods. This study utilized a mixed-method sequential explanatory design with a follow-up explanations variant, which prioritizes the initial quantitative phase and uses the subsequent qualitative phase to explain the quantitative results. The study comprised three phases. First, a document analysis led to determining the status of fortification policies and a needs assessment for regulation change in the 20 Latin American countries, followed by the development of the NeuroAdvocacy Toolkit. The toolkit development was informed by the scientific literature and voices from the target audience regarding preferred mechanisms for knowledge transfer and utilization. Second, a quantitative phase collected survey data from purposefully selected Latin American key opinion leaders through the Measurement Instrument

for Determinants of Innovations (MIDI) to identify the barriers and facilitators for implementing the toolkit as an innovative knowledge translation strategy. The surveys were conducted through an online platform in Spanish. And third, a qualitative phase gathered interview data about the perspectives of Latin American key opinion leaders in pediatric neurosurgery (purposefully selected from the survey respondents) on implementing and disseminating the toolkit to policymakers. The interviews were conducted through an online platform in Spanish. This phase concluded by integrating quantitative and qualitative data to gain a deeper understanding of how to address the critical factors.

Results. The document analysis in the study's first phase triangulated different sources of information to identify the status of food fortification policies in Latin America and develop a reliable needs assessment for regulation change. The data gathered allowed categorizing the 20 countries according to the priority to implement regulatory changes to strengthen fortification policies. Four countries are in level 1 priority with an urgent need for regulation change, 14 countries are in level 2 with a high need for regulation change, one country is in level 3 with a medium need, and one is in level 4 with no need for regulatory change. After being introduced to the NeuroAdvocacy Toolkit, 30 key opinion leaders in pediatric neurosurgery from 20 countries responded to the MIDI questionnaire. Their responses allowed identifying 20 facilitators, seven potential facilitators, and two barriers to implementing the Toolkit as a knowledge translation strategy targeting policymakers in the region. Twenty-four interviews with key opinion leaders yielded three themes describing 1) the attitudes toward using the Toolkit, 2) the ideal delivery strategies to policymakers, and 3) how to face potential challenges when bringing policymakers on board during the implementation and dissemination process. Finally, integrating quantitative and qualitative data permitted a deeper understanding of overcoming potential barriers and strategically leveraging facilitating factors when disseminating the Toolkit to the target policymakers. Although the MIDI allowed identifying the main barriers and facilitators for implementing the NeuroAdvocacy Toolkit, the subsequent interviews allowed visualizing alternatives for operationalizing the determinant factors. Key opinion leaders' behaviors, influenced by subjective norms, social norms, and perceived roles, can spearhead effective data-driven advocacy. Organizational support can enhance the implementation and dissemination of the NeuroAdvocacy Toolkit by consolidating neurosurgical guild unity and promoting alliances with universities, other academic institutions, and other professional societies; also, obtaining support from non-governmental organizations and patients' associations as critical stakeholders. Gaining support from supranational organizations such as the WHO and PAHO, materialized through a statement or resolution, can accelerate the dissemination process and promote the promulgation, enactment, and enforcement of MFF policies in most of the countries represented in this study.

Conclusions. Most Latin American countries have a compelling need to update, scale up, implement, optimize surveillance, and guarantee the sustainability of mandatory food fortification policies to prevent neural tube defects. The NeuroAdvocacy Toolkit is an innovative knowledge translation strategy enabling key opinion leaders in pediatric neurosurgery to influence policymakers' decisions toward strengthening fortification policies in Latin America. Critical determinant factors can act as barriers or facilitators to implementing and disseminating the Toolkit. Recognizing them is essential to tailor strategies to approach and call policymakers to action, with the ultimate goal of saving thousands of children in Latin America from being born with a devastating but preventable condition and promoting a healthy and fulfilling start to their lives.

KEYWORDS

Knowledge translation; Translational knowledge; Implementation science; Policy dissemination; Neural tube defects; Food fortification; Mixed-methods design

DEDICATION

I dedicate this work to individuals living with neural tube defects and their families in the hope of changing the landscape and diminishing the challenges they face due to preventable congenital malformations.

ACKNOWLEDGMENTS

I want to express my most profound appreciation to my dissertation chair, Joseph Bocchino, BA, MBA, EdD, as well as my committee, Phillip Van der Wees, PT, Ph.D., and Gail L. Rosseau, MD, FACS, FAANS, for effectively mentoring and guiding me throughout a transformational and revealing process as a doctoral student, advocate, researcher, and leader at every step of the process in the most inspirational and assertive way.

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LIST OF ABBREVIATIONS

ASOLANPED: Latin American Association for Pediatric Neurosurgery (for the initials in Spanish)

GAPSBiF: The Global Alliance for the Prevention of Folic Acid-Sensitive Spina Bifida

ISPN: International Society for Pediatric Neurosurgery

KOL: Key opinion leader

KT: Knowledge translation

MFF: Mandatory food fortification

MIDI: Measurement Instrument for Determinants of Innovation

NTD: Neural tube defect

PAHO: Pan American Health Organization

WHO: World Health Organization

The NeuroAdvocacy Toolkit: A Knowledge Translation Strategy to Strengthen Food Fortification Policies to Prevent Neural Tube Defects in Latin American Countries.

A Mixed-Method Study

Chapter 1: Introduction

Thousands of children can be saved from being born with a neural tube defect (NTD), a disabling congenital condition that affects the proper development of the brain and spine. A large percentage of the cases are preventable by implementing mandatory food fortification (MFF) with folic acid, an evidence-based public health measure that has shown to be efficacious, practical, safe, feasible, and cost-effective in preventing NTDs (CDC, 2020c; Kancherla, 2018; Pachón et al., 2013). Despite these facts, worldwide only 63 countries have implemented this evidence-based policy, while most have focused on just one type of staple food (primarily wheat flour) (FFI, 2022; Kancherla, Botto, et al., 2022), while other essential staples are left out, hindering that this intervention reaches the most vulnerable population.

Different determinant factors acting as barriers or facilitators for the reach, adoption, implementation, and scaling-up of MFF as an evidence-based policy are evident in the literature (CDC, 2020a; Estevez-Ordonez et al., 2018; Field et al., 2018; Kancherla, 2018; Kancherla, Botto, et al., 2022; Martinez et al., 2021). They comprise individual and contextual factors that may vary according to specific circumstances. However, there is scarce information in the literature regarding theories, models, frameworks, or knowledge translation interventions that address how to overcome those barriers or leverage the facilitators to implement MFF effectively and successfully to prevent NTDs.

In Latin America, despite meaningful progress in public health policies regarding MFF for the prevention of NTDs, the reach of these policies is still insufficient. The presence of MFF legislation is uniform in the Latin American region for wheat products; in contrast, it is incomplete, in some cases voluntary, and often null for maize and rice, two essential staple foods in the diet of millions of Latin Americans (FFI, 2022; Rosenthal et al., 2014; Zaganjor et al., 2016). A scoping review identified key barriers and facilitators for implementing MFF (Ghotme, 2018). On the one hand, some of the obstacles include insufficient translation of the evidence to support MFF policies and a lack of willingness from local authorities in many countries to either enact regulations for this evidence based-policy or to provide sufficient oversight to ensure that industry and importers follow the rules for mandatory folic acid fortification (Estevez-Ordonez et al., 2018; Martin et al., 2011; Mills, 2017). On the other hand, advocacy and leadership of neurosurgical individuals and groups stand out as potential facilitators for knowledge translation to policymakers due to their accumulated experience dealing with these conditions and their high standing in society (Estevez-Ordonez et al., 2018).

Statement of the Problem

A lack of knowledge translation strategies is responsible, in part, for the incomplete enactment, enforcement, and scaling-up of MFF as an evidence-based policy to prevent NTDs in Latin American countries, hindering the protection of thousands of children from these disabling conditions. There is no evidence in the scientific literature of studies attempting to identify the factors contributing to implementing knowledge translation strategies that aim to influence policymakers' decisions regarding MFF to prevent NTDs in Latin American countries or worldwide.

The consequences of not addressing the problem have an impact on four levels. First, in public health, due to an increased incidence of cases, pregnancy terminations, stillbirths, morbidity, and mortality. Second, at a societal level, due to increased costs to the healthcare system for unnecessary allocation of resources and efforts to treat a preventable condition. Third, at a family level, causing an increased burden of disease to caregivers and family dysfunction, as well as increased use of family time and resources. Fourth, at the individual level, these patients present significant long-term physical disability, need for complex care, dependence on different aids, and psychosocial issues.

Purpose

The study's overall purpose was to describe the factors contributing to developing and implementing a knowledge translation (KT) strategy aiming to influence policymakers in Latin American countries regarding MFF to prevent NTDs. The strategy involved the participation of key opinion leaders (KOL) at the Latin American Society for Pediatric Neurosurgery (ASOLANPED). A core strategy component was developing a KT toolkit, denominated the NeuroAdvocacy Toolkit, aimed to broker knowledge to policymakers. The ultimate goal was to design a dissemination strategy tailored to the needs for regulatory change and contextual aspects of Latin American countries.

Research Questions

This study answered the following overarching research question: *how may we describe the factors contributing to the development and implementation of a KT strategy aiming to influence policymakers regarding MFF for preventing NTDs in Latin American countries?*

This question gave rise to quantitative, qualitative, and mixed-methods research questions, presented in Table 1.1.

Table 1.1 Quantitative, qualitative, and mixed-methods research questions of the study

QUANTITATIVE RESEARCH QUESTION	**QUALITATIVE RESEARCH QUESTIONS**	**MIXED-METHODS RESEARCH QUESTION**
What are the determinant factors influencing the use of the NeuroAdvocacy Toolkit as an innovation to promote robust MFF policies in Latin America?	How do the KOL describe their attitudes toward implementing and disseminating the NeuroAdvocacy Toolkit to translate knowledge to policymakers in their countries? What are the perceptions of KOL about appropriate dissemination mechanisms of the NeuroAdvocacy Toolkit?	In what ways do the interview data reporting the views of KOL about using the NeuroAdvocacy Toolkit help to explain the quantitative results about the determinant factors for implementing the innovation?

Note: MFF: mandatory food fortification; KOL: key opinion leaders

Statement of Potential Impact

This study generated knowledge regarding effective KT strategies to strengthen public health measures to prevent NTDs by bridging the chasm between scientific evidence and implementing public policies for MFF (bridging the T3 and T4 moments of the translational research continuum, which implies translating knowledge from scientific evidence to populations). This KT process is associated with impacting policies for improved disease prevention and reduced costs for medical care (Waldman & Terzic, 2010). The present study included the development of a KT strategy (the NeuroAdvocacy Toolkit) and analyzing the critical factors for implementing and disseminating it, aiming to influence policymakers in Latin American countries regarding MFF policies for the prevention of NTDs. The ultimate goal of the KT strategy is to increase the likelihood that research evidence on the prevention of NTDs reaches policymakers and influences their decisions to ensure the reach, adoption, implementation, scale-up, and sustainability of MFF as a robust evidence-based policy to prevent NTDs. In the long term, properly implementing and enforcing MFF policies will eventually lead to improved health outcomes for individuals, impacting families, society, and public health.

On the other hand, the development, implementation, and dissemination of the KT strategy proposed in this study can help address some of the unmet needs of global neurosurgery in its five domains: strengthening health systems, education, research, practice, and advocacy. Global neurosurgery prioritizes improving health outcomes and decreasing health disparities for humans affected by neurosurgical conditions or requiring neurosurgical care worldwide (Park et al., 2016).

Conceptual Framework

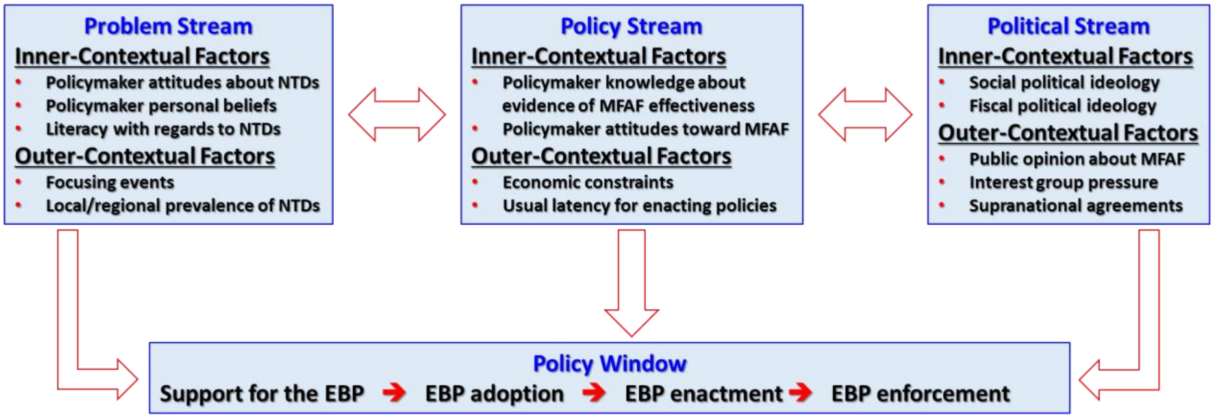
This study’s primary constructs are:

- Mandatory food fortification
- Determinant factors (barriers and facilitators) of innovation
- Knowledge translation strategies
- Knowledge brokers (key opinion leaders)
- Knowledge users (policymakers)
- Dissemination of evidence-based policies
- Stakeholder engagement
- Advocacy, leadership, and lobbying

The reason for prioritizing those primary constructs was that the evidence of MFF's efficacy, safety, and cost-effectiveness as a successful evidence-based policy is already compelling and has been available for more than three decades (CDC, 2020c; De-Regil et al., 2015, 2016; FFI, 2022; Kancherla, 2018; Martinez et al., 2021; Pachón et al., 2013; Tablante et al., 2019). Therefore, this study focuses on the mechanisms to bridge that gap by translating knowledge to decision-makers and influencing the scale-up and optimization of MFF policies while understanding the determinant factors for implementing and disseminating such strategies.

Kingdon’s model describes how the convergence of problem, policy, and political streams opens a window for policy entrepreneurs to promote new policies that enter the agenda of policymakers (Kingdon, 2014). However, this model does not account for the critical factors influencing the uptake of a specific evidence-based policy. Aaron’s model incorporates those factors, but it does not consider the three streams of Kingdon’s model. Therefore, a combination of both models integrated streams and critical factors based on a published experience in mental health using this approach (Aarons et al., 2011). Figure 1.1 illustrates the conceptual framework created explicitly for this study using both models.

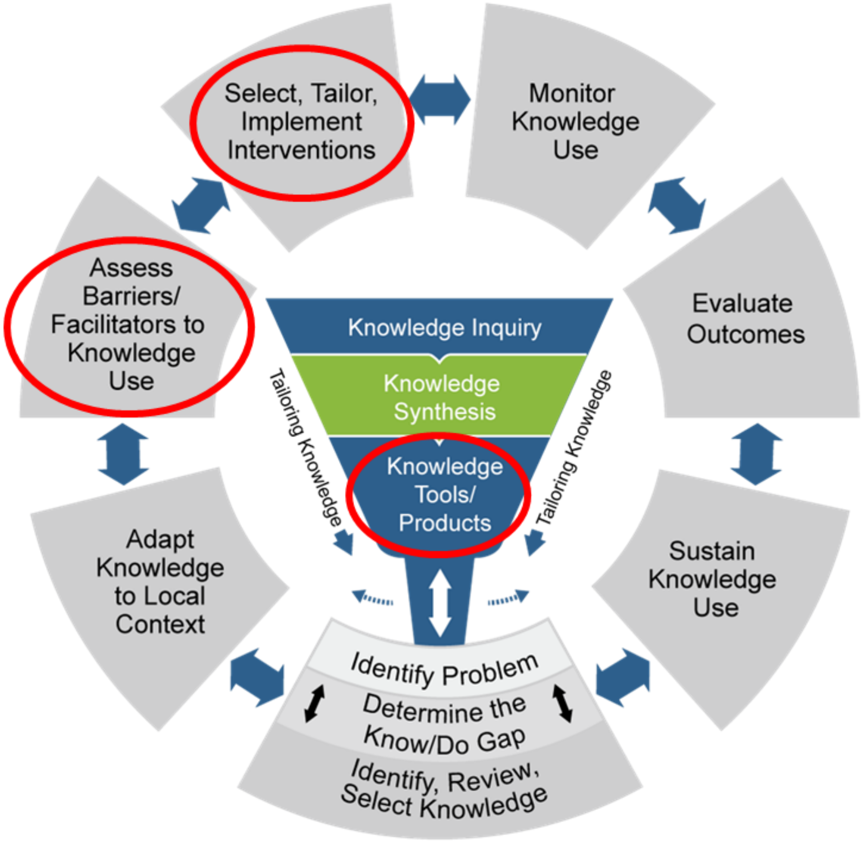
Figure 1. 1 A conceptual framework combining Kingdon's and Aaron's models for alignment of multiple streams and contextual factors to disseminate mandatory food fortification as an evidence-based policy to prevent neural tube defects



Note. Ghotme - Own work, *Based on Purtle, Dodson & Brownson (2018)*

The Knowledge to Action framework addresses the process of translating knowledge to actions as an iterative, dynamic, and complex process. It concerns the creation (knowledge funnel) and application (action cycle) of knowledge (Graham et al., 2006; Straus et al., 2011). Although the framework constitutes a cycle, users may need to utilize the phases out of sequence, depending on the project. In this case, the development of a knowledge tool was followed by the assessment of determinant factors for knowledge use and the selection, tailoring, and implementation of a KT intervention (Figure 1.2).

Figure 1. 2 Specific steps of the Knowledge to Action Framework used in this study



Note. Adapted from the Knowledge to Action Framework (Graham, 2006), retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16557505 (2020)

Summary of the Methodology

This study used a mixed-method explanatory sequential design to describe the factors contributing to the development and implementation of a KT strategy aiming to influence policymakers regarding MFF to prevent NTDs in Latin American countries. The selected design used the follow-up explanations variant, which prioritizes the initial quantitative phase and uses the subsequent qualitative phase to explain the quantitative results (Creswell & Plano Clark, 2017). The rationale for collecting quantitative and qualitative data was to obtain a deeper understanding of the critical factors for developing and implementing the innovation (the NeuroAdvocacy Toolkit), along with the KOL's engagement, motivation, intention to act, and mechanisms for disseminating it. Studying those aspects together is unaccountable with one source of data only.

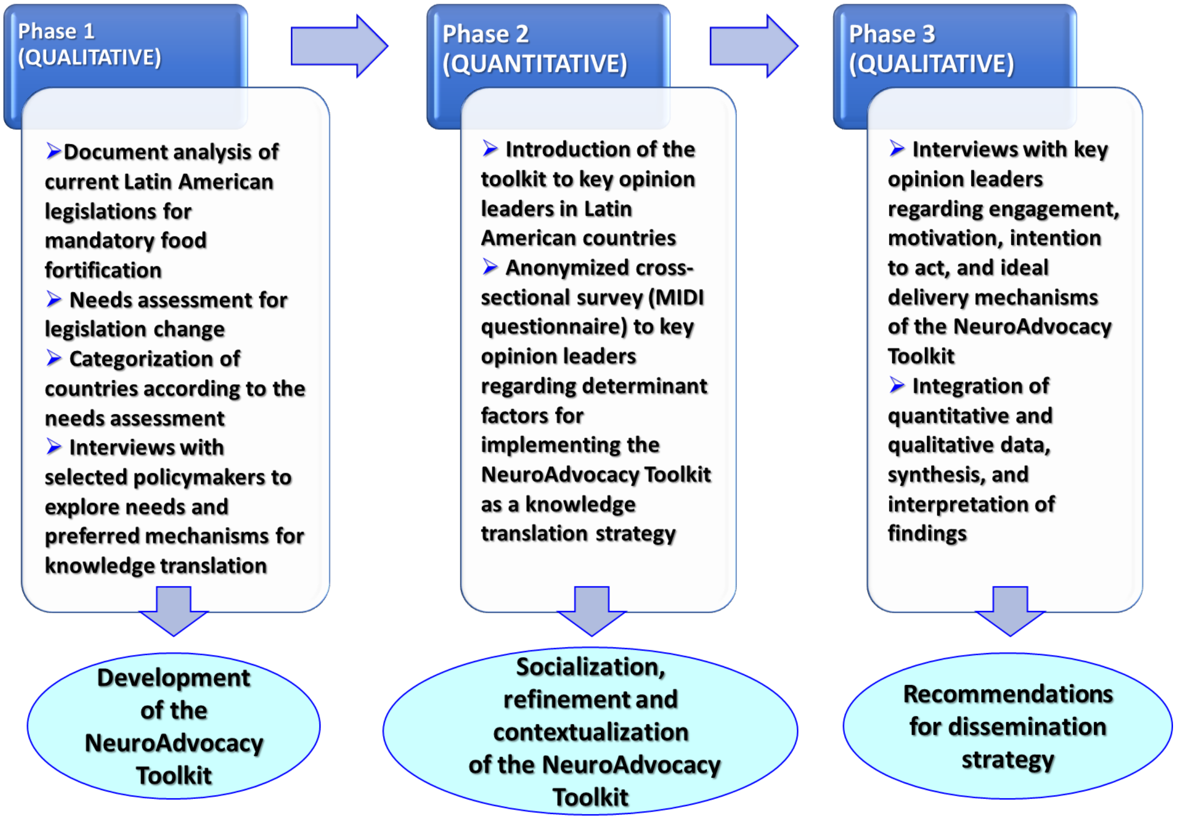
In dissemination and implementation research, mixed-method studies are the preferred design to identify the determinant factors acting as barriers or facilitators to implementing innovations. Besides, they help develop strategies and conceptual models of implementation, monitoring the implementation process, and increase the probabilities of the long-term sustainability of successful innovations (Palinkas & Cooper, 2018).

The selection of this design was founded on a pragmatic worldview combining quantitative and qualitative approaches. It drew elements of the multiple streams model for policy dissemination (Kingdon, 2003, 2014) and the Knowledge to Action Framework (Graham et al., 2006).

The study followed Maxwell's interactive model for research design to align the theoretical framework with the goals, research question, and methodology (Maxwell, 2012). It generated trustworthy, credible, confirmable, and transferable data on effectively using a toolkit to translate knowledge to decision-makers for strengthening evidence-based policies to protect thousands of children from NTDs as disabling but preventable conditions.

The study comprised three sequential phases, illustrated in Figure 1.3. The three-phases layout facilitated a logical sequence of the study's main activities and outputs.

Figure 1. 3 Phases, activities, and outputs of the study



Note: Ghotme, own work, created with SmartArt. MIDI: Measurement Instrument for Determinants of Innovations

In the first phase of the study, a document analysis provided factual data regarding the status and content of current legislation for MFF in the 20 Latin American countries, along with the national prevalence of NTDs and nutritional situation. The data gathered were codified to explore common ground (or lack thereof) in terms of policies, followed by a needs assessment for regulatory change contextualized to each country. According to the needs assessment, countries were classified into four categories: urgent need, high need, medium need, and no need for regulatory change. To include the voices of the innovation's target audience in designing the Toolkit, semi-structured interviews with pre-set topics were conducted with three selected policymakers from different countries to explore goals, expectations, and preferred mechanisms for knowledge translation. This phase's output was the NeuroAdvocacy Toolkit's development as the innovative KT strategy.

The second phase gathered quantitative survey data from KOLs at the national pediatric neurosurgery societies in Latin America regarding the determinant factors for implementing the NeuroAdvocacy Toolkit. Before data collection, the toolkit was introduced and explained to the KOLs at in-person scientific and online meetings. Subsequently, the Measurement Instrument for Determinants of Innovations (MIDI) was applied online, in Spanish, through SurveyMonkey®, an open-source software tool. The survey was pilot-tested on three participants and adjusted accordingly. Data were processed in SPSS version 27. Quantitative data analysis of the survey answers included descriptive statistics focused on the proportion of respondents in agreement with the statements inquired. The frequency of responses for each factor was analyzed according to the respondents' country and then organized through a joint display table for contingency analysis. This phase yielded additional refinement of the NeuroAdvocacy Toolkit in response to the identified barriers and facilitators to the innovation by the KOL in a way that retains the core components but contains customizable elements adaptable to local contexts.

The third phase collected qualitative data from semi-structured interviews with the KOLs. The questions explored their engagement, motivation, intention to act, and ideal delivery mechanisms of the NeuroAdvocacy Toolkit. The content of the interview protocol was grounded in the quantitative results of the study's second phase. The interview questions focused on the central phenomena related to their perspectives on the factors influencing the implementation of the NeuroAdvocacy Toolkit. The interview protocol was pilot-tested on one participant, purposefully selected from those who had completed the survey in Phase 2, and adjusted accordingly. All interviews were conducted online, in Spanish, through the Zoom® platform, and recorded in a secure storage location. The recorded interviews were transcribed verbatim through the Microsoft 360® transcript software. Data were analyzed and coded for thematic analysis of the participants' perspectives. The analysis was performed at two levels: within each case (individual interviewees) and across the cases (Creswell & Plano Clark, 2017). A matrix structured in terms of the themes, subthemes, and codes was used for displaying and further developing the results, including the verbatim quotes that addressed or supported those categories (Maxwell, 2012). Memoing and bracketing procedures were used to mitigate the potentially deleterious effects of the researcher's preconceptions. Trustworthiness was secured by triangulating different sources of information, member checking, rich and thick descriptions of the cases, and reviewing and resolving disconfirming evidence.

Finally, quantitative and qualitative data were synthesized and integrated. A joint display table was developed to illustrate how the qualitative results enhance the quantitative results. The value added by the qualitative explanations was interpreted to provide a deeper understanding of the MIDI questionnaire findings and additional insights and nuances on overcoming barriers and leveraging facilitators for the KT strategy. At the end of this phase, a set of recommendations tailored to each participating country was elicited for implementing and disseminating the NeuroAdvocacy Toolkit.

Limitations

Some of the study limitations included potential threats to internal and external validity. The first threat to internal validity was the lack of a comparison group; therefore, other events occurring within the study's timeframe may have generated the observed results (Portney, 2020). In this case, using a single group was justified because the study did not have an experimental manipulation. Instead, participants were approached in their natural setting. Finally, the results of this study are generalizable only to Latin American countries due to their unique social, cultural, and political reality.

There were also threats to trustworthiness, such as the risk of researcher bias for the investigator being part of the strategy as a researcher and, simultaneously, an advocate participating in policy dissemination. Therefore, it was essential not to consider the researcher's influence as a problem but to understand it and use it productively (Maxwell, 2012). Bracketing procedures helped in mitigating this threat. Besides, there was a potential risk for KOL's reactivity affecting their responses due to their awareness of being part of a study. However, reactivity facilitated a deeper understanding of the phenomena studied and more relevant and actionable findings. The use of multiple methods for data collection allowed for controlling threats to trustworthiness through triangulation, complementarity, and expansion procedures.

Finally, since the surveys and interviews were conducted in Spanish and all data were translated back into English, there was a possibility of confusion, ambiguities, or errors arising from the nuances of language. Back translation and reconciliation procedures were carried out to ensure quality, accuracy, and equivalence of meaning between the participants' answers and target texts.

Definition of Key Terms

Neural tube defects

NTDs are a group of congenital malformations caused by incomplete closure of the neural tube during the early stages of embryonic development at the primary neurulation stage (O'Rahilly

& Müller, 2001). NTDs include anencephaly, iniencephaly, craniorachischisis, encephalocele, spina bifida aperta, spina bifida occulta, and other types of spinal dysraphism.

Food fortification

Food fortification practices deliberately increase the content of essential micronutrients, i.e., vitamins and minerals (including trace elements), to improve the food supply's nutritional quality and provide a public health benefit with minimal risk to health (Allen et al., 2006).

Mandatory food fortification

Mandatory food fortification (MFF) is a regulation that requires food manufacturers to add specific vitamins (such as folic acid) or minerals, or both, to specified foods to address a significant public health need (CDC, 2020a).

Evidence-based intervention

Evidence-based interventions include programs, practices, processes, policies, or guidelines whose efficacy and effectiveness have been proven or informed by research and evaluation (National Center for Healthy Safe Children, 2020; Rabin et al., 2008).

Evidence-based policy

Evidence-based policies are public health actions informed by scientific evidence, but the decisions will depend on prevailing values and priorities. The decision-making process often requires the interplay of advocacy, lobbying, and more complex social and political negotiations than only appraising evidence and formulating recommendations (Rychetnik et al., 2004). MFF with folic acid is an example of an evidence-based policy aimed at preventing NTDs.

Knowledge translation (KT)

KT is a dynamic and iterative process that includes the synthesis, dissemination, exchange, and ethically sound application of knowledge to improve health, provide more effective health services and products and strengthen the healthcare system (CIHR, 2020; Straus et al., 2011).

Knowledge translation strategy

A KT strategy aims to increase awareness and utilization of research evidence in health, including printed educational materials, educational meetings, educational outreach, local opinion leaders, audit and feedback, and reminders (Barac et al., 2014).

Local opinion leaders

Also known as key opinion leaders (KOL). In the health sciences field, they are "health professionals nominated by their colleagues as educationally influential" (O'Brien et al., 1999).

MIDI questionnaire

The Measurement Instrument for Determinants of Innovations (MIDI) is an instrument that maps the determinants that influence the use of innovation in practice (Fleuren et al., 2014). It was the selected instrument to gather data in the quantitative phase of this study.

Public health intervention

Public health interventions are actions or programs applied to multiple members in a community aiming to produce identifiable outcomes that can deliver a net benefit to the population and individuals. Public health interventions include policies of governments and non-government organizations, laws/regulations, organizational development, community development, education of individuals and communities, engineering and technical developments, service development and delivery, communication, and social marketing (Rychetnik et al., 2004).

Regulation

A regulation broadly implies the imposition of government rules backed by the use of penalties specifically intended to modify the economic behavior of individuals and firms in the private sector to enforce compliance with higher-order norms that affect the population at large (OECD, 2008). Regulations can include laws, decrees, resolutions, policies, and norms. Throughout this dissertation, the terms regulation, legislation, and policies might have been used interchangeably to refer to mandatory food fortification rules promulgated, enacted, and enforced by state authorities.

Stakeholder

Stakeholders are individuals or groups responsible for or affected by health- and healthcare-related decisions that can be informed by research evidence (Concannon et al., 2014).

Stakeholder engagement

In research, stakeholder engagement entails “a bi-directional relationship between stakeholder and researcher that results in informed decision-making about the prioritization, conduct, and use of research” (Concannon et al., 2014).

Toolkit

A toolkit is a type of KT strategy consisting of the packaging of multiple resources that codify explicit knowledge, templates, pocket cards, guidelines, algorithms, and summaries geared to share knowledge, educate, or facilitate behavior change (Barac et al., 2014). Toolkits result from multifaceted combinations of sources such as guidelines for practice, audio-visual materials, and electronic publications. They communicate messages aimed at improving health and changing practices to diverse audiences, including healthcare practitioners, patients, community and health organizations, and policymakers (Barac et al., 2014). The core innovation of this research study is the NeuroAdvocacy Toolkit.

Translational research continuum

The translational process, also known as the translational spectrum, is a continuum of knowledge, processes, skills, and practice reflected by clinical and translational science, whose amalgamation and integration are essential to the successful application of new scientific discoveries to the creation of community wellness (Waldman & Terzic, 2010). The continuum is constituted by five moments or steps. T0 includes preclinical and foundational research that informs research with humans. T1 involves translation to humans through clinical interventions and initial settings, including proof of concept studies and phase I and II clinical trials. T2 implies translation to clinical settings to inform evidence-based guidelines, including phase III trials. T3 involves translation to practice and implementation in real-world settings, including phase IV trials and clinical practice guidelines. T4 implies translation to populations associated with improved disease prevention and reduced costs for medical care, including population-based outcome studies. The present study intends to bridge the chasm between the T3 and T4 moments of the continuum. Finally, T5 involves translating the population-based effects to the policies derived from it, including social healthcare, macroeconomics, and political measures for access to healthcare and education (Waldman & Terzic, 2010).

Translational science

The field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process (NCATS, 2020).

Chapter 2: Literature Review

NTDs are a set of severe congenital malformations of the central nervous system due to an absent, incomplete, or impaired closure of the neural tube in the embryonic stage, leading to significant neurological deficits, disability, and related complications in patients affected with these conditions (Greene et al., 2014). NTDs constitute a substantial cause of pregnancy termination, stillbirths, mortality, morbidity, and long-term disability. Annually, up to three of every 1,000 children can be born with an NTD, including anencephaly or spina bifida, with a global estimated rate of 300,000 new cases per year (Blencowe et al., 2018; Zaganjor et al., 2016). In more than 70% of the cases, the cause is a maternal folic acid deficiency or insufficiency (FFI, 2022). However, other risk factors have been identified, including gestational diabetes, genetic abnormalities, and teratogenic exposure to medications and other physical or chemical agents (Mitchell, 2005).

Despite substantial efforts to understand the genetics, pathophysiology, and surgical treatment of NTDs, the natural history of these conditions continues to exhibit high morbidity and marked impairment of the quality of life of affected patients (Estevez-Ordonez et al., 2018). Except for children with lethal malformations, patients with NTDs can undergo successful corrective surgery after birth, or during the intrauterine stage, in countries with installed healthcare capacity to perform such procedures. Notwithstanding, and despite successful neurosurgical treatments, these patients might face different long-term health issues in physical, cognitive, psychological, and social areas, leading them to require additional surgeries and several treatments and aids during their lifetime. Furthermore, the calculated direct and indirect costs of care for individuals with NTDs are enormous, which ensures profound inequities and disparities in disease burden, especially for low and middle-income countries (Estevez-Ordonez et al., 2018).

With this landscape, the ideal scenario is the primary prevention of NTDs. Mandatory food fortification is a successful public health evidence-based policy to prevent folic acid-sensitive NTDs, which has been available for several decades (Crider et al., 2011). Globally, MFF of cereal grains is only implemented in about 60 countries, preventing nearly 62,000 cases of all preventable NTDs as of the year 2020, and accounting for only 22% of the NTDs that could be prevented; there are an additional 200,000 preventable cases in more than 100 countries that do not implement MFF with folic acid (Kancherla, Wagh, et al., 2022). As a public health intervention, scientific evidence has shown that food fortification is a practical, safe, feasible, and cost-effective policy. It also decreases costs associated with healthcare and helps countries achieve their sustainable development goals (Hoddinott, 2018; Högler et al., 2016; Kancherla, Roos, et al., 2022). Despite these facts, only 92 countries worldwide have adopted a mandatory fortification policy for cereal grains. From those, only 63 countries include folic acid in their fortification standard, and the majority focus solely on one staple food, wheat flour (FFI, 2022; Kancherla, Botto, et al., 2022). Many women of reproductive age are vulnerable across the globe as they do not use enriched wheat flour and its derivates as an ingredient in their regular diet or traditional recipes, such as corn masa (Heather C. Hamner et al., 2011; Marchetta et al., 2015; Marchetta & Hamner, 2016; Minsalud Colombia, 2015). This situation hinders the protection of many children from these devastating but preventable conditions.

Purpose

This literature review aimed to synthesize the relevant scientific publications about NTDs, their relation to folic acid levels, and the main preventive measures, including policies for food fortification. It also aimed to identify the barriers and facilitators to implementing those policies, the role of neurosurgical advocacy, and the gaps that future research could address to advance in translating knowledge to decision-makers willing to protect thousands of children from these congenital anomalies.

Methods

The search strategy covered PubMed, Scopus, CINAHL, and SciELO databases; grey literature sources such as Open Grey and Pro-Quest; and repositories from the Centers for Disease Control (CDC), the World Health Organization (WHO), and the Food Fortification Initiative (FFI). The search had no language or publication type restrictions and covered the timeframe between 1980, when the first publications on the relationship between nutritional deficiencies and NTDs started to appear, and 2022. It included the following key terms: neural tube defects, folic acid, food fortification, culture and beliefs, health legislation, barriers and facilitators, implementation, public health intervention, evidence-based policy, knowledge translation, global neurosurgery, and advocacy.

This literature review reflects a body of knowledge built from disciplines such as medicine, neurosurgery, nutrition, pediatrics, obstetrics, public health, and epidemiology. It provides a comprehensive overview of the strategies to decrease the impact of NTDs as disabling conditions and their controversial aspects.

Description and Critique of Scholarly Literature

Neural tube defects: General aspects

NTDs are a group of congenital malformations caused by incomplete closure of the neural tube during the early stages of embryonic development at the primary neurulation stage, usually between the 23rd and 26th day following conception (O’Rahilly & Müller, 2001). NTDs can be classified as open if neural tissue is exposed or covered only by a membrane and closed if healthy skin covers the defect. According to etiopathogenesis, these congenital malformations can be folic acid-sensitive NTDs caused by maternal folate insufficiency and folic acid-resistant NTDs, when the malformation does not relate to folic acid insufficiency. NTDs include anencephaly, iniencephaly, craniorachischisis, encephalocele, spina bifida aperta, spina bifida occulta, and other types of spinal dysraphism. These congenital anomalies are defined as follows:

Anencephaly. This severe and fatal NTD consists of the absence of a significant portion of the brain, skull, and scalp that occurs during embryonic development (O'Rahilly & Müller, 2001).

Craniorachischisis. This extremely severe and invariably fatal NTD is due to complete primary neurulation failure no later than 20–22 days after conception. It consists of anencephaly and a contiguous and complete bony defect of the spine with exposure to neural tissue (Naveen et al., 2010; Polat et al., 2005).

Encephalocele. This late neurulation defect occurs during the 4th gestational week, consisting of a midline protrusion of cranial contents outside the skull. This defect is due to a disturbance in the separation of the surface ectoderm (epithelial layer) from the neurectoderm (nervous tissue) just after the closure of the neural folds. The internal skull defect usually locates in the midline. In contrast, the external skull defect may vary with the bony surroundings of the defect in the scalp or the facial skeleton, leading to topographic classification in occipital, cranial vault, frontoethmoidal, and basal encephaloceles (Hoving, 2000).

Iniencephaly. This severe and almost uniformly fatal NTD consists of a variable deficit of the occipital bones, resulting in an enlarged foramen magnum; a partial or total absence of cervical and thoracic vertebrae; abnormal vertebral fusion accompanied by incomplete closure of the vertebral arches or bodies; significant shortening of the spinal column due to marked lordosis and hyperextension of the malformed cervicothoracic spine; and an upward-turned face and mandibular skin directly continuous with that of the chest due to the lack of neck (C. P. Chen, 2007).

Spina bifida aperta. It is also known as open spina bifida, spina bifida cystica, or cystic spina bifida. In this NTD, an open bony defect of the posterior vertebral arches leads to herniation of neural tissue and meninges (Naveen et al., 2010). The two forms of cystic spina bifida are meningocele and myelomeningocele, which can occur at any level of the vertebral column but are more common in the lumbar and sacral areas. A meningocele is a saccular herniation of meninges and cerebrospinal fluid through a bony defect of the spine, usually covered by healthy skin. Myelomeningocele (MMC) is the most common type of spina bifida; it is characterized by herniation of the spinal cord, nerves, or both through a bony defect of the spine (Naveen et al., 2010).

Spina bifida occulta. It is also known as closed spina bifida. In this type of spinal dysraphism, a defective closure of the neural tube causes a set of ‘covered’ spinal cord lesions that include lipomyelomeningocele, split cord malformation (diastematomyelia), meningocele manqué, ectodermal inclusion tumor or cyst, dermal sinus tract, neurenteric cyst, and tight filum terminale. These lesions are often concealed or occult and may be asymptomatic, therefore detected later in life; however, in the majority of cases, cutaneous (hypertrichosis, capillary hemangioma, subcutaneous lipoma, dermal sinus, caudal appendage, atretic meningocele) and orthopedic (vertebral or lower extremity anomalies) stigmata exist, allowing early diagnosis (Lapsiwala & Iskandar, 2004).

Pathophysiology of NTD and the role of folic acid in neural tube closure

Closure of the neural tube is a crucial process of embryogenesis during the third and fourth weeks of gestation when most women are usually unaware that they are pregnant. A harmonic closure promotes the healthy development of the central and peripheral nervous systems (Blom, 2013). Failure of this process can result in NTDs, which have a multifactorial etiology with the interplay of genetic and environmental factors. Even though chromosomal and single-gene disorders are among the genetic factors related to NTDs, the inheritance pattern favors a multifactorial polygenic or oligogenic model, as opposed to an effect of single genes with partial penetrance (Harris & Juriloff, 2007). Meanwhile, environmental factors are related to seasonal changes, geographical areas, and socioeconomic status (Blom, 2013). On the other hand, some parental conditions constitute specific risk factors for NTDs, such as gestational diabetes, maternal obesity, maternal use of antiepileptic drugs such as valproic acid, maternal hyperthermia, and paternal occupational exposure (Agopian et al., 2013; Blom, 2013; Greene et al., 2014).

Undoubtedly, the leading risk factor in developing an NTD is diminished folate status (Bailey & Hausman, 2018). Folate is a general term used to describe the many different forms of water-soluble vitamin B9, including folic acid, dihydrofolate (DHF), tetrahydrofolate (THF), 5, 10-methylenetetrahydrofolate (5, 10-MTHF), and 5-methyltetrahydrofolate (5-MTHF) (Crider et al., 2011). The primary form of folate circulating in the blood is 5-methyl tetrahydrofolate (5-methyl-THF); therefore, it is the standard form of measuring and reporting serum folate levels (Choi et al., 2006). On the other hand, folic acid is the synthetic form of folate used in supplements and fortified foods as it is more stable during storage and processing, including cooking or baking (Choi et al., 2006). After ingestion and absorption, folic acid is easily converted to folate, increasing serum folate concentrations across populations (CDC, 2020a).

Serum folate deficiency, also known as vitamin B9 deficiency, is a low level of folate and derivatives in the body, below the range of 7 nmol/L for serum folate and <227 nmol/L for red blood cells folate, usually due to inadequate dietary intake or absorption; however, it can also be caused by increased folate needs or increased excretion or loses. Serum folate deficiency has been associated with NTDs, megaloblastic anemia, and chronic disease risk (Darnton-Hill, 2019). Moreover, the folate concentration needed to support rapid cell division at the neural tube closure is much higher; therefore, it requires a higher cut-off (<25.5 nmol/L for serum folate and <748-906 nmol/L for red blood cells folate) to provide maximum protection against folate-dependent NTDs (Chen et al., 2019). Folate levels below this cut-off are referred to as folate insufficiency. At the population level, red blood cell folate concentrations (a better marker of the long-term folate status of an individual) should be above 400 ng/mL (906 nmol/L) in women of reproductive age to achieve the most significant reduction of NTDs (CDC, 2022).

The underlying mechanisms by which folate deficiency or insufficiency induces NTDs have been associated with impairment of cell division due to genetic variations in folate transport and metabolism, as well as the presence of autoantibodies against the folate receptor, leading to a maternal immunological response impeding folate uptake (Osterhues et al., 2013).

Because of the failed neural tube closure in the embryo, the neural tissue endures prolonged exposure to the amniotic fluid environment. The neuroepithelium initially presents relatively normal neuronal differentiation, with the development of spinal motor and sensory function above and below the lesion level. As gestation progresses, the exposed spinal cord becomes hemorrhagic. Neurons die due to the toxicity of the amniotic fluid, leading to axonal disconnections and loss of function (Copp et al., 2015).

Clinical manifestations

Infants born with NTDs can present various clinical manifestations and health concerns throughout their lives, including physical, cognitive, emotional, and social issues. Physical problems include hydrocephalus, craniovertebral junction anomalies such as Chiari malformation, tethered cord, spinal deformities such as scoliosis and kyphosis, bladder or bowel incontinence, limb deformities, and inability to walk (Copp et al., 2015). Cognitive issues include intellectual disabilities, although infrequent, and difficulties in learning to construct and assimilate information (Taylor et al., 2013). On the other hand, psychological complaints include a higher incidence of depressive symptoms and lower self-esteem (Copp et al., 2015). Meanwhile, social issues involve family dysfunction (Holmbeck et al., 2006), less social interaction, more dependent behaviors, and decreased autonomy (Friedman et al., 2009).

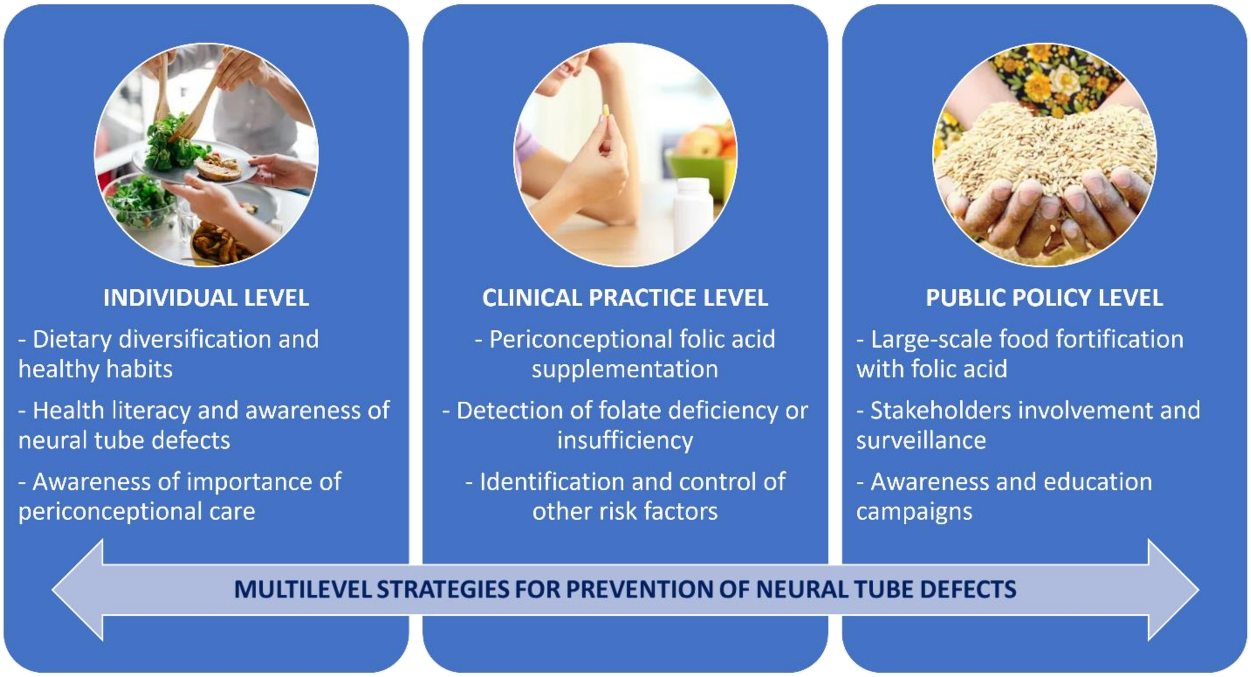
Treatment

Craniorachischisis, anencephaly, and iniencephaly are extremely severe NTDs incompatible with prolonged extrauterine life, usually leading to stillbirths or pregnancy terminations. Therefore, conservative treatment or palliative measures are the standard of care for the affected neonates born alive. On the other hand, surgical treatment is the gold standard for encephaloceles, spina bifida aperta, and many cases of spina bifida occulta. Different neurosurgical techniques can successfully correct these birth anomalies and prevent the complications associated with untreated NTDs. They include prenatal or postnatal repair of MMC, treatment of associated hydrocephalus, posterior fossa decompression of the Chiari type II malformation, encephalocele correction, lipomyelomeningocele repair, and cord untethering (Estevez-Ordonez et al., 2018). Most cases of spina bifida occulta are asymptomatic; if they remain like that, they usually benefit from conservative management and close routine follow-up. Surgical indications for spina bifida occulta include intractable spine or limb pain, progressive spinal deformity associated with tethered cord, worsening neurogenic bladder and bowel, and symptomatic Chiari. Despite successful surgeries for correcting NTDs, the prevalence of long-term complications and disability remains high; therefore, prevention efforts are essential to decrease the rate of these congenital anomalies and their consequences.

Strategies to prevent neural tube defects

Multilevel prevention strategies can be combined to decrease the prevalence of NTDs. Figure 2.1 summarizes the main strategies addressing different etiologic conditions and illustrates the interconnectivity and complementarity of preventive measures since they are not mutually exclusive. This dissertation focuses on folate deficiency or insufficiency primary prevention strategies at the public policy level.

Figure 2. 1 Multilevel strategy for prevention of neural tube defects



Note: Ghotme, own work, created with SmartArt

Folic acid supplementation. Dietary supplements are oral products that contain a dietary ingredient meant to supplement nutrients in the diet (CDC, 2020a). Folic acid supplementation is explicitly the act of taking a supplement that contains folic acid, usually in the form of a vitamin pill, every day (CDC, 2020a).

The literature synthesized in a Cochrane review shows a protective effect of daily folic acid supplementation (alone or in combination with other vitamins and minerals) in preventing NTDs compared with no interventions/placebo or vitamins and minerals without folic acid (De-Regil et al., 2015). Supplementation may also reduce other congenital malformations such as cleft lip, cleft palate, and congenital cardiovascular defects. Supplementation with folic acid is recommended globally for women before conception until the first trimester. WHO also recommends that women of reproductive age take intermittent iron and folic acid supplements, especially in populations with a prevalence of anemia above 20% (De-Regil et al., 2015). Nevertheless, these supplementation strategies do not significantly impact public health since less than 4% of the population takes vitamin supplements, and less than half of the pregnancies are planned and get access to preconception assessment and counseling (Ray et al., 2004).

Food fortification initiatives. Food fortification is the practice of deliberately increasing the content of an essential micronutrient, i.e., vitamins and minerals (including trace elements) in food, to improve the nutritional quality of the food supply and to provide a public health benefit with minimal risk to health (Allen et al., 2006). Folic acid fortification is a specific process by which synthetic folic acid is added to staples, aiming to increase the blood folate levels in the population (CDC, 2020a). As a public health measure, this process can be mandatory or voluntary.

Mandatory food fortification (MFF) is a regulation that requires food manufacturers to add specific vitamins (such as folic acid) or minerals, or both, to specified foods to address a significant public health need (CDC, 2020a). In contrast, voluntary food fortification is a process that allows food manufacturers to choose what vitamins and minerals they add to food as long as they abide by the regulations established in each country (Food Standards, 2020).

Scientific evidence supporting food fortification. A substantial body of evidence supports that regulations that enforce mandatory folic acid fortification of one or more grain cereals and their derivates induce a significant decrease in the incidence of NTDs and their associated morbidity and mortality (Atta et al., 2016; Garrett & Bailey, 2018; Kancherla et al., 2014). As an evidence-based policy, MFF is practical since it does not require women to change behaviors (such as taking supplements) to improve their periconceptional folate status (Martinez et al., 2018, 2021; Pachón et al., 2013). It is also safe, given that programs implemented in many countries have no adverse consequences (Field et al., 2018). MFF is feasible since over a hundred countries already have mandatory fortification with micronutrients of different foods, including maize flour (19 countries), oil (34 countries), rice: (8 countries), salt (126 countries), and wheat flour (91 countries) (Global Fortification Data Exchange, 2022). It is also feasible because countries with existing industrial milling infrastructure can immediately fortify staple foods and prevent more than 50,000 cases annually (Kancherla, 2018). Last, and most importantly, it is cost-effective because fortifying food is inexpensive and saves lives and millions in resources and efforts (CDC, 2020b).

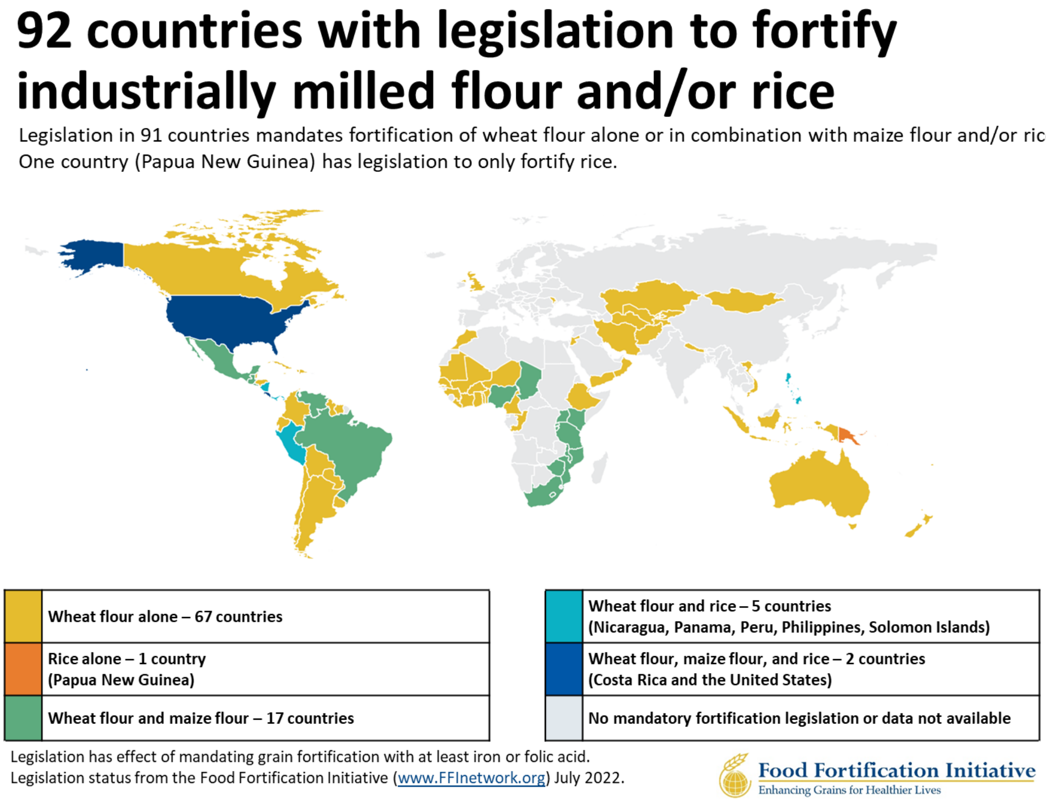
Controversial evidence against food fortification. Despite MFF being a groundbreaking public health intervention to prevent NTDs, other congenital disabilities, and several non-congenital health issues, there are reports of potential risks; however, they have been refuted with solid scientific evidence. Excessive folic acid intake may mask a vitamin B12 deficiency, potentially resulting in neurologic damage (Mills, 2017). However, the available evidence indicates that folic acid intakes of up to 1 mg/day, the adult upper level of intake, will not mask the diagnosis of vitamin B12 deficiency (Berry, 2019). At the same time, the upper level's relevance for younger age groups, particularly children, is unclear because vitamin B12 deficiency is rare in the pediatric population (Mills, 2017). Moreover, Wald et al. and Pachon et al. have stated that there is no scientific basis for setting an upper level of intake for folate and proposed that the upper level should be eliminated since it acts as a barrier to large-scale fortification (Pachón et al., 2021; Wald et al., 2018).

Although there is the potential for increased folic acid intake to interfere with certain medications, the available scientific evidence does not demonstrate any clinically significant interaction with therapeutic medicines from folate intakes up to 1 mg/day (Choi et al., 2006).

One source of resistance to MFF policies is the belief that they limit consumers' choice regarding opting for non-fortified products; however, this is not the main issue in many low and middle-income countries, where poverty remains the limiting factor to access processed foods for most of the population (Allen et al., 2006).

Global situation of MFF policies. Only 92 countries in the world (47%) have regulations that enforce MFF of cereal grains with micronutrients (Figure 2.2), primarily focused on wheat flour and its derivates (FFI, 2022); from those, just about 63 countries include folic acid in the fortification policy. Even though the existing industrial milling infrastructure provides the immediate potential to fortify wheat flour in another 71 countries and, thus, prevent 57,000 additional cases of congenital anomalies of the brain and spine annually (Kancherla, 2018), many countries in Africa, Asia, Europe, and Oceania do not implement fortification of staples with folic acid.

Figure 2. 2 World map illustrating mandatory micronutrient fortification status for wheat flour, maize flour, and rice



92 countries with legislation to fortify industrially milled flour and/or rice

Legislation in 91 countries mandates fortification of wheat flour alone or in combination with maize flour and/or rice.
One country (Papua New Guinea) has legislation to only fortify rice.

🟨	Wheat flour alone – 67 countries	🟦	Wheat flour and rice – 5 countries (Nicaragua, Panama, Peru, Philippines, Solomon Islands)
🟧	Rice alone – 1 country (Papua New Guinea)	🟦	Wheat flour, maize flour, and rice – 2 countries (Costa Rica and the United States)
🟩	Wheat flour and maize flour – 17 countries	⬜	No mandatory fortification legislation or data not available

Legislation has effect of mandating grain fortification with at least iron or folic acid.
Legislation status from the Food Fortification Initiative (www.FFInetwork.org) July 2022.

Food Fortification Initiative
Enhancing Grains for Healthier Lives

Note: Used with permission from the Food Fortification Initiative (FFI, 2022).

Only three countries in Europe (Moldova and Kosovo, and more recently, the United Kingdom) have embraced mandatory folic acid fortification (DEFRA, 2021; FFI, 2022; Global Fortification Data Exchange, 2022), resulting in more than a thousand pregnancies affected by preventable spina bifida and anencephaly every year in that continent (Kancherla, Botto, et al., 2022). The reasons for the endurance of this prevalence are multifactorial. For instance, a study conducted in Italy addressed the transition in dietary habits affecting the Mediterranean diet, previously shown to be protective against NTDs, to a more “North American” diet as one potential cause for this phenomenon (Fischer et al., 2017). On the other hand, increasing migration of people from African countries and Eastern Europe could have also changed the landscape of dietary habits and access to quality food in some communities living in Southern Europe. Fisher et al. argue that folic acid supplements alone are not enough to decrease the incidence of NTDs; therefore, efforts for food fortification, among others, are needed (Fischer et al., 2017). In 2021, the United Kingdom mandated adding folic acid to wheat flour, which was previously fortified with other micronutrients. However, the amount of folic acid is still being stipulated (DEFRA, 2021).

In 2021, the International Society for Pediatric Neurosurgery (ISPN) recommended that all governments enact policies for MFF with folic acid of centrally produced staples to provide almost all women of reproductive age who eat fortified foods with at least an additional 150 μg/day of folic acid, according to the WHO recommended guidelines (Caceres et al., 2021).

In a global context, despite countries having existing policies for fortification of cereal grains with folic acid, most of them focus only on one staple (mainly wheat flour) (FFI, 2022), leaving groups of people who favor other food sources (such as maize flour or rice) in their diet without the benefit of getting folic acid-enriched products. In some regions, vulnerable communities do not access industrially-processed, fortified wheat flour and derivate products (Hamner et al., 2011; Marchetta et al., 2015; Sarah C. Tinker et al., 2012) and base their diet on rice, corn masa, yucca (cassava), teff, or quinoa for geographic, historical, cultural, or ethnic reasons or because those grains constitute the only staple. Therefore, those countries with existing policies can benefit from updating and scaling up MFF policies to include other staples with the recommended guidelines for folic acid while optimizing surveillance and ensuring the sustainability of existing policies.

Most countries with MFF policies in place have systems for surveilling implementation. However, documentation of compliance with those policies, the roles and responsibilities between agencies, the cost of regulating fortification, and enforcement strategies, are often lacking (Marks et al., 2018).

Partnerships joining efforts from multiple stakeholders are crucial since they combine diverse expertise and perspectives. The Global Alliance for the Prevention of Spina Bifida F (GAPSBiF), a multidisciplinary coalition of neurosurgeons, pediatricians, geneticists, epidemiologists, food scientists, and fortification policy experts, was formed to advocate for MFF of staple foods worldwide (Shlobin, Roach, et al., 2022).

A recent call to action from the scientific community led by GAPSBiF, published in The Lancet Global Health, urges the World Health Assembly to pass a resolution for universal mandatory folic acid fortification (Kancherla, Botto, et al., 2022). Such a resolution could accelerate the slow pace of NTD prevention globally and assist countries in reaching their 2030 Sustainable Development Goals on decreasing child mortality and promoting health equity. The cost of inaction is profound and disproportionately impacts susceptible populations worldwide, with a more significant impact in low-income and middle-income countries.

MFF regulation in Latin America. Latin America is the term used to describe the 20 independent republics in North, South, and Central America that speak Romance languages, after being colonized by the Latin nations Spain, Portugal, and France. Latin America consists of 20 countries (Figure 2.3) and 14 dependent territories, covering approximately 19,197,000 km^2 (7,412,000 sq. mi). The region spans from Mexico to Tierra del Fuego and includes much of the Caribbean, constituting almost 13% of the Earth’s land surface area. As of the first half of 2022, the estimated population of Latin America and the Caribbean was more than 656 million, with a combined nominal GDP of US$5,188,250 million and a GDP PPP of 10,284,588 million USD in 2019 (*Latin America - Wikipedia*, 2022).

Figure 2. 3 Latin American region

Note. Pertaining countries colored in blue, by Ghotme - Own work, created with mapchart.net

In a scientific meeting held in Bolivia in 2006, the Latin American Association for Pediatric Neurosurgery (ASOLANPED) promulgated the Declaration of Santa Cruz. This document reinforces that the high incidence of NTDs in Latin American countries is a social problem preventable by implementing MFF. The declaration also recommended that the region's governments support this policy and consider other environmental factors that could be related to NTDs in the specific Latin American context (Dabdoub et al., 2014). However, the Declaration of Santa Cruz did not provide detailed guidance on how to translate the evidence to influence government agents' support of the policy.

Meanwhile, Latin American countries have made meaningful progress in public health policies regarding MFF and the prevention of NTD. Table 2.1 crosses data from three sources (FFI, 2022; Rosenthal et al., 2014; Zaganjor et al., 2016) that report the existence of legislation for MFF in Latin American countries and their prevalence of NTDs. It shows that the presence of MFF regulatory acts is almost uniform in the region for wheat flour. In contrast, it is incomplete (for instance, not including folic acid in the fortification standard or adding folic acid concentrations below the recommended guidelines), in some cases voluntary, and often null for maize (corn) and rice, two essential staple foods in the diet of millions of Latin Americans. The fortification status correlates directly with a decreasing NTD prevalence in some countries with more robust fortification policies while remaining persistently high in others, especially those with incomplete fortification status (only one staple food fortified or current fortification below the recommended guidelines). It is noteworthy that Costa Rica exhibits positive deviance since this country has successfully implemented policies on MFF of the three main staple foods, which has led to the minimum level of NTDs reported when a successful strategy for folic acid fortification is applied.

Table 2. 1 Type of fortification legislation and neural tube defects (NTDs) prevalence in Latin American countries

COUNTRY	LEGISLATION FOR FOOD FORTIFICATION			PREVALENCE OF NTDs PER 10,000 BIRTHS
	WHEAT FLOUR	MAIZE FLOUR	RICE	
Argentina	Mandatory	None	None	11.9
Bolivia	Mandatory	None	None	11
Brazil	Mandatory	Mandatory	None	24.3
Chile	Mandatory	None	None	10.1
Colombia	Mandatory	None	None	11
Costa Rica	Mandatory	Mandatory	Mandatory	4.8
Cuba	Mandatory	None	None	10
Dominican Republic	Mandatory	Voluntary	None	11
Ecuador	Mandatory	None	None	8
El Salvador	Mandatory	Mandatory	None	8
Guatemala	Mandatory	Mandatory	None	27.9
Haiti	Mandatory	None	None	18
Honduras	Mandatory	None	None	17.4
Mexico	Mandatory	Mandatory	None	11
Nicaragua	Mandatory	None	Mandatory	8
Panama	Mandatory	None	Mandatory	8
Paraguay	Mandatory	None	None	8
Peru	Mandatory	None	Voluntary	20
Uruguay	Mandatory	None	None	17.5
Venezuela	Mandatory	Mandatory	Voluntary	17

Note. Ghotme – own work, based on Food Fortification Initiative, 2022; Global Fortification Data Exchange, Kancherla, 2022; Zaganjor et al., 2016; and Rosenthal et al., 2013. Although Puerto Rico is considered part of Latin America, it was excluded from this table since the regulations for fortification are under the United States legislation. NTDs: Neural tube defects.

Barriers and facilitators to the implementation of MFF as an evidence-based policy

Evidence-based policies are public health actions informed by a consideration of the scientific evidence, but the decisions made will depend on determinant factors and prevailing values and priorities; therefore, this process often requires the interplay of advocacy, lobbying, and more complex social and political negotiations, than only appraising evidence and formulating recommendations (Rychetnik et al., 2004).

The literature points to different determinant factors acting as barriers or facilitators for the reach, adoption, implementation, and scaling-up of MFF with micronutrients, including folic acid, as an evidence-based policy. They comprise individual and contextual factors, internal or external, that may vary according to specific circumstances. However, there is scarce information in the literature regarding theories, models, frameworks, or knowledge translation interventions that address how to overcome those barriers or leverage the facilitators to effectively and successfully implement MFF to prevent NTDs.

Barriers. Table 2.2 summarizes the main barriers to the implementation of MFF policies. Despite substantial evidence of the efficacy and effectiveness of MFF as a successful public health intervention, one of the evident barriers in the literature is a lack of willingness from local authorities in many countries to either enact regulations for this evidence based-policy or to provide sufficient oversight to ensure that industry and importers follow the rules for mandatory folic acid fortification (Estevez-Ordonez et al., 2018; Martin et al., 2011; Mills, 2017). One potential reason for that is the concern that exposure to high doses of folic acid might cause an increased risk of different disorders. Other aspects, including perceived costs of fortification by the food industry and socio-political reasons, might also play a role.

Higher than normal serum folate levels have been associated with health issues such as cancer, asthma, cognitive problems, twin pregnancy, and autism and may mask vitamin B12 deficiency (Fischer et al., 2017). However, scientific evidence does not confirm these risks (Berry, 2019; Wald et al., 2018). Although masking of vitamin B12 deficiency in older adults with macrocytic anemia has been described if they are only treated with folate and not folic acid (Mills, 2017), in modern practice, it is unlikely that vitamin B12 deficiency masking would happen (Berry, 2019). Moreover, the evidence points in the opposite direction since no singular study has enough level of evidence to recommend against food fortification on a massive scale. For instance, a rare condition causes slow processing of folates (Crider et al., 2011). However, it does not lead to toxic serum folate levels in individuals receiving folic acid supplements at the recommended doses since folic acid is a water-soluble vitamin excreted in the urine when it reaches excessive serum concentration.

The ambiguous role of synthetic folic acid in promoting subclinical cancers, mainly colorectal cancer, has led to the hesitation of some countries, mainly in Europe, to introduce a public health intervention for MFF (Smith et al., 2008). Nevertheless, the increased incidence of colorectal cancer is more attributable to improved screening for that type of cancer. Quite the opposite, there is evidence of a protective effect for pancreatic cancer with increasing dietary folate intake (Jägerstad, 2012). Additionally, one study discusses folic acid fortification's role in a higher risk of malaria in African countries (Nzila et al., 2016). However, this finding has been controversial since folic acid supplements usually contain iron, whose high levels reportedly increase the risk of malaria; meanwhile, other studies have shown a protective effect of folates against that parasitic illness. The authors propose a dose-dependent effect, whereby intake of low doses of folic acid (which corresponds to the daily intake from food fortification) would have a marginal impact on malaria disease.

Different dietary habits rooted in local or national cultures may also act as barriers leading to a low reach of MFF as an impactful measure to prevent NTDs. For instance, Mexican American women, a vulnerable immigrant population in the United States whose offspring have a high incidence of NTDs, rely on non-fortified products such as corn masa as the main component of their traditional recipes (Hamner et al., 2011). This cultural practice, along with other potential factors such as race/ethnicity and acculturation, is associated with lower folate intake and low serum-folate levels among women of reproductive age in that group (Hamner et al., 2011; Marchetta & Hamner, 2016). Hence, the fortification of wheat flour has a weak influence on these communities since the basis of their dietary habits does not include wheat flour products but other non-fortified cereal grains such as non-fortified maize flour, a common ingredient in corn masa and other traditional recipes made with locally grown or imported grains. In that sense, studies modeling fortification of traditional foods like corn masa found a positive potential to selectively increase total folic acid intake among Mexican-American women without exceeding the tolerable upper intake level for folic acid (Hamner et al., 2013; Tinker et al., 2012).

Table 2. 2 Critical determinant factors acting as barriers and facilitators to adopt mandatory food fortification policies

Barriers	Type of factor		Facilitators
Lack of translational knowledge by coordinating level officials	Individual	👥	Advocacy/leadership of physicians and professional organizations to broker knowledge to policymakers
Concerns on potential adverse effects of high level intakes of folic acid			
Bureaucratic processes delay adoption and enactment of policies	Contextual	🏢	Established infrastructure of milling industry in many countries with potential for immediate fortification
Focus in wheat flour and neglect of other food sources or traditional foods			Commitment and willingness of local milling industry to adopt fortification policies, since they see it as part of their social liability
Race/ethnicity, acculturation of immigrant groups			Interdisciplinary approaches and modelling of fortification of traditional foods
Lack of willingness from local authorities to adopt folic acid fortification as a public health measure in some countries	External	🌎	Influence of supranational organizations on regional and local law/policy makers
Influence of food importers, for their non-fortified products to enter countries, in virtue of free trade agreements (FTAs)			Private/public partnerships (industry, government, academia, and civil society)

Note. Based on a scoping review (Ghotme, 2018)

Facilitators. The literature also suggests facilitators for the implementation of MFF policies, summarized in Table 2.2. One of the facilitators is the existing milling infrastructure, which creates a potential for immediate fortification in many countries (Kancherla, 2018). Also, supranational policies encourage local governments to achieve Sustainable Development Goals by 2030, including ending hunger and improving the population's health status, as is the case for preventing NTDs (Kancherla et al., 2019). On the other hand, private/public partnerships, adequate monitoring, and quality control are among the main components of successful staple food fortification programs in Latin America. They might also be critical elements for the sustainability of those programs (Martorell & de Romaña, 2017).

The role of Global Neurosurgery in neurosurgical advocacy

Neurosurgical conditions are usually devastating, and their care is highly demanding in terms of costs and effort. However, the involvement of neurosurgeons in public health initiatives is scarce. Their participation, advocacy, and lobbying can be impactful in promoting evidence-based policies and integrating the neurosurgical burden into national health planning systems (Veerappan et al., 2022).

Global neurosurgery is an “area of study, research, practice, and advocacy that prioritizes improving health outcomes and achieving health equity for all people worldwide who are affected by neurosurgical conditions or need neurosurgical care” (Park et al., 2016). The literature identifies five global neurosurgery domains: practice, research, health systems strengthening, advocacy, and education (Shlobin, Sharma et al., 2022).

There are different ways in which individuals, scientific organizations, other civil society groups, and academia engage in global neurosurgery to address the global challenges faced in many low- and middle-income countries. Key strategies include surgical camps, educational programs, training programs, health system strengthening projects, health policy changes/development, and advocacy (Haglund & Fuller, 2019). However, current Neurosurgery residency training programs or Pediatric Neurosurgery fellowships do not comprise curricula that prepare neurosurgeons to be competent in assuming a role in public health advocacy. It is essential to consider the challenges and benefits of international neurosurgical training programs to effectively promote the development of neurosurgical care and prevention strategies for NTDs in low- and middle-income countries (Gandy et al., 2020).

The research and advocacy domains of Global Neurosurgery strive to understand local neurosurgical epidemiology to drive contextually adapted models of neurosurgical practice, to study the social determinants of neurosurgical conditions in all populations, and the diverse disease trends that occur across different socioeconomic groups locally and abroad (Barthélemy et al., 2018). These domains also promote using qualitative and quantitative methods to identify the socio-economic effects of disparities in access to neurosurgical care and to study the impact of innovative, enduring solutions for neurosurgical inequity. Finally, they promote partnering with non-neurosurgical researchers to produce interdisciplinary team science approaches and participate in local, national, regional, and global initiatives to influence policies that regulate the healthcare ecosystems of patients with neurosurgical conditions (Barthélemy et al., 2018).

Organized neurosurgery plays an essential role in neurosurgical advocacy. The liaison committee between the WHO and the World Federation of Neurosurgical Societies (WFNS) works to advance access to quality care for neurosurgical patients globally (Rosseau et al., 2018). National and regional neurosurgical societies play an important role in advancing the global neurosurgical agenda, including ways to influence public policies impacting the incidence and effects of conditions that affect the human nervous system. In low- and middle-income countries, contributions include advocating for compiling information regarding the neurosurgical disease burden and accurate reporting of human health resources, and may also include evaluation of resource-stratified interventions, policies, and equipment (Rosseau et al., 2018).

Neurosurgical efforts have explored different advocacy mechanisms, including economic contributions to campaigns of lawmakers who support policy issues important to neurosurgery (Agarwal et al., 2020). However, a survey of nearly half of pediatric neurosurgeons affiliated with the American Society for Pediatric Neurosurgery (ASPN) revealed that members prioritized public health and clinical issues that affected children over economic matters (LoPresti et al., 2019). The survey yielded data regarding pediatric neurosurgeons' attitudes that may assist with designing a successful advocacy program. Most respondents favored drafting position statements on critical issues and partnerships with larger organizations to pursue an advocacy agenda (LoPresti et al., 2019).

Few publications address the role of neurosurgeons as KOL and how they might act as knowledge brokers to facilitate the adoption, implementation, and scaling-up of MFF as an evidence-based policy to prevent NTDs. The ISPN constituted a Spina Bifida Global Taskforce with the multi-national and multidisciplinary collaboration of individuals and organizations interested in the primary prevention of major folic acid-sensitive NTDs. This organization stated that pediatric neurosurgeons are essential science-based advocates for MFF policies, with the potential to spearhead the protection of thousands of children in all countries (Caceres et al., 2021).

One seminal paper to this dissertation highlights the central role that neurosurgeons and organized neurosurgery can play in advocating for a more comprehensive, global-scale folate fortification to avoid the most common and severe birth congenital malformation that affects the human nervous system due to their accumulated experience dealing with these conditions and their high standing in society (Estevez-Ordonez et al., 2018). These authors propose that assertive, proactive, informed advocacy for folate fortification should be a central and integral part of the neurosurgical approach to NTDs. Furthermore, they recommend eight steps to materialize this advocacy, as listed below.

1) Neurosurgeons and neurosurgical professional organizations must serve as powerful advocates for MFF with folic acid
2) Forming partnerships with local and international colleagues to advance basic and clinical research
3) Supporting improved registry and surveillance efforts on a local and global scale

4) Advocating for increased prenatal screening of NTDs
5) Supporting the establishment of comprehensive countrywide centers of excellence to integrally approach NTDs through a combination of advocacy, international collaboration, and funding
6) Working to establish and expand partnerships between their institutions and existing NTD centers in developing countries
7) NTD advocacy organizations and organized neurosurgical groups must expand the availability of multidisciplinary conferences on NTD prevention and multidisciplinary management across the world
8) International initiatives can provide country-level information on NTD prevalence and local prevention and can serve as partners to effect significant change

Inferences for the current study

NTDs are devastating congenital anomalies that can diminish the affected individuals' survival, health, and quality of life and impact families, society, and public health. MFF with folic acid, the most effective public health intervention to prevent NTDs, has been available for more than three decades, but still, more than 100 countries fail to fortify food with folic acid despite being a robust evidence-based policy. This situation generates inequities in the burden of disease on vulnerable populations, which is a current problem demonstrated by an increasing number of recent publications addressing it. Separate disciplines, including medicine, nutrition, pediatrics, public health, and epidemiology, have identified gaps and opportunities for implementing strategies to adopt MFF as a public health intervention. However, there is a lack of cross-disciplinary research to move forward and include relevant stakeholders in the dialogue, aiming to scale up this evidence-based policy and reach thousands of communities that may benefit from the intervention.

Important determinant factors acting as barriers and facilitators for implementing MFF as an evidence-based policy are evident in the literature. Furthermore, the literature allows inferring that policymakers of most Latin American states may lack knowledge of the benefits of scaling up their policies for MFF to prevent folic acid-sensitive NTDs, improve the health status of their communities, and promote the protection of a large number of children from these disabling but preventable conditions. Not addressing this problem continues to pose negative consequences on four levels: public health, society, family, and individuals. However, there is scarce information in the literature on how to address this problem and to what extent knowledge translation interventions can help achieve the goal of influencing policymakers' decisions. Future exploration of this problem might consider theories, models, and frameworks for materializing the role of neurosurgeons and neurosurgical societies and the KT strategies that could leverage that advocacy to ensure the reach, adoption, implementation, scaling-up, and sustainability of MFF as a robust evidence-based policy to prevent NTDs.

Conceptual Framework

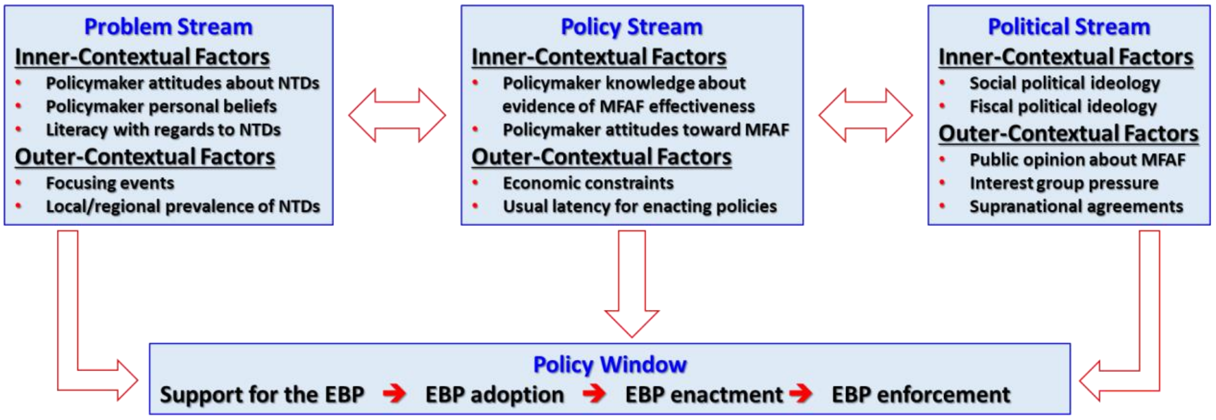
As discussed above, there is a robust body of evidence on MFF's efficacy, safety, and cost-effectiveness as a successful public health intervention to prevent NTDs (CDC, 2020c; FFI, 2022; Kancherla, 2018; Pachón et al., 2013). Therefore, this study focuses on the KT strategies to influence policymakers in Latin America to update, optimize, enact and enforce MFF policies, eventually leading to health outcomes impacting individuals, society, and public health.

This study's primary constructs are mandatory food fortification, determinant factors (barriers and facilitators) of innovation, knowledge translation strategies, knowledge brokers

(KOL), knowledge users (policymakers), dissemination of evidence-based policies, stakeholder engagement, advocacy, leadership, and lobbying. For this study, these primary constructs are prioritized over secondary constructs such as health outcomes, prevalence, incidence, NTD treatment, folic acid supplementation, and voluntary fortification.

Kingdon's model describes how the convergence of problem, policy, and political streams opens a window for policy entrepreneurs to promote new policies that enter the agenda of policymakers (Kingdon, 2014). However, this model does not account for the critical factors influencing the uptake of a specific evidence-based policy. Aarons' model incorporates those factors, but it does not consider the three streams of Kingdon's model. Therefore, both models could integrate streams and critical factors based on a published experience in mental health using this approach (Aarons et al., 2011). Figure 2.4 illustrates the conceptual framework specifically designed for this study using both models.

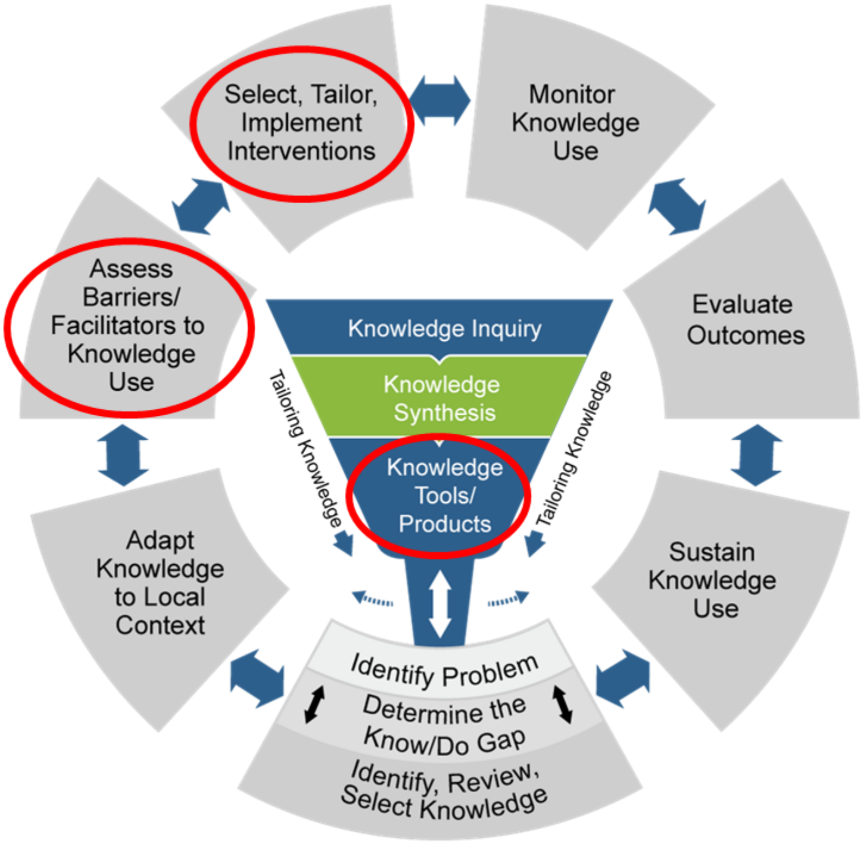
Figure 2. 4 A conceptual framework combining Kingdon's and Aaron's models for alignment of multiple streams and contextual factors to disseminate MFAF as an EBP to prevent folic acid-sensitive NTDs



Note. Ghotme - Own work, *Based on Purtle, Dodson & Brownson (2018)*

The Knowledge to Action framework addresses the process of translating knowledge to action as an iterative, dynamic, and complex process. It concerns the creation (knowledge funnel) and application (action cycle) of knowledge (Graham et al., 2006; Straus et al., 2011). Although the framework constitutes a cycle, users may need to utilize the phases out of sequence, depending on the project. In this case, the development of a knowledge tool is followed by the assessment of determinant factors for knowledge use and the selection, tailoring, and implementation of a KT intervention (Figure 2.5).

Figure 2. 5 Specific steps of the Knowledge to Action Framework used in this study



Note. Adapted from the Knowledge to Action Framework (Graham, 2006), retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16557505 (2020)

Chapter 3: Methods

Overview of Methodology

This study answered the following overarching research question: *how may we describe the factors contributing to the development and implementation of a KT strategy aiming to influence policymakers regarding MFF for preventing NTDs in Latin American countries?*

This question gave rise to quantitative, qualitative, and mixed-methods research questions, presented in Table 3.1.

Table 3. 1 Quantitative, qualitative, and mixed-methods research questions of the study

QUANTITATIVE RESEARCH QUESTION	QUALITATIVE RESEARCH QUESTIONS	MIXED-METHODS RESEARCH QUESTION
What are the determinant factors influencing the use of the NeuroAdvocacy Toolkit as an innovation to promote robust MFF policies in Latin America?	How do the KOL describe their attitudes toward implementing and disseminating the NeuroAdvocacy Toolkit to translate knowledge to policymakers in their countries? What are the perceptions of KOL about appropriate dissemination mechanisms of the NeuroAdvocacy Toolkit?	In what ways do the interview data reporting the views of KOL about using the NeuroAdvocacy Toolkit help to explain the quantitative results about the determinant factors for implementing the innovation?

Note: MFF: mandatory food fortification; KOL: key opinion leaders

The study's overall purpose is to describe the factors contributing to developing and implementing a KT strategy aiming to influence policymakers in Latin American countries regarding MFF to prevent NTDs. The KT strategy relies on neurosurgeons' and professional organizations' advocacy and leadership in brokering knowledge to policymakers and other stakeholders. The ultimate goal was to design a dissemination strategy tailored to the needs for regulatory change and contextual aspects of Latin American countries.

This study used a mixed-method explanatory sequential design to describe the factors contributing to developing and implementing the KT strategy with the NeuroAdvocacy Toolkit as the central component. The selected design utilized the follow-up explanations variant, which prioritizes the initial quantitative phase, and uses the subsequent qualitative phase to explain the quantitative results (Creswell & Plano Clark, 2017). The rationale for collecting quantitative and qualitative data was to obtain a deeper understanding of the critical factors for developing and implementing the innovation (the NeuroAdvocacy Toolkit), along with the KOL's engagement, motivation, and intention to act in disseminating it. Studying those aspects together cannot be achieved only with one data source.

In dissemination and implementation research, mixed-method studies are the preferred design to identify the determinant factors acting as barriers or facilitators to implementing innovations. Besides, they help develop strategies and conceptual models of implementation, monitoring the implementation process, and increase the probability of the long-term sustainability of successful innovations (Palinkas & Cooper, 2018).

The selection of this design was founded on a pragmatic worldview combining quantitative and qualitative approaches. It draws elements of the multiple streams model for policy dissemination (Kingdon, 2003) and the Knowledge to Action Framework (Graham et al., 2006).

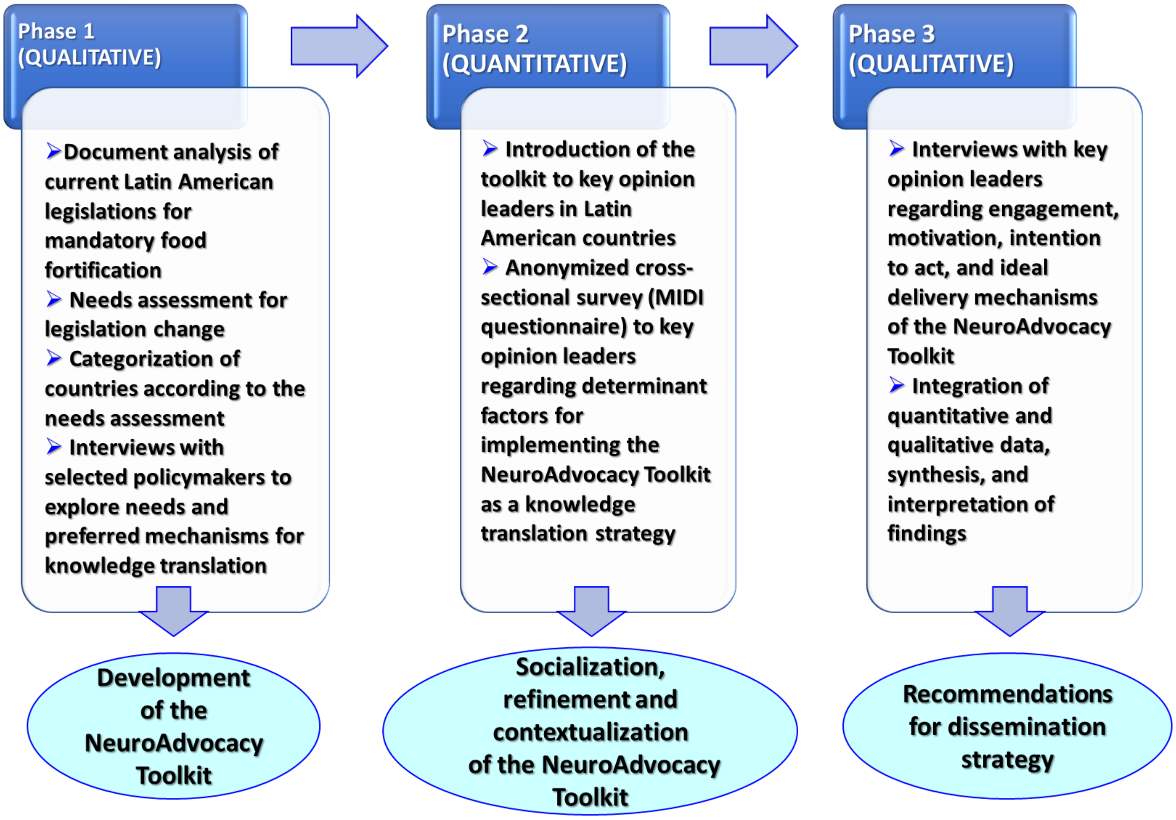
The study follows Maxwell’s interactive model for research design to align the theoretical framework with the goals, research question, and methodology (Maxwell, 2012). It generated trustworthy, credible, confirmable, and transferable data on effectively achieving knowledge translation mechanisms to decision-makers for adopting evidence-based policies to protect thousands of children from NTDs, as disabling but preventable conditions.

The central hypothesis of this study implies that diverse determinant factors can act as barriers and facilitators for developing and implementing the NeuroAdvocacy toolkit. Several factors described in the literature can be present in different degrees, or sometimes absent, according to specific contexts in which the innovation intends to promote change. Testing the hypothesis involved utilizing a validated instrument to identify influencing factors for implementing innovations. To explain the results generated by the quantitative assessment of determinant factors, phenomena such as motivation, engagement, and intention to broker knowledge to policymakers in Latin American countries are crucial for a deeper understanding of the role of KOL in implementing the NeuroAdvocacy Toolkit. Furthermore, the KOL perspectives and their attitudes towards advocacy, leadership, and lobbying constitute additional phenomena whose exploration provides insightful notions for future dissemination of the innovation. The combination of the data obtained from this study’s quantitative and qualitative inquiries addressed the factors influencing the implementation of the NeuroAdvocacy Toolkit and the development of a tailored dissemination strategy for approaching policymakers and calling them to action.

Research Procedures

The study comprised three sequential phases, illustrated in Figure 3.1. The three-phases layout proposes a logical sequence of the study's main activities and outputs.

Figure 3. 1 Phases, activities, and outputs of the study



Note: Ghotme, own work, created with SmartArt. MIDI: Measurement Instrument for Determinants of Innovations

Phase 1

In the first phase of the study, a document analysis provided factual data regarding the status and content of current legislation for MFF in the 20 Latin American countries, along with the local prevalence of NTD and nutritional situation. The data gathered were codified to explore common ground (or lack thereof) in terms of policies, followed by a needs assessment for regulatory change contextualized to each country.

Sampling. Phase 1 included documents from the 20 Latin American countries, including publicly available official documents about MFF policies, epidemiological data regarding the prevalence of NTDs, and national nutritional situation surveys to evaluate the MFF's status and perform the needs assessment for regulatory change.

Data collection. Document analysis provided data regarding the status and content of current legislation for MFF in Latin American countries concerning the nutritional practices and the prevalence of NTDs. Data were collected from three sources:

1) Public legislation records, repositories of the Food Fortification Initiative, and the Global Fortification Data Exchange were the primary sources of specific regulations regarding MFF.
2) Publicly available epidemiological data from official sites and peer-reviewed publications
3) Periodical results regarding the national nutritional situation for each country, when available

A data collection matrix/instrument in Excel helped to organize data and facilitate comparisons among regulations, epidemiological data, and nutritional situations.

Data analysis. The data gathered were codified to generate a needs assessment for regulatory change contextualized to each country. The needs assessment facilitated discerning which Latin American countries require modifications of current regulations to enhance MFF's reach, adoption, implementation, scaling-up, and sustainability.

According to the needs assessment, countries were classified into mutually exclusive categories reflecting the priority for regulatory change (See Chapter 4 for a detailed description of the categories and the criteria to allocate countries to each of them).

Output. This phase's output was the NeuroAdvocacy Toolkit's design and development as the innovative KT strategy. To include the voices of the innovation's target audience in designing the Toolkit, semi-structured interviews with pre-set topics were conducted with three selected policymakers to explore goals, expectations, and preferred mechanisms for knowledge translation. The interview protocol, whose topics were refined after the completion of the needs assessment, is presented in Appendix A.

Phase 2

For this quantitative phase, a cross-sectional survey was utilized to gather data from KOL at the national pediatric neurosurgery societies in Latin America regarding the determinants for implementing the NeuroAdvocacy Toolkit. The survey instrument was adapted from a published and validated questionnaire that evaluates the determinants for implementing innovations (Dugstad et al., 2014; Fleuren et al., 2014). The instrument is described in detail in the data collection subsection.

Sampling. This stage approached all Latin American pediatric neurosurgical societies, pediatric chapters of national neurosurgical associations, or organized groups of pediatric neurosurgeons through ASOLANPED, with a greater emphasis on those countries identified as having an urgent or high need for action, according to the needs assessment in Phase 1. The recruitment rate was 100% of the 20 pertaining societies. Purposive sampling aided in identifying one to three KOL per participating country among the executive boards of the neurosurgical societies. These participants were men and women, ages 35 to 75 years old, with postgraduate degrees, whom their peers identified as local KOL due to their experience, advocacy, leadership, and lobbying abilities. In total, the number of respondents for the survey was 30. As a preliminary step to data collection, the innovation, i.e., the NeuroAdvocacy Toolkit, was introduced and explained to the KOL at in-person and online scientific meetings held in Latin American countries.

Data collection. The second phase comprised gathering quantitative survey data via the online application of the Measurement Instrument for Determinants of Innovations (MIDI) questionnaire through SurveyMonkey®, an open-source software tool.

The MIDI maps the determinants that influence the use of innovation in practice (Fleuren et al., 2014). It originally started from 50 potentially relevant innovation determinants and initially focused on healthcare organizations. Further development and refinement of the instrument used a systematic review, a Delphi panel, and empirical studies, leading to 29 potential determinant factors classified into four categories according to their association with the innovation, the user, the organization, and the socio-political context (Fleuren et al., 2014; Fleuren et al., 2004). See Appendix B for a detailed description of the 29 determinant factors organized into four categories.

The MIDI, validated in languages such as Dutch, English, and Norwegian (Dugstad et al., 2014; Fleuren et al., 2013), offers a comprehensive framework and allows the quantification of the presence or absence of a determinant. The MIDI questionnaire was adapted and operationalized to fit the purposes of this study. Adaptations to the instrument were made in consultation with the author of the MIDI. Appendix B contains the operationalization and response scale for each determinant factor adapted for this study.

The questionnaire was translated into Spanish by a native speaker. The translated version of the questionnaire was assessed by a separate independent translator (who did not know the original text) and translated back into the original language. For reconciliation, the original text was compared with the back translation to look for potential issues where the meaning was confusing or slightly off, leading to a refined version of the questionnaire in Spanish. Afterward, it was validated and adjusted through pilot surveys with five experts in the field. The validated questionnaire was then pilot-tested on three respondents purposefully selected from Argentina, Colombia, and Costa Rica, looking for comprehensibility. Minor adjustments were made for clarity without affecting the meaning of statements or answers; therefore, the pilot survey data were included in the final quantitative analysis.

Data analysis. Data were processed in SPSS version 27. Descriptive analysis of the survey responses included frequency of responses for each factor and proportion of positive responses. For this study, ordinal variables (Likert scales) were considered positive when the participants predominantly selected the options “agree,” “completely agree,” or their equivalent. Only the “yes” option was considered a positive response for nominal variables. Although the MIDI questionnaire does not have a standard cut-off to establish how determinant a factor can be for a specific innovation, an 80/20 rule was applied to assess the answers based on previous experiences in the application and interpretation of the responses to the questionnaire (Fleuren, personal communication, 2020). If one specific factor had a percentage of agreement of less than 20% of the time, it was considered a barrier; explicit adjustment strategies must be placed to overcome that anticipated barrier to implementation. If another factor had a percentage of agreement of more than 80% of the time, it was considered a facilitator; no specific actions are needed to adjust the implementation strategy for that factor, or its presence could leverage implementation and dissemination plans. An individualized analysis was performed for factors with an agreement percentage between 20 and 80% and then considered potential barriers or facilitators. See Chapter 4 for a detailed explanation of the factors' assessment using the rule mentioned earlier.

Subsequently, the frequency of responses for each factor was organized in a joint display table according to the respondents' country in the categories elicited in Phase 1 related to the need for regulatory change. The table facilitated examining, on a granular level, potential differences between participants' responses, depending on the priorities for regulatory change in their countries. The analysis was conducted independently for each of the 29 factors in a descriptive way and was not inferential or hypothesis-driven.

Output. This phase resulted in the refinement of the NeuroAdvocacy Toolkit in response to the identified barriers and facilitators to the innovation by the KOL in a way that retains the core components but contains customizable components, adaptable to local contexts.

Phase 3

A multiple case study design was utilized for collecting and analyzing the data in this qualitative phase through interviews with the KOL. The instrumental multiple cases explored KOL's engagement, motivation, intention to act, and ideal delivery mechanisms of the NeuroAdvocacy Toolkit.

Sampling. For Phase 3, a new purposive sampling based on Phase 2 allowed selecting a representative group of KOLs for personal interviews, including at least one KOL per participating country. Participants were also men and women, ages 35 to 75 years old, with postgraduate degrees. Twenty-four interviews were conducted to reflect diverse perspectives on the phenomena evaluated.

Interview protocol development. The content of the interview protocol was grounded in the quantitative results of the study's second phase. The interview protocol, including the pre-set topics, is presented in Appendix C. The interview protocol was pilot-tested on one participant, purposefully selected from those who had completed the survey in Phase 2. Minor adjustments were made for clarity without affecting the meaning of pre-set topics or questions; therefore, the pilot interview data were included in the final qualitative analysis.

Data collection. The interview questions reflect pre-set topics focused on the central phenomena related to their perspectives on the factors influencing the implementation of the NeuroAdvocacy Toolkit. These phenomena included but were not limited to engagement, motivation, intention to act, and anticipated delivery mechanisms of the NeuroAdvocacy Toolkit. All interviews, which lasted approximately 20 to 30 minutes, were conducted online, in Spanish, through the Zoom® platform, except for an interviewee from one country where the platform use was unavailable due to national regulations. In this case, the interview was conducted through a WhatsApp® video call, and audio was recorded using a conventional recorder. All data were stored in a secure storage location.

Data analysis. The recorded interviews were transcribed verbatim through the Microsoft Office 360® transcription software. Data were analyzed and coded for thematic analysis of the participants' perspectives. The steps in the qualitative analysis based on Creswell & Plano Clark (2017) included:

1) Preliminary exploration of the data by reading through the transcripts
2) Coding the data by segmenting and labeling the text
3) Using codes to develop themes by aggregating similar codes together
4) Connecting and interrelating themes

5) Constructing a case narrative composed of descriptions and themes
6) Cross-case thematic analysis

The analysis was performed at two levels: within each case and across the cases (Creswell & Plano Clark, 2017). A matrix structured in terms of the themes, subthemes, codes, and representative verbatim participant's quotes was used for displaying and further developing the results in a way that reflected the qualitative data, including the verbatim quotes that addressed or supported those categories (Maxwell, 2012).

Memoing and bracketing procedures were used to mitigate the potentially deleterious effects of the researcher's preconceptions. Trustworthiness was secured by triangulating different sources of information, member checking, rich and thick descriptions of the cases, and reviewing and resolving disconfirming evidence.

Finally, quantitative and qualitative data were synthesized and integrated. A joint display table was developed to illustrate how the qualitative results (expressed in themes and direct quotes) enhance the quantitative results in terms of the most relevant determinant factors. The value added by the qualitative explanations was interpreted to provide a deeper understanding of the MIDI questionnaire findings and additional insights and nuances.

Output. This phase's output was a set of recommendations for the NeuroAdvocacy Toolkit's dissemination strategy, with fidelity to the core generalizable components and flexible elements tailored to participating countries.

Limitations of the Study

Some of the limitations of the proposed project included potential threats to internal and external validity. The first threat to internal validity is the lack of a comparison group; therefore, other events occurring within the study's timeframe may have generated the observed results (Portney, 2020). In this case, using a single group was justified because the study did not have an experimental manipulation. Instead, participants were approached in their natural setting. Finally, the results of this study are generalizable only to Latin American countries due to their unique social, cultural, and political reality.

There were also threats to trustworthiness, such as the risk of researcher bias for the investigator being part of the strategy as a researcher and, at the same time, an advocate participating in promoting policy implementation and dissemination. Therefore, it is essential not to consider the researcher’s influence as a problem but to understand it and use it productively (Maxwell, 2012). Bracketing procedures helped in mitigating this threat. Besides, there was a potential risk for KOL’s reactivity affecting their responses due to their awareness of being part of a study. However, reactivity can facilitate a deeper understanding of the phenomena studied and more relevant and actionable findings. Using multiple methods for data collection served to control threats to trustworthiness through triangulation, complementarity, and expansion procedures.

Since the surveys and interviews were conducted in Spanish and the results were processed, analyzed, and reported in English, there was a possibility of confusion, ambiguities, or errors arising from the nuances of language. Back translation and reconciliation procedures were performed to ensure quality, accuracy, and equivalence of meaning between the participants' answers and target texts. See the data collection subsections in this chapter for more details regarding the translation, back translation, and reconciliation procedures.

Human Participants and Ethics Precautions

The three stages of this study involved human participants who answered surveys and interviews as professional experts. Although they did not constitute a vulnerable population, and participation in the study involved no greater than minimal risk (under 45 CFR 46 / 21 CFR 56 regulations), respect for human subjects was granted throughout the study. Strict privacy and confidentiality measures were in place to protect anyone who might be identifiable. Therefore, the project was submitted through the GW Integrated Research Information Software (iRIS) and approved by The Office of Human Research (OHR) of the George Washington University for Institutional Review Boards review and monitoring (IRB# NCR203004, 03/22/2021).

Entering and remaining in the study was entirely voluntary to ensure participants' autonomy, and refusal to participate did, by no means, affect the participants' status regarding their relationship with ASOLANPED, their national neurosurgical organization, or their activities in clinical practice.

From a justice standpoint, successful strategies to prevent NTDs decrease inequities, improve the health status of their communities, and promote the protection of vulnerable children from these disabling but preventable conditions.

Risks and benefits

Participants may have benefited from receiving updated information on NTDs and effective ways to prevent them, as well as training in knowledge translation strategies that might, in turn, have led to boosting their advocacy and leadership in promoting health and preventing conditions related to the field. There was no material compensation for participating in this study, but the research budget covered expenses caused by attending the study activities. This study involved no physical harm to participants; however, the surveys and interviews required dedicated time (approximately 10 minutes for the online survey and 20 minutes for a remote interview) and had the potential to elicit feelings of discomfort. Additionally, some participants might have hesitated to expose their opinions due to fear of stigma or discrimination based on the specific situation of their countries in terms of legislation to prevent NTDs or sociopolitical context.

Privacy and confidentiality

Privacy and confidentiality were ensured continuously during the recruitment and further phases of the study, and data protection complied with the United States and local Latin American regulations. The surveys were anonymized to protect participants' privacy. For the interviews, the names were replaced with a consecutive alphanumeric code on all study materials, and all identifiable information was removed from the study formats. All study information was stored securely in a locked cabinet and a password-protected file in a computer that was only accessible to authorized research personnel. Once the study finished, records containing personal information were deleted or shredded. Any information about individuals' research involvement will not be disclosed without written permission unless required by law. The study results published in scientific meetings or journals might contain identifying information about the participating countries but no identifiable data pertaining to individuals.

Participants were instructed not to discuss their answers or results with other participants. However, non-identifiable participants' answers obtained during the study's second phase were disclosed in the qualitative phase for explanatory purposes during the interviews. Only the audio part of the interviews was sent to the transcription service. Recordings will not be used in presentations or for any reason other than data analysis. When reporting the results, any direct quotes were attributed to pseudonyms.

Informed consent and potential challenges

A separate informed consent form per phase was available through online software tools. An introductory page contained all the information and included the option for clicking agreement and electronic signature. Participants could also accept or decline being contacted for further follow-up interviews or verification procedures. Records of the agreement were kept electronically and were stored securely in a password-protected file on a computer that is only accessible to authorized research personnel.

Potential challenges were considered during the informed consent process, including a limited understanding of the research’s implications. Participants received understandable language information and visual aids when needed to mitigate this challenge. Knowledge verification was encouraged before signing the consent form. For any questions or concerns raised by participants regarding the study, the student researcher was available synchronously (by chat) at predetermined timeframes and asynchronously (by e-mail).

Chapter 4: Results

This study used a mixed-method explanatory sequential design to describe the factors contributing to developing and implementing a KT strategy to influence policymakers regarding MFF to prevent NTDs in Latin American countries. The main results of the three phases, including the toolkit development, are presented sequentially, followed by an integration of the quantitative and qualitative data.

Phase 1: Status of MFF Legislation in Latin America and Need for Regulatory Change

A thorough document analysis led to identifying the regulatory status of MFF for the 20 Latin American countries and categorizing them according to the needs assessment for regulatory change. This categorization pondered five factors: prevalence of NTDs, coverage of current fortification regulations, the fortification standard in those regulations, the daily intake of non-fortified cereals, and the percentage of industrialization of the main cereal grains. Each factor was pondered in a range from zero to three points to determine the level of priority by which a country requires to update and optimize regulations for mandatory fortification (Table 4.1). The lower the score, the higher the need for regulatory change.

The scores for each domain were estimated in comparable intervals. For instance, for the NTD prevalence domain, the maximum score was given to the lowest prevalence achieved with MFF policies (five cases or less per 10,000 live births) (CDC, 2020c, 2020a), and the subsequent scores were allocated in groups of five.

Table 4. 1 Priority for regulation change ponderation scale

ASPECT	POINTS
NTD PREVALENCE (per 10,000 live births)	
Prevalence > or = 20	0
Prevalence between 11 and 19	1
Prevalence between 6 and 10	2
Prevalence < or = 5	3
MANDATORY FORTIFICATION, INCLUDING FOLIC ACID	
No mandatory fortification in place including folic acid	0
Mandatory fortification of 1 staple food	1
Mandatory fortification of 2 staple foods	2
Mandatory fortification of 3 staple foods	3
FOLIC ACID CONCENTRATION IN FORTIFICATION STANDARD	
No folic acid in the fortification standard	0
Folic acid below the recommended standard (<5 mg/kg)	1
Folic acid standard between 0.5 and 1 mg/kg	2
Folic acid standard between 1.1 and 2 mg/kg	3
CEREAL GRAIN DAILY INTAKE (WHEAT, CORN, RICE) IN GRAMS/PER CAPITA/PER DAY	
Daily intake of non-fortified food > or = 200	0
Daily intake of non-fortified food between 101 to 199	1
Daily intake of non-fortified food between 51 to 100	2
Daily intake of non-fortified food < or = 50 or fortification in place	3
INDUSTRIALIZATION PERCENTAGE (PER TYPE OF CEREAL GRAIN)	
Percentage of reported industrialized food processing 0-30%	0
Percentage of reported industrialized food processing 31-60%	1
Percentage of reported industrialized food processing 61-90%	2
Percentage of reported industrialized food processing 91-100%	3

This ponderation led to establishing four levels of priority in acting to change regulations:

Priority 1 (0 to 5 points): Urgent need for regulatory change

Priority 2 (5.1 to 10 points): High need for regulatory change

Priority 3 (10.1 to 14.9 points): Medium need for regulatory change

Priority 4 (15 points): No need for regulatory change

Table 4.2 displays the needs assessment results for every country with the granular detail of the five domains leading to the individual scores. Dominican Republic, Haiti, Peru, and Venezuela require urgent regulatory changes to effectively fortify staple food with folic acid (Priority 1). Fourteen countries have a high need for regulatory change; this group includes Argentina, Bolivia, Brazil, Colombia, Chile, Cuba, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Paraguay, and Uruguay (Priority 2), whereas Panama was categorized in Priority 3 with a medium need for regulatory change. Only one country, Costa Rica, was classified in Priority 4 with no need for regulatory change since it has extensive coverage of fortification of staple foods with folic acid with the recommended standards and the region’s minimum prevalence of NTDs achievable with this policy.

Table 4. 2 Priorities for regulation change in Latin American countries according to the needs assessment

COUNTRIES	NTDs PREVALENCE	MANDATORY FORTIFICATION	FOLIC ACID CONCENTRATION IN FORTIFICATION STANDARD				CEREAL GRAIN DAILY INTAKE				INDUSTRIALIZATION PERCENTAGE PER CEREAL GRAIN				TOTAL POINTS	PRIORITY IN REGULATORY CHANGE
			Wheat flour	Maize flour	Rice	Average	Wheat flour	Maize flour	Rice	Average	Wheat flour	Maize flour	Rice	Average		
Argentina	1	1	3	0	0	1.0	3	3	3	3.0	3	3	3	3.0	9.0	2- High need
Bolivia	1	1	3	0	0	1.0	3	1	1	1.7	2	0	0	0.7	5.3	2- High need
Brazil	0	2	3	3	0	2.0	3	3	1	2.3	3	3	3	3.0	9.3	2- High need
Chile	2	1	3	0	0	1.0	3	2	3	2.7	3	0	0	1.0	7.7	2- High need
Colombia	2	1	3	0	0	1.0	3	2	1	2.0	3	0	2	1.7	7.7	2- High need
Costa Rica	3	3	3	3	3	3.0	3	3	3	3.0	3	3	3	3.0	15.0	4- No need
Cuba	2	1	3	0	0	1.0	3	2	0	1.7	3	0	0	1.0	6.7	2- High need
Dominican Republic	1	1	3	0	0	1.0	3	3	0	2.0	0	0	0	0.0	5.0	1- Urgent need
Ecuador	2	1	3	0	0	1.0	3	1	1	1.7	3	0	0	1.0	6.7	2- High need
El Salvador	2	2	3	2	0	1.7	3	3	3	3.0	3	0	0	1.0	9.7	2- High need
Guatemala	0	2	1	3	0	1.3	1	3	3	2.3	0	0	0	0.0	5.7	2- High need
Haiti	1	0	0	0	0	0.0	2	2	1	1.7	3	0	0	1.0	3.7	1- Urgent need
Honduras	1	1	3	0	0	1.0	3	0	2	1.7	3	0	0	1.0	5.7	2- High need
Mexico	1	2	3	3	0	2.0	3	3	3	3.0	3	1	0	1.3	9.3	2- High need
Nicaragua	2	2	3	0	2	1.7	3	1	3	2.3	3	0	0	1.0	9.0	2- High need
Panama	2	2	3	0	2	1.7	3	2	3	2.7	3	0	3	2.0	10.3	3- Medium need
Paraguay	2	1	3	0	0	1.0	3	1	3	2.3	3	0	3	2.0	8.3	2- High need
Peru	0	1	3	0	0	1.0	3	2	0	1.7	0	0	0	0.0	3.7	1- Urgent need
Uruguay	1	1	3	0	0	1.0	3	2	3	2.7	3	0	1	1.3	7.0	2- High need
Venezuela	1	0	0	0	0	0.0	1	1	2	1.3	3	0	0	1.0	3.3	1- Urgent need

Toolkit Development

The scientific literature, data on the current status of MFF policies in Latin America, the needs assessment, and voices from the target audience informed the NeuroAdvocacy Toolkit development and its core components. This last interaction with the target audience as future knowledge users occurred through semi-structured interviews with three policymakers purposefully selected in Colombia, Chile, and Costa Rica. The interviews conducted in this phase had an exploratory purpose. Participants reviewed the toolkit drafts, suggested adjustments, and discussed preferred knowledge transfer and utilization mechanisms.

Drawing from the interview data, Table 4.3 summarizes the conventional sources of information that policymakers and their teams seek when guiding their decisions based on scientific evidence, the main challenges in gathering information or using the knowledge obtained, and the mechanisms they foresee could help to overcome those challenges.

The interviewees also discussed their preferred mechanisms for receiving and using knowledge to inform their decisions about adopting or implementing public policies. They highlighted the need to access scientific evidence, the essential role of experts in a particular field in translating that evidence, and how a toolkit like the one proposed to them in this stage could accelerate knowledge comprehensibility and utilization.

Table 4. 3 Conventional sources of information, challenges, and strategies for knowledge utilization according to selected policymakers interviewed in Phase 1

CONVENTIONAL SOURCES OF INFORMATION	USUAL CHALLENGES	POTENTIAL STRATEGIES TO OVERCOME CHALLENGES
Health bulletins from supranational organizations	**Reluctance to adapt to local contexts, other priorities**	**Access to knowledge translation mechanisms/generate awareness**
Government agencies	**Bureaucracy**	**Generate awareness, enhance national registries**
Expert advisor committee	**Different priorities/agenda**	**Advocacy/lobbying/ awareness**
Scientific journals, databases	**Language barriers, excessively technical information, time-consumption**	**Access to knowledge translation mechanisms**

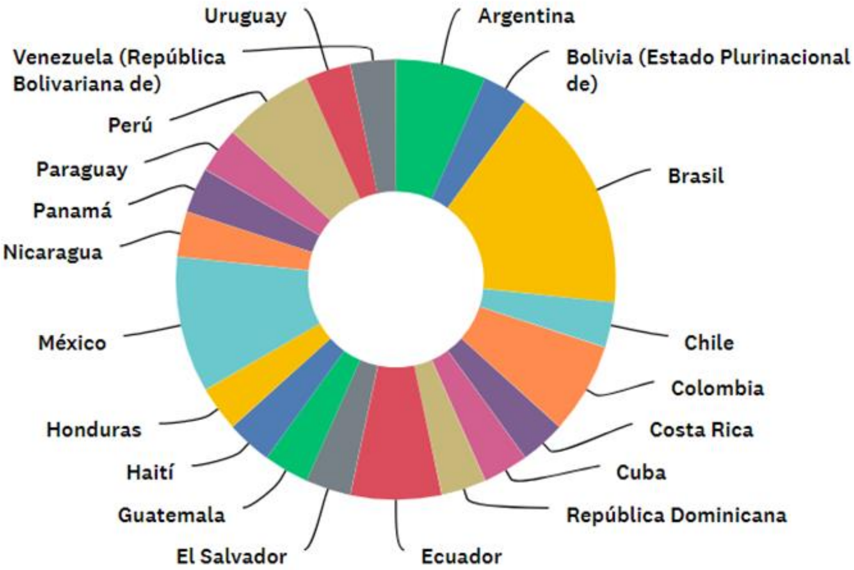
The toolkit, designed in a visually appealing format, includes a slide deck to present a five-minute “elevator pitch” before policymakers, containing critical facts, data, and an interactive map illustrating each country’s legislation status and need for regulatory change. It ends with a call to action to update, scale up, implement, ensure sustainability, and optimize surveillance of fortification policies with folic acid. The toolkit’s second piece is a printable infographic sheath summarizing the pitch deck's information, highlighting a call to action. The third element is an evidence brief that organizes some of the best scientific data in a visual and interactive format for a quick consult, with hyperlinks that give free access to the full-text Pdf articles. The last toolkit component summarizes successful legislations from Costa Rica and the United States as reliable models of complete and adequate coverage of the fortification of cereal grains and the lowest prevalence of NTDs achievable with these policies. Current toolkit elements are presented in Spanish, the native language of the innovation's intended users and target audience; nevertheless, it is customizable for English, Portuguese, and French versions.

The four pieces constituting the Toolkit can be consulted and downloaded free of charge at www.neuroadvocacy.info, a web page specifically created for this purpose. After obtaining official endorsement by ASOLANPED, the toolkit was introduced to an estimated 270 Latin American pediatric neurosurgeons, residents, and fellows at in-person scientific meetings held in Mexico, Ecuador, Peru, and Brazil. Additionally, it was introduced through several virtual meetings to another 325 pediatric neurosurgeons practicing in 20 Latin American countries.

Phase 2: Quantitative Strand

After being introduced to the NeuroAdvocacy Toolkit, 30 KOL (22 men and eight women, aged 35 to 75) responded to the survey using the MIDI questionnaire. The recruitment rate for this phase was 94%, and the response rate was 100%. Participants from the 20 Latin American countries were included, with a greater representation of those with a larger community of pediatric neurosurgeons, such as Brazil or Mexico (Figure 4.1).

Figure 4. 1 Distribution of the survey respondents' countries of practice



Participants' responses were tabulated, and the percentage of positive responses was calculated for each factor independently. For this study, ordinal variables (Likert scales) were considered positive when the participants predominantly selected the options "agree," "completely agree," or their equivalent. Only the "yes" option was considered a positive response for nominal variables. An 80/20 rule was applied to assess the answers. If one specific factor had a percentage of agreement of less than 20% of the time, it was considered a barrier; explicit adjustment strategies must be placed to overcome that anticipated barrier to implementation. If another factor had a percentage of agreement of more than 80% of the time, it was considered a facilitator; no specific actions are needed to adjust the implementation strategy for that factor, or its presence could leverage implementation and dissemination plans. An individualized analysis was performed for factors with an agreement percentage between 20 and 80%, which were considered either potential barriers or facilitators. For factors 4 (complexity) and 26 (unsettled organization), the rule was applied inversely since those factors are expected to behave as usual barriers to implementation, i.e., the lower the percentage of agreement, the lower the need to implement specific actions to overcome these factors.

First category: determinants associated with the innovation.

Answers in this category were homogeneous. Responses consistently allowed classifying all factors associated with the Toolkit as implementation facilitators (Table 4.3). Therefore, no specific actions are required to adjust the implementation strategy for these seven factors, and the Toolkit attributes could leverage implementation and dissemination plans.

Table 4. 4 Determinant factors in implementing the NeuroAdvocacy Toolkit associated with the innovation

Determinants associated with the innovation				
Determinant	**Name**	**Description**	**Percentage of agreement**	**Type of factor**
1	**Procedural clarity**	The extent to which the innovation is described in clear steps/procedures	93.3%	Facilitator
2	**Correctness**	The degree to which the innovation is based on factually correct knowledge	93.3%	Facilitator
3	**Completeness**	The degree to which the activities described in the innovation are complete	96.7%	Facilitator
4	**Complexity**	The degree to which the implementation of the innovation is complex	3.3%	Facilitator
5	**Compatibility**	The degree to which the innovation is compatible with the	100%	Facilitator

		values and working method in place		
6	**Observability**	Visibility of the outcomes for the user	93.3%	Facilitator
7	**Relevance for client**	The degree to which the user believes the innovation is relevant for policymakers	100%	Facilitator

Note: For factor 4, the percentage of agreement was considered inversely since it is expected to behave as a barrier to implementation (the lower the agreement percentage, the lower the need to implement specific actions to overcome this factor)

Second category: determinants associated with the user

Responses in this category were also homogeneous. Participants' answers consistently allowed classifying all factors associated with the user as facilitators of implementation (Table 4.4). Therefore, no specific actions are required to adjust the implementation strategy for these 11 factors, and the intended users' knowledge, attitudes, and beliefs could leverage implementation and dissemination plans.

Table 4. 5 Determinant factors in implementing the NeuroAdvocacy Toolkit associated with the user (key opinion leaders)

Determinants associated with the user				
Determinant	**Name**	**Description**	**Percentage of agreement**	**Type of factor**
8	**Personal benefits/drawbacks**	The degree to which using the innovation has advantages or disadvantages for the users themselves	92%	Facilitator
9	**Outcome expectations**	Perceived probability and importance of	100%	Facilitator

		achieving the client objectives as intended by the innovation		
10	**Professional obligation**	The degree to which the innovation fits in with the tasks for which the user feels responsible when doing their work	96.3%	Facilitator
11	**Client satisfaction**	The degree to which the user expects policymakers to be satisfied with the innovation	100%	Facilitator
12	**Client cooperation**	The degree to which the user expects policymakers to cooperate with the innovation	93.3%	Facilitator
13	**Social support**	Support experienced or expected by the user from important social referents relating to the use of the innovation (for example, from colleagues, other professionals they work with, heads of department, or management)	90.0%	Facilitator
14	**Descriptive norm**	Colleagues' observed behavior: the degree to which colleagues use the innovation	93.3%	Facilitator
15	**Subjective norm**	The influence of important others on the use of the innovation	83.3%	Facilitator
16	**Self-efficacy**	The degree to which the user believes they can implement the activities involved in the innovation	100%	Facilitator

17	**Knowledge**	The degree to which the user has the knowledge needed to use the innovation	90.0%	Facilitator
18	**Awareness of content of innovation**	The degree to which the user has learned about the content of the innovation	96.7%	Facilitator

Third category: determinants associated with the organization (national neurosurgical societies and ASOLANPED)

Responses in this category were heterogeneous (Table 4.5). Participants' answers led to classifying factors 19 (the absence of formal ratification by management) and 25 (the lack of designation of a coordinating individual or group) as barriers to implementing the innovation. Since ASOLANPED has officially endorsed the initiative, specific action is needed to adjust the implementation strategy for these two factors targeting the national neurosurgical associations. The remaining eight factors are either facilitators or potential facilitators, requiring minimum adjustments, if any, to take advantage of them to leverage implementation and dissemination plans.

Table 4. 6 Determinant factors in implementing the NeuroAdvocacy Toolkit associated with the organization (national neurosurgical societies and ASOLANPED)

Determinants associated with the organization				
Determinant	**Name**	**Description**	**Percentage of agreement**	**Type of factor**
19	**Formal ratification by management**	Formal ratification of the innovation by management, for example, by including the use of the innovation in policy documents	16.7%	Barrier

20	**Replacement when staff leave**	Continuity of policies and initiatives despite staff transitioning the organization	70%	Potential facilitator
21	**Staff capacity**	Adequate staffing in the department or in the organization where the innovation is being used	70%	Potential facilitator
22	**Financial resources**	Availability of financial resources needed to use the innovation	73.4%	Potential facilitator
23	**Time available**	Amount of time available to use the innovation	76.7%	Potential facilitator
24	**Material resources and facilities**	Presence of materials and other resources or facilities necessary for the use of the innovation as intended (such as equipment, materials, or space)	73.4%	Potential facilitator
25	**Coordinator**	The presence of one or more persons responsible for coordinating the implementation of the innovation in the organization	13.3%	Barrier
26	**Unsettled organization**	The degree to which there are other changes in progress (organizational or otherwise) that represent obstacles to the process of implementing the innovation, such as re-organizations, mergers, cuts, staffing changes, or the simultaneous implementation of different innovations	6.7%	Facilitator

27	**Information accessible about the use of innovation**	Accessibility of information about the use of the innovation	70%	Potential facilitator
28	**Performance feedback**	Feedback to the user about progress with the innovation process	63.3%	Potential facilitator

Note: For factor 26, the percentage of agreement was considered inversely since it is expected to behave as a barrier to implementation (the lower the agreement percentage, the lower the need to implement specific actions to overcome this factor)

Fourth category: determinant associated with the socio-political context

Most respondents considered that the innovation fits in with existing legislation and regulations established by the competent authorities in Latin America (Table 4.6). Therefore, no specific actions are required to adjust the implementation strategy for factor 29, which could actually leverage implementation and dissemination plans.

Table 4. 7 Determinant factor in implementing the NeuroAdvocacy Toolkit associated with the Latin American socio-political context

Determinant associated with the socio-political context				
Determinant	**Name**	**Description**	**Percentage of agreement**	**Type of factor**
29	**Legislation and regulations**	The degree to which the innovation fits in with existing legislation and regulations established by the competent authorities	83.3%	Facilitator

Determinant factors according to country categories

After analyzing data from all respondents respective to each factor, the frequency of positive responses was organized in a joint display table according to the respondents' country location in the four priorities elicited in Phase 1: no need, medium need, high need, and urgent need for regulatory change (Table 4.7). The table facilitated examining, on a granular level, potential trends between participants' responses, depending on the priorities for regulatory change in their countries. The analysis was conducted independently for each of the 29 factors and was not inferential or hypothesis-driven. This descriptive analysis applies only to the respondents included in the study and their respective countries.

The factors associated with the innovation, user, and socio-political context were consistently facilitators for all country categories. In contrast, factors associated with the organization showed a more heterogeneous pattern, especially for factors 23 (time availability), 24 (availability of material resources and facilities), and 28 (performance feedback). This heterogeneity in the response pattern was found in the countries of categories 2 (high need for regulatory change) and 3 (medium need for regulatory change), although this last category corresponds to only one participant.

Table 4. 8 Determinant factors in implementing the NeuroAdvocacy Toolkit according to country categories for priority in regulatory change

Frequency of positive responses according to country category	DETERMINANT FACTORS																												
	Associated with the innovation (NeuroAdvocacy Toolkit)							Associated with the user (key opinion leaders)											Associated with the organization (national neurosurgical organization and ASOLANPED)										Associated with socio-political context
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Priority 1: Urgent need (n=5)	5	5	5	0	5	5	5	4	5	5	5	5	4	5	4	5	5	5	1	5	5	5	5	5	2	1	4	4	4
Priority 2: High need (n=23)	22	21	22	1	23	22	23	22	23	23	23	22	22	22	18	23	20	22	3	15	15	17	17	16	4	0	18	18	21
Priority 3: Medium need (n=1)	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	0	0	0	1	0	1
Priority 4: No need (n=1)	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1

Note: ordinal variables (Likert scales) were considered positive when the participants predominantly selected the options "agree," "completely agree," or their equivalent. Only the "yes" option was considered a positive response for nominal variables. For factors 4 and 26, the response was considered inversely since they usually behave as barriers to implementation (the lower the the number of positive responses, the lower the need to implement specific actions to overcome this factor).

Color code:

Facilitator
Potential facilitator
Potential barrier
Barrier

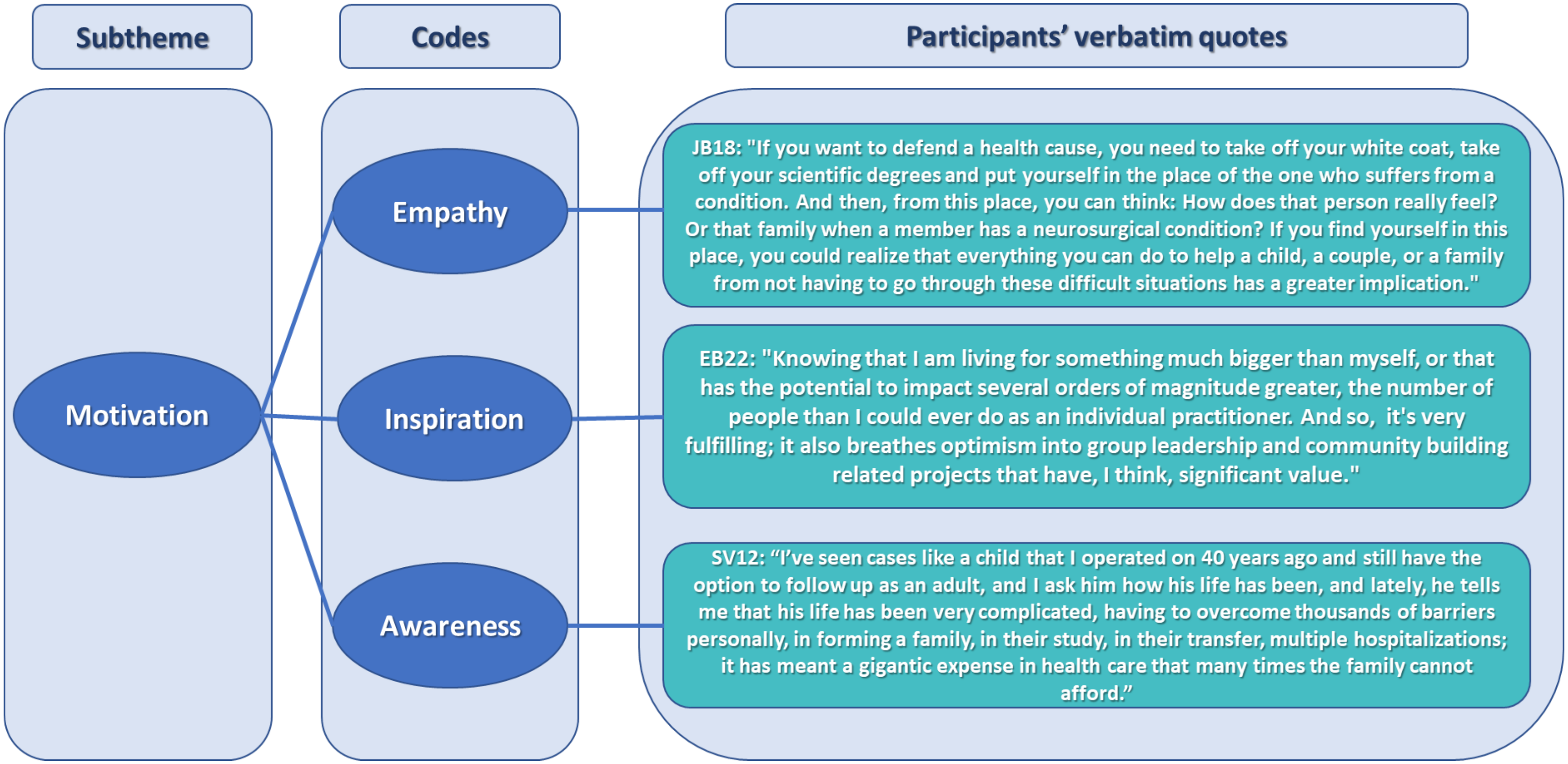
Phase 3: Qualitative Strand

Twenty-four KOL purposefully selected from the survey respondents (16 men and eight women, aged 35 to 75) participated in online semi-structured interviews (recruitment rate 100%, response rate 100%). Again, participants from the 20 Latin American countries were included, with a greater representation of Brazil and Mexico for having a larger community of pediatric neurosurgeons. The qualitative data yielded three themes, nine subthemes, and 34 codes describing the attitudes toward using the Toolkit, the ideal delivery strategies to policymakers, and how to face potential challenges during the implementation and dissemination process effectively.

Theme 1: Attitudes toward using the toolkit

Participants in this phase richly described their attitudes toward using the NeuroAdvocacy Toolkit as an innovative KT strategy to approach policymakers in their own countries. Four subthemes (motivation, engagement, intention to act, and potential drawbacks) grouped 11 codes representing these attitudes. Most participants expressed positive and proactive attitudes toward brokering knowledge to policymakers, including empathy, inspiration, awareness, confidence, gratification, commitment, emulation, and readiness (Figures 4.2, 4.3, and 4.4). These phenomena are congruent with the determinants associated with the toolkit and the intended users reflected in the MIDI questionnaire. Nonetheless, some participants also expressed a few potential drawbacks regarding their future involvement in using the toolkit, including hesitation due to time constraints or the need to prioritize clinical practice, inertia or apathy, and potential frustration from poor policymakers' attention to the initiative (Figure 4.5). Although these potential drawbacks were not evident in the quantitative phase, they represent real-life scenarios when it comes to putting the innovation into action.

Figure 4. 2 Theme 1: Attitudes toward using the NeuroAdvocacy Toolkit. Subtheme 1: Motivation

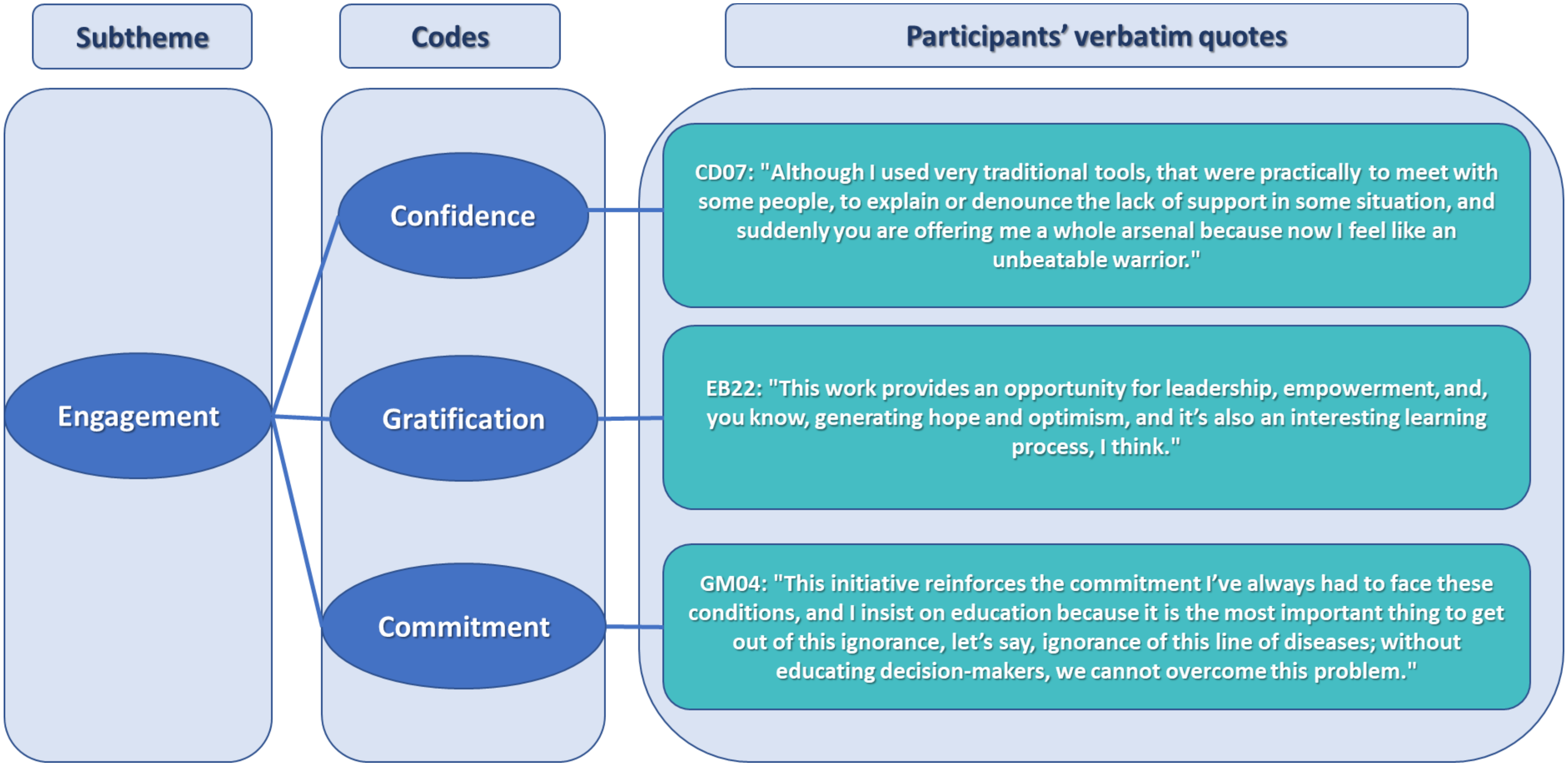


JB18: "If you want to defend a health cause, you need to take off your white coat, take off your scientific degrees and put yourself in the place of the one who suffers from a condition. And then, from this place, you can think: How does that person really feel? Or that family when a member has a neurosurgical condition? If you find yourself in this place, you could realize that everything you can do to help a child, a couple, or a family from not having to go through these difficult situations has a greater implication."

EB22: "Knowing that I am living for something much bigger than myself, or that has the potential to impact several orders of magnitude greater, the number of people than I could ever do as an individual practitioner. And so, it's very fulfilling; it also breathes optimism into group leadership and community building related projects that have, I think, significant value."

SV12: "I've seen cases like a child that I operated on 40 years ago and still have the option to follow up as an adult, and I ask him how his life has been, and lately, he tells me that his life has been very complicated, having to overcome thousands of barriers personally, in forming a family, in their study, in their transfer, multiple hospitalizations; it has meant a gigantic expense in health care that many times the family cannot afford."

Figure 4. 3 Theme 1: Attitudes toward using the NeuroAdvocacy Toolkit. Subtheme 2: Engagement

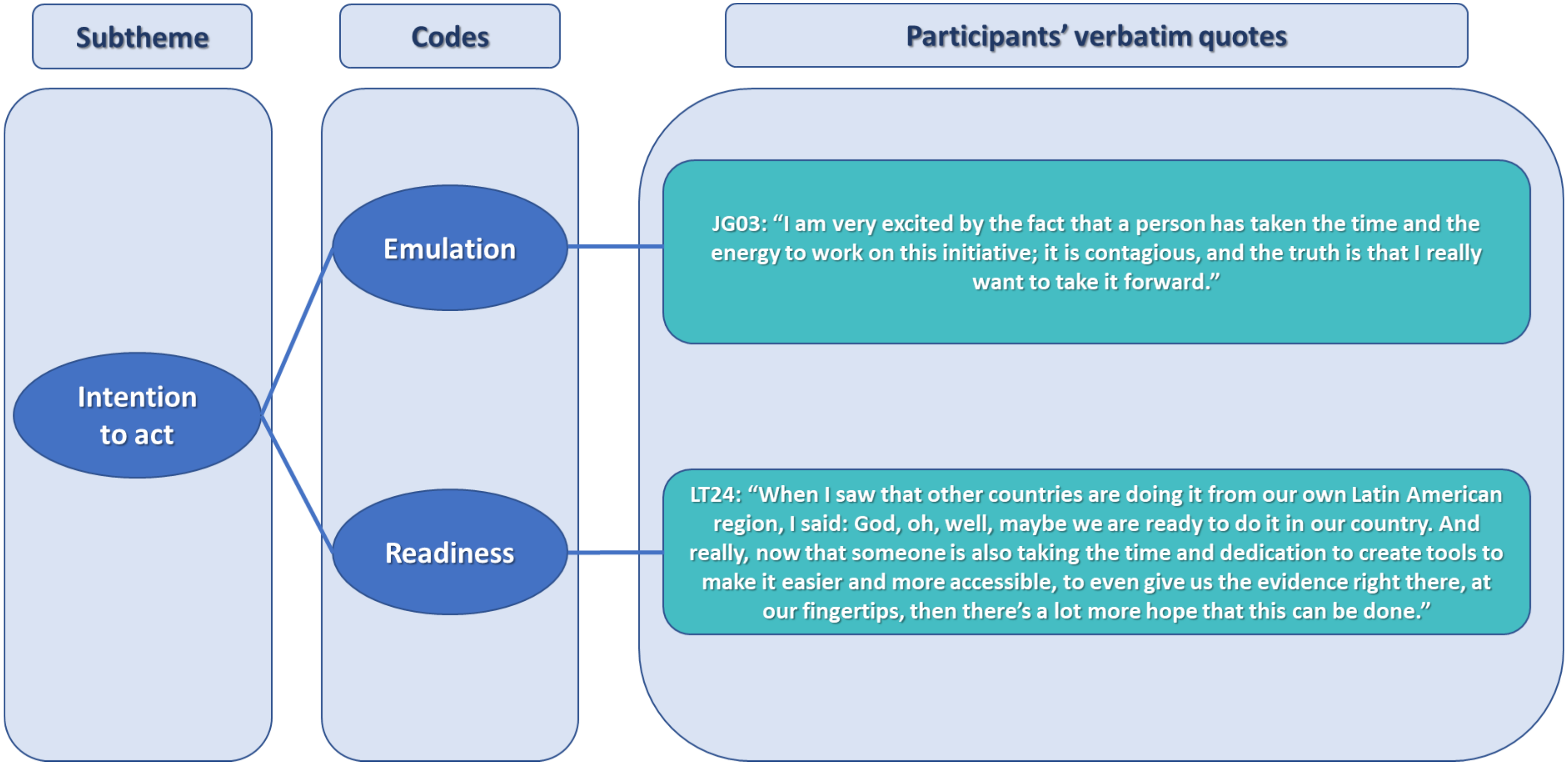


CD07: "Although I used very traditional tools, that were practically to meet with some people, to explain or denounce the lack of support in some situation, and suddenly you are offering me a whole arsenal because now I feel like an unbeatable warrior."

EB22: "This work provides an opportunity for leadership, empowerment, and, you know, generating hope and optimism, and it's also an interesting learning process, I think."

GM04: "This initiative reinforces the commitment I've always had to face these conditions, and I insist on education because it is the most important thing to get out of this ignorance, let's say, ignorance of this line of diseases; without educating decision-makers, we cannot overcome this problem."

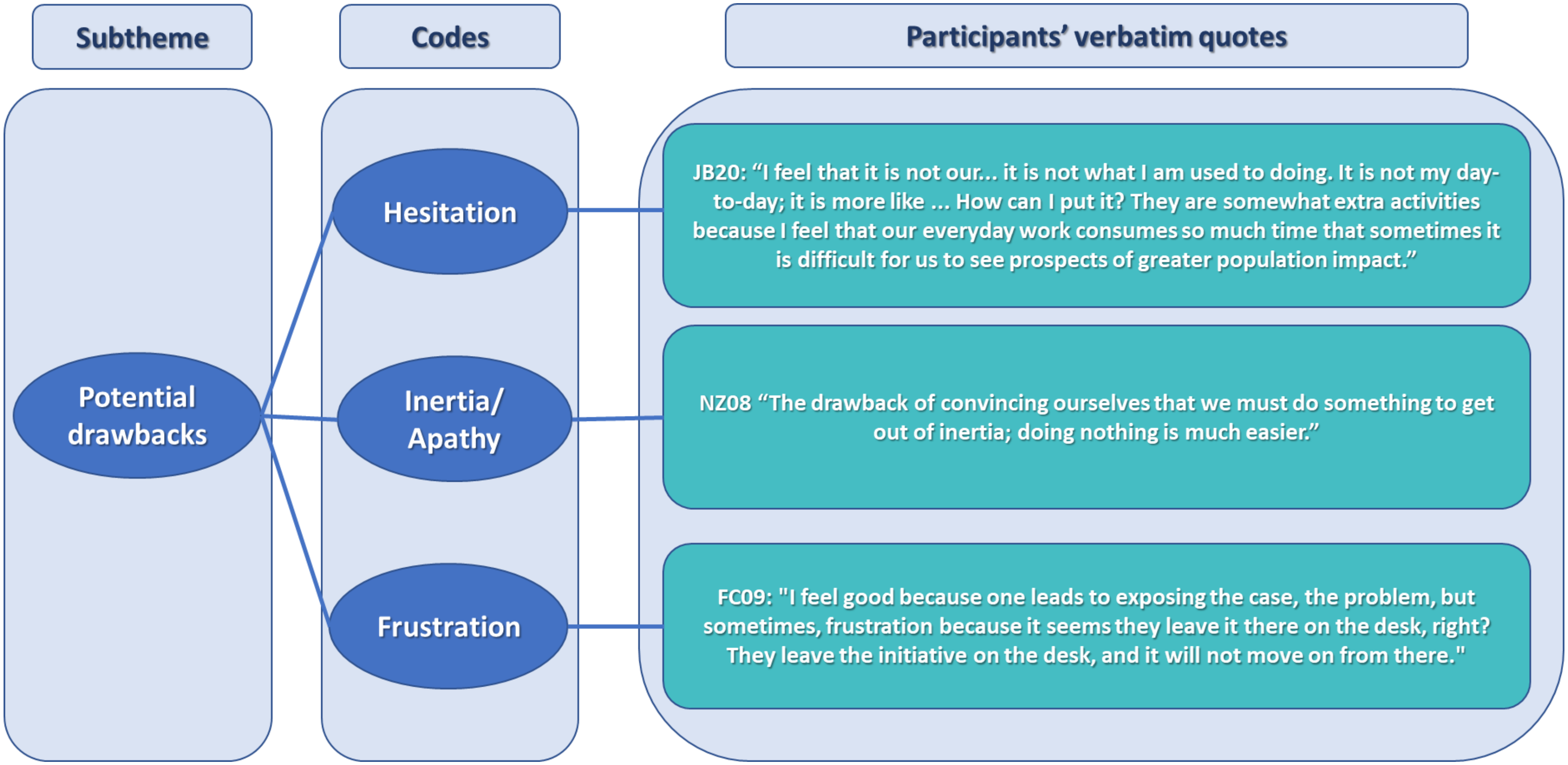
Figure 4. 4 Theme 1: Attitudes toward using the NeuroAdvocacy Toolkit. Subtheme 3: Intention to act



JG03: "I am very excited by the fact that a person has taken the time and the energy to work on this initiative; it is contagious, and the truth is that I really want to take it forward."

LT24: "When I saw that other countries are doing it from our own Latin American region, I said: God, oh, well, maybe we are ready to do it in our country. And really, now that someone is also taking the time and dedication to create tools to make it easier and more accessible, to even give us the evidence right there, at our fingertips, then there's a lot more hope that this can be done."

Figure 4. 5 Theme 1: Attitudes toward using the NeuroAdvocacy Toolkit. Subtheme 4: Potential drawbacks



JB20: "I feel that it is not our... it is not what I am used to doing. It is not my day-to-day; it is more like ... How can I put it? They are somewhat extra activities because I feel that our everyday work consumes so much time that sometimes it is difficult for us to see prospects of greater population impact."

NZ08 "The drawback of convincing ourselves that we must do something to get out of inertia; doing nothing is much easier."

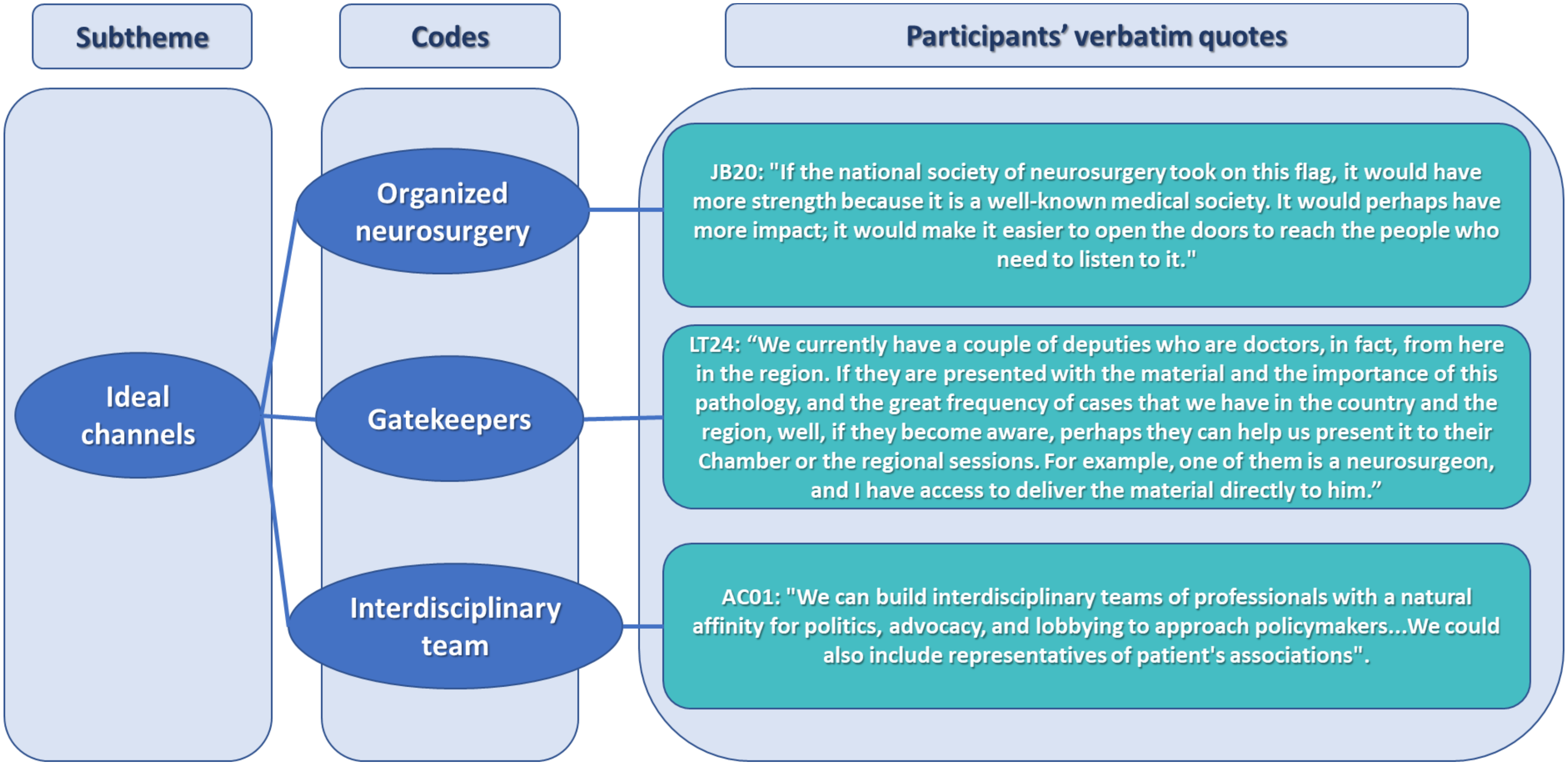
FC09: "I feel good because one leads to exposing the case, the problem, but sometimes, frustration because it seems they leave it there on the desk, right? They leave the initiative on the desk, and it will not move on from there."

Theme 2: Strategies to deliver the NeuroAdvocacy Toolkit to policymakers

The interviewees, positioned as KOL, discussed the ideal mechanisms by which they could deliver the toolkit more effectively. Three subthemes (ideal channels, initial approaches, and follow-up strategies) grouped nine codes representing these mechanisms.

The figure of a gatekeeper (personal contacts, intermediaries, colleagues working on the policymaker role) was preeminent, as well as the idea of using collective efforts of organized neurosurgery and interdisciplinary teams to move the initiative forward and not as an individual quest (Figure 4.6). For the initial approach, there was consensus among participants that organizing an in-person meeting with policymakers or their delegates would be more impactful than making the first interaction virtually. Although they recognize the value of online platforms, especially in post-pandemic times, participants do not prefer virtual meetings, e-mails, or sharing digital material without a previous in-person meeting for the initial knowledge translation moment with policymakers. Most interviewees see virtual meetings as having a role in follow-up sessions (Figure 4.7). Participants pointed out systematic, continuous, and persuasive follow-up strategies to increase the probabilities of policymakers' knowledge use and intention to act (Figure 4.8).

Figure 4. 6 Theme 2: Delivery strategies of the Toolkit to policymakers. Subtheme 5: Ideal channels

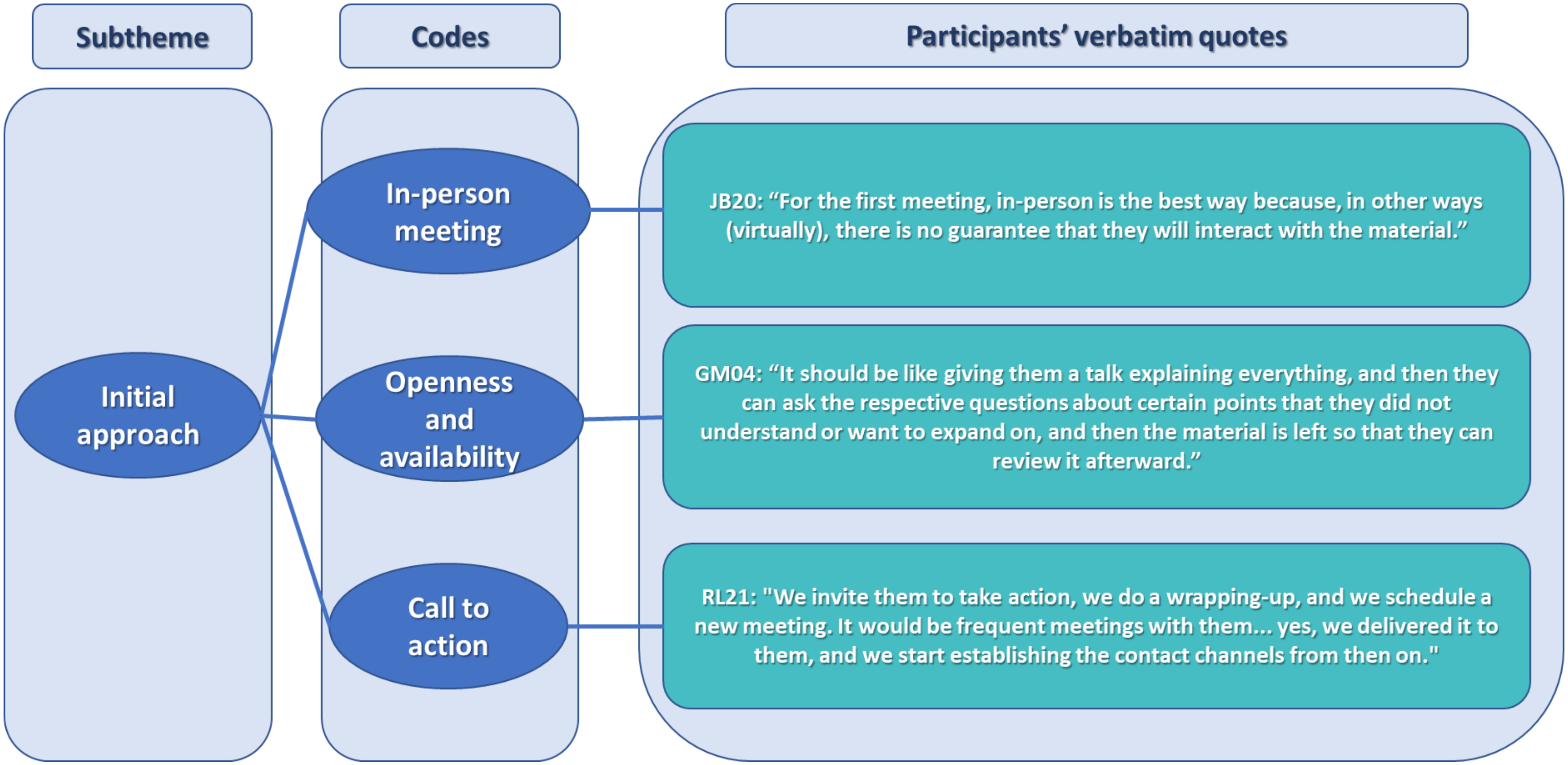


JB20: "If the national society of neurosurgery took on this flag, it would have more strength because it is a well-known medical society. It would perhaps have more impact; it would make it easier to open the doors to reach the people who need to listen to it."

LT24: “We currently have a couple of deputies who are doctors, in fact, from here in the region. If they are presented with the material and the importance of this pathology, and the great frequency of cases that we have in the country and the region, well, if they become aware, perhaps they can help us present it to their Chamber or the regional sessions. For example, one of them is a neurosurgeon, and I have access to deliver the material directly to him.”

AC01: "We can build interdisciplinary teams of professionals with a natural affinity for politics, advocacy, and lobbying to approach policymakers...We could also include representatives of patient's associations".

Figure 4. 7 Theme 2: Delivery strategies of the Toolkit to policymakers. Subtheme 6: Initial approach

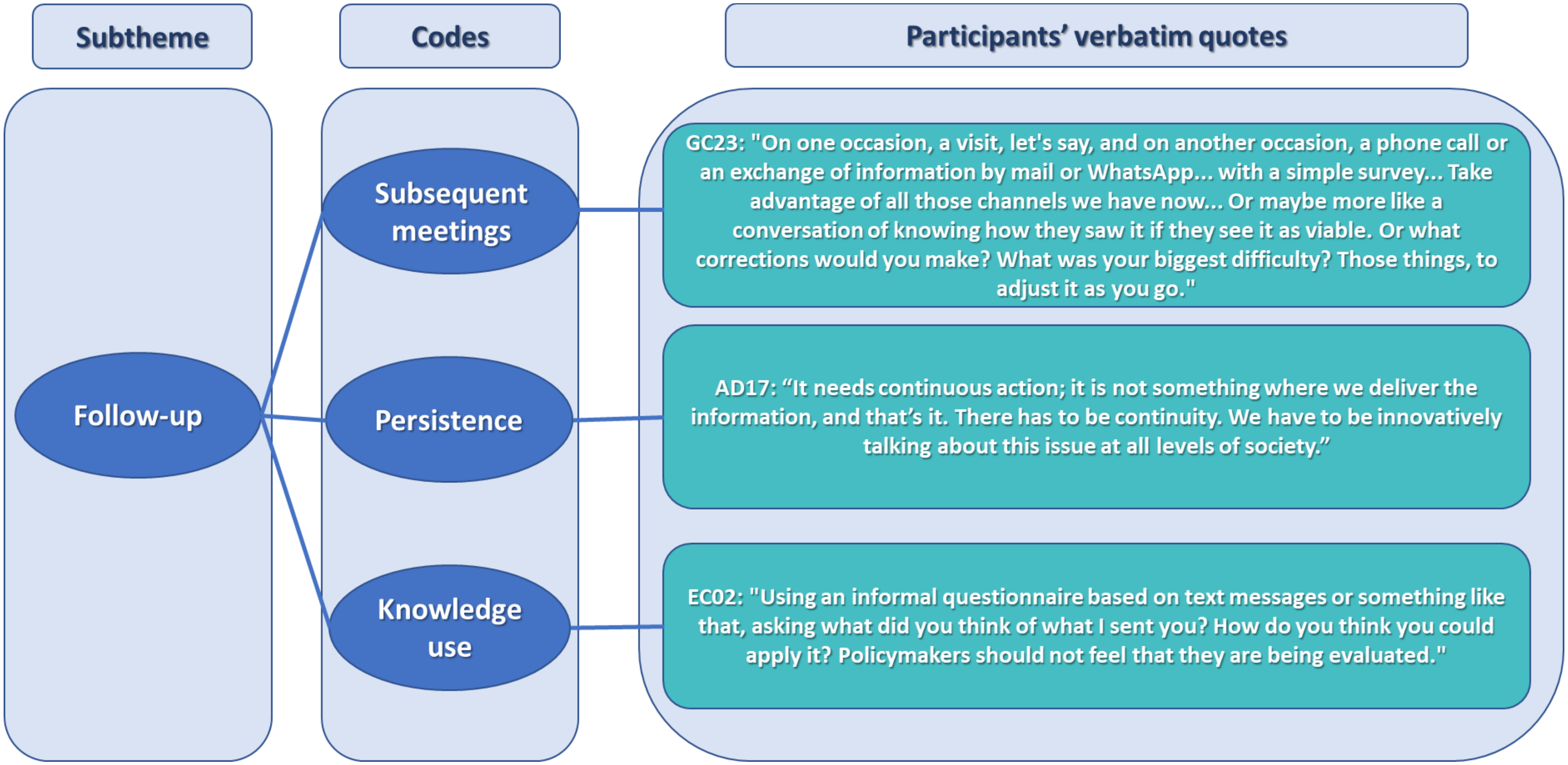


JB20: "For the first meeting, in-person is the best way because, in other ways (virtually), there is no guarantee that they will interact with the material."

GM04: "It should be like giving them a talk explaining everything, and then they can ask the respective questions about certain points that they did not understand or want to expand on, and then the material is left so that they can review it afterward."

RL21: "We invite them to take action, we do a wrapping-up, and we schedule a new meeting. It would be frequent meetings with them... yes, we delivered it to them, and we start establishing the contact channels from then on."

Figure 4. 8 Theme 2: Delivery strategies of the Toolkit to policymakers. Subtheme 7: Follow-up strategies



GC23: "On one occasion, a visit, let's say, and on another occasion, a phone call or an exchange of information by mail or WhatsApp... with a simple survey... Take advantage of all those channels we have now... Or maybe more like a conversation of knowing how they saw it if they see it as viable. Or what corrections would you make? What was your biggest difficulty? Those things, to adjust it as you go."

AD17: "It needs continuous action; it is not something where we deliver the information, and that's it. There has to be continuity. We have to be innovatively talking about this issue at all levels of society."

EC02: "Using an informal questionnaire based on text messages or something like that, asking what did you think of what I sent you? How do you think you could apply it? Policymakers should not feel that they are being evaluated."

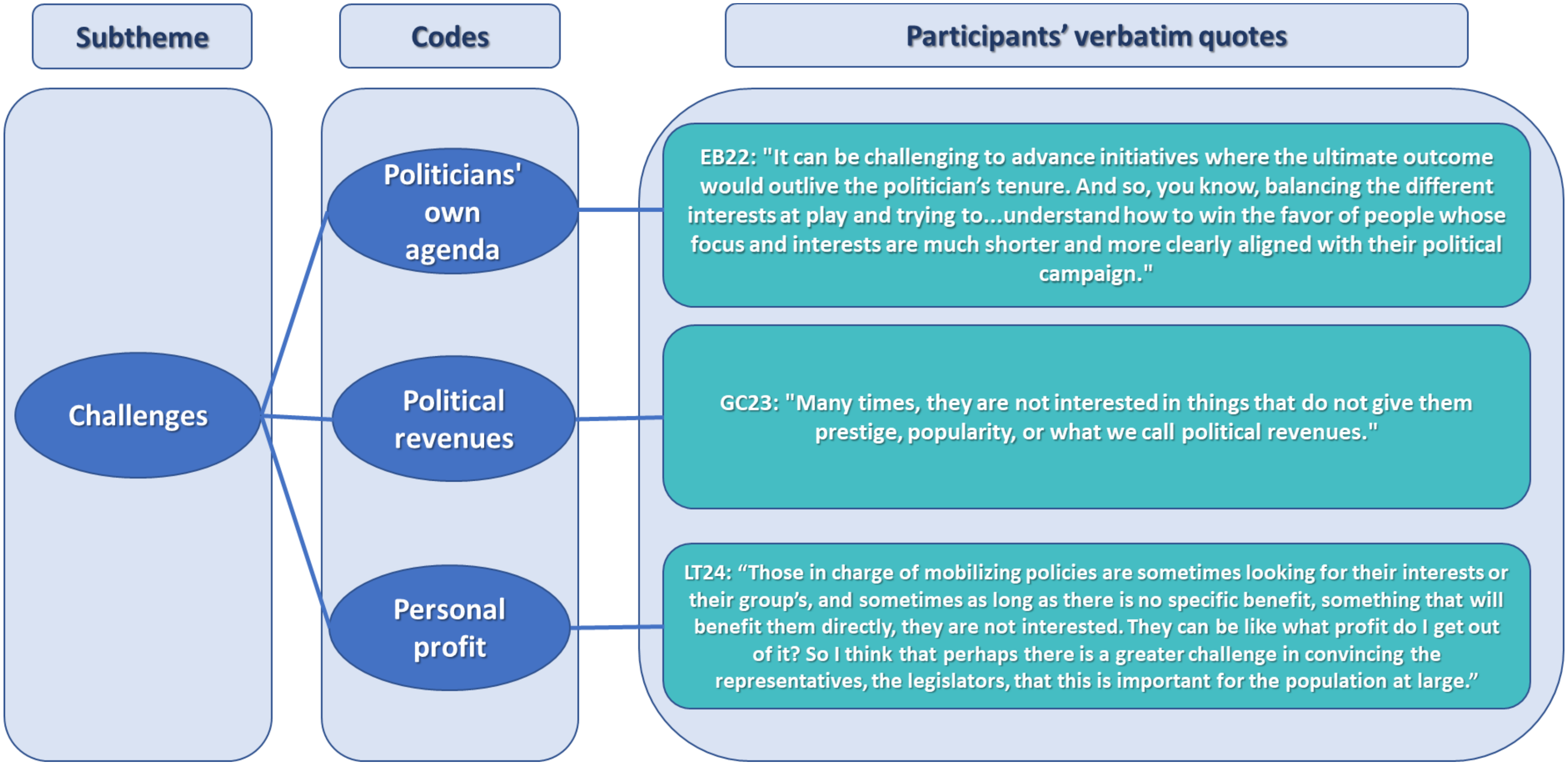
Theme 3: Bringing policymakers on board

Participants described the challenges that might be faced and the strategies to increase the likelihood of convincing and encouraging policymakers to strengthen MFF to prevent NTDs. Fourteen codes representing these aspects were grouped into two subthemes (challenges and strategies).

The main challenges included politicians prioritizing their own agenda or seeking political revenues or personal profit (Figure 4.9), excessive bureaucracy, policymaker’s lack of knowledge or understanding of the problem’s dimension and the need to take action, distrust among parties or stakeholders (Figure 4.10), indolence, cynicism, and negativity. Participants particularly highlighted science skepticism as an emergent challenge in the post-pandemic era (Figure 4.11).

On the other hand, the interviewees explained the strategies that could spearhead policymakers’ engagement in strengthening MFF policies, including visualizing political rewards associated with legislating for the greater good, managing objections effectively and anticipating solutions to potential problems elicited by policymakers, promoting persuasive encounters instead of intending to impose change (Figure 4.12), generating public awareness and support, maintaining a flexible mindset to adapt to local contexts and changing situations, understanding the decision-makers agenda, and explaining the positive cost/benefit balance of MFF policies (Figure 4.13).

Figure 4. 9 Theme 3: Bringing policymakers on board. Subtheme 8: Challenges part I

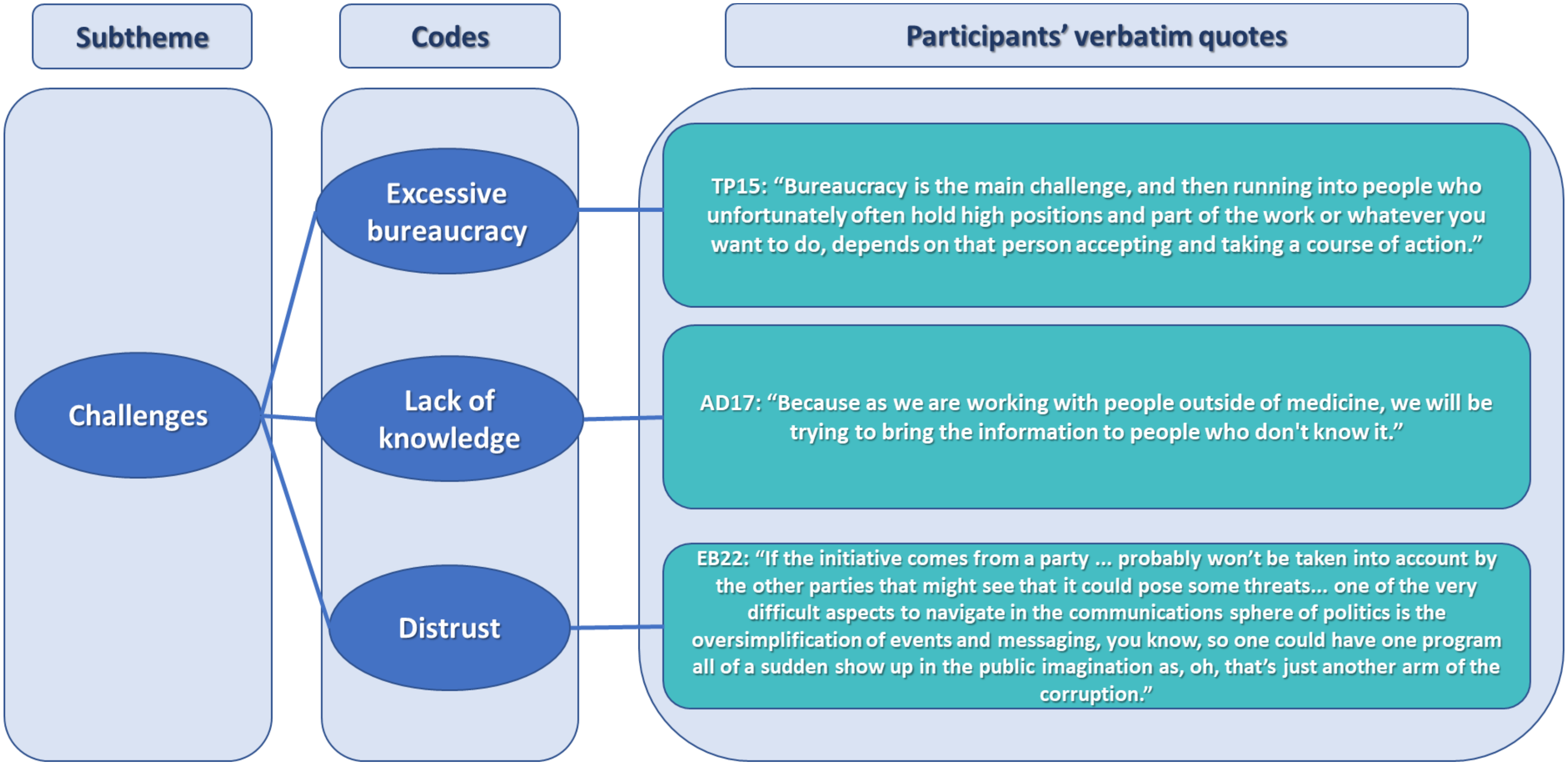


EB22: "It can be challenging to advance initiatives where the ultimate outcome would outlive the politician's tenure. And so, you know, balancing the different interests at play and trying to...understand how to win the favor of people whose focus and interests are much shorter and more clearly aligned with their political campaign."

GC23: "Many times, they are not interested in things that do not give them prestige, popularity, or what we call political revenues."

LT24: "Those in charge of mobilizing policies are sometimes looking for their interests or their group's, and sometimes as long as there is no specific benefit, something that will benefit them directly, they are not interested. They can be like what profit do I get out of it? So I think that perhaps there is a greater challenge in convincing the representatives, the legislators, that this is important for the population at large."

Figure 4. 10 Theme 3: Bringing policymakers on board. Subtheme 8: Challenges part II

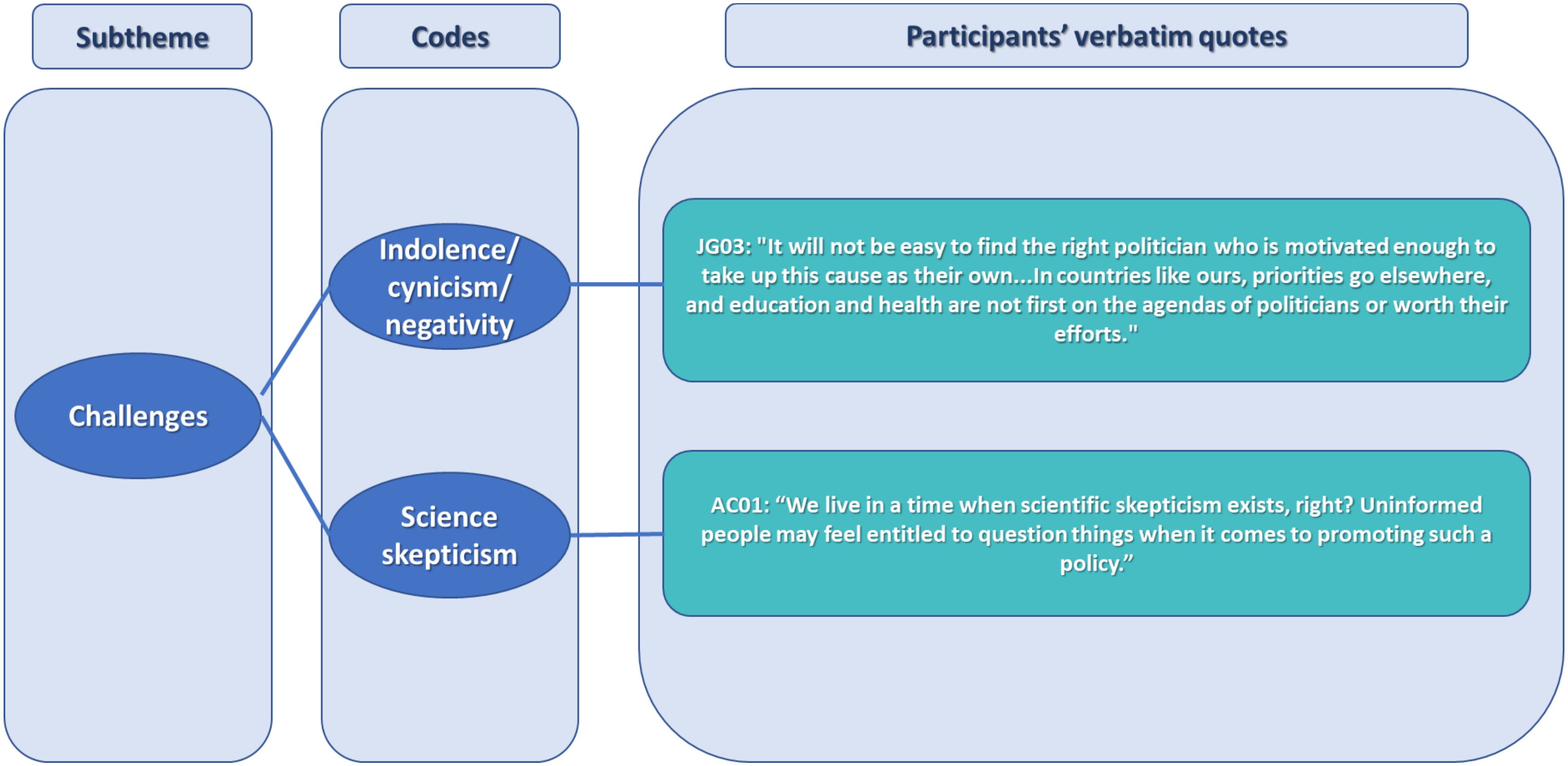


TP15: "Bureaucracy is the main challenge, and then running into people who unfortunately often hold high positions and part of the work or whatever you want to do, depends on that person accepting and taking a course of action."

AD17: "Because as we are working with people outside of medicine, we will be trying to bring the information to people who don't know it."

EB22: "If the initiative comes from a party ... probably won't be taken into account by the other parties that might see that it could pose some threats... one of the very difficult aspects to navigate in the communications sphere of politics is the oversimplification of events and messaging, you know, so one could have one program all of a sudden show up in the public imagination as, oh, that's just another arm of the corruption."

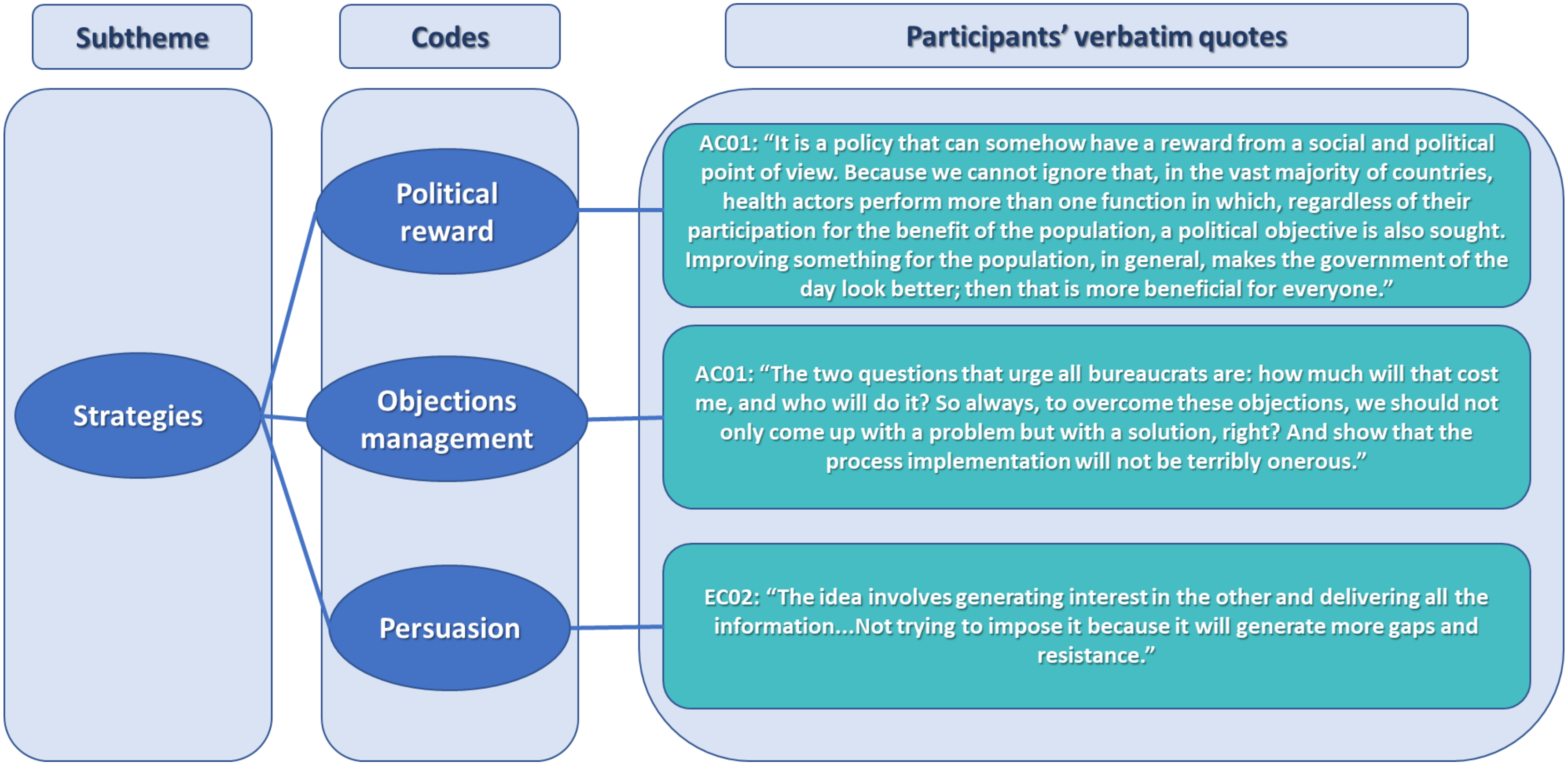
Figure 4. 11 Theme 3: Bringing policymakers on board. Subtheme 8: Challenges part III



JG03: "It will not be easy to find the right politician who is motivated enough to take up this cause as their own…In countries like ours, priorities go elsewhere, and education and health are not first on the agendas of politicians or worth their efforts."

AC01: "We live in a time when scientific skepticism exists, right? Uninformed people may feel entitled to question things when it comes to promoting such a policy."

Figure 4. 12 Theme 3: Bringing policymakers on board. Subtheme 9: Strategies, part I

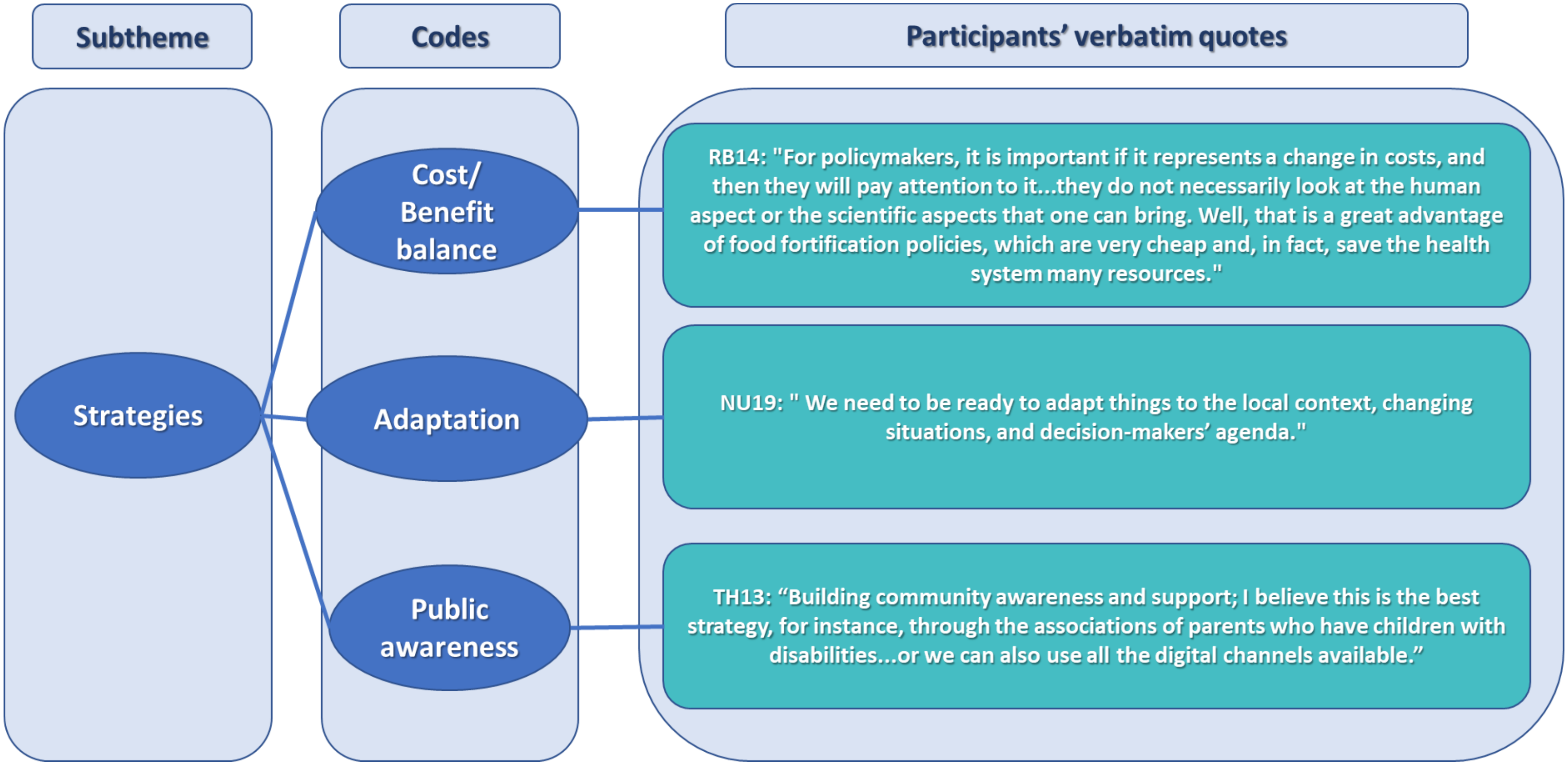


AC01: “It is a policy that can somehow have a reward from a social and political point of view. Because we cannot ignore that, in the vast majority of countries, health actors perform more than one function in which, regardless of their participation for the benefit of the population, a political objective is also sought. Improving something for the population, in general, makes the government of the day look better; then that is more beneficial for everyone.”

AC01: “The two questions that urge all bureaucrats are: how much will that cost me, and who will do it? So always, to overcome these objections, we should not only come up with a problem but with a solution, right? And show that the process implementation will not be terribly onerous.”

EC02: “The idea involves generating interest in the other and delivering all the information...Not trying to impose it because it will generate more gaps and resistance.”

Figure 4. 13 Theme 3: Bringing policymakers on board. Subtheme 9: Strategies, part II



RB14: "For policymakers, it is important if it represents a change in costs, and then they will pay attention to it...they do not necessarily look at the human aspect or the scientific aspects that one can bring. Well, that is a great advantage of food fortification policies, which are very cheap and, in fact, save the health system many resources."

NU19: " We need to be ready to adapt things to the local context, changing situations, and decision-makers' agenda."

TH13: "Building community awareness and support; I believe this is the best strategy, for instance, through the associations of parents who have children with disabilities...or we can also use all the digital channels available."

Integration of Quantitative and Qualitative Data

A joint display table was developed to illustrate how the qualitative results (expressed in themes and direct quotes) enhance the quantitative results in terms of the most relevant determinant factors grouped in the four MIDI categories (Table 4.8). The value added by the qualitative explanations was interpreted to provide a deeper understanding of the MIDI questionnaire findings and additional insights and nuances.

Table 4. 9 Joint display of quantitative (MIDI questionnaire) and qualitative (interviews) results for the sequential explanatory integration of data on overcoming barriers and leveraging facilitators to implement and disseminate the NeuroAdvocacy Toolkit

MIDI CATEGORY	OVERCOMING BARRIERS AND STRATEGICALLY LEVERAGING OF FACILITATORS	ILLUSTRATIVE QUOTES
DETERMINANTS ASSOCIATED WITH THE TOOLKIT	Seizing the toolkit attributes	GZ16: "As a strategy, it seems excellent to me, it is very clear, very didactic, and very easy to understand, obviously for professionals who work on this, but I am sure that it is so well laid out, so friendly that a legislator or even a school teacher can understand it perfectly."
	Expansion of the toolkit utilization to other stakeholders	CD05: "It seems to me that it is a job very well done, well planned, and above all, empathic...it is not boring; it is dynamic, helps to understand, it is written and done with words and phrases that are easy to understand, not only for one as a surgeon, but for the people, for the citizen, so I think the language is very clear, precise, I think everybody will understand it."

	Training in toolkit use / Preparedness to manage objections	JJ10: “Learning to address the possible objections they may raise in that first discussion, try to solve those that the legislators have placed there so that they spend a very short period and move on to the next step of the process.”
DETERMINANTS ASSOCIATED WITH THE USERS	Subjective norm	JB20: "It seems to me that pediatric neurosurgeons should support strategies aimed at prevention and public health because they do play a role in transferring knowledge to the population beyond the surgical work we do."
	Social norm	JJ10: “There would be no problem because, within the statutes of the pediatric chapter of our Neurosurgical Association, one of the missions is to support this type of initiative.”
	Perceived roles	CC05: “We play a fundamental role in society; we can change lives, and we only have to want to do it and wish for it. It is hard work. I’m not going to deny it. It demands a lot of time and sacrifice, not only physically because our surgeries are very complex, but also time, family, and resources because sometimes one has to take part not only in clinical practice and healthcare but also dedicate time in contributing to society.”
	Boosting effective advocacy role	GP06: "Our role is crucial; since we are pediatric neurosurgeons, we can influence society not only from a clinical or academic standpoint but also from an administrative point of view and from influencing public policies, although there are few cases focused on this point."
DETERMINANTS ASSOCIATED WITH THE ORGANIZATION	Alliances with academic institutions/other societies	NZ08: “We need to work in collaboration with societies, not only neurosurgery but also gynecology and obstetrics, and pediatrics because they also see the complications of neural tube defects. The more allies we get, the better. Also consider urology, orthopedics, and the Medical Women’s Association.”

	Support from professional societies	JJ10: “The person going to do this must receive significant backing and support...they must have support at the national level but also from ASOLANPED at the Latin American level. Don’t let them fight this fight alone.”
	Support by non-governmental organizations (NGOs)	GC23: "Through a foundation, there are foundations here that are highly respected for their prestige, for their help in every way to the most vulnerable people, the poorest people, and these foundations have much prestige and are highly accepted by the political class and by people in general."
	Guild unity	CC05: “Not that I say one thing and another person says, but I can do it this other way; it would generate disunity...Authority and information are diluted, and policymakers, well, you see, won’t give it importance...If we all work together, and everyone moves in the same direction, pulling the same boat, I think that we can work wonders.”
DETERMINANT ASSOCIATED WITH THE SOCIOPOLITICAL CONTEXT	Support by supranational organizations	RB14: “It is ideal to have the support of organizations of the stature of the WHO and PAHO. If we have an agreement or a resolution from PAHO/WHO, it is a little easier to go directly to the Ministry of Health and gain their attention.”

Chapter 5: Interpretations, Conclusions, and Recommendations

To date, this is the first study using a mixed-methods design to describe the determinant factors for developing, implementing, and disseminating a knowledge translation strategy to influence Latin American policymakers to strengthen MFF policies including folic acid to prevent NTDs.

A mixed-methods design facilitates greater depth and stakeholder inclusion in several ways described, in terms of this study, for the specific approach of policy implementation and dissemination research (Brownson et al., 2018; Creswell & Plano Clark, 2017). First, mixed-methods designs are more suitable to involve participants in the study as relevant stakeholders to understand the detailed nuances of promoting policy change and empowering and engaging them in implementing the research findings that might impact their communities (Milat et al., 2014). Second, strategies devised to translate knowledge aiming to influence policymakers' decisions benefit from a mixed-methods evaluation design to gather quantitative and qualitative data to explore the involvement of individuals in the components of the intervention but also the generation of change (Palinkas & Cooper, 2018). Third, bridging a knowledge gap in the translational continuum requires broadening the approaches and leveraging opportunities for collaboration; these conditions are possible with a mixed-methods approach and are more complicated when conducting intradisciplinary quantitative or qualitative research independently (Repko & Szostak, 2020). Fourth, a mixed-methods approach fosters the application of different ontologies, epistemologies, and methodologies in one study, combined in a pragmatic worldview or flowing in a dialectic stance (Creswell & Plano Clark, 2017); this feature stimulates dialogue among investigators of different fields to create common ground on how to approach policy change. Finally, mixed-methods approaches in translational research not only ensure greater cross-disciplinary inclusion but are also inclusive in the sense that non-academic participants can be an active part of the generation, exchange, transfer, translation, utilization, and integration of knowledge.

This study also represents the first formal validation of the MIDI questionnaire in Spanish and the first time the instrument is applied to measure determinant factors of an innovation targeting public policies to bridge the gap between the T3 and T4 moments of the translational continuum. The instrument has proven helpful in the healthcare, welfare, informatics, and education sectors; however, its generalizability to other settings had not been tested before this study (Dugstad et al., 2019; Fleuren et al., 2014). Therefore, the authors of the MIDI invited implementation researchers to use and explore the instrument in other settings where similar processes may occur when implementing an innovation (Fleuren et al., 2014). For this study, the MIDI offered an objective view of the determinants affecting the implementation of the NeuroAdvocacy Toolkit as an innovation aiming to influence policymakers' decisions regarding fortification policies.

Using a knowledge transfer toolkit serves as a powerful aid in promoting policy change (Barac et al., 2014). Although international neurosurgical organizations such as ASOLANPED and the ISPN have issued a call to action and prompted member neurosurgeons to advocate for MFF policies to prevent NTDs (Caceres et al., 2021; Dabdoub et al., 2014), their directives lacked detailed guidelines on how to translate the evidence to influence government agents' support of the policy. The NeuroAdvocacy Toolkit represents a vehicle to channel efforts from the neurosurgical community and convey strong messages to crucial decision-makers when advocating for MFF policies to prevent NTDs. It could also serve as a model to facilitate advocacy for other causes, such as primary prevention of traumatic brain and spine injury and prevention and early detection of central nervous system tumors in the pediatric population.

The scientific literature provides examples of using knowledge transfer toolkits in other health settings, such as healthcare education and implementation of clinical practice guidelines and health programs (Barac et al., 2014; Straus et al., 2013), as well as entirely different settings to promote knowledge translation in areas such as finances (Carrillo et al., 2006), geospatial science (Sajeva et al., 2020), foreign affairs (Napier, 2005), and science integration for secondary schools (Guasch et al., 2020). This study is the first reported experience involving developing and implementing a KT toolkit in the global neurosurgery field, which had great acceptance among the neurosurgical community and almost unrestricted self-reported support, a crucial element when implementing and disseminating an innovation (Brownson et al., 2018).

The NeuroAdvocacy Toolkit is a conduit for behavior change in KOL and policymakers. It could even permeate other sectors and stakeholders. The main barriers to change within the system related to evidence-informed policies imply ontological, methodological, and epistemological challenges than can permeate intellectual, relational, and institutional levels (Stevenson et al., 2012) but also real-world problems such as policymakers' agenda and priorities. On the other hand, potential facilitators to change include broadening the phenomenon to focus on large-scale interventions, the use of more expansive methods that integrate different disciplines and relevant stakeholders, public-private partnerships, network bridging, and institutional alignment (Stevenson et al., 2012). Those barriers may be overcome, and the facilitators can and should be leveraged by integrating a transdisciplinary generation of knowledge, translational science, and a systems-thinking approach.

From a researcher and advocate's experience, while conducting the study, the conceptual framework specifically designed for this study (combining Kingdon's multiple streams model

(Kingdon, 2003, 2014) and Aarons' model for assessing the determinant factors for the uptake of evidence-based policies (Aarons et al., 2011)) was materialized through the actual implementation of the NeuroAdvocacy Toolkit to approach and exchange knowledge with official agents at the Colombian Ministry of Health. While governmental agendas are set in the problems or political streams, solutions are usually generated in the policy stream. However, the possibility of items rising on a decision agenda is enhanced if all three streams converge (Kingdon, 2014). Integrating knowledge of the critical factors for policy implementation and seizing the window of opportunity for brokering knowledge led to consolidating a formal process for a new resolution draft scaling up the micronutrient fortification policy to include maize flour and rice in the Colombian regulation. This new resolution is in progress for official governmental approval.

Moreover, the Colombian government sponsored an initiative to promote a WHO resolution prompting the implementation of MFF policies worldwide, which is now on the agenda for the next WHO Executive Board to be voted in the forthcoming World Health Assembly in May 2023. See in Appendix D the diplomatic concept note issued by Colombia as a member state of the WHO Executive Board. The document was informed by drawing elements from the NeuroAdvocacy Toolkit resulting from iterative processes and knowledge exchange interactions. It is presented in this dissertation with permission from the Colombian authorities.

Interpretation of Specific Findings in the Study Phases

Needs assessment

Ninety percent of Latin American countries have a compelling necessity for regulatory change regarding MFF policies. Generating change requires multiple stakeholders' involvement and knowledge translation strategies to impulse actions by regional policymakers. This study confirms the NeuroAdvocacy Toolkit's utility to serve in this capacity and presents an objective way to determine priority elements according to the specific context of each country. Through a customizable scale that allows the granular analysis of regulatory aspects and epidemiological data, KOL and interdisciplinary teams can tailor advocacy activities to specific domains of MFF, such as implementing the policy, improving enactment by the food industry, and optimizing the policy surveillance or making national registries more robust.

Implementing and disseminating the NeuroAdvocacy Toolkit can convey a sense of urgency at the decision-makers level by understanding the critical determinant factors and the strategies explained in the following subsections.

Quantitative strand

Quantitative data obtained through the MIDI questionnaire were instrumental in answering the research question: what are the determinant factors influencing the use of the NeuroAdvocacy Toolkit as an innovation to promote robust MFF policies in Latin America? Key opinion leaders in pediatric neurosurgery from the twenty countries helped determine 20 facilitators, seven potential facilitators, and two barriers to implementing the Toolkit as a knowledge translation strategy to policymakers in the region.

Factors associated with the innovation, the users, and the sociopolitical context constitute facilitators in implementing and disseminating the Toolkit; similarly, most factors related to the organization are facilitators or potential facilitators and can be leveraged to achieve the goals. On the other hand, two barriers were associated with the organization (neurosurgical societies). This phenomenon responds to the fact that 38% of the survey respondents reported an absence of a formal pediatric neurosurgery chapter or organized society in their countries. When present, nearly half of the participants mentioned that this society, chapter, or association does not include missional activities to advise, promote or influence public policies concerning children's health. Specific actions are needed to adjust the implementation and dissemination strategies for these two factors, including meetings between ASOLANPED leadership and local neurosurgical associations to formally ratify the initiative and boost advocacy and lobbying competencies in designated team members.

Analyzing the determinant factors according to the country categories allows the local KOLs, the national neurosurgical associations, and ASOLANPED leadership to customize specific actions to enhance the implementation and dissemination strategies for the NeuroAdvocacy toolkit.

Qualitative strand

The detailed descriptions in the qualitative phase of the study enabled answering the qualitative research questions: how do the KOL describe their engagement, motivation, and intention to act in implementing and disseminating the NeuroAdvocacy Toolkit to translate knowledge to policymakers in their countries? And what are the perceptions of KOL about appropriate dissemination mechanisms of the NeuroAdvocacy Toolkit? The codified qualitative data allowed identifying three themes related to the implementation expressed as 1) the attitudes toward using the Toolkit, 2) the ideal delivery strategies to policymakers, and 3) how to face potential challenges to bring policymakers on board effectively during the implementation and dissemination process.

Participants described motivation in terms of empathy toward their patients and caregivers, awareness of the high burden people living with NTD and their families have to face along the vital cycle, and inspiration for doing a greater good. They described engagement in terms of confidence in using the toolkit to broker knowledge to policymakers, gratification for opportunities to advocate for an impactful evidence-based policy, and commitment to the initiative. Intention to act was prompted by emulation of efforts and readiness to start the process of implementing and disseminating the innovation. A few KOL also described potential drawbacks during the implementation and dissemination of the KT strategy, namely hesitation to participate due to time constraints, the anticipation of apathy or inertia leading to maintaining the status quo, or frustration by not observing policymakers' use of the knowledge transferred to them.

Participants described the strategies to deliver the toolkit in terms of ideal channels to approach policymakers, including initiatives from organized neurosurgery and interdisciplinary teams instead of individual efforts, involving patients and families associations and contacting gatekeepers to facilitate the process. For the initial approach, participants favored in-person meetings, maintaining openness and availability to explain the toolkit material and spontaneous questions in lay terms and wrapping up the encounter with a call to action to policymakers highlighting the specific further steps. They also emphasized the need for ongoing follow-up activities such as scheduling new virtual or in-person meetings, e-mails, and phone calls, as well as devising practical mechanisms to assess policymakers’ knowledge use in a way that they do not feel evaluated or overwhelmed.

When bringing policymakers on board, participants identify potential challenges, including laborious bureaucratic processes, lack of knowledge by decision-makers, distrust among stakeholders, indolence, cynicism, and negativity. The interviewed KOL identified science skepticism as an emergent threat that has also been described for other fields in public health, such as contagious diseases, vaccination, or climate change, and is usually linked to science literacy (Rutjens et al., 2021, 2022; Scheitle & Corcoran, 2021). In parallel, participants recognize strategies to defeat the identified challenges, namely generating public awareness regarding NTDs and preventative strategies, using persuasion and objection management techniques, making the policy's favorable cost/benefit balance and the possibility of political rewards visible to policymakers, and finally, being prepared to adapt to changing decision-makers agendas and priorities.

Quantitative and qualitative integration

Integrating the quantitative and qualitative data permitted a deeper understanding of how to overcome potential barriers and devise strategic leveraging of facilitating factors when disseminating the Toolkit to the target policymakers. Achieving this integration required the mixing of quantitative and qualitative data, which also enabled answering the mixed-methods research question: in what ways do the interview data reporting the views of KOL about their motivation, engagement, and intention to act help to explain the quantitative results about the determinant factors for implementing the NeuroAdvocacy Toolkit?

After merging quantitative and qualitative data, the iterative analytic process provided essential information through emergent themes and additional insights and nuances when aiming to influence policymakers regarding MFF policies in Latin America. Although the MIDI allowed identifying the main barriers and facilitators for implementing the NeuroAdvocacy Toolkit, the subsequent interviews allowed visualizing alternatives for operationalizing the determinant factors. First, combining survey and interview data made more evident the elements of the toolkit that make it suitable for the knowledge translation process and how to take advantage of those attributes to expand the innovation to involve other stakeholders as potential users beyond the neurosurgical community. Second, KOL behaviors influenced by subjective norms, social norms, and perceived roles can spearhead effective data-driven advocacy. Third, organizational support can enhance the implementation and dissemination of the NeuroAdvocacy Toolkit by consolidating neurosurgical guild unity and promoting alliances with universities, other academic institutions, and other professional societies, including nutrition, pediatrics, urology, orthopedics, rehabilitation disciplines; also, obtaining support from non-governmental organizations and patients' associations as critical stakeholders. Fourth, gaining support from supranational organizations such as the WHO and PAHO, materialized through a statement or resolution, can accelerate the dissemination process and promote the promulgation, enactment, and enforcement of MFF policies in most of the countries represented in this study.

Reflections on the knowledge translation process

This study generated knowledge regarding effective KT strategies to include an evidence-based public health measure to prevent NTDs into Latin American policymakers' agenda. The gap between robust scientific evidence and policy implementation, i.e., from knowledge to action, has surpassed three decades. By seizing the window of opportunity for knowledge brokering described by Kingdon's multiple streams model, the implementation and dissemination of the NeuroAdvocacy Toolkit can aid in bridging the chasm between the T3 and T4 moments of the translational research continuum regarding primary prevention of neural tube defects.

The NeuroAdvocacy Toolkit development and refinement benefitted from evidence-informed data and the rich perspectives of selected Latin American KOL and policymakers. The implementation and dissemination of the innovative strategy also require the involvement and interaction of multiple stakeholders and approaches that reflect the diverse perspectives and mechanisms for the primary prevention of NTDs.

Stakeholder engagement, in this case, the involvement of Latin American pediatric neurosurgeons as KOLs, can increase the likelihood that policymakers use the scientific evidence to enhance the reach, adoption, implementation, scale-up, and sustainability of MFF as a robust evidence-based policy to prevent NTDs. During the study, the KOL were exposed to the KT strategy, reflected on their societal role, and experienced a renovated impulse to advocate for health causes. This study also exemplifies how knowledge translation constitutes a productive way to materialize actions in global neurosurgery.

The exposition of KOL to the NeuroAdvocacy Toolkit ignited the transformation of Latin American pediatric neurosurgeons from being passive stakeholders to active change agents in MFF with micronutrients as robust evidence-based policies to prevent congenital malformations.

Conclusions

Most Latin American countries have a compelling need to update, scale up, implement, optimize surveillance, and guarantee the sustainability of mandatory food fortification policies to prevent neural tube defects. The NeuroAdvocacy Toolkit is an innovative knowledge translation strategy enabling key opinion leaders in pediatric neurosurgery to influence policymakers' decisions toward strengthening fortification policies. Although the NeuroAdvocacy Toolkit was originally designed to be used by pediatric neurosurgeons, and this study tested its implementation by users from that particular group, the toolkit attributes make it suitable to be used by different actors willing to implement and disseminate it, with minimum training or alteration of the core components.

Critical determinant factors can act as barriers or facilitators to implementing and disseminating the Toolkit. Recognizing them is essential to tailor strategies to approach and call policymakers to action, with the ultimate goal of saving thousands of children in Latin America from being born with a devastating but preventable condition and promoting a healthy and fulfilling start to their lives.

The role of pediatric neurosurgeons in caring for children with congenital malformations extends beyond surgical care and includes advocacy initiatives to promote context-specific, science-driven policies for preventing NTDs. Championing, advocating, and lobbying for MFF policies exemplifies the Latin American pediatric neurosurgeons' potential to impact the population's health positively.

Recommendations

Although sociocultural and political differences among Latin American countries exist, the following recommendations apply to the Latin American region at large, based on the consistency and homogeneity of findings in this study regarding the determinant factors for implementing the NeuroAdvocacy Toolkit as a KT strategy.

- The implementation and dissemination process of the NeuroAdvocacy Toolkit should consider specific contextual aspects and needs of each Latin American country.

- The Toolkit contents should be translated into Portuguese for implementation and dissemination in Brazil. In the case of Haiti, the contents should be translated into French and Haitian Creole. In both cases, the idea is to bring on board multiple stakeholders in those countries to support the initiative.
- For some countries, greater consolidation of organized neurosurgery is ideal for taking the initiative forward. ASOLANPED and large national societies can support and advise small associations or groups of pediatric neurosurgeons, as well as individual champions leading the process in countries without an evident neurosurgical organization.
- ASOLANPED can lead the formal ratification of the initiative and the implementation and dissemination process by national societies of pediatric neurosurgery in Latin America.
- More junior neurosurgeons, residents, and fellows can benefit from training in communication, persuasion, advocacy, and lobbying techniques to enhance their abilities as key opinion leaders.
- Senior pediatric neurosurgeons can reorient efforts at this stage of their careers to take advantage of their experience and wisdom to lead the way and guide younger colleagues in advocacy and lobbying activities.
- Gatekeepers can facilitate initial contact with policymakers and pave the way to more productive interactions.
- In-person meetings are ideal for the first approach to policymakers, followed by diverse and creative ways to follow up and measure knowledge utilization.

- A resolution by a supranational organization such as the WHO encouraging member states to adopt or strengthen existing MFF policies will serve as a catalyst to accelerate the process and dilute potential resistance from particular stakeholders.
- Advocating for primary prevention of NTDs by no means implies impairing continuous efforts to provide quality, humane and person-centered care to individuals living with neural tube defects. Quite the opposite, those individuals generate a source of inspiration to expand the horizons for innovative ways of incorporating meaning in a pediatric neurosurgery career.

Implications for Future Research

When MFF are effectively implemented, enacted, and enforced, they bring about consistent health outcomes in the population by reducing the prevalence of NTDs by approximately 50% after three to five years of implementation. For Latin America, new inquiries elicited from the findings presented here but beyond the scope of this study include the following research questions:

- What is the degree of fidelity in delivering the KT intervention?
- What elements of the dissemination strategy require flexibility to respond to specific contextual factors?
- How is the reception of evidence-based policy-related information by policymakers?
- How well does the intervention inform and motivate policymakers to address this problem?

- How effective are the strategies for disseminating and translating knowledge in generating uptake of the program?
- How did the program permeate different levels or sectors related to the policy to support its enactment and enforcement?
- How do we ensure the sustainability of the KT strategy in promoting knowledge use to achieve health outcomes?

Objective indicators in future research efforts should include implementation and dissemination science outcomes such as self-reported support of the policies, self-reported knowledge use, and observed knowledge use by policymakers (Brownson et al., 2018). Teachout et al. described a framework for conducting implementation science research in large-scale food fortification programs (Teachout et al., 2021) that can be helpful in future research initiatives derived from the promulgation and enactment of MFF policies. Another objective indicator of the impact of MFF policies is the periodical assessment of blood folate levels in women of reproductive age as a monitoring and evaluation measure (Bailey & Hausman, 2018).

After proper translation and adaptation, the NeuroAdvocacy Toolkit has the potential to serve as a KT strategy for other world regions, which will necessarily elicit new research questions regarding the determinant factors for implementing and disseminating the innovative strategy outside Latin American countries.

Like translational science, global neurosurgery is a young field of research. Both will benefit from growing research ideas to address unmet needs from interdisciplinary and diverse perspectives. Promulgation, enactment, and enforcement of MFF policies are the first steps of a long process that requires using a lens that accounts for the complexity of the process and stakeholder mapping and involvement to guarantee the sustainability of micronutrient fortification policies and the prevention of congenital disorders. In addition to policymakers, critical stakeholders are the food industry, distributors (including importers and exporters), consumers, clinicians of different fields, and patient associations. They can be natural allies in the quest to prevent NTDs and other congenital malformations through MFF policies.

Other preventable causes of NTDs also require building a body of evidence to promote further knowledge translation. Non-folate-sensitive NTDs constitute a large window of opportunity to generate translational knowledge in different moments of the research spectrum.

Application to Other Settings

Although the findings of this study are generalizable to Latin American countries regarding MFF policies, the procedures carried out in this research can inspire the conduction of similar studies in other world regions and other fields of research in global neurosurgery. The scale to assess the needs for regulatory change presented in this dissertation applies to different continents and other situations of interest in preventing neurosurgical conditions.

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APPENDIX A: Phase 1. Interview protocol to policymakers

Thank you for agreeing to participate in this study. This interview will be recorded, and only the audio component of the recording will be transcribed. All the materials will be destroyed after the completion of the study. All the answers will be confidential, and you are encouraged not to use specific names. Please, feel free to answer all questions or pass on any questions that might make you uncomfortable or do not want to answer.

If that is OK with you, I will start the recording now.

1. Exploratory question: Please, state your name and current position in (state agency or legislative body). For how long have you been appointed to this position? What are the roles of your team members?
2. Leading question: When you or your team need scientific information to guide your decisions, what mechanisms do you usually employ to obtain that information?
    a. Follow-up question: How are those mechanisms working for you?
    b. Follow-up question: What are the main challenges when gathering scientific information?
    c. Follow-up question: What strategies do you use to overcome those challenges?
3. Leading question: Tell me about your experience in applying and monitoring current legislation on mandatory food fortification
    a. Follow-up question: In your opinion, what are the main obstacles to implementing food fortification programs
    b. Follow-up question: What factors make it easier to implement such programs?

   c. Follow-up questions: What would you consider crucial aspects in monitoring the application of current policies?

4. Leading question: Are there any plans for other food fortification policies to improve human health conducted by the (state agency or legislative body)?
   a. Follow-up question: What kind of evidence do you or your team usually seek when designing a policy for mandatory food fortification?
   b. Follow-up question: What would be your preferred mechanisms and formats to receive and use evidence-based knowledge?
5. Leading question: What would be the role of an expert in the field when exchanging knowledge to inform your decisions?
   a. Follow-up question: What would be the ideal ways for that expert to convey the knowledge so you and your team can readily use it to inform your decisions?
   b. Follow-up question: How can a toolkit containing slides, infographics, evidence briefs, and executive summaries of successful legislation serve the purposes of obtaining and using evidence-based knowledge?
   c. Follow-up question: What other elements would you add to such a toolkit?
6. Is there any comment you would like to add to what you have shared in this interview?

Thank you very much for participating in this interview. If necessary, would it be OK to contact you for further follow-up questions about this interview?

APPENDIX B: Phase 2. Adaptation and operationalization of the MIDI questionnaire

THE NEUROADVOCACY TOOLKIT:
DESCRIPTION AND OPERATIONALIZATION OF THE DETERMINANTS OF INNOVATION MEASUREMENT INSTRUMENT (MIDI)

Determinants associated with the innovation				
Determinant	**Name**	**Description**	**Operationalization**	**Response scale**
1	**Procedural clarity**	The extent to which the innovation is described in clear steps/procedures.	The NeuroAdvocacy Toolkit clearly describes the activities I should perform and in which order.	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
2	**Correctness**	The degree to which the innovation is based on factually correct knowledge	The NeuroAdvocacy Toolkit is based on factually correct knowledge	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
3	**Completeness**	The degree to which the activities described in the innovation are complete	The NeuroAdvocacy Toolkit provides all the information and materials needed to work with it properly	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
4	**Complexity**	The degree to which the implementation of the innovation is complex	The NeuroAdvocacy Toolkit is too complex for me to use	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
5	**Compatibility**	The degree to which the innovation is compatible with the values and working method in place	The NeuroAdvocacy Toolkit is a good match for how I am used to working	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
6	**Observability**	Visibility of the outcomes for the user, for example, whether the outcomes of a particular treatment are clear to the user	The outcomes of using the NeuroAdvocacy Toolkit are clearly observable	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree

7	**Relevance for the target audience**	The degree to which the user believes the innovation is relevant to the target audience	I think the NeuroAdvocacy Toolkit is relevant for the policymakers in my country	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
			I think the intended effects of the NeuroAdvocacy Toolkit are relevant to the population of my country	

Determinants associated with the user

Determinant	Name	Description	Operationalization	Response scale
8	**Personal benefits/drawbacks**	The degree to which using the innovation has advantages or disadvantages for the users themselves	Using the NeuroAdvocacy Toolkit means I can contribute significantly to my neurosurgical society and, in general, to children in my country.	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
			Using the NeuroAdvocacy Toolkit can be time-consuming and add extra workload to my regular activities	
			Will using the NeuroAdvocacy Toolkit make my work as a pediatric neurosurgeon more valuable since I will see fewer children with devastating neural tube defects	
9	**Outcome expectations**	Perceived probability and importance of achieving the client objectives as intended by the innovation	Importance: Policymakers should be more aware of the impact of neural tube defects on the individual, family, society, and public health levels	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
			Probability: I expect that using the NeuroAdvocacy Toolkit will achieve that policymakers will take	(1) most definitely not, (2) definitely not, (3) perhaps not, perhaps (4) definitely, (5) most definitely

			action to improve fortification policies.	
10	**Professional obligation**	The degree to which the innovation fits in with the tasks for which the user feels responsible when doing their work	I feel it is my responsibility as a professional and member of my national neurosurgical society to use the NeuroAdvocacy Toolkit to encourage policymakers to improve fortification policies	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
11	**Client satisfaction**	The degree to which the user expects the target audience to be satisfied with the innovation	Policymakers will generally find it useful if I deliver the NeuroAdvocacy Toolkit to them	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
12	**Client cooperation**	The degree to which the user expects the target audience to cooperate with the innovation	Policymakers will generally cooperate if I use the NeuroAdvocacy Toolkit	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
13	**Social support**	Support experienced or expected by the user from important social referents relating to the use of the innovation (for example, from colleagues, other professionals they work with, heads of	I can count on adequate assistance from my national neurosurgical society if I need it to use the NeuroAdvocacy Toolkit	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree

		department, or management)	I can count on adequate assistance from the Latin American Association of Pediatric Neurosurgery (ASOLANPED) if I need to use the NeuroAdvocacy Toolkit	
14	**Descriptive norm**	Colleagues' observed behavior: the degree to which colleagues use the innovation	In your opinion, what proportion of the colleagues in your national neurosurgical society will use the NeuroAdvocacy Toolkit?	(1) not a single colleague (2) almost no colleagues (3) a minority (4) half (5) a majority (6) almost all colleagues (7) all colleagues
15	**Subjective norm**	The influence of important others on the use of the innovation	Normative beliefs: To what extent do the members of your neurosurgical society expect you to use the NeuroAdvocacy Toolkit?	(1) most definitely not, (2) definitely not, (3) perhaps not, perhaps (4) definitely, (5) most definitely
			Motivation to comply: When it comes to working in accordance with the NeuroAdvocacy Toolkit, to what extent do you comply with the opinions of the ASOLANPED?	(1) very little (2) little (3) not a little, not a lot (4) a lot (5) a great deal
16	**Self-efficacy**	The degree to which the user believes they can implement the activities involved in the innovation	Do you think you can put the NeuroAdvocacy Toolkit into practice?	(1) most definitely not, (2) definitely not, (3) perhaps not, perhaps (4) definitely, (5) most definitely
17	**Knowledge**	The degree to which the user has the knowledge needed to use the innovation	I know enough to use the NeuroAdvocacy Toolkit.	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree

18	**Awareness of content of innovation**	The degree to which the user has learned about the content of the innovation	To what extent are you informed about the content of the NeuroAdvocacy Toolkit?	(1) I'm not familiar with the innovation (2) I'm familiar with the innovation, but I haven't read it through (yet) (3) I'm familiar with the innovation, and I have glanced through it (4) I'm familiar with the innovation, and I have read through it thoroughly
Determinants associated with the organization				
Determinant	**Name**	**Description**	**Operationalization**	**Response scale**
19	**Formal ratification by management**	Formal ratification of the innovation by management, for example, by including using the innovation in policy documents.	Has your national neurosurgical society set up formal arrangements relating to the use of the NeuroAdvocacy Toolkit (in policy plans, work plans, and others)	(1) no (2) yes
20	**Replacement when staff leave**	Replacement of staff leaving the organization	In my national neurosurgical society, there are arrangements in place so that staff who use the NeuroAdvocacy Toolkit and leave the organization are replaced in good time by staff who are/will be adequately prepared to take over	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
21	**Staff capacity**	Adequate staffing in the department or in the organization where the innovation is being used	There are enough people in our national neurosurgical society to use the NeuroAdvocacy Toolkit as intended	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
22	**Financial resources**	Availability of financial resources needed to use the innovation	There are enough financial resources available to use the NeuroAdvocacy Toolkit as intended	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree

23	**Time available**	Amount of time available to use the innovation	Our national neurosurgical society provides me with enough time to include the NeuroAdvocacy Toolkit as intended in my yearly activities	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
24	**Material resources and facilities**	Presence of materials and other resources or facilities necessary for the use of the innovation as intended (such as equipment, materials, or space)	Our organization provides me with enough materials and other resources or facilities necessary for the use of the NeuroAdvocacy Toolkit as intended	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
25	**Coordinator**	The presence of one or more persons responsible for coordinating the implementation of the innovation in the organization	In my organization, one or more people have been designated to coordinate the process of implementing the delivery of the NeuroAdvocacy Toolkit	(1) no (2) yes
26	**Unsettled organization**	The degree to which there are other changes in progress (organizational or otherwise) that represent obstacles to the process of implementing the innovation, such as re-organizations, mergers, cuts, staffing changes, or the simultaneous implementation of different innovations	In addition to implementing the NeuroAdvocacy Toolkit, are there any other organizational changes affecting the implementation of the innovation now or in the foreseeable future (reorganization, merger, cuts, staffing changes, other innovations)?	(1) no (2) yes
27	**Information accessible about the use of innovation**	Accessibility of information about the use of the innovation	It is easy for me to find information in my organization about using the NeuroAdvocacy Toolkit as intended	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree

28	**Performance feedback**	Feedback to the user about progress with the innovation process	In my neurosurgical association, feedback is regularly provided about progress with the use of the NeuroAdvocacy Toolkit	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree
Determinants associated with the socio-political context				
Determinant	**Name**	**Description**	**Operationalization**	**Response scale**
29	**Legislation and regulations**	The degree to which the innovation fits in with existing legislation and regulations established by the competent authorities	The activities listed in the innovation fit in well with existing legislation and regulations	(1) totally disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) totally agree

APPENDIX C: Phase 3. Interview protocol to key opinion leaders

Thank you for agreeing to participate in this study. This interview will be recorded, and only the audio component of the recording will be transcribed. All the materials will be destroyed after the completion of the study. All the answers will be confidential, and you are encouraged not to use specific names. Please, feel free to answer all questions or pass on any questions that might make you uncomfortable or do not want to answer.

If that is OK with you, I will start the recording now.

1. Exploratory question: Please, state your name and current position in your national society for pediatric neurosurgery. For how long have you been appointed to this position? What are your roles in the organization?
2. Leading question: Tell me about your opinion on the role of pediatric neurosurgeons as health advocates.
    a. Follow-up question: Walk me through your experiences in advocating for health initiatives.
    b. Follow-up question: How does it make you feel when participating in such initiatives?
    c. Follow-up question: What benefits does participation in these activities bring for a medical specialist like you?
3. Leading question: What are the main challenges when advocating for a health cause?
    a. Follow-up question: What strategies do you use to overcome those challenges?
    b. Follow-up question: Are there any potential drawbacks when participating in such causes?

4. Leading question: To your knowledge, are there any plans for further food fortification policies to improve human health in your country?
    a. Follow-up question: What kind of evidence do you think policymakers usually seek when designing a policy for mandatory food fortification?
    b. Follow-up question: What would be the preferred mechanisms and formats to receive and use evidence-based knowledge in your country?
5. Leading question: After being introduced to the NeuroAdvocacy Toolkit, tell me about your general opinion on the toolkit as a strategy to translate knowledge to policymakers
    a. Follow-up question: In your opinion, what elements of the toolkit make it suitable for knowledge transfer to policymakers?
    b. Follow-up question: What element, if any, would you change to enhance the likelihood that the toolkit meets its purpose?
6. Leading question: How motivated do you feel, like an expert in the field, to use the NeuroAdvocacy Toolkit to inform policymakers' decisions?
    a. Follow-up question: What would be the ideal ways to approach those policymakers?
    b. Follow-up question: What mechanisms do you think will be more effective when trying to deliver the NeuroAdvocacy Toolkit to the policymakers?
    c. Follow-up question: What obstacles, if any, do you anticipate when approaching policymakers and delivering the toolkit?
    d. Follow-up question: What circumstances would make it easier to deliver the toolkit to policymakers?

7. Leading question: After delivering the NeuroAdvocacy Toolkit, what would be a good way to follow up on the knowledge utilization by the policymakers?
    a. Follow-up question: To what extent would you be willing to be contacted again by the policymakers for follow-up questions?
    b. Follow-up question: To what extent would you like to contact policymakers for further verification of knowledge use?
8. Is there any comment you would like to add to what you have shared in this interview?

Thank you very much for participating in this interview. If necessary, would it be OK to contact you for further follow-up questions about this interview?

APPENDIX D. Diplomatic Concept Note from the Colombian Government to the World Health Organization Secretariat

El futuro es de todos
Gobierno de Colombia

Government of Colombia
Ministry of Health and Ministry of Foreign Affairs
Concept Note

Proposed agenda item - Prevention of congenital malformations through food fortification with micronutrients and draft resolution

Context

The 63rd World Health Assembly, held in 2010, reviewed the report on congenital malformations prepared by the WHO Secretariat and its importance as a cause of prenatal and neonatal mortality, as well as mortality in children under five years of age. As a result, the WHA adopted resolution WHA63.17, recognizing that congenital disorders are due to various causes and determinants, including preventable factors such as infectious or nutritional factors. The text also promoted primary prevention and improvement of the health of children with congenital disorders and requested the Member states to:

- Develop and strengthen registration and surveillance systems as recommended by WHO-Nutrition in collaboration with other departments and the USCDC.
- Develop expertise and build capacity for the prevention of congenital disorders and care of affected children;
- Increase coverage, allocate resources, and formulate plans for effective prevention measures, including vaccination against rubella, folic acid supplementation, and programs addressing tobacco and alcohol use among pregnant women and women who are trying to conceive;
- Raise awareness of the importance of newborn screening programs and their role in identifying infants born with congenital malformations;
- Support families who have children with congenital malformations and associated disabilities;
- Strengthen research on major congenital disorders and promote international cooperation to prevent them.

Additionally, the resolution requested the Director General to support the Member States in developing national plans for implementation of effective interventions to prevent and manage congenital malformations within their national maternal, newborn, and child health plan, strengthening health systems and primary care, including improved coverage of vaccination against diseases such as measles and rubella, of addressing tobacco and alcohol use among pregnant women and women trying to conceive, along with **food fortification strategies, for the prevention of congenital malformations, and promoting equitable access to such services**.

However, this resolution, adopted more than ten years ago, was the latest mandate from the World Health Assembly to the Member States and the WHO Secretariat on these causes of prenatal and neonatal mortality, which continue to be of significant impact and importance.

According to the World Health Organization (WHO), **303,000 newborns die yearly in the first four weeks of life due to congenital anomalies**. The most common and severe congenital disorders are neural tube defects, including spina bifida, encephalocele, anencephaly, cardiac malformations, and Down syndrome. Although it is not possible to assign a specific cause to about 50% of congenital anomalies, some causes and risk factors have been identified, such as socioeconomic and demographic factors, genetic factors, infections, maternal nutritional status, and environmental factors.

In this sense, the WHO has stated that it is possible to prevent some congenital anomalies, for example, with fundamental preventive measures such as vaccination, sufficient intake of folic acid and iodine by women of reproductive age, ensuring an adequate supply of vitamins and minerals in the diet (through the fortification of staple foods or the provision of supplements), as well as appropriate prenatal care.

Colombia recognizes neural tube defects, such as anencephaly, encephalocele, and spina bifida, as among the most severe congenital disorders. Worldwide, 300,000 children are born with this condition, and 100,000 will die unnecessarily each year. Regarding the morbidity of these diseases, children who survive these congenital anomalies have a lifelong neurological impairment and require multiple surgeries, a significant need for complex care that, unfortunately, is never curative.

Although most neural tube defects are multifactorial in origin, folic acid deficiency or insufficiency during the periconceptional stage directly correlates with the prevalence of these defects. The scientific evidence has shown that most neural tube defects are sensitive to maternal folic acid levels and can be prevented by mandatory fortifying foods such as wheat, corn, rice, or other staple foods with folic acid. However, only 23% of these congenital disorders are currently being prevented worldwide.

A recent call to action from the scientific community, published in The Lancet Global Health, urges the World Health Assembly to pass a resolution for universal mandatory folic acid fortification. Such a resolution could accelerate the slow pace of spina bifida and anencephaly prevention globally and assist countries in reaching their 2030 Sustainable Development Goals on child mortality and health equity. The cost of inaction is profound and disproportionately impacts susceptible populations in low-income and middle-income countries.

Benefits of fortifying staple foods with micronutrients

Food fortification was discussed at the United Nations Food Systems Summit 2021 and Nutrition for Growth 2021, where investment and government commitments took place. Some particular benefits of fortifying foods with micronutrients are described below:

1. Food fortification ensures adequate levels of maternal micronutrients like folic acid before conception. Most congenital malformations and disorders, such as spina bifida and other neural tube defects, uniformly occur before pregnancy is known, making vitamin supplements taken during pregnancy ineffective.
2. Although folic acid supplementation is effective when started at least three months preconceptionally, this measure has limited coverage since less than half of pregnancies are planned, and only 4% of women of reproductive age take oral supplements. Moreover, adolescents and vulnerable populations that cannot access health services are left unprotected.
3. Only mandatory fortification of staple foods results in widespread maternal micronutrient levels sufficient to prevent spina bifida and other congenital malformations.
4. At the recommended levels, large-scale fortification with micronutrients, including folic acid (vitamin B9), iron, vitamin A, iodine, and zinc, is very safe, effective, and cost-beneficial. For example, incidence rates of spina bifida in countries with fortification are consistently 8/10,000 live births. Rates without fortification are orders of magnitude higher (50-120/10,000 with focal epidemics of >150/10,000).
5. In terms of the cost-effectiveness of this prevention measure, every dollar invested in fortification results in many thousands of dollars of savings in future health care costs. For instance, the cost per death averted through mandatory folic acid fortification is estimated to be U$957.
6. Iron, folic acid, zinc, vitamin A, and other B vitamins help prevent nutritional anemia, which improves productivity, maternal health, and cognitive development.
7. Fortifying with folic acid may also have a role in the child's mental health.
8. Zinc helps children develop, strengthens immune systems, and lessens complications from diarrhea.
9. Vitamin A helps individuals fight infections and helps prevent childhood blindness.

Objectives of the inclusion of the prevention of congenital malformations as an agenda item of the 76th WHA in 2023.

Given that congenital malformations are a public health problem, Colombia has considered it essential to revitalize and promote within the WHO the agenda on the preventive approach to congenital malformations. These disorders include spina bifida, anencephaly, other neural tube defects, cardiovascular malformations, cleft lip and palate, and other congenital disorders. Consequently, Colombia requests to **incorporate this item in the 152nd Session of the WHO Executive Board to be held in January 2023**.

The proposed novel resolution, to be discussed and agreed upon by the Member States, **brings together the synergies of food and health systems and seeks the following objectives**:

- Decrease inequities in the access to quality food and health interventions through social protection measures for the population's most vulnerable and disadvantaged sectors by articulating the synergies of the food and health systems.
- Diminish the unnecessary and costly allocation of resources and efforts to treat conditions that are by other means preventable
- Mitigate the impact that preventable congenital malformations have on public health systems, society, families, and individuals
- Promote that WHO Member States strengthen their commitment to the prevention of congenital malformations and other conditions as part of their regular health programs and maternal and child health promotion through mandatory fortification of staple foods with folic acid, iron, vitamin A, iodine, and zinc, according to each country's context, needs, ethnicity, and cultural realities
- Facilitate the promulgation, update, optimization, scaling up, implementation, and surveillance of fortification policies with harmonized standards in line with WHO recommendations to achieve a population impact.
- Promote the integration of multiple stakeholders and sectors in articulating efforts to implement sustainable large-scale fortification while supporting periodic monitoring and surveillance of fortification status, fulfillment of harmonized standards, quality control of enriched products, and micronutrient serum levels among women of reproductive age

Impact on Sustainable Development Goals (SDGs)

Food fortification with micronutrients such as folic acid, iron, vitamin A, iodine, and zinc has a direct impact on at least three SDGs and three targets, as depicted in the following table:

SDG	DESCRIPTION	TARGET	DESCRIPTION	TANGIBLE IMPACT OF THE PROPOSED RESOLUTION
2 ZERO HUNGER	End hunger, achieve food security and improved nutrition, and promote sustainable agriculture	2.2	By 2030, end all forms of malnutrition, including achieving, by 2025, the internationally agreed targets on stunting and wasting in children under 5 years of age, and address the nutritional needs	Different multinational surveys demonstrate that folate deficiency and insufficiency are endemic worldwide among women of reproductive age. Population maternal folate levels correlate directly with the

			of adolescent girls, pregnant and lactating women, and older persons	population incidence of spina bifida, anencephaly, other neural tube defects, major cardiovascular malformations, cleft lip and palate, and other congenital conditions. Large-scale food fortification with micronutrients is an efficacious, cost-effective, safe, and feasible measure to address the nutritional needs of adolescent girls, women of reproductive age, and pregnant and lactating women.
3 GOOD HEALTH AND WELL-BEING	Ensure healthy lives and promote well-being for all at all ages	3.2	By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births	Large-scale food fortification with micronutrients aids in the reduction of anemia by 50% and the reduction of low birth weight. It also decreases iodine deficiency disorders such as brain damage to millions of children, goiter, cretinism, stillbirth, miscarriage, and physical impairment. Class I medical evidence for over 30 years demonstrates the effectiveness of mandatory folic acid fortification in reducing spina bifida, anencephaly, and other neural tube defects, along with other systemic congenital
		3.4	By 2030, reduce by one-third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being	

				malformations. Additionally, this evidence-based policy prevents other conditions like visual and skin disorders related to vitamin A deficiency, gastrointestinal disorders, and cognitive impairment related to zinc deficiencies, among other diseases.
10 REDUCED INEQUALITIES	Reduce inequality within and among countries	10.3	Ensure equal opportunity and reduce inequalities of outcome, including by eliminating discriminatory laws, policies, and practices and promoting appropriate legislation, policies, and action in this regard	Being born with a preventable disability is a clear source of inequality, particularly affecting vulnerable populations. Public policies enforcing mandatory fortification of staple foods with micronutrients will help overcome inequities in the access to quality food and robust evidence-based public health interventions

Documents supporting the proposed resolution for food fortification with micronutrients to prevent congenital malformations and other disorders:

- https://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_10-sp.pdf
- https://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R17-sp.pdf
- WHO/CDC/ICBDSR. Birth defects surveillance: a manual for programme managers. Geneva: World Health Organization; 2014.
- WHO/CDC/ICBDSR. Birth defects surveillance: atlas of selected congenital anomalies. Geneva: World Health Organization; 2014.
- Birth defects surveillance: a manual for programme managers, second edition. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO
- Birth defects surveillance: quick reference handbook of selected congenital anomalies and infections. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

- Birth defects fact sheet. Updated February 2022 https://www.who.int/news-room/fact-sheets/detail/birth-defects
- Comprehensive implementation plan on maternal, infant, and young child nutrition. http://apps.who.int/iris/bitstream/handle/10665/113048/WHO_NMH_NHD_14.1_eng.pdf;jsessionid=0D5460B0638196F0A94C6E905FB4CA45?sequence=1
- FAO Second International Conference of Nutrition - Framework for action. Recommendation 42. https://www.fao.org/3/i4465e/i4465e.pdf
- WHA58.24. https://apps.who.int/gb/ebwha/pdf_files/WHA58/WHA58_24-en.pdf
- UN Food systems summit 2021: the coalition for healthy diets. https://www.who.int/initiatives/food-systems-for-health/the-coalition-of-action-on-healthy-diets-from-sustainable-food-systems-for-children-and-all
- Why fortify: Save Lives: https://www.ffinetwork.org/savelives
- Preventing birth defects, saving lives, and promoting health equity: an urgent call to action for universal mandatory food fortification with folic acid. The Lancet Global Health. https://www.sciencedirect.com/science/article/pii/S2214109X22002133

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بسم الله الرحمن الرحيم

In the name of Allah, the Merciful

En el nombre de Allah, el Misericordioso