

The challenge of global elimination policies: A case study of malaria and other diseases of poverty

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DEDICATION

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RESUMEN

Malaria es una prioridad en los programas de salud pública global. Cada año se registran cerca de 800 mil a un millón de muertes. Las áreas endémicas más afectadas por esta enfermedad parasitaria son las regiones con altos índices de pobreza y miseria donde la estructura poblacional es piramidal y de base amplia. Los niños y las mujeres embarazadas son los grupos que sufren el impacto de esta enfermedad transmitida por vectores del género *Anopheles spp.* Alrededor de 90 países en el mundo reportan casos autóctonos y transmisión activa. Enormes esfuerzos se han realizado a través del tiempo con el propósito fundamental de aliviar su carga y efecto devastador en la salud de las poblaciones afectadas como la carga que conlleva sufrir de esta patología.

En esta investigación se presenta una combinación de abordajes metodológicos, ontológicos y axiológicos, que permiten dar cuenta de los diferentes componentes intrínsecos y extrínsecos, que afectan las dinámicas de transmisión y control de la malaria. Las limitaciones son inherentes a la capacidad del investigador, y es bastante probable que ese documento no presente la totalidad de factores y determinantes que interactúan en el sistema complejo que abarca la problemática de la malaria. Sin embargo, se hace un gran esfuerzo por combinar paradigmas desde el positivista hasta el constructivismo histórico, para contribuir en la comprensión de este fenómeno y comparar evidencias cualitativas y cuantitativas en áreas endémicas de Colombia y las Américas. El propósito es reconstruir las trayectorias y experiencias para el desarrollo y estructuración de modelos mejorados de control acordes a los contextos específicos donde la malaria y otras patologías de la pobreza mantienen su presencia contribuyendo como determinantes para que en ocasiones las enfermedades resurjan desafiantes tanto para los sistemas de atención en salud como para las políticas de control que se implementan. Los capítulos I y II dan cuenta de este ejercicio académico, en donde el establecimiento de paradigmas, preguntas ontológicas, epistemológicas, axiológicas y metodológicas son delimitadas en términos de variables como tiempo, poblaciones y lugares.

El proceso de análisis inicia con una revisión narrativa de textos indexados y grises que dan cuenta de las transformaciones históricas de los conceptos de control, eliminación y erradicación. Esta lectura ha permitido comprender e interpretar que en el tiempo y según las estructuras políticas, económicas, sociales y culturales en la línea del tiempo analizada, siglo XX y parte del Siglo XXI, la malaria requiere un abordaje tras-disciplinar y de multinivel, y adicionalmente sacar la problemática del modelo *biologicista* a un contexto bio-socio-político más incluyente y amplio. La malaria es un fenómeno complejo y como tal las estrategias de control, eliminación y erradicación obligan a

reconocer los logros parciales de cada intervención implementada a través del tiempo. La búsqueda de “balas mágicas” es un proceso constante de reconocimiento de todas las partes y actores involucrados, desde los investigadores, la academia, las instituciones hasta la participación activa permanente de las comunidades afectadas, y de acercamiento entre lo público y lo privado. Esta detallada descripción aparece en el capítulo III, el cual se titula: **Concepts evolution of malaria control, elimination and eradication. Historical Review**, el cual fue sometido al Journal of Malaria.

Posteriormente y con el propósito de correlacionar y triangular las evidencias primarias y secundarias, se realiza la presentación del estudio de campo y revisión narrativa de la situación de eliminación de malaria en Colombia y Latin América, el cual aparece en el capítulo IV, con el título de: **Proportion of Fever Attributable to Malaria in Colombia: Potential indicators for tracking progress towards malaria elimination**. El estudio descriptivo y de corte transversal, permitió identificar en diferentes escenarios epidemiológicos y socio-demográficos, características comunes relacionadas con las dinámicas de transmisión de la malaria. Las regiones endémicas seleccionadas para Colombia, comparten problemas estructurales a los de otras regiones maláricas en América Latina. Los problemas del sector productivo primario: agricultores, mineros, pescadores, y migrantes o desplazados, muestran la injusticia social de las políticas de estado y la inequidad entre regiones. La débil gobernanza y pobre inversión como la ausencia de modelos de desarrollo, para áreas rurales y peri-urbanas están causalmente relacionadas con las pobres condiciones de vida y la presencia de enfermedades de la pobreza. Los sistemas de información y alerta temprana de brotes y epidemias es casi inexistente. Los registros semanales de casos y la vigilancia de falla terapéutica, o de resistencia a los insecticidas esta pobremente documentada. La proporción de asintomáticos aunque baja sigue siendo el problema que se evidencia en los años sesenta durante la primera era de erradicación.

Desde el Desarrollo de las Metas del Milenio, se han retomado los conceptos de eliminación para aquellas regiones con programas de control de eventos de baja frecuencia pero de interés en salud pública. En el caso de Colombia, el Bocio Endémico y la política de yodación de la sal como estrategia costo efectiva de eliminación de este problema, se impulso desde finales del Siglo XIX. Sin embargo en 1998, se declaro al país libre de Bocio. Desafortunadamente, la ausencia de programas de monitoreo y evaluación, no ha permitido su eliminación y por el contrario la ausencia de políticas de control y seguimiento oportunas a la yodación de sal, como de las poblaciones afectadas, nos permite decir que hoy esta enfermedad sigue estando presente en niños en edad escolar y en mujeres embarazadas, con las consecuencias en el desarrollo cognitivo y de

aprendizaje de los escolares pobres de regiones deprimidas. En el capítulo V, se revisa la política y el retroceso de control que ha tenido el Bocio Endémico en Colombia, y nos ejemplifica, las debilidades de acompañamiento y sistemas de vigilancia en programas de control hasta alcanzar la meta del Zero. El capítulo aborda nuevamente desde el constructivismo la transformación en el tiempo de la política de control y su retroceso : **Historical Review of the current sanitary policy of goiter elimination in Colombia, 1990-2012**

Finalmente, en el capítulo VI, hay una reflexión y triangulación de fuentes, con el propósito de cuestionar los logros y desafíos a los que los programas de control y de salud pública se enfrentan en la búsqueda de reducir la carga de enfermedad, y sus efectos en bucle causal para los mas pobres y desprotegidos. No menos importante, se plantean nuevas preguntas de investigación que en consulta de fuentes aparentemente están sin respuesta, y requieren adicionales investigaciones operativas, y el desarrollo de intervenciones novedosas, que impacten en la incidencia de la enfermedad desde la prevención primaria, pero apoyada en programas de promoción de la salud, atención primaria en salud, y el fortalecimiento de los sistemas de información.

En conclusiones, los resultados confirman la necesidad de definir mecanismos de vigilancia, evaluación y monitoreo de los programas de eliminación. El acompañamiento permanente a los servicios de salud de las áreas endémicas, como el desarrollo de políticas y modelos de desarrollo, para las áreas mas vulnerables, con necesidades particulares, requieren dada su complejidad abordajes integrales, donde las estructuras primarias de la sociedad, puedan disminuir las brechas de equidad, y reducir al máximo las injusticias sociales con apoyo participativo y activo de la comunidad.

SUMMARY

Malaria is a priority disease on the global public health agenda, with between 800 thousand and one million deaths reported annually. The endemic areas most affected by this parasitic disease have high poverty rates across broad population groups. Children and pregnant women suffer the biggest impacts from this disease, which is transmitted by *Anopheles spp.* mosquitoes. About 90 countries worldwide report indigenous cases with active transmission. Enormous efforts are on-going to alleviate the disease burden and its devastating effect on health in vulnerable populations.

This research presents a combination of methodological, ontological, and axiological approaches in order to further understand the intrinsic and extrinsic components of malaria which affect the dynamics of transmission and control measures. Limitations are inherent in the ability of the researcher, and this document is unlikely to fully present all factors and determinants which interact in the complex system of malaria. Nonetheless, it reflects a major effort to combine paradigms from positivism to historical constructivism. The purpose of this work is to contribute to the understanding of this phenomenon and compare qualitative and quantitative evidence in malaria-endemic areas of Colombia and the Americas. Additional effort is made to reconstruct the trajectories and experiences of control and prevention and recognize elements to improve models of control, considering the specific contexts where malaria and other diseases of poverty persist. In Chapters I and II, the realities and nature of the problem are defined, specifically to establish paradigms as well as ontological, epistemological, axiological and methodological questions, while the objective of the research is defined in terms of variables such as time, people and places.

The analysis process begins with a narrative review of gray literature and indexed texts covering the historical transformations of concepts of control, elimination and eradication of malaria. The compilation of sources interprets the effect of political, economic, social and cultural structures on trends of malaria and diseases of poverty. Additionally, the problem of elimination of infectious diseases is followed from a "biologist model" to a more inclusive and broad bio-socio-political context. Malaria is a complex phenomenon, and control/ elimination /eradication strategies should not underestimate the importance of partial achievements from interventions implemented over time. The search for "magic bullets" is a constant and continual process of recognition by all involved actors, including researchers, academic and public-private institutions, as well as sustained active participation by the affected communities. The detailed description of this process is presented in Chapter III, **Concepts evolution of malaria control, elimination and eradication. Historical Review**, as submitted to the Journal of Malaria.

In order to correlate and triangulate the primary and secondary evidence, field work to identify epidemiological markers of advancement and a narrative review on the status of elimination of malaria in Colombia and Latin America are analyzed. These findings are reported in Chapter IV, **Proportion of fever attributable to malaria in Colombia: Potential indicators for tracking progress towards malaria elimination**. A cross-sectional survey descriptive study, conducted in two regions of Colombia, aimed to identify risk factors (epidemiological and socio-demographic) and baseline characteristics related to the dynamics of malaria transmission. These two regions shared similar structural problems with other malaria endemic regions of Latin America. The field results are strongly correlated with the narrative review. Part of the problem is explained through the primary productive sector, which consists of farmers, miners, fishermen, and migrants/displaced persons, reflecting social injustice and inequalities between regions under the same public policies. Poor governance and reduced infrastructure investment for the health and education sectors, combined with scarce development models for rural and peri-urban areas, produce inadequate living conditions which perpetuate diseases of poverty and high rates of maternal and infant mortality. Information systems for early prediction of outbreaks and epidemics are inadequate or non-existent. Recording of cases on a weekly basis and monitoring of therapeutic failures and insecticide resistance are poorly documented. The proportion of asymptomatic individuals, despite the low reported rates, remains a clinical and epidemiological problem.

In the objectives of the Millennium Development Goals, the concepts of elimination particularly focused interest on public health programs. In the case of Colombia, other diseases of poverty can be used as epidemiological markers of the goals achieved. Using the example of endemic goiter, the policy of salt iodization has been adapted as the most cost effective strategy for elimination. By 1998, Colombia declared the country free of goiter. Unfortunately, the lack of monitoring and evaluation programs has hindered appropriate follow up to ensure continued iodization of salt. This study indicates that the disease is still prevalent in school children and pregnant women. In Chapter V, entitled **Historical review of the current sanitary policy of goiter elimination in Colombia, 1990-2012**, a review on the control policy addresses the decline from a constructivism paradigm.

In Chapter VI, the impact of this research to improve the policy of elimination, considering local examples which are widely generalizable to other endemic areas in the same region of the Americas, is presented. New research questions for additional operational research and the development of novel interventions which impact on the incidence of disease are articulated.

In conclusion, these results confirm the need to define mechanisms for monitoring and evaluation of programs for elimination. Given the complexity of the health problems, strategies of control must consider reducing inequities, social injustice, and, importantly, the gender component, which are consequences of violence in Colombia.

Chapter I Introduction

Public health researchers consider a wide range of diseases and try to study their determinants, thereby offering a foundation for action and for planning and intervention strategies. Health systems and control programs design models that characterize populations in terms of the distribution and magnitude of a specific health problem. Interventions are selected and implemented based on a cost benefit analysis and on the effectiveness demonstrated by predictive models. Supply and demand relationships determine the quality and coverage of public health programs and establish indicators for monitoring and evaluation. The most important goal of a health system, according to the WHO, is to promote universal health care, ensuring that all people receive health care without suffering financial hardship as a result; unfortunately, many health systems have not yet arrived at this point(1). As Kenneth Arrow suggested, the health care economy is affected by markets and “the special economic problems of medical care can be explained as adaptations to the existence of uncertainty in the incidence of disease and in the efficacy of treatment” (2). This assumption is commonly observed in low-, middle-, and high-income countries. On one side, there are transmissible diseases, classified as either diseases of poverty like most vector borne pathologies i.e. dengue, chikungunya, leishmaniasis, zika yellow fever, or as chronic infectious diseases, like HIV or TB. On the other side, the study and control of chronic diseases with long periods of latency, like cancer, cardiovascular diseases and obesity related to diabetes, represent high costs to health systems and public policies. In addition, implementing health promotion and disease prevention strategies (from basic to primary and secondary prevention) requires substantial economic investments in both qualified human resources and in physical infrastructure. Long-term variations in the patterns of disease transmission and presentation, in terms of time and location, cannot be forecasted.

In addition to this epidemiological transition, demographic changes are also evident in all regions of the world. Permanent migration between continents, political unrest and resulting flows of refugees present a challenge for control and elimination programs to achieve their stated goals. Related programs and reforms are designed in consideration of the principles of universality and solidarity in providing medical care; unfortunately, program coverage and access does not always extend to various segments of the population.

The purpose of this study is to look at health policies designed to eliminate and eradicate diseases prevalent in endemic regions, but under conditions of widespread poverty. The factors and determinants of policy/program success or failure are also discussed and correlated with the socio-economic structure of the countries.

1.1 From outbreaks and epidemics to elimination and eradication

Those who study the history of communicable disease epidemiology consider several important outbreaks and epidemics from which to glean lessons for today. From the plague of Athens in 500 BC and the Black Death in Europe in 1330, through to the cholera epidemic in London in 1840, (studied extensively by Sir John Snow) and the most recent Ebola epidemic in 2014, each success and failure along the way has contributed to our understanding of the natural history of disease and to the development of palliative or curative procedures.

In the 20th century, considerable advances in science and technology led to several innovations with enormous utility in the field of disease control. Public health and epidemiological evidence has been being consolidated through scientific publications and science and technology networks, reflecting the needs of and considering the differences between particular regions, health systems and epidemiological profiles. In a similar way, international policy has evolved to meet specific health priorities. Since the mid-1950s, considerable efforts to reduce social injustice between regions have been implemented. Health for all by the year 2000 was the proposal of the 1970s, unfortunately with limited results but enough evidence to support new international policies of health. The Millennium Development Goals (MDGs) was another global strategy for reducing inequities between regions and was implemented between 2000 and 2015. In this strategy, efforts focused on decreasing the burden of disease caused by malaria, HIV, and TB. Other diseases of poverty were neglected and new alliances were created to alleviate hunger, malnutrition, and diseases of poverty, suffering and discrimination among vulnerable populations around the world. Table 1 shows the MDGs. The focus here on reducing poverty and empowering women, from an equity perspective, contributed substantially to reducing infant and maternal mortality, a health priority in all regions.

It is important to mention that throughout the history of public health, several victories have been won, mainly in the field of elimination and eradication. The most celebrated of these was smallpox eradication in 1977. To achieve this goal, eradication efforts were supported by health sectors, strong political interventions and the widespread use of an inexpensive vaccine that was simple and easy to administer. Smallpox eradication was possible because of an existing, well-known and highly efficacious vaccine and because of well-organized health services with strategic plans and periodic evaluation of the state of immunization. Successful eradication has been attributed to the implementation of an efficient surveillance system, including permanent monitoring to detect and forecast epidemics and outbreaks, which was essential to eventually declaring the world free of smallpox (3)(4)(5).

Other important successes on the way to elimination and eradication include the global reduction of measles incidence by 91%, between 2000 and 2006; concerted efforts to eliminate Rubella in Europe and the reduction of American Trypanosomiasis incidence in Latin America by

Table 1. UN Millennium development goals

The goals	Action
1. Eradicate extreme poverty and hunger	<ul style="list-style-type: none"> • Reduce by half the proportion of people living on less than a dollar a day • Reduce by half the proportion of people who suffer from hunger
2. Achieve universal primary education	<ul style="list-style-type: none"> • Ensure that all boys and girls complete a full course of primary schooling
3. Promote gender-equality and empower women	<ul style="list-style-type: none"> • Eliminate gender-disparity in primary and secondary education, preferably by 2005, and at all levels by 2015
4. Reduce child mortality	<ul style="list-style-type: none"> • Reduce the mortality rate among children under five by two-thirds
5. Improve maternal health	<ul style="list-style-type: none"> • Reduce the maternal mortality ratio by three-quarters
6. Combat HIV/AIDS, malaria and other diseases	<ul style="list-style-type: none"> • Halt and begin to reverse the spread of HIV/AIDS • Halt and begin to reverse the incidence of malaria and other major diseases
7. Ensure environmental sustainability	<ul style="list-style-type: none"> • Integrate the principles of sustainable development into countries' policies and programs; reverse loss of environmental resources • Reduce the proportion of people without sustainable access to safe drinking water by half • Achieve significant improvement in the lives of at least 100 million slum dwellers, by 2020
8. Develop a global partnership for development	<ul style="list-style-type: none"> • Develop further an open trading and financial system that is rule-based, predictable and non-discriminatory, including a commitment to good governance, development and poverty reduction (nationally and internationally) • Address the least-developed countries' special needs. This includes tariff- and quota-free access for their exports, enhanced debt relief for heavily-indebted poor countries, cancellation of official bilateral debt and more generous official development-assistance for countries committed to poverty-reduction • Address the special needs of landlocked and small island developing states

	<ul style="list-style-type: none"> • Deal comprehensively with developing countries' debt problems through national and international measures to make debt sustainable in the long-term • In cooperation with the developing countries, develop decent and productive work for youth • In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries • In cooperation with the private sector, make available the benefits of new technologies, especially information and communications technologies http://www.un.org/millenniumgoals/index.html
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Source: United Nations www.un.org/millenniumgoals/index.html#

more than 70%, between 1983 and 2000(6), (7). Most recently, Colombia was declared free of the neglected tropical disease, onchocerciasis, more commonly known as “river blindness”(8). The list could be extended to malaria advances in Mesoamerica that reduced transmission considerably, and to reductions in the number of leprosy and tuberculosis cases.

1.2 From elimination to reintroduction: Iodine Disorder Deficiency

Currently, global elimination policies mainly focus on infectious diseases, however other diseases of poverty such as endemic goiter, associated with iodine deficiency disorder, are also targets of elimination. Iodine deficiency disorders were first treated by consumption of algae rich in iodine. Later, this was replaced with iodized salt, introduced in the early 1900s. Over time, the consumption of iodized salt contributed to eliminating this condition in many countries. Unfortunately, in New Zealand, Australia, and some European countries, iodine deficiency disorder continues to be an important public health problem. It is even more common in developing countries like Colombia. Primary prevention strategies have strongly recommended low consumption of salt to prevent cardiovascular diseases. However, there is a trend towards consuming more processed foods, rich in iodized salts. In Colombia, the first reported cases of goiter occurred around 1820-1823. By 1990, the country was declared free of endemic goiter. By 2013, a study conducted by Valero, Franco and Cuellar showed a frequency of this pathology of 15 to 30% among children between the ages of 6 and 14 years old in Bogota. Iodine in urine was also measured and almost 80% of children excreted more than 200 mg/ml, suggesting over consumption of iodized salt. Both disorders, related to iodine consumption, are associated with thyroid diseases. These findings suggest that the elimination policy for goiter disease has not been controlled, monitored or evaluated sufficiently. The population is further affected by the absence of control and supervision of the iodized salt industry(9).

1.3 Malaria case study: A disease of the poor and neglected

Malaria is one of the major diseases of poverty and several agencies provide financing to decrease the socio-economic impact and burden of the disease. The eradication and global control strategy popular from 1948 to 1990 changed approach to meet the objectives of the MDGs, which promoted a new era of elimination and eradication. This new global approach to eliminating and eradicating malaria has faced a considerable number of challenges. The number of agencies financing basic and applied research in this area is insufficient. The WHO malaria program recognizes that funding remains scarce, starting from USD 100 million in 2000 to USD 1.94 billion in 2012 and USD 1.97 billion in 2013(10). Given the limited number of indicators reached, the global community is transitioning to a new set of 17 goals, called the Sustainable Development Goals (SDGs), which will employ a multidisciplinary approach to reduce poverty and hunger and to improve education and nutrition conditions(11). Table 2 shows the goals for malaria 2016-2030.

Table 2. Objectives, activities and indicators suggested by the Global Technical Strategy for Malaria 2016–2030 Source: (11) modified by author

Planning Objectives	Indicators of monitoring and evaluation		Final Indicator
	By year		
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	≥40%	≥75%	≥90%
2. Reduce malaria case incidence globally compared with 2015	≥40%	≥75%	≥90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

According to World Health Organization, 3.2 billion people lived in malaria endemic areas in 2015 (12). The Malaria Report 2010-2015 estimated 207 million cases of malaria and about 627,000 related deaths in 2012. By 2013, more than 198 million malaria cases were recorded and estimated 584,000 malaria (93 countries). Of all malaria deaths globally, 90% occur in sub-Saharan Africa. The main causes of death in the world are presented in Table 3. Respiratory infections account for 3.9 million deaths annually, followed by malaria, with uncertainty ranging from 1.3 to 3.0 million deaths per year(13). Some differences in the figures can be observed due to methodological variations

insources and procedures from surveillance to meta-analysis and systematic reviews. Internal and external validity is considerable and has also affected the figures estimated.

The total number of malaria cases around the world has fallen from 500 million at the end of the 20th century to fewer than 200 million clinical cases in the current era of malaria elimination. According to the WHO Health Report 2015, malaria has been reduced globally by 30% (10).

Table 3. Annual global deaths from infectious diseases, in millions per year: 1990-2010, 2010, 2013. Source: (13)(14)(15)

Infectious Disease	Deaths in Millions 1990-2010 (15)	Deaths in Millions 2010 (14)	Deaths in Millions 2013 (13)
Respiratory Infections	3.4-2.8	3-4	3.9
Malaria	1.9-1.7	2	1.3 - 3.0
HIV/AIDS	0.30-1.15	1	2.5
Diarrhea	2.5-1.4	5-6	1.8
Tuberculosis	ND-1.2	1	1.7
Neglected Tropical Diseases	ND	ND	0.5

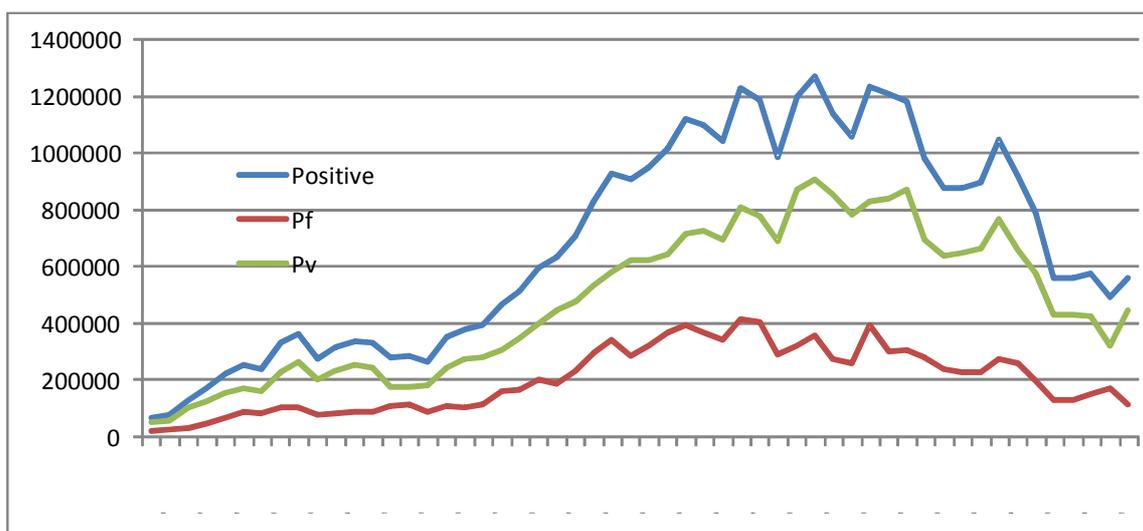
In the Americas, malaria incidence has fallen by 50%. Unfortunately, the crude analyses do not show the differences between regions. The serial reporting of cases since 1959 shows an irregular trend of malaria patterns. Earlier reports consolidated all of the cases by country. However, the Malaria Americas Report 2012, classifies countries by relative level of risk. Haiti, Guyana, Suriname, Venezuela, Colombia, Peru and Brazil account for the highest number of cases (16, 17); mainly in poor areas, with high rates of migration. Most health indicators, like access to and coverage of health services and public services, are considerably low, corresponding to high rates of infant and maternal mortality in the same regions (18).

In Latin America, slight reductions in malaria incidence started in the mid-nineties (19)(20). The latest report from the Pan-American Health Organization (PAHO) 2013 for malaria in the Americas gives 2012 statistics. In this report, the highest Annual Parasite Incidence (21) are in Mexico, Haiti, Guyana, Suriname, Venezuela and Brazil (19). The malaria problems in the Amazon region, eight

countries, are explained by non-program related processes of colonization, illegal economies, and intense mineral extraction from the soil. Regional demographic indicators show the presence of indigenous populations with high levels of unsatisfied basic needs (UBN), limited presence of health services (most of them of very basic level), and geographical barriers to access (22), (23), (24, 25), (18)

In Central America, the malaria situation must be analyzed for both continental countries and the Caribbean islands. The country with the highest prevalence rates, including mortality, is Haiti. In Mesoamerica, Mexico faces the greatest challenges to reducing the malaria burden. In South America, Guyana, Suriname and Brazil are affected by socio-economic and political conditions that undermine living conditions. Figure 1 shows the distribution of confirmed malaria cases. The Pf/Pv ratio is around 1:4; there was a 15% reduction of cases between 2000 and 2004 (16). By 2005, the number of cases had returned to 2000 levels. Between 2005 and 2008, cases fell again by almost 50%. There was no further reduction from 2008 to 2012 (assuming similar denominators). The incidence of *Plasmodium vivax* has increased considerably during the last decade, while *Plasmodium falciparum* malaria cases have fallen, as have the number of deaths attributed to this species. In Latin America, a malaria case is defined as any individual presenting with symptoms compatible with malaria and a positive blood smear. Trend differences between Pv vs. Pf cases have been observed since 2011 onwards.

Figure 1. Annual distribution of positive blood smear cases of malaria by passive case detection, showing the relation between *Plasmodium falciparum* and *Plasmodium vivax* in Latin America from 1959-2012. Source: adapted by the author from PAHO Malaria Report 2012-2014 (16, 17) and WHO Malaria Report 2015 (10)



In the Andean region, Venezuela and Peru showed the most positive cases of malaria. Countries located in the Southern Cone, Argentina, Chile and Bolivia (southern part bordering Argentina) showed a considerable reduction and are considered to be in pre-elimination phase. However, additional analyses must be carried out to compare these figures to seasonal variations, treatment failure, treatment, and coverage of the malaria control program.

1.3.1 Transformation of malaria control policy in Colombia

Depending on the period of analyses and the structure of comparison, the malaria situation in Colombia varies. Analyses conducted between 1960 and 2014 suggest patterns similar to the rest of Latin America, that is, reduction of *P. falciparum* and increase of *P. vivax* mortality and morbidity rates (20, 26, 27). Of the several analyses conducted for Colombia, most suggest that the health sector reform implemented in 1993, introducing the General Social Security System, known as Law 100, could not have supported reduction trends in endemic regions. In fact, the period 1993-2006 showed an increase eight times the incident rates during the period 1960-1975 (28), (29). As other authors mention, there are seasonal variations. However, it is not possible to assess if peaks occur every five, ten or thirty years, given that different variables have been included into the analyses. Some authors have explained the malaria patterns as a consequence of El Niño Southern Oscillation (30) phenomenon (27) and climate abnormalities (26). Socio-economic, political and cultural determinants can also explain the malaria transmission dynamics (18, 28, 29). The primary structures of society are powerfully associated with one another and geospatial analyses of these variables show strong correlations, thereby offering an explanation for malaria persistence, resurgence and the need for innovative approaches to elimination and eradication.

The lowest level of documented malaria cases in Colombia was in 1960, as a consequence of the worldwide Malaria Eradication Campaign (20), (31). However, since that time, morbidity has steadily increased, with prevalence of *Plasmodium falciparum* species giving way to *Plasmodium vivax* as the most troublesome species. Recent analyses clearly show a seasonal cycle of thirty years; starting with the low incidence of malaria in 1960 after eradication was introduced, and reaching maximum incidence between 2000 and 2005, similar to peaks between 1950 to 1955, just before the eradication era. All this evidence suggests that Colombia needs new strategies and programs to control and possibly eliminate malaria. Any new initiative must take account of several factors. First, Colombia is still experiences political unrest in endemic regions, with poor economic growth and socio-ecological conditions suitable for malaria transmission. Second, pre-elimination and elimination in Colombia need continuous control programs and ongoing human resource management and training, accompanied by adequate health service planning strategies at national and local levels as well as modern technology for evaluation and monitoring. Third, the surveillance system must guarantee a high level of data quality and make sentinel surveillance for prompt

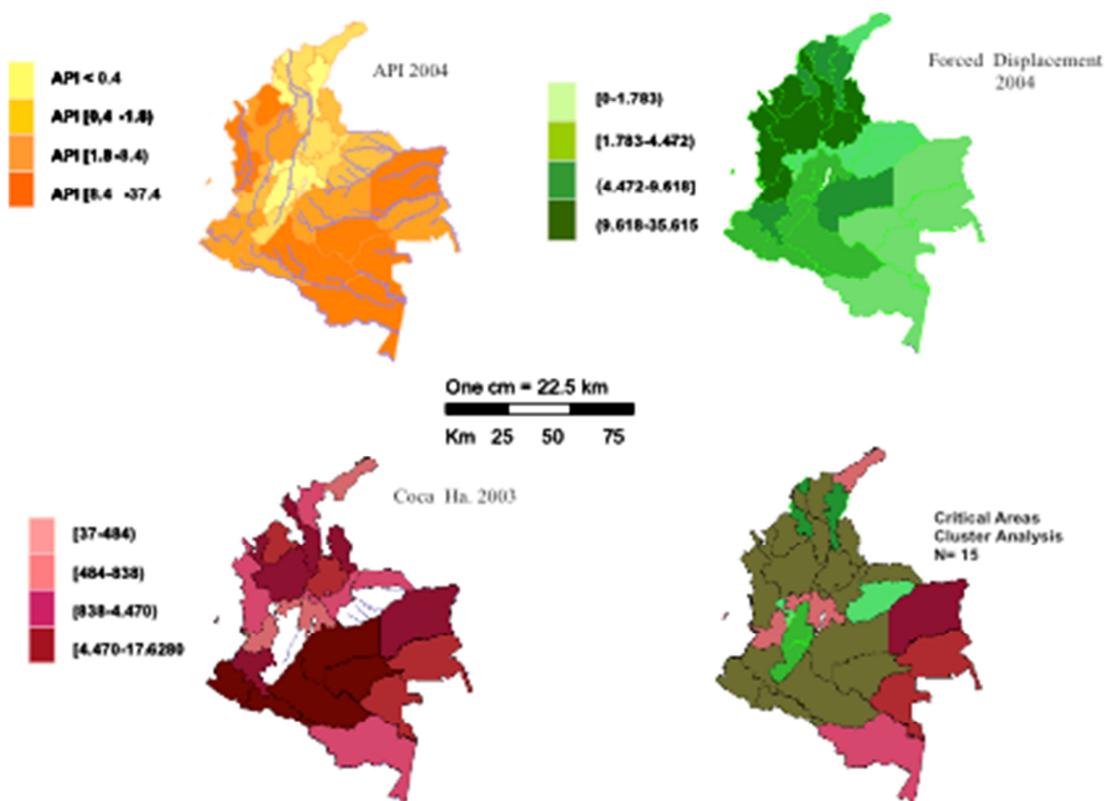
malaria detection a priority. Reports of parasite resistance and treatment failure in infected patients are limited.

A successful push towards elimination must include ongoing updates of the census and of the population at risk. The last census in Colombia was carried by 2005 and most of the population at risk denominators in use are projections—a situation that limits accurate forecasting and appropriate development of malaria indicators. We rely on estimations of these data as surveillance systems are weak and health workers' access is limited, especially in areas experiencing serious political unrest and terrorism. In other words, current malaria reporting likely underestimates the real situation in endemic areas.

Malaria transmission dynamics in Colombia corresponds to the tropical conditions in the affected areas, these being less than 2,000 meters above sea-level in 85% of rural areas. The afro communities of the Pacific Coast and several indigenous communities in Caqueta and Putumayo (Koreguajes), Guajira (Wayus) Catatumbo region (Motilonos) and Uraba region (Zenues, Emberas) are the most affected populations, where ethnic and cultural plurality are massive. Mass internal migration, mainly due to forced displacement from endemic to non-endemic areas, has also contributed to malaria's resurgence. Unplanned colonization and the indiscriminate exploitation of resources and the environment have had a considerable impact on malaria, primarily through deforestation. The economic development models implemented so far have not improved poverty conditions in rural or urban areas. Inequities persist and municipalities in categories 4 to 6,¹ all facing the same difficulties and inequities, have high transmission levels of most communicable diseases due to poor investment in health and development projects. Municipalities are categorized by level of decentralization and poverty. Map 1 presents the geo-spatial distribution of malaria in Colombia.

¹ The municipal category is a synthetic development index designed by Colombia's National Planning Department (NPD). Municipalities in categories 5 and 6 are less economically developed than municipalities in categories 1, 2 and 3. Such stratification considers 14 requirements to classify a municipality as decentralized and able to manage their own health budget.

Map 1. Spatial malaria distribution in Colombia. Source: prepared by the author



The Global Malaria Eradication program was implemented in 1956 under the dictatorship of Gustavo Rojas Pinilla². It assumed a vertical structure from the beginning, aided by financial and technical support from international agencies. Given the political conditions at the time, the program worked like a military operation and possessed a suitable administrative, technical and operational structure. The program underwent several changes in the mid-1960s due to evidence of anti-malarial drug resistance in Tumaco, on the Pacific Coast (1961). The 1960s were also characterized by the emergence of social resistance movements. Budget constraints led to malaria personnel organizing themselves to form a labor union (ANDEMINSAP) that supported strikes and caused disruptions during control activities. At that time, personnel were also assigned to other control measures and responsibilities, such as for yellow fever, dengue and vaccination campaigns. As a result, Colombia experienced increased malaria incidence rates from the 1980s onwards.

In spite of the limitations of under-reporting, which prevents a full understanding of the trends and dynamics of malaria transmission, malaria in Colombia shows three main trends during the second

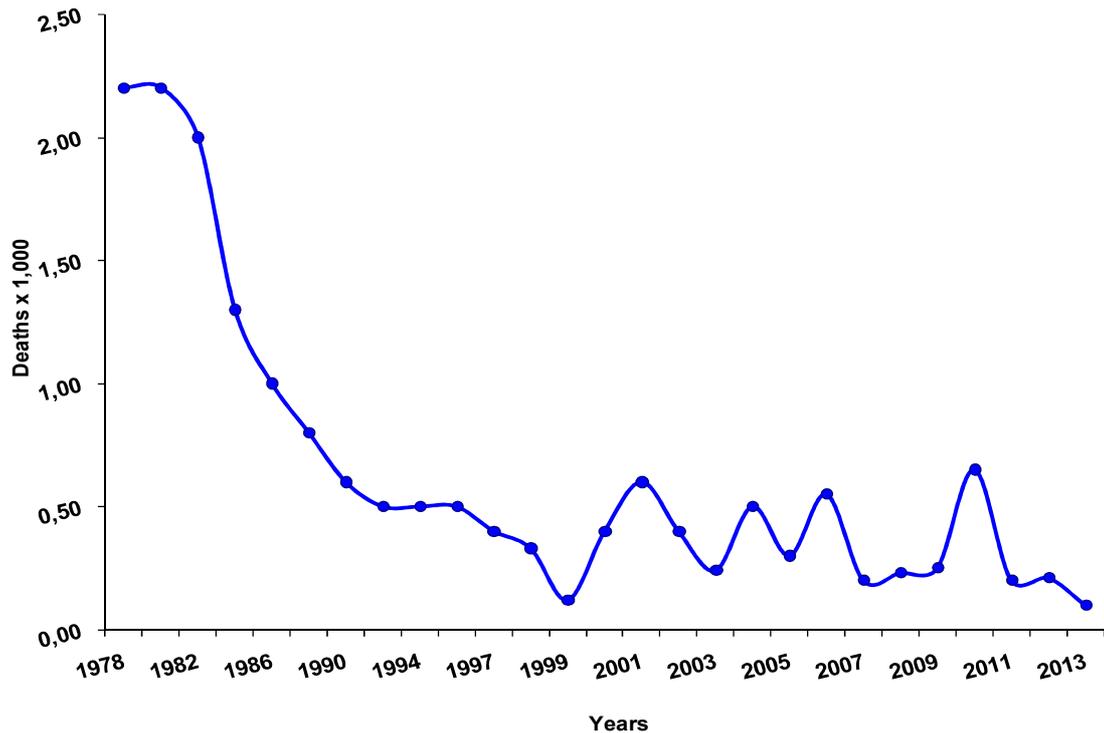
² Decree No. 2968, Ministry of Public Health with recommendations of the Public Health Cooperative Service, 8th General Assembly of the World Health Organization

half of the 20th century: (i) reduced mortality, (15) a steady increase in morbidity, and (15) considerable variation in the ratio of confirmed *P. vivax* to *P. falciparum* malaria cases (32),(33).

Figure 2 shows the reduced malaria mortality rate, which fell from 2.5 per 1,000 in 1978 to 0.4 per 1,000 in 2005. The main factors associated with the malaria campaign's success included tremendous financial support from both the state and international health agencies; appropriate administrative, technical and operational structures; good supervision and evaluation at all levels; and favorable reception by local/affected communities. Unfortunately, other major factors persisted, including: limited action to promote awareness of the illness, its transmission mechanisms and the need for preventive measures; precarious housing, often located in flood-prone areas; poor health service infrastructure in rural areas and associated isolation (poor roads and communication networks), low education and economic development levels and disorganized political participation in government spheres (18).

At the beginning of the 1970s, the malaria control program received little in the way of international financing and human resources. The decade was characterized by mass, disorganized colonization, which left few resources to adequately cover eradication efforts in the affected areas. At the same time, consolidated areas were unprotected and received limited advice/counseling for controlling epidemics in colonized areas. There was insufficient monitoring and diagnosis, low interest in health organizations, poor inter-sectoral communication and collaboration (because they no longer represented votes), decreased training resources at all levels and insufficient awareness and prevention measures. Technical problems were exacerbated by increased vector-resistance to insecticides and parasite-resistance to medication.

Figure 2. Colombia's mortality rate due to malaria, 1978-2013. Source: prepared by the author with data from the Vector Borne Diseases Program at the Ministry of Social Protection of Colombia, 2013



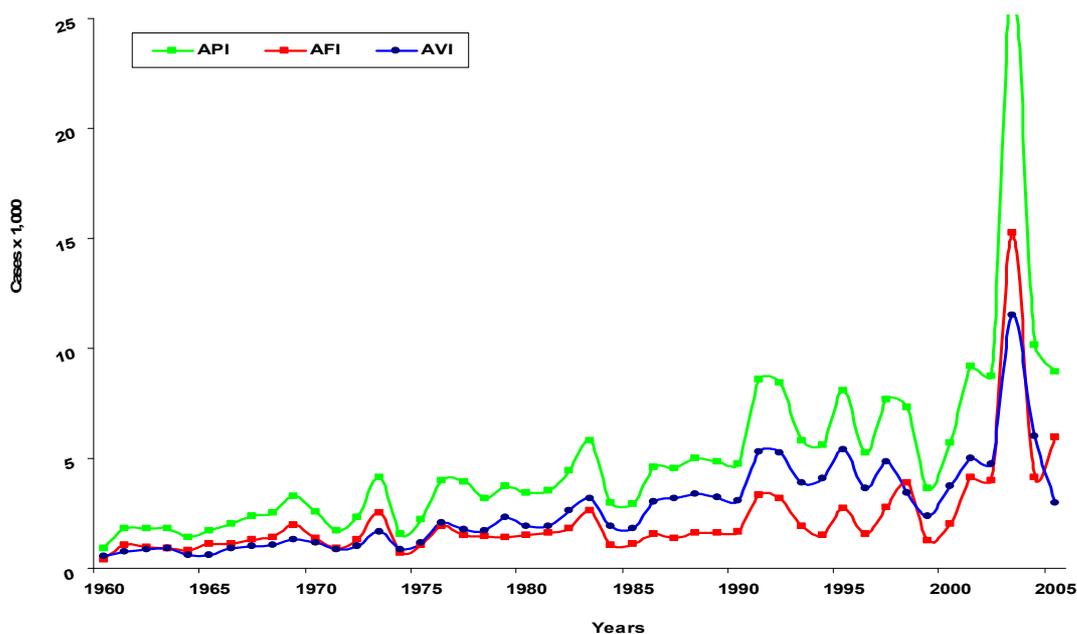
1.3.2 The current malaria situation in Colombia

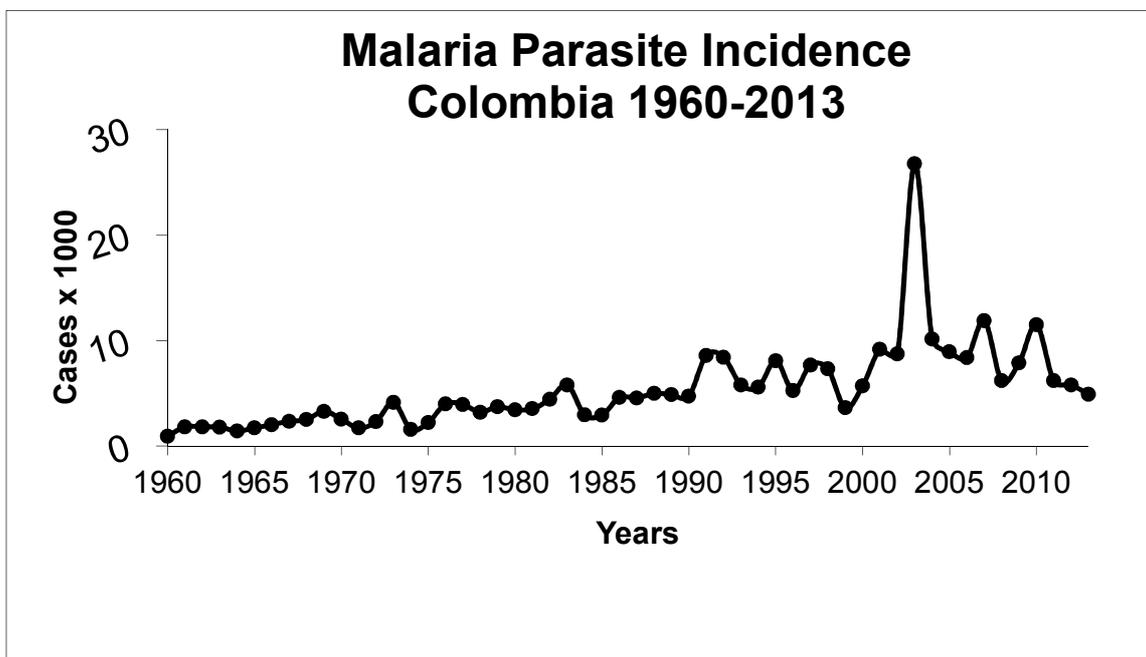
In the late 1990s, the malaria control program changed its approach, moving from a vertical to a horizontal control program. The old and new government departments created by the 1991 constitution assumed all functions and plans related to control, not only for malaria but also for other endemic vector borne diseases like dengue, leishmaniasis, yellow fever, etc. Colombia ranks among the countries with the highest malaria incidence in the Americas, with a relatively high percentage of *Plasmodium vivax* cases and *Plasmodium falciparum* being the most pathogenic in areas less than 1,800 meters above sea level. *Falciparum* malaria transmission was reduced by 85% due to DDT spraying during the malaria eradication campaign.

Since the National Malaria Control Program's (NMCP's) inception in 1970, security concerns have prevented NMCP from covering many areas of the country. Areas particularly at risk of malaria include the lower Cauca River region, the tropical areas of the Pacific Coast, the high Sinu River region and the Urabare region. More than 160,000 cases were reported in 2003. In 2005, the National Surveillance System (SIVIGILA) recorded 107,866 malaria cases: 46,771 cases of *P. falciparum* and 79,101 cases of *P. vivax* (34).

Nowadays, financial support for malaria control activities comes almost exclusively from the Ministry of Social Security, which contributed over USD 13 million to malaria control in 2003 (35). Attempts to strengthen the national program through the Global Fund have only concentrated on fringe municipalities, excluding more than 50% of the most endemic areas. In accordance with the Global Malaria Control Strategy and the principles of the Roll Back Malaria Partnership (35), the MoH launched a renewed NMCP in 1998. Its goals include: (i) improved diagnosis and treatment; (ii) selective vector control including use of insecticide treated nets (ITNs) or mosquito-repellent chemicals; (iii) mosquito breeding control and targeted indoor residual spraying (36); (iv) public health surveillance strengthening, including entomological and vector resistance surveillance; and (v) intersectoral and social participation. Figure 3 presents the annual malaria incidence by parasite species between 1960 and 2015. There is an inversion in the relation of *P. falciparum* cases vs. *P. vivax* cases from the 1970s onwards.

Figure 3. Annual parasite incidence (21); annual *Falciparum* incidence (37) and annual *Vivax* incidence (AVI) per 1,000: 1960-2015. Source: author's calculations from IQUEN and MSP and NHI databases





The distribution by municipality shows that 511 Colombian municipalities (45% of the total) presented evidence of permanent malarial transmission in 2002, and 75% of these registered moderate and high risk API.³ Urban malarial incidence has grown during the last decade, affecting more than 20 municipalities in which the control program was once successful (38), (39), (34).

According to the WHO's 2014 statistics, Colombia registered an infant mortality rate of 0.2 cases per 1,000 by 2000 (40). Those in the age group 15 to 45 years represented 60% of total cases, indicating that those in the most productive age brackets are most affected by the clinical disease. The age group 5-14 years was the second most affected, representing around 22% of cases, and having a significant impact on school absenteeism.

The predominant malaria transmission vectors in Colombia are: *Anopheles albimanus*, *Anopheles darlingi* and *Anopheles nuñeztovari*. The secondary vectors include *A. pseudopunctipennis*. All of them are highly adaptable, especially under conditions of salinity (41).

Anti-malarial drug resistance depends on the region and most of the related evidence is not used during drug-policy decision making. The different approaches taken by local research groups on the one side and international health agencies on the other make it difficult to consolidate findings, mainly because of the varying sources and amounts of financing.

³The malaria control program in Colombia considers three levels of transmission: high risk is more than 10 cases x 1,000 and moderate risk is more than 1 case/1,000.

CHAPTER II Rationale, Aim, Research Questions, Objectives and Methodology

2.1 Research aims

The purpose of this research was to compile qualitative and quantitative information associated with historical concepts and changes in public health strategies around malaria elimination and eradication in the second half of the 20th century, and correlate these findings with economic, systemic, and epidemiological data and the distribution of poverty-related infectious diseases. This process made it possible to evaluate the factors affecting the success or failure of relevant public health policies and to advocate for updated models in the context of the health attention system model in both low and middle income countries. The findings could help to improve the success rate of current interventions and offer scientific evidence on which to base policy decisions around public health programs and health system reforms. This, in turn, could contribute to more effective elimination and control programs at both local and international levels.

Improving service quality and promoting the supervision, inspection, and surveillance of its functions is the essence of public health. Smallpox eradication contributed greatly to the health and wellbeing of millions of people, particularly those in the poorest populations, and is considered to be the most important epidemiological and public health achievement of the 20th century (42)(43). Efforts to eradicate other diseases are also underway. Polio is one example; unfortunately, some states remain infected with wild poliovirus but are not currently exporting it (Cameron, Nigeria, Somalia) while others are no longer infected by wild poliovirus, but remain vulnerable to international spread (Equatorial Guinea, Ethiopia, Iraq, Israel, Syrian Arab Republic) (10)(43)(44). Another great example is the reduction of rubella cases and regional efforts to eliminate and ultimately eradicate the disease (45).

The malaria case study presented in this thesis seeks to further the concepts of elimination and eradication so as to make further public health progress a reality.

2.2 General Objective

To describe, characterize and evaluate the evidence related to strategies of disease elimination and eradication, and to compile data and information for malaria, in particular, through developing a case study of elimination for endemic regions in Latin America, with special emphasis on Colombia.

2.3 Specific Objectives

1. To compile and consolidate primary and secondary information related to malaria control, elimination and eradication concepts and their transformation over time.
2. To analyze trends in malaria statistics and data as well as to estimate the frequency and distribution of *Plasmodium spp.*, both symptomatic and asymptomatic, in endemic areas with evidence of malaria transmission.
3. To evaluate the current status of other historical elimination efforts, such as policies to control goiter disease after its elimination from Colombia in 1990.
4. To outline a basic plan towards elimination as a framework for national and regional policy.

2.4 Study approach

The present study combines descriptive information, and analytical comparison between regions and populations. Extensive literature review has also been incorporated in order to complete and update the state of knowledge of elimination and infectious diseases. Chapter III presents the history of malaria and the evolution of concepts related to its control from the perspective of a middle-income country (Colombia) that has adopted relevant international policies. The methodology consisted of a narrative review of the literature from both the 20th and 21st centuries. Chapter IV presents the results of a cross sectional study, carried out in two regions of Colombia, endemic for malaria: the Pacific Coast and the Caribbean Coast. The proportion of asymptomatic cases, defined as any individual with a positive rapid diagnostic test (15), was investigated by sampling four villages in Tumaco, three villages in Bocas de Satinga, and six villages in Cordoba. Chapter V offers a narrative review of the history of endemic goiter elimination in Colombia and its resurgence. It describes the current situation, 30 years after the formal declaration to eliminate the disease by 1990, and the high frequency of thyroid diseases and excessive iodine consumption in a sample of 130 school-aged children (6 to 14 years of age).

The thesis concludes with a chapter on the lessons learnt from malaria control and elimination and the public health implications for other elimination plans and for public health related policies in general.

2.5 Study population

The focus is on the Latin America context and the population at risk and living in endemic areas for infectious diseases of poverty. The main analyses and discussion are about malaria trends and the impact of related policies since 1950, with special attention to the Era of Elimination, during which the Millennium Development Goals were implemented. Table 4 presents the most prevalent infectious diseases in this region and the most affected populations. The distribution of the population at risk, classification of areas by vulnerability and its main diseases and percent of global burden are also given.

Table 4. Ranking of NTDs in LACs by Prevalence and Distribution(46). Source: Hotez PJ, Bottazzi ME, Franco-Paredes C, Ault SK, Periago MR (2008) The Neglected Tropical Diseases of Latin America and the Caribbean: A Review of Disease Burden and Distribution and a Roadmap for Control and Elimination. *PLoS Negl Trop Dis* 2(47): e300. doi:10.1371/journal.pntd.0000300

<http://127.0.0.1:8081/plosntds/article?id=info:doi/10.1371/journal.pntd.0000300>

Disease	Population Currently Infected in LAC	Population At Risk in LAC	Major Vulnerable Populations or Geographic Areas	Number LAC Countries Infected	Percentage of LAC Population Infected (% Poor People Infected)	Percent Global Disease Burden in LAC	Reference
Trichuriasis	100 million	523 million	Poor rural & urban slums	27	17.8% (46.9%)	16.6%	[19]
Ascariasis	84 million	514 million	Poor rural & urban slums	27	15.0% (39.4%)	10.4%	[19]
Hookworm	50 million	346 million	Poor rural	26	8.9% (23.5%)	8.7%	[19]
Chagas disease	8-9 million	25-90 million	Poor rural & urban slums	13	1.6% (4.1%)	99.8%	[43,44]
Schistosomiasis	1.8 million	36 million	Poor rural	4 with > 1,000 cases	0.3% (0.8%)	0.9%	[31]
Blinding trachoma	1.1 million	ND	Poor rural	3	0.2% (0.5%)	1.3%	[54]
Lymphatic filariasis	720,000	8.9 million	Urban slums & poor rural	7	0.1% (0.3%)	0.6%	[20,33]
Dengue	552,141 reported in 2006	ND	Urban slums	23	0.1% (0.2%)	ND	[62]
Cysticercosis	400,000	75 million	Poor rural	15	<0.1% (0.2%)	ND	[37]
Cutaneous (CL) and visceral (VL) leishmaniasis	62,000 CL 5,000 VL	ND	Urban slums & poor rural	18	ND	ND	[52]
Leprosy	47,612 new cases	ND	Poor rural & urban slums	22	<0.1% (<0.1%)	11.4%	[56]
Onchocerciasis	64 new cases in 2004	515,675	Poor rural	6	<0.1% (<0.1%)	0.3%	[20,35,36]
Jungle yellow fever	86 new cases in 2004	ND	Jungle & urban slums	4	<0.1% (<0.1%)	<0.1%	[63]

ND, not determined.
doi:10.1371/journal.pntd.0000300.t001

The population at risk in Latin America in 2008, the year of Hotz et al's analyses, was around 105 million inhabitants in low-, middle- and high-risk endemic areas. The following countries reported autochthonous cases: Argentina, Belize, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Dominican Republic, Suriname and Bolivarian Republic of Venezuela.

A case of malaria in Latin America is defined as a patient with fever or any other symptom compatible with malaria and with a positive blood smear. In Colombia, 80% of the territory is endemic for vector-borne diseases, with malaria affecting 500 municipalities (See Annex 1).

2.6 Research Questions

This thesis was designed and researched considering four guiding questions. These questions were elaborated from positivist, neo positivist, and critical theory paradigms (48-57).

The following questions were considered:

1. The epistemological question: What is the current knowledge of the problem?
2. The ontological problem: What has actually been achieved?
3. The methodological approach: What information do qualitative and quantitative methods reveal?
4. The axiological difficulty: How do questions of ethics bear on the problem?

Table 5 shows the research questions constructed for each level of analysis. From the reality and object of study, to the relation between researcher and the level of knowledge about the topic selected. Ethical aspects are considered as an additional level of analysis, covering national and international regulation and its implications for populations affected by malaria.

Other considerations arise from the main research questions, such as:

- Poverty relates to income inequality and out-of-pocket payments waste of the population affected by diseases of poverty
- Infectious diseases are communicable or transmissible diseases
- Elimination refers to a country or region that has not experienced transmission for a minimum of three years

In the specific case of malaria, a reductionist approach to control focuses on human protection, vector control, parasite detection and treatment. Here, other elements related to the structure of the society are included in the analyses. The risk factors for persistence of a disease are often considered as biological determinants; however this study presents other determinants such as socio-economic and political aspects of the societal structure and their implications for further innovating policies towards control and elimination.

The author evaluates risk factors according to the positivist paradigm, which presents some limitations as this approach is not sufficient for explaining the complete phenomenon. For this reason, the author draws upon critical theory and historical materialism to offer additional interpretations. Completing the broader picture depended on access to the information published and the heterogeneity of population.

Table 5. Research questions and paradigms used by the researcher

Epistemological Question What is the relation between the researcher and the things that can be known? (Scientific approaches to that reality)	Ontological Question What is the form or nature of the reality? (Object of the study)	Methodological Question How can the researcher discover that which can be known?	Axiological Question For the population affected, what is fundamentally important to investigate? How can the population contribute and participate? What is value of the investigation?
<p><i>A</i> <i>Positivist paradigm</i> suggests the following questions: Is current scientific knowledge sufficient for eliminating and eradicating the magnitude and frequency of poverty-related diseases in low- and middle-income countries? To what extent has malaria frequency been reduced in Colombia and Latin America during the last 15 years? Can this reduction be explained by the elimination and control strategy in place?</p>	<p><i>The Critical Theory paradigm</i> requires us to answer: How do social, political, cultural and economic determinants contribute to increasing or decreasing the frequency of infectious diseases (to zero)? How are ethnic minorities and vulnerable populations affected by public health problems related to poverty and poor development models? How can social determination contribute to solving problems arising from endemic infectious diseases of poverty?</p>	<p>Public health problems and research questions cannot be solved through one single methodology. Quantitative methods: Is the reduction of malaria in Latin America and Colombia statistically significant? Qualitative Methods: Does the evidence from primary and secondary data support a declaration of malaria pre-elimination or elimination in Latin America and Colombia?</p>	<p>In Colombia, health research is supervised by the MoH. Legal aspects that regulate the investigation include: 1. Decree 8430 1993 2. Resolution 13437, 1991 Creation of Ethics Committee by MoH. Is this research experimental? Are human lives or patients involved? How many people will benefit from the results of this study? Is there any conflict of interest by the author?</p>

In light of the conceptual framework outlined above, the following research question has been formulated:

What qualitative and quantitative indicators are required to show that a country is close to eliminating and eradicating priority infectious diseases and which elements must be included in surveillance

systems to adequately and permanently evaluate and monitor the status of transmission, to maintain transmission rates at zero and to contain any imported cases?

To answer this research question, the author conducted descriptive studies and systematic narrative reviews of the scientific literature. Primary, historical analyses of the evolution of malaria concepts are presented to shed light on the state of elimination and eradication in endemic regions over time. Moreover, results of cross-sectional surveys carried out in areas endemic for malaria in Colombia are included. Studying the asymptomatic malaria cases in two areas where the risk of transmission is high, helps one to understand the phases of pre-elimination and elimination of malaria. Policies and processes towards eliminating goiter in Colombia are reviewed to confront the current prevalence of goiter and salt consumption in the country. These two diseases offer contrasting cases of control and elimination phases; malaria in a current state of elimination, and goiter disease post-elimination and with evidence of recrudescence due to excessive iodine consumption and the absence of policies to regulate it.

2.7 Methodology

Qualitative and quantitative methods were used to answer the research questions. Please see below for details.

2.7.1 Narrative systematic review

The first step was identifying the research question. MeSH (medical subject heading) and DeCS (scientific descriptor) terms were selected to search Embase, Pubmed, Scielo and Bireme databases. Documents published in Spanish, English and Portuguese were included in the search. MeSH terms included: elimination, control, eradication, diseases or poverty, infectious diseases, malaria trends. DeCS (Spanish terms: eliminación, control, erradicación, enfermedades de la pobreza, enfermedades infecciosas, tendencias en malaria

All databases were accessed from the Library of the Universidad Nacional de Colombia and captured in Endnote X7. After creating a list of references, the abstracts were read and duplicate records were eliminated. The repository of Colombia was consulted, in order to identify and include "grey literature", such as research reports and other relevant literature not published in peer-review scientific journals.

2.7.2 Quantitative Analyses

Data were captured in Excel. The descriptive statistics included the mean comparison and ANOVA of qualitative variables. Qualitative variables were compared using 2x2 tables. The level of

significance was estimated at 5%. The means and proportions were estimated using Stata 13. For variables with normal distribution, parametric methods were applied, and non-parametric tests were estimated otherwise. Crude and adjusted estimations are shown in tables and figures.

2.8 Ethical considerations

This research followed the ethical process as set out by the Colombia Ministry of Health. The proposal was approved by the School of Medicine's Ethics Committee, Universidad Nacional de Colombia, Bogota. Each participant was informed about the study's methods and duration prior to any interview or focus group discussion; a health service representative was present to answer questions or doubts in all such cases. The study follows the principles of Declaration of Helsinki, and the Resolution 8430, Ministry of Health of Colombia, 1993. According to law regulation for investigation this project is considered of not risk.

The informed consent form is shown in Annex 2

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Chapter III. Concepts evolution of malaria control, elimination and eradication.

Historical Review

Title: Concepts evolution of malaria control, elimination and eradication.

Short: Concepts of malaria. Public Health Interventions

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3.1 Abstract

Introduction: The concepts of control, elimination and eradication of communicable diseases are now structural elements of new global health policies. In the case of malaria, we use both conceptual and operational definitions that contribute to reducing the negative impact of this disease on the progress and wellbeing of low-and middle-income countries.

Objective: To trace the historical evolution of malaria elimination efforts, from eradication services to current international health policies based on global and regional control and elimination programmes through a narrative review of the scientific information.

Results: These changes reflect the perceptions of health authorities and the scientific community on the possibility of eradicating malaria based on scientific developments, existing health policies and (un)successful experiences during the implementation of programs to combat the disease in regions with varying transmission dynamics and health care models, in particular.

Conclusion: It is now recognized that in the processes of malaria control, elimination and eradication it is necessary to use operational definitions and applied interventions that correspond to geographical, eco-epidemiological and social-economic determinants, as well as participatory models of assessment and monitoring appropriate to the structure of national and local health systems, as basic requirements for the success of these programs.

Keywords: elimination, malaria eradication, health policy, history (source: MeSH, NLM)

Evolution of the malaria control, elimination and eradication concepts

3.2 Introduction

Malaria is a complex problem for the global health, with more than 250 million clinical cases annually. In 2012, there were nearly one million deaths, mostly children under five and pregnant women. It is the fourth leading cause of mortality, which is significant considering that it is a "completely preventable and treatable" disease [1-5], [6, 7]

Approaches to control and transmission dynamics has shown different results throughout history[8]. From the Global Malaria Eradication Program (GMEP) of the 1950s, to the current proposal to take progressive steps towards elimination in accordance with the Millennium Development Goals by 2015, each initiative has had its own set of successes and failures.

Changes in the concepts of malaria control, elimination and eradication since their appearance on the world stage have been a complex process. International health agencies and local health services have consolidated basic operational definitions that allow us to understand how multidimensional conditions in endemic countries pose a challenge for programs that aim to reduce the malaria disease burden.

In the last decade, reductions in morbidity and mortality due to malaria have been associated with the use of comprehensive and multilevel control tools ([3, 9], [10]). These programs have benefited from great financial investments, a network of highly qualified experts and global coordinating agencies. The guidelines proposed by these scientific and financial networks include mathematical modelling of the variables associated with persistence and resistance, in combination with predictive models of the effectiveness of different control strategies under various scenarios.

Field experiences have shown limited success of these control measures in terms of effectiveness and sustainability over time in areas of high vulnerability[11-13]. Challenges for the scientific community, such as treatment failure, outbreaks and imported cases in areas nearing elimination, have become a priority.

This review aims to build a holistic conceptual framework of malaria control, elimination and eradication efforts since the twentieth century and presents various models of reduced incidence (close to zero) for regions that have achieved the goal of low transmission. We show that addressing malaria control is a complex problem and new approaches should include the use and application of systems theory.

3.3 Current definitions of the concepts of control, elimination and eradication

(Table 1)

One of the statements that best describes our perception of malaria comes from the World Health Organization's (WHO) World Malaria Report 2010, in which malaria is referred to as "a tenacious, ever-changing foe" [3]. However, from the Hippocratic era to the middle of the last century, the recognition of the magnitude of the malaria burden and the complex factors that enable its resurgence and re-emergence, despite the control measures implemented, saw malaria defined as "the most serious communicable disease in the world"[14-16]

Before analysing how the concepts and implementation policies for control, elimination and eradication of malaria have changed over the last half of the last century, it is helpful to understand the context of the current definitions of these terms in order to compare and contrast with those enacted during GMEP, where there was debate over the most appropriate definition of the term eradication and confusion between the terms extinction and elimination [17, 18]. Strictly defining these terms not only benefits health programme planning and implementation by giving "practical strategic parameters" for execution, but it also avoids misinterpretation of the actual goals [18-20],[21]

Control is an organised public effort to implement cost-effective intervention measures against malaria according to the particular conditions of transmission in a defined area [22], to "restrict the movement of an infectious agent below the level that would result if individuals acted on their own to control the disease " [23]. The control is local but still follows global and national guidelines. For this reason, there may be differences in the optimal levels of reduction of disease burden in different regions [24], [25] for malaria to stop being considered a public health problem [4].

Elimination can be defined as the interruption of malaria transmission in a defined geographic area, i.e., the incidence of locally-acquired cases is zero [1], [9, 26]. However, it is inevitable that cases will be imported from areas where malaria remains endemic to those areas with no local transmission. This proximity to endemic areas and constant movement of people and other socio-economic determinants from these areas is called *vulnerability*[18]. Mathematical models have focused on defining a low level of local transmission, which could explain why certain areas can not reach the status of elimination or interruption of transmission due to the risks of imported cases. Cohen et al. have proposed the term "non-endemic malaria control" as a state different from control, also called "controlled low endemic malaria" and "elimination". However, WHO clarified that despite the *vulnerability* of an area, it may be possible to achieve a zero incidence when vector control measures make transmission unlikely[5]. Eco epidemiological and health systems, as well as parasite and vector genetics in a specific region, are grouped under the term *receptivity*

[18]. The interactions and effects of *vulnerability* and *receptivity* in an area are referred to as the *malariogenic potential* or *malariogenic environment*. The characterisation of these variables for different areas with the presence of malaria has important implications for the development and sustainability of programmes. As the magnitude of transmission in a given area decreases, highly sensitive and specific systems must be implemented due to the difficulty of detection in low transmission settings [27], [28, 29]. For elimination of malaria, *the basic reproductive number* should be less than one ($R_0 < 1$). (R_0) is the "measure of effective transmission of the disease," or the number of malaria cases effectively transmitted from a single case during the infection. It is an expression of the efficiency of the vector capacity, host susceptibility, and infectiveness of the parasite [3].

To declare a country free of malaria, the local case record must be zero for three consecutive years [4]. In addition, the re-establishment of transmission is said to have occurred once there is a third consecutive local case after an imported case per year, for a period of two successive years for *P. falciparum* and three-years for *P. vivax*[5].

Eradication is defined as the permanent reduction to zero of the incidence of infection in the world [4]. Its character is binary, that is, a disease can be eradicated or not, although some authors recognise the practical impossibility of certifying the absence of the organism and can only make approximations from the dynamics of the populations involved: human, vector, parasite [14, 21, 30]. Eradication is considered to be the ultimate aim in the on going fight against malaria [31, 32].

Table 1. Features current conceptual and epidemiological aspects concerning the terms elimination, eradication and control.

Conceptual features	Control	Elimination	Eradication
Etymology	French control testing or inspection	Latin <i>ex y limen</i> 'beyond a threshold'	Latin <i>ex y radix</i> 'uproot'
The Individual. Transmission dynamics of infection and disease occurrence	Reducing transmission to a level where it no longer represents a public health problem or that is acceptable, presumably ($R_0=1$).	Reduction of local transmission * to an incidence of zero or a very low default level not necessarily zero ($R_0<1$).	Permanent reduction to zero of the incidence of infection ($R_0=0$).
The Community. Endemic cases vs. imported	Should report imported cases to the site of origin as well as the presence of locally acquired cases and identify contacts.	Seeks to reduce to zero locally-acquired cases and recognises that introduced cases are inevitable †.	There are no cases of malaria in the world, neither locally-acquired nor imported.
Geographic area	The control is local but guided by a global perspective with local and regional policy according to each situation.	Elimination occurs in a single country, continent or other generally limited geographic area with common characteristics.	Worldwide ‡.
Runtime	It is by definition a set of permanent measures.	Being involved with a "threshold", elimination is not a final process but a reversible, temporary achievement.	Its achievement depends on the time countries and regions spend on achieving elimination in particular.

* Local transmission is that indigenous transmission that would persist even if all imported cases were prevented.

† An introduced case is one that is secondary to a known imported case. Locally-acquired cases are those cases secondary to alternative transmission cases.

‡ Regional eradication is an "oxymoron" because of the ever-present risk of importation of the pathogen and the continuing need for control measures. Sources: [33-35], [6, 26, 36-47]. Adapted by the author

3.4 Brief review of programmes to combat malaria

To facilitate better understanding, we outline the history of international malaria knowledge starting from early last century, its fundamental theoretical basis, approaches to addressing the disease, the failures encountered along the way, and milestones in the history of epidemiological and social knowledge, not only for malaria but also for other infectious diseases. To do this, we perform a theoretical temporal division based on what we consider to be the major events, scientific thought, and health authorities during the last century and the present. This division is not strict but didactic and does not intend to unify visions or ignore the opinions and disagreements encountered during each period; we recognise that they are still valid.

3.4.1 First half of the twentieth century

Without ignoring other eras of control, we consider the first scientific basis for malaria *control* to be the nineteenth century developments by Alphonse Laveran and Ronald Ross who discovered the parasite that causes the disease and documented its transmission cycle [48]. First, in the Bacteriological Era, was the identification of the parasite or causal agent, and later in the Entomological Era, from a perspective based on causality and in vivo models, work on Vector-Borne Diseases, including malaria, presented models of human experimentation. The control measures used were mainly sanitary engineering activities related to the water tanks where *Anopheles* larvae grow, such as the draining of swamps, or local use of physical or chemical methods (such as Paris Green) aimed at larval control. In the early twentieth century, the debate was between implementing large-scale vector control campaigns to "quickly solve the problem" [49] or investing in local case management and environmental health. Examples of such activities include those conducted by private organisations like the Rockefeller Foundation, designed to improve sanitation and health in port territories mainly in Latin America and to conduct behavioural research of tropical diseases. In Colombia, these commissions had an impact not only on health, but also on business decisions and on the policies of the country in border or coastal areas. At the end of the First World War, coverage with larval control, insecticide spraying with pyrethrum extract and restoration of areas — known to Italian malariologists as *bonifica integrale*[50]— coupled with the use of mosquito nets, microscopic diagnosis and treatment with quinine in the 1930s could have *eliminated* the disease in most Western European countries. However, these control measures were only economically feasible in places with significant resources and broad interests in incurring the costs for example in industrialised cities or in military camps. "In most rural areas, man was powerless to control the disease" [50]. Then, with the emergence of Dichloro-diphenyl-trichloroethane (DDT), previously synthesised by Zeidler in 1874, and thanks to the observations of Müller in Switzerland in 1939 [51, 52], the first contact residual insecticide to decrease the number of required applications was first used during typhus epidemics and later for vector control of malaria. The use of DDT and chloroquine in the first era of eradication improved the outlook for rural areas such that there was an increase in the drive for global achievements, setting the scene for programmes based on an etio-pathogenic approach that marked the second half of the century [53], [13, 54].

3.4.2 Second Half of the Twentieth Century

This period is the one that perhaps offers the most lessons in the history of disease control. At the end of the 1940s, it was thought that malaria control through DDT spraying should be recurring, and the views of certain malariologists who believed in that increasing spraying coverage would lead to suspending DDT use in the future were not welcome [50]. In 1947, the recommendations of the Pan American Health Organization (PAHO) favoured household spraying with DDT in malaria endemic regions under local control programmes. In Colombia, these control activities were conducted by the Malaria Division of the Inter American Cooperative Public Health Service [55-57]. In parts of the Caribbean, with support from UNICEF, these local malaria control programmes were integrated with others, with the intention of eradicating *Aedes aegypti*, the vector of yellow fever and dengue [57].

However, in 1951, in Greece, experiences with DDT in certain regions showed that once the interruption of local malaria transmission had been achieved, spraying could stop but transmission would return [58]. The time needed to stop this transmission was four years for *P. falciparum* and five years for *P. vivax* [48]. But the emergence of resistance of *Anopheles sacharovi* against DDT in Greece suggested that the time required to maximise the efficiency of the insecticides and simultaneously suspend transmission over large geographic areas should last long enough to achieve these objectives but not so long as to allow the vectors to develop resistance [59]. These measures together accounted for the basis of what became known as "*malaria eradication*" in the 1950s. Confidence in the potential efficiency of residual insecticide spraying, even over other traditional control measures, led to the perception that "there was no time to lose in the eradication of the disease while it was possible to control the vector" with the insecticides available [36].

In 1950, Uganda held the WHO's Fourth Expert Committee on Malaria, referred to as the Kampala Conference [41]. It recognised the relationship between the disease and the development of affected countries, especially in Africa. It recommended that governments make it a priority to implement "malaria control organisations" that would reduce the burden of disease in order to subsequently direct resources and efforts to other public health programmes. It also recognised the need for financial resources and trained personnel to implement these organisations.

In 1954, the eradication strategy adopted by the XIV Pan American Sanitary Conference was instituted in 1955 by the Eighth World Health Assembly, under the Global Malaria Eradication Programme (GMEP) [60]. Colombia, adhering to international health policy, created the National Malaria Eradication Service [61] in 1956 (8), which replaced the previous Malaria Division and was dependent on the Ministry of Public Health. The GMEP had four phases: preparation, attack, consolidation and maintenance. The campaign was marked by economic and logistical efforts in the country that, with cooperation from PAHO and WHO, sought to educate and empower the people affected and build capacity among medical and technical personnel. During the preparatory phase, the territory was divided into 18 zones according to its particular ecological conditions, including tropical ecological characteristics, the presence of different vector species and the high burden of disease. However,

diversity of these features in a given zone made malaria in Colombia a public health problem more complex than in other countries in the region and one that was compounded by internal political and military conflicts. It is now recognised that this campaign had important implications for the practice of malariology, namely to be directed from and coordinated by central agencies that assumed a rigid system based on local compliance to the rules issued within the guidelines for spraying homes with DDT. However, continuation of other control measures, known at the time as the destruction of larval breeding swamps and reducing human contact vector, bites reduction [49] did not receive equal support. Moreover, the global nature of the programme was affected by the WHO's recognition in 1956 that existing barriers to proper implementation in Africa (long transmission season, high degree of endemism and weak infrastructure) led to low coverage of the programmes on this continent [55]. Some authors believe that the "discrepancies" between the Kampala Conference, the GMEP guidelines and low coverage of local programmes in Africa [62] were the result of extrapolating local experiences, which although successful, only represented a limited number of possible epidemiological scenarios for the disease. Other flaws that were recognised during the implementation of GMEP included the creation of autonomous services structures dissociated from the general health system and with low adaptive capacity, the lack of importance given to reports of parasite resistance to chloroquine, and little regard for local cultural characteristics in programme planning [9, 49]. In addition, research on control measures and antimalarial drugs declined markedly during the GMEP period. It was before the emergence of chloroquine resistance in Thailand and Colombia and the U.S. involvement in the wars in Korea and Vietnam that illustrated the continued need for research and prompted resumed efforts to develop new strategies for disease control [9, 63].

Thus, in the absence of results consistent with the overall policy of eradication, which excluded regions of sub-Saharan Africa and Madagascar, the need for a pre-eradication period for countries not were ready to embark on the goal of eradication was recognized. The period would serve to strengthen health infrastructure at the same time as carrying out the preparatory phase. However there were no clear models of what the minimum health infrastructure required to achieve these goals should look like. Soon the lack of local health services and limited political and financial commitment yielded different programme results between regions, mainly characterised by the resurgence of transmission after it was suspended in the phase attack. The consolidation phase that followed was the most affected and showed the extent of the impact of health systems in epidemiological models of disease transmission. Considering the current definition of the concept of eradication, PEGM comprised a "series of national malaria elimination often successful" in which the incidence of local transmission was reduced or brought to zero, with the ever-present possibility of importation and introduction of cases and the need for continued surveillance and control measures to maintain these achievements. During the VIII and X Expert Committees, WHO used an annual parasite incidence of less than 0.5/1000 as an indicator of when total coverage with insecticide could be stopped? In this case, the use of a threshold confirms that the programmes were aiming more towards elimination rather than eradication as we know it today[64].

Based on the limited results obtained, it was decided to extend insecticide spraying activities and in many areas the consolidation phase reverted to attack phase [65], while others, declared free of the

disease, were expected to support them financially [66]. Field workers experienced burnout [67] compounded by the redirection of resources by major donors to public health problems deemed more urgent, as happened in 1963 when the total revenue fell by more than half because the U.S. stopped making contributions to the WHO's Special Account for Malaria, thereby endangering its sustainability. Elsewhere, in order to avoid losing the results achieved during the GMEP, efforts and resources were concentrated in areas that were "paradoxically, the least affected". In 1968, a report was published stating that the pre-eradication period was indefinite owing to the nature of control programmes [68]. This situation led to the WHO, in 1969, recognizing that the malaria eradication was not feasible in some countries and thus they should focus on implementing control measures instead to develop "economically viable methods for the complete elimination of the disease" [69]. This statement, therefore, is considered to be one of the main manifestations of the global paradigm shift from *eradication* programmes to control measures.

Despite limitations in their achievements GMEP found a reduction in the global distribution of malaria, increased contact with communities through the establishment of volunteers in diagnosis and treatment activities, and successfully influenced health programme planning in some countries [49]. The GMEP eliminated the disease in regions at the boundaries of the overall distribution of malaria. The countries that achieved elimination shared similar characteristics: political stability, political and financial commitment to eradicating malaria, good organisational and technical infrastructure, high quality staff training, well-developed and functional general health services, absence of internal and external conflicts, and no large population movements from neighbouring countries with malaria.

In 1972 and 1973, the Garki project took place in Nigeria [70]. This project implemented control measures (residual insecticides with propoxur and mass treatment with pyrimethamine sulfalene) in a population with high and steady transmission of malaria. The project resulted in a marked decrease in entomological inoculation rates, incidence of fever, infant mortality rates and prevalence of parasites. Its importance lies in demonstrating the impact of control measures in areas of high and steady transmission. In this period, one of the major changes was the understanding of the control measures as an alternative goal (reducing incidence and mortality) to the ultimate goal of eradication [71, 72], [73].

The achievements of countries between 1950 and 1978 were important on the road to reducing malaria worldwide. For example, in the Americas, 22 countries achieved the elimination of malaria in this period, 37 countries in Europe as well as Japan, Australia and Singapore [48]. During the eighties, many countries continued to implement programmes with the goal of "eradication", especially those committed to GMEP initially and who were on the edges of the distribution area of malaria. Between 1970 and 1990, Tunisia, Greece, Kuwait, Libya, Maldives, among others, were certified as malaria free countries by the WHO, and achieved elimination just as Europe and Australia had.

In Colombia, during the National Malaria Eradication Service, there was a significant decrease in morbidity in the first five years of program implementation and a reduction in the malaria risk area from 93% to 85%. However, following this achievement, signs of resurgence and persistence of the disease

occurred. This was reflected in an increased *annual parasite index* [37] from 2.19 per 1000 in the period 1960-1974 to an IPA of 8.9 per 1000 in the period 1994 -2004 although the *annual rate of blood tests* (IAES) remained consistently below the minimum percentage required for the diagnosis of malaria in populations at risk. This was due mainly to the lack of sustainability in the measures used following the withdrawal of technical and financial support from international agencies in the 1970s, such that the country could not achieve elimination status[14]. Differences in achieving elimination between countries led to the enactment of the Global Control Strategy of the Ministerial Assembly of Amsterdam, in 1992, which sought to reduce the impact of the disease in affected countries through control measures tailored to local eco- epidemiological characteristics and the health infrastructure and capabilities available.

Subsequently, in 1998 the Roll Back Malaria (RBM) initiative was born to increase the coverage of control measures, mainly in sub-Saharan African countries. The RBM was supported by the UN, NGOs, the private sector and was participatory at different levels, with the primary purpose of reducing transmission or even eliminating malaria from their territories.

3.4.3 Period from 2000 to the present

The Millennium Development Goals targets for 2015 recognise many of the achievements to date in controlling malaria. Among the related goals, stated either directly or indirectly, are the fourth goal (reduce by two thirds the mortality rate among children under five years) and the sixth goal (stop and reduce the incidence of malaria and other infectious diseases). The year 2000 gave rise to the Abuja Declaration. Held in Nigeria, the summit of African countries sought to cover 60% of the population at risk with key malaria interventions by 2005, especially for children under five and pregnant women. Some of the control tools that have had the greatest impact to date are the distribution and use of insecticide treated nets (ITN), long acting combination therapies based on artemisinin, and rapid diagnostic tests. With these strategies, the possibility of eliminating malaria and eradicating it in the long term attracted the interest of international political and financial leaders and in 2007, the Bill and Melinda Gates presented eradication as the ultimate goal to which global efforts aiming to combat the disease should contribute[10]. However, given past experiences and the different transmission states where malaria is found in the world, it was not possible to set a timeframe in which to achieve this goal, meaning the goal is a long-term one. Currently, the phases described by WHO for the transition from control programs to elimination and finally eradication, are more gradual than those initially promulgated during GMEP, which were based primarily on an "attack phase" to reduce the burden of disease. Thus, those countries with endemic malaria areas with high and stable transmission and without experience in elimination. This need has led to admit that "eradication is not feasible with currently available tools[63], [16]. It can be inferred that these tools are useful for countries with low and unstable transmission and with experience in elimination programmes, but not for those with high and stable transmission, which have remained under the control programme paradigm.

In 2008, the Global Malaria Action Plan was approved by the association for Roll Back Malaria and aimed to reduce the number of malaria deaths in the world to nearly zero by 2015, eliminating malaria in 8-10 countries and countries that were in the pre-elimination phase in 2008 and eradicating malaria in the long term through progressive elimination in countries [74].

According to the WHO, of the 109 endemic countries in 2007, 80 were in the control phase, 12 in transition to elimination, 11 in elimination, and 6 in preventing reintroduction [3]. Since 2007, three new countries (UAE, Morocco and Turkmenistan) have been added to the list of countries certified malaria-free by the WHO [1]. Today New Guinea and the tropical African regions are considered to be the last endemic epicentres of stable malaria.

3.5 Concepts of malaria eradication in the twentieth and twenty-first centuries (Table 2)

As we have seen, the term eradication has had different meanings and interpretations over the last century. These changes took place gradually as shown in Table 2. It should be noted that this comparison uses the term "eradication" as it appears in the literature, so as we saw above, deep conceptual differences between the current uses of the term and that used in the middle of the last century may exist. Contrasting the today's definition of "elimination" of with "regional eradication" and "elimination" as it had been used over the past century has already been done by others [8]. We believe, however, that by explicitly comparing the term eradication as it has been used in anti-malaria programmes may allow for a better understanding of the conceptual basis from which these programmes were formed.

As seen in Table 2, one of the main engines of the last half century that made the world change the focus of its programs from malaria control strategies to "eradication" was the appearance of DDT as a scientific tool to quickly reduce rapidly the vectors of causing disease transmission. The vision of the mosquito and the parasite as enemies to kill is reflected in the military terminology "campaign" to eradicate malaria.

This, coupled with political and economic interests meant that approaches concentrated on fighting the vector and the parasite, diverting attention away from the environmental conditions where this was taking place[75].

Historically, the main obstacles to progress in controlling and eliminating the disease were the lack of flexibility of eradication programs, the inability to adapt to the particular regional situation and the lack of coordination between the control and research programmes. The role of national epidemiological services in achieving long-term sustainable elimination in endemic areas must also be highlighted. Many authors recognise the need to invest not only in the technological advancement of control measures but also in the epidemiological infrastructure required for data collection, analysis, monitoring and surveillance [31].

Accordingly, the understanding of eradication as the triumph of man in the process of understanding a disease that has existed for centuries, the biological characteristics of all actors involved and "its close relationship with certain conditions of life and work and with certain production processes" indicates that the perception of the term today differs greatly from that of the scientific community and health authorities of the last century. At that time, although determinants of disease transmission and biological control had already been recognised, the definition and implementation of eradication programmes were contingent upon the use of chemicals. Understanding eradication beyond this approach is perhaps the most important achievement in the history of programmes combatting malaria, so that even to achieve elimination, countries are required to maintain a "sustained commitment to medium and long-term health systems and required human capacity", as stated by the WHO [1, 2].

The experiences of malaria eradication programmes, has allowed us to design programmes for the eradication of other transmissible diseases and to coordinate based on the various determinants and structures of health systems with successful results, as with the Intensified Smallpox Eradication Program [29, 76]. The various cost calculations for smallpox eradication programmes were favourable; when eradication efforts began; transmission of the disease was already reduced in several countries. Unlike malaria, certain characteristics were present and responsible for the success of these smallpox eradication programs, like the development of immunity, the availability of an effective vaccine, the characteristic clinical picture and the possibility of surveillance. For the Polio Eradication Program, begun in 1988, there has been a substantial reduction in the incidence of the disease and a reduced number of polio-endemic countries (from 125 in 1988 to 6 in 2003), but it is necessary to recognise that in some African countries, weak health infrastructure, communications, transport, among other things, have prevented the interruption of transmission [21].

Currently, we identified a number of key considerations for choosing between eradication approaches that are (a) scientific: available technologies to interrupt transmission and interventions to affect the host's ability to fight disease (b) focus on operational biological systems of the parasite, vector and host, and (c) economic: finance, time duration and geographic region of concern (14). Multidisciplinary and intersectoral approaches, biosocial-models, and systems theory approaches as suggested by Valero et al. (33) are also proposed. The active participation of communities is essential for monitoring, inspection and control programmes.

Figure 1 compares the phases of GMEP and the stages currently recommended by WHO for countries with low to moderate endemic patterns. Although the term eradication 50 years ago is now recognised as elimination, these two graphs show significant adjustments in phases or requirements of moving from control to elimination. Although the technical details may vary between the two models, a retrospective analysis found similarities, such as the maintenance phase of the First Elimination and prevention of reintroduction of the New Elimination and consolidation with elimination. The main difference, apart from the conceptual definition of "*eradication*" would then be in the preparatory and attack phases, which could be related to current control measures (to rapidly reduce the burden of disease). It is remarkable that 50 years ago, the time spent on the preparatory and attack phases was 5 years before moving on

to the consolidation phase, while nowadays we do not know how long it will take countries to achieve the "first reorientation of its programme" towards the *pre-elimination* stage. As discussed below, there are countries that are limited in their ability to progress towards elimination, thus control could be considered as an alternative to the goal of elimination, not theoretically but from a pragmatic point of view.

Table 2. Global overview of malaria and transformations in the concepts of eradication

Period	Late nineteenth and early twentieth century	1940-1969	1970-2000	2000-2011
Global malaria situation				
Health policies	Local control programmes.	Global Malaria Eradication Programme (GMEP)	Reorientation of control programmes. 1998: Roll Back Malaria Initiative	Millennium Development Goals. Funds and research agendas in the accelerated elimination phase and eradication as the ultimate goal.
Scientific developments	Discovery of the parasite cycle, first residual insecticides, use of quinine. Development of mathematical models of transmission.	Development of new antimalarial: chloroquine, amodiaquine, proguanil, pyrimethamine, Appearance of the first cases of resistance.	Artemisinin Development (1972), mefloquine (1985).	Development of ACT*. RTD*, long-lasting, insecticidal treated nets.
Interpretations of the term eradication of global malaria cases				
Geographic area	1916: Eradication of malaria in the Western hemisphere	Eradication applies to specific local, state, national, and regional areas and extends to the periphery to all areas from which there may be reinfection. In practice, there are areas where eradication is not feasible.	Eradication can only be global. Regional eradication is therefore an oxymoron.	2007: Global level. Certification of freedom from malaria is given to countries and there is a recognised need for joint support between regions.

Estimated time	Since control measures were the paradigm of that time, deadlines had not been set for the sustained reduction or eradication of malaria.	It is a time-limited campaign that will last 4-5 years, followed by three years of consolidation.	It is recognised that eradication cannot be conceived as a short-term programme.	Eradication is a long-term, not a short-term goal.
Incidence of infection	Mainly, sought reduction in morbidity and mortality in specific areas.	Eradication seeks to end malaria transmission without resumption at the end of it. WHO* later set a threshold of "manageable proportions" based on API $<0.5/1000$ and in 1964 $<0.1/1000$.	Reduction to a level that does not constitute a public health problem.	2007: Permanent reduction to zero of the incidence of infection through the progressive elimination of malaria in countries.
Pathogen situation	For control measures to prevail, we would expect significant reductions in transmission incidence of certain pathogens without the cessation of transmission.	1961: You can not survive even a single pathogen ("Sunset/extinction")	No possibility of reintroduction of the pathogen from another geographical area.	2006: In practice it is impossible to certify the extinction of the parasite with certainty.
Need for control measures	There has been controversy between the vector control and drug administration vs. investment in local health systems and economic development.	1952: There is no need to continue with residual insecticides. 1962: Eradication is maintained even in the absence of any preventive measures. 1969: Control measures are necessary and valid in regions where eradication is not feasible.	1984: In the case of regional eradication, there is no need to actively monitor control measures, monitoring and rapid response to imported cases; are able to keep the area free of disease.	2007: The new strategy is to move quickly with the tools available while researching new developments.

* **Abbreviations used:** API Annual Parasite Index, WHO World Health Organization, RDT rapid diagnostic tests, ACT artemisinin-based combination therapy.
Sources:[3], Adapted by the authors.

Main tools currently available

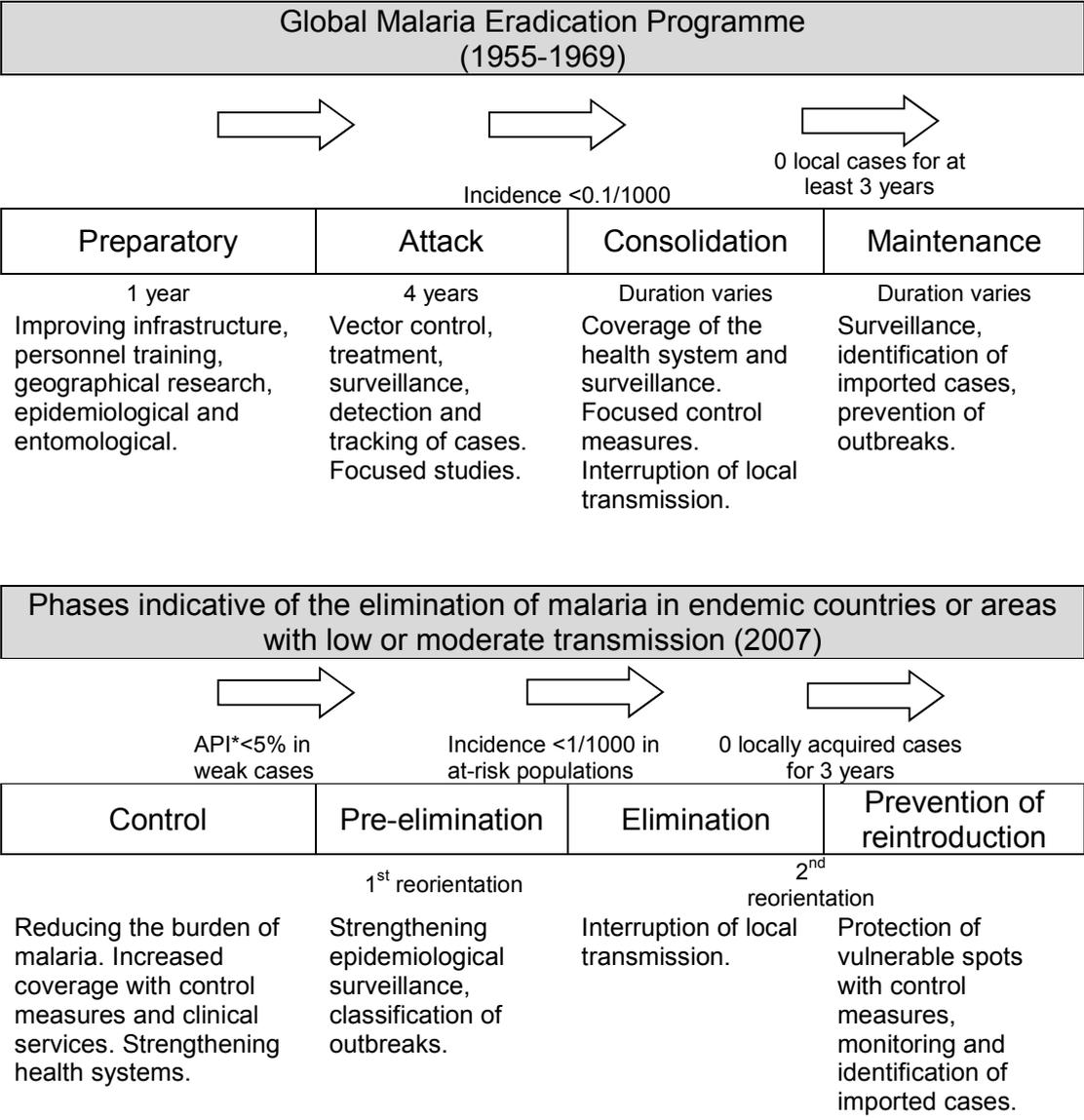
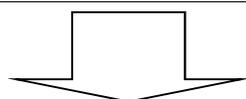


Figure 1. Comparison between the GMEP phases and the phases set by the WHO for certification of malaria-free status. **Sources:**[48], [50].Adapted by the authors.

* **Abbreviations used:** *RDT* positive index sheets or rapid diagnostic tests.

Vector control RI*, ITN*, larvacide, environmental control	Diagnostic Clinical diagnosis, RDT * for <i>P. vivax</i> and <i>P. falciparum</i> DM *, molecular and serological tests.	Drugs ACT*, quinine, primaquine, sulfadoxine- pyrimethamine for IPT* in pregnant women among others	Epidemiological surveillance Public health surveillance, reporting and investigation of cases, and monitoring antimalarial resistance and RI	Health systems Different models of systems with different equity, access, and quality indicators	Other conditions associated with the presence of disease.
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Main needs in relation to current tools					
New interventions in cases of exophilic and exophagic vectors and in areas of high transmission, ideally one application with long-term effect (genetic modification).	Quality control for RDT and DM in the field and PDR that is more sensitive, easy to apply in states asymptomatic individuals at low parasite density and identify individuals with G6PD*.	Maximize available drugs and develop new ones that can be mass administered in a single dose, effective against all stages of the parasite and its species and with specific indications for age group and type of programme.	Improve information systems to monitor changes in pathology and epidemiology using mobile telephone or internet to limit to rigorous transmission.	Research on health systems with universal access, equity and effectiveness in the delivery of services at all levels. Integration of diagnostic tests in health services.	Social science research and education in community participation on vector control and environmental planning



Current goals	
Control Programmes	Elimination Programmes
2000 Abuja Declaration, Millennium Development Goals	2007: Shrinking the malaria map.
2005: Reduce the number of malaria cases and deaths by 2000 by 50% in 2010 and 75% or more (almost zero) in 2015.	2008: Countries in areas of low and unstable transmission can proceed to malaria elimination. 2011: Eliminate malaria from 8 of the 10 countries that are in pre-elimination phase by 2015.
2008: Countries in areas with high and stable transmission can proceed to large-scale front measures to reduce the intensity of transmission. 2011: Coverage for 80% of the population at risk with control measures.	

Figure 2. Current tools for and main goals of control and elimination. Data based on reports of malERA group (Malaria Eradication Research Agenda initiative).

* Abbreviations used: G6PD glucose-6-phosphate dehydrogenase, DM diagnosis by microscopy, RI residual insecticides, ITNs insecticide treated nets (long-term), ACT artemisinin-based combination therapy, intermittent presumptive treatment IPT.

Sources: [1, 3], [3], [77-86], [87] **Adapted by the authors.**

3.6 The future of malaria: From defining concepts to the real success of the programmes

One of the assumptions for eradicating malaria is that there is no animal reservoir that can interfere and cause resurgence in human transmission [10]. Understanding this limited epidemiological characteristic in humans has been reinforced by the impact on the incidence of disease transmission of control measures that act primarily on the triad vector, man, and parasite. However, even during the GMEP, the results obtained from such a view were far closer to the goal of achieving a sustainable and time-limited campaign, reducing case incidence to zero. The teachings of GMEP have been well documented [49], however, in the face of eradication proposals and discussions that have been reintroduced in this millennium, it is necessary to consider the following:

3.6.1 Strict focus on humans, the parasite and the vector and the possibility of eradication

Historically, man's fight against malaria has been strictly biological but always influenced by the social and cultural characteristics of different regions. This means that theoretically at least, it is recognised that eradication depends on more than just the effectiveness of the control measures employed. Control measures are effective when they reach a coverage level of at least 80% of the population and are essential in the early stages of vector control for reducing malaria morbidity [88]. Indoor spraying with residual insecticide plays an important role in the process of elimination as it is intended to terminate the viability of the remaining pockets of transmission.

Thus, during the "New Age of Malaria Elimination", we consider additional measures to promote malaria eradication. Research areas include vaccine development, genetic modification and the possibility of action blocking drugs on transmission (in single doses) to replace artemisinin-based therapies [10]. It is important to note that, unlike GMEP, the current trend is toward recognising the limitations of existing tools and the need for developing in parallel a research agenda with one of control.

Still, even though today there is growing consensus regarding the need for infrastructure investments in health and epidemiological services, scientific research seems to be directed mainly to developing chemical compounds with specifications dictated by international agencies. These details include chemical composition, ease of use, effectiveness, dosage, limited therapeutic properties (in terms of pathogens, treatment therapy versus intermittent presumptive therapy, among others) and rapid diagnostic tests with lower costs and better results in the field (currently rapid diagnostic tests for *P. vivax* have lower sensitivity and specificity for *P. falciparum*, so the case deserves special attention, requiring a treatment regimen that includes drugs with action against hypnozoites. The interest in focusing efforts and resources on these measures is based on the importance of ensuring sustainability of the results obtained with current control

measures, in terms of significant reduction of the burden of disease and eventual elimination in certain geographic areas [74], [88]. However, control measures based on chemical compounds appear to have a lifespan, within which the benefits are undeniable, but once there are biological responses by the organisms where they work or are new circumstances that reduce its effectiveness, the results are also potentially short-lived.

Since the temporary nature of these chemicals' effectiveness has been recognised, it is questionable whether this methodology is prolonging indefinitely a strategy for *action - reaction* between organisms in the transmission dynamics and pharmaceutical science. While the focus of the fight against malaria requires measures for each of its components, vector control is imperative (with measures other than the use of ITNs and residual insecticide spraying). A balanced global approach is perhaps more effective and less costly if it relies less on biological adaptations of the vector and parasite. Thus, although theoretically we have taken a big step forward in advocating a comprehensive approach to malaria (as well as other infectious diseases), in practice it is still necessary to expand interest and redirect efforts towards improving all conditions that influence its persistence.

3.6.2 *What to expect from malaria programmes in accordance with the current tools and outlook*

One question that arises amidst the achievements is which the way forward is [67]. According to WHO models, designed based on efficiency studies of current control tools and assuming that all things remain the same, with the tools currently available, it is possible to effect substantial changes in the global map of malaria. Such changes consist of a 75% reduction in the incidence and age redistribution of malaria cases. Under this scenario, the decrease in the number of people at risk in the world would also increase the proportion of countries that can transition their programmes towards elimination. However, since the main malaria programmes are geared towards achieving this goal, many scientific authorities have noted that the changes we expect to see in the endemic characteristics of certain regions represent operational challenges that test the continuity of interest and support from the international economic and political organisations. These challenges include changes in the pre-test probability associated with changes in the prevalence of the disease [10]; the significance of changes in immunity associated with the variation in intensity of the exposure periods of individuals; the impact of new epidemiological characteristics on measures to reduce the rate of infection or clinical disease, such as those aimed at sporozoites and asexual forms of the parasite [85]; the increase in costs per case treated as incidence decreases; and reducing the percentage of the population at risk and therefore the need for measures such as Intermittent Presumptive Treatment in children and pregnant women [82], among others.

In addition to these factors that require authorities to adapt to prevailing new epidemiological conditions, today it is recognized that although the financial contributions from international funds increased during the

period 2004 - 2009, the 1.800 billion dollars raised in 2010 were far from the 6 billion dollars required to achieve global coverage. Thus, the WHO has deemed the achievements of current control measures as "sustainable, but fragile" [82]. Figure 2 shows the tools that are currently used in control and elimination programmes and the major challenges facing current research agendas.

In the context of current strategies, the process to follow involves the progressive reduction of malaria transmission from local levels ("natural margins in endemic areas where the disease is not as entrenched") to regional and global, leading to what has been called "*Shrinking the malaria map*", as different states of transmission currently existing each country (control, pre-elimination, elimination, prevention of reintroduction) [89], [90]. This becomes important when you consider that many endemic areas with high and stable transmission of malaria have not had successful experiences with control programmes and therefore cannot even reorient their programs to pre-elimination stage. Some authors have focused on other areas in which malaria transmission is heterogeneous, because the malaria community is particularly looking for the appropriate distribution of resources, combining elements of control and pre-elimination and not exclusive programmes [91], [92].

Furthermore, it is recognized that reorienting programmes towards elimination requires a joint commitment of countries in the same region as reducing the transmission of malaria in border areas decreases the possibility of imported cases and thus the threat to local achievements[93]. In this particular situation, one of the points in favour of collaboration between countries in the same region is that despite the large economic investments required to implement eradication programmes, it is less costly to "prevent the reintroduction of border cases than to indefinitely maintain control measures on a large scale " [94]. Some reports, for example, mention the utility of planning an elimination programme in cases where socio-political conflicts and displacement hamper authorities' access to areas with populations at risk. Although the goal of eradication, put back on the table in this millennium, sought to incorporate control programmes and elimination as the most important goals for eradicating malaria, gaps remain in developing methods for monitoring remote areas, identifying barriers to access to health systems, and generating greater investment in developing diagnostic and immune prophylactic methods, particularly for cases of residual malaria in specific regions [61], [86]

3.7 Conclusions and recommendations

The purpose of this review was to highlight and to trace the historical development of fields of knowledge, from the periphery to the centre, that have characterised the process of constructing the terminology used in the control, elimination and eradication of malaria. However, it is important to mention that malaria is a complex public health problem in which there are various interacting determinants, health system actors and dynamics between multiple levels, making the process of reconstructing these concepts somewhat challenging [95].

This review evidence how these approaches and concepts emerged and transformed during a period of great social, political and economic change in the 20th and 21st centuries. It identifies some of the factors and actors associated with the shrinking global malaria map, in time and space. The reciprocal relationship between the definition of concepts and the implementation of programs in the history of the health policies of malaria in the first two centuries suggests: first, continuous learning by international and regional scientific and health authorities; second, and no less important, the possibility of innovation in interventions from basic research to public health practice with approaches that complement existing measures as they delve into the different malaria scenarios; and third, the consequent enrichment in planning new strategies to reduce the problem and in the definition and achievement of objectives at different levels of intervention.

The state of the art shows limitations in financing to make sustainable the elimination planning and the main challenges include the control of case importation, the limited evidence of self-medication in poor areas where health system can not guarantee enough coverage of prompt diagnose and early treatment as well as barriers of access in remote areas under political unrest. Most of these endemic areas where malaria persists do not have adequate surveillance systems and monitoring indicators. Understanding the complex determinants and intrinsic and extrinsic relationships that influence resistance, resurgence and persistence of the disease have been previously studied and have described malaria as a disease "intimately associated with poverty, without having a causal relation or being of direct consequence " [30]. Thus, the challenge for the malaria community is not only technological innovation but also other cost effective operational measures, so that some countries can reorient their programmes towards pre-elimination, unless these new scientific tools radically change the way we see malaria transmission, as was the case of a vaccine that specifically targeted parasitic states to influence transmission or/in consideration of the complex genetic and antigenic characteristics of the parasite and therefore development of immunity. For these countries especially, the research strategy for new control measures can be harmful considering that a large part of health efforts are directed to this work.

Community participation in the process of organizing programmes and prioritizing areas according to vulnerability is important[61]. Additionally, empowering and constructing social networks facilitate and help

to improve processes such as diagnostic methods, mosquito net distribution, surveillance of areas experiencing a resurgence of cases, and proper distribution of resources. Monitoring and evaluation should include representatives of these networks who would participate in periodic evaluations carried out by the public and private health authorities involved in the next stages of eradication, elimination and control. In addition, and not less important this elimination Era has the priority to reduce the environmental impact of insecticide massive use as well as improve the coverage of the programmes in cluster areas where limited changed of data and statistics have been demonstrated.

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3.10 Conflict of Interest Statement

The statements and claims made in this article involve their authors and not of the Universidad Nacional de Colombia. The authors declare no conflict of interest.

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CHAPTER IV. Proportion of Fever Attributable to Malaria in Colombia: Potential indicators for tracking progress towards malaria elimination

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4.1 Abstract

Objective: To **establish** the proportion of asymptomatic malaria cases in two endemic areas of Colombia and compare the findings of malaria elimination with other endemic areas in the region.

Methods and Population: Cross-sectional surveys were carried out in 2011 and 2014 in two endemic regions of malaria in Colombia, the Caribbean and Pacific Coast. Informed and written consent were obtained from each volunteer. Capillary blood samples were obtained and examined through microscopy and RDT. Temperature was measured from the ear and a socio-demographic and clinical questionnaire was completed for each patient. In addition a narrative review was conducted to correlate state of malaria elimination in Colombia in comparison to other countries of the Amazon Region.

Results: A total of 548 volunteers were sampled by active case detection in Cordoba and Nariño. The proportion of positive malaria cases was 3% (17/548). Malaria mixed infections were the most prevalent event at 47% (8/17). Fever prevalence, that is temperature over 38.0°C, was 2.7% (15/548), but only two febrile patients tested positive for malaria. The prevalence of asymptomatic malaria cases among all positive cases was 88%. Studies about subclinical malaria are limited on the region. The financial resources impact the sustainability of control programs in several countries in The Americas and surveillance system is major responsibility at public health sector.

Conclusion: Asymptomatic malaria cases and mixed infections represent the main challenge for malaria control and elimination programs and public surveillance systems in Colombia. In regions with dense populations and high migration levels, vulnerability to infection is high. The presence of imported cases affects control and elimination efforts, reducing the Basic Case Reproduction Rate < 1 . Similar results have been found for the countries from the Amazon Region. Innovation in surveillance and innovation in community participation are required.

Key words: malaria elimination, febrile, malaria control, asymptomatic, active case detection, surveillance, mixed infection

4.2 Introduction

Malaria persists as the major global public health problems. Traditionally, solutions have centered on a biological approach, such as treating the parasitic infection and vector control, without taking socio-economic and environmental factors into account. This paradigm has proved insufficient for advancing control strategies and progressive elimination. The main challenge has been early diagnose and prompt treatment. Unfortunately, failure treatment in clinical cases and adherence to radical affect the process, outcome and impact indicators of control programs.

In Latin America, the first chloroquine resistance case was registered in Tumaco, Colombia in 1960. (1), (2). One possible factor contributing to the spread of drug resistance in the region was the frequency of presumptive treatment for all febrile cases without follow up, and not radical treatment for all positive confirmed cases (3), (4), by first Eradication Era . More recently the failures treatment are associate to poor treatment adherence and self-medication with natural herbs as a consequence of limited access to health malaria services (5).

New global malaria elimination efforts guided by the WHO's Global Technical Strategy (WHO, 2015) and RBI's action and investment framework (6) (RBM 2015) point to several key elements, including better knowledge of malaria epidemiology patterns at different endemic levels, which can be used to estimate the potential impact of novel malaria reduction strategies (7),(8),(9). Integrated strategies tailored to specific endemic settings, such as combined therapies, intermittent preventive treatments (IPT), and rapid diagnostic testing(10), have been shown to reduce case-fatality rates associated with *P. falciparum*.(11), (12), (13). However, this is not the case for *P. vivax*, owing to its dormant forms in the liver and the possibility of relapse, and to the reservoir of asymptomatic cases. In addition, the high rates of mixed malaria infections in countries like Colombia limit the possibilities for elimination. Mixed malaria infections are widely correlated with inadequate treatment and self-medication, with limited quality control strategies for blood samples, and with considerable difficulties accessing health services, thereby preventing patient control during the pathogenic period(14, 15).

In Latin America, global pre-elimination and elimination strategies have led to the introduction of various integral strategies at three levels: parasite, host, and vector (16),

(17). In this context, (i) few studies have considered the impact of asymptomatic cases on the basic case reproduction rate (R_0), and (ii) there is still a need to define and quantify the proportion of fever attributable to malaria and its implications for elimination in different endemic settings(18-23). The purpose of this study was to explore the association between malaria infection and fever as a potential way of tracking progress towards malaria control and elimination in low endemic areas and to compare the changes in species' transmission patterns. To do this, we assessed the level and distribution of symptomatic and asymptomatic cases and related the findings to potential transmission risks as a basis from which to develop improved models of control and elimination in Colombia.

4.3. Methods and study population

The study was conducted in two endemic areas in Colombia: Nariño, department on the Pacific coast, and Cordoba, a department on Caribbean coast. Blood samples were obtained from both urban and rural areas of Nariño in San Andres de Tumaco(1°48'24"N 78°45'53"W) and the municipality of Olaya Herrera (2°20'49"N 78°19'32"W). This region is endemic for falciparum malaria in a 80% and population is mainly Afro-Colombian. In Cordoba, the study concentrated on Puerto Libertador(7°53'17"N 75°40'18"W) and the municipality of Montelibano(7°58'16"N 75°25'05"W), both endemic areas for vivax malaria but high prevalence of transmission of other vector borne diseases. Cordoba department registers 9% of total positive cases detected by the National Malaria Surveillance System of Colombia(24).

A complementary qualitative systematic review was conducted, using Embase, Pubmed, and Bireme databases, covering the period 2000-2015. Search terms included asymptomatic, fever attributable to malaria, elimination, eradication and control of malaria in South America and Colombia. Several search equations were elaborated to obtain more precise information related to malaria elimination and control indicators. The references were captured in Endnote X7 and Zotero. Duplicate records were identified and eliminated. All abstracts meeting the inclusion criteria were read and selected for complete analyses of frequency and association measures.

We compared cross sectional surveys conducted in 2011 and 2014, and 1995 cross sectional survey data for San Francisco village(25). This dataset was presented by the

World Malaria Atlas (26). This area was classified as an high endemic risk (API >100 per 1000 inhabitants); unfortunately, around 3,000 inhabitants were displaced and the village San Francisco over the Rosario River, disappeared due the long period of political unrest, making no feasible additional studies (27), (5) .

The coordinator of malaria control program verified from a list the village with current evidence of autochthonous cases reported. In each village the community was invited to participate and after writing consent the sampling was conducted. Sampling by convenience was done, and participants located in each information post with help of local leaders. Protocols of security for humanitarian mission were activated according to particular conditions. From each volunteer a capillary blood sample was taken one for a thick blood smear, and for Rapid Diagnose Test, RDT, manufactured by Standard Diagnostic Inc. Asymptomatic cases were defined as any person without symptomatology compatible to malaria, but showing a positive RDT. Fever was defined as any patient with more than or equal to 38,0 Celsius degrees according to WHO Guidelines. Treatment of malaria episodes: individuals with malaria infections di were treated according to malaria guidelines of the National Control program in Colombia(28), (29). In Latin America a case of malaria is defined as all patient with or without symptomatology and positive presence of parasites. The descriptive statistics and association were estimated using Stata 13. The level of significance was at 5%.

4.4 Ethical considerations

The study was undertaken according to the basic principles of the Helsinki declaration and Resolution 8430 of the Ministry of Health of Colombia, October 4th, 1993. The study was cleared by the Ethical Committee, of the Faculty of Medicine at the Universidad Nacional de Colombia, Bogota. In addition, informed consent was obtained from all study participants. For volunteers under 18 years old, the parents or legal guardian authorized participation, as per Articles 23 and 24 of Resolution 8430, 1993. According to national norms, the investigation was classified as a minimal risk study, as per Article 11.

4.5 Results

A total of 528 subjects were sampled. Table 1 shows the prevalence of positive cases, defined as infected with or without symptomatology.

Table 1. Socio-demographic characteristics of the sampled population

Municipality and Population	Population Sampled	Malaria Prevalence RDT Positive %	Main Occupation/Situation of Community Members
TumacoUrban (102,495)	117	0	Agriculture
Tumaco Rural (87,000)	112	0,9	Fishing
Bocas de Satinga, Olaya Herrera (27,359)	235	1,7	Fishing
Puerto Libertador (47,643)	51	5,9	Displaced, miners
Montelibano (81,351)	13	30.8	Displaced, subsistence farmers

The four sampled villages experienced intense political unrest and had a high proportion of displaced populations, mainly in Cordoba Rural areas. According to CODHES, Colombia recorded five million displaced people by 2013(30). From field observations the self medication was confirmed. The consumption of herbal infusions to reduce fever is very common in all areas, but in Tumaco, people prepare infusions of Cinchona Bark while all drug stores close to the temporary field station sold the tonic, "Arquin", each 100 ml containing 0.566g of chloroquine. Given the limited diagnostic services in the area and the cost of transport to a well-equipped health center, most people with fever or malaria-compatible symptomatology take these available products.

Table 2. Malaria case distribution by municipality and species

Code	Age	Sex	Village	Municipality	Department	To	Diagnose RDT	Occupation
5	29	F	Tierraadentro	Monte Libano	Cordoba	36,1	Mixed	Housewife
20	5	M	Tierraadentro	Monte Libano	Cordoba	36,6	Vivax	Infant
28	27	M	Displaced	Monte Libano	Cordoba	36,6	Mixed	Unemployed
47	40	F	Terminal	Puerto Libertador	Cordoba	36,7	Vivax	Housewife
7	50	F	Tierraadentro	Monte Libano	Cordoba	36,8	Vivax	Housewife
10	2	F	Tierraadentro	Monte Libano	Cordoba	36,8	Mixed	Housewife
301	30	F	Porvenir	Tumaco	Nariño	37,0	Falciparum	Bingo
52	23	M	Juan Jose	Puerto Libertador	Cordoba	37,0	Vivax	Army
64	63	M	Juan Jose	Puerto Libertador	Cordoba	37,1	Mixed	Farmer
2064	42	F	Displaced	Olaya Herrera	Nariño	37,3	Mixed	Housewife
2173	33	F	Satinga	Olaya Herrera	Nariño	37,4	Falciparum	Housewife
2037	20	F	Satinga	Olaya Herrera	Nariño	37,5	Mixed	Housewife
2232	51	M	Satinga	Olaya Herrera	Nariño	37,8	Falciparum	Farmer
2017	15	M	Bellavista	Olaya Herrera	Nariño	37,8	Mixed	Student
19	6	M	Tierraadentro	Monte Libano	Cordoba	38,7	Vivax	Infant
2030	37	M	Satinga	Olaya Herrera	Nariño	38,7	Mixed	Fisher
55	19	M	Juan Jose	Monte Libano	Cordoba	39,2	Vivax	Farmer

Table 2 shows the demographic and clinical characterization of the detected malaria cases. Prevalence did not differ by sex or occupation. The findings suggest that *P. vivax* and mixed infections are a key public health problem in those areas. The age distribution of cases kept the historical epidemiology for these areas. The ages affected by the infection and disease are grouped between 15-45 yrs. However, 70% of infected subjects were asymptomatic and the proportion of fever attributable to malaria was 42%.

San Francisco Village study: Historical comparison 1995

This Village was located on Tumaco rural area, over the Rosario River. A total of 1,685 thick blood smears were taken. 41 (2.4%) patients reported fever, i.e. temperature $\geq 38^{\circ}\text{C}$, and 151 (8.9%) tested positive for parasites microscopically (6.2% *P. falciparum* and 2.3% *P. vivax*). The total proportion of positive cases in febrile episodes was 86% (19/22) and 8.7% (132/1,512) in afebrile subjects. The crude odds ratio of the association fever/parasitemia was 9.9 (95% confidence intervals, CI, 5.2%-18.7%, *p-value* < 0.0001). After adjusting for age and sex, the OR was 10.8 (95% CI 5.6-20.8, *p-value* < 0.0001). The crude proportion of fever attributable to malaria (PAF) was a 41.7% (95% CI 31.3%- 55.3%) and 42% (95% CI, 38.1- 44.1, *p-value* < 0.001) after adjusting for age and sex (31).

On this particular survey fever due by malaria increased with the level of parasite density and, consequently, the frequency of fever associated to malaria decreases with age (31). After adjusting for age and sex, the odds of fever was 12.1 times higher among individuals exposed to *Plasmodium vivax* malaria parasites compared to those who were not exposed. Although, a high association was also observed among those exposed to *Plasmodium falciparum* malaria, OR=11.4, it was slightly lower. However, the proportion of fever attributable to *Plasmodium falciparum* was 33.2% higher than the fraction of fever attributable to *Plasmodium vivax*, where the proportion of fever attributable to malaria was =16.4% (31).

During the last 20 years, there is a slight reduction of asymptomatic and the PAF. The population of San Francisco was in the middle of all actors in the armed conflict, and population was forced to displace. Additional surveys are not possible, however the other regions sampled keep similar epidemiological conditions and same socio-economic factors which affect both Tumaco and the Pacific coast endemic areas.

Table 3 presents most relevant aspects of the malaria control program of the eight countries on the same Amazon Region where Colombia also share similar eco-epidemiological conditions. These findings suggest limited actions of surveillance and budget constraint. The case detection in some areas combine intensified active case detection. The activities are responsibility of the public sector, the review do not find the private health sector participation in most of the countries. The surveillance system in Colombia and other countries present data from years before 2013, there is not available data for more recent years. The surveillance system is not opportune and sensible in case detection. It is widely suggest levels of under report around 35% (15)

Table 3. Results of the Qualitative Review of Malaria Pre-elimination and elimination:
Study case of countries on the Amazon Region. (32-42)

Strategies	Promotion and Prevention	Vector Borne Control	Health System
Country	Early detection Outbreak prediction		Strengthening, Planning, surveillance, operative research
Peru	Active, Passive and Intensive case detection _ACD;PCD;ICD	Impregnated bed nets. Insecticides spraying , Control of swamps	Surveillance irregular, Studies to establish insecticide susceptibility and research strategies is limited
Colombia	Passive Case Detection Combined treatment is free in public health sector Only few groups conduct active case detection	Distribution of bed nets to all age groups Irregular Indoor residual spray Some communities reject impregnated bed net due to bad smell and allergic in children	International partnerships with Global Fund, Swiss TPH, PAHO NIH-USA Public health and academic sector with limited access to financial support
Bolivia	Combine treatment is free, artemisinin treatment partially effective	Programs of distribution of impregnated bed nets Indoor residual spray	Responsibility of actions mainly in public health sector
Ecuador	PCD, combined treatment is free by public health sector	There is not evidence in the efficacy of indoor residual spray Free distribution of impregnated bed nets	Combined therapy is distributed by public health sector free
Venezuela	PCD, ACD, Case detection by volunteers Diagnose by microscopy	Residual spray	Information capture is by hand and does not allow analyses to policy making decision

Guyana	PCD	Massive bed net distribution, residual indoor spray limited results	Limited evidence and resources for operative research
Surinam	ACD, PCD, Intense Case Detection	Indoor spray residual, Impregnated bednets, Protection to pregnant women	Educational campaigns and promote of Behavioral changes
Brazil	ACD, PCD, ICD	Indoor and outdoor residual spray, Impregnated Bed nets, swamp elimination	Limited Sentinel surveillance of insecticide vector susceptibility Limited evidence of interventions efficacy

4.6 Discussion

The findings show that *P. vivax* malaria is still endemic in Cordoba, while *P. falciparum* continues to be the main problem in Tumaco. However, the frequency and distribution of *P. vivax* and mixed infections indicate a weak effectiveness of malaria treatment in terms of prescriptions, delayed access and limited supervision by health actors. As other authors refer, *Plasmodium vivax* represents de 80% of clinical malaria cases in Latin America and the Caribbean Island, meanwhile *Plasmodium falciparum* remains as a main cause of mortality 6 deaths per 100.000 inhabitants (32, 43)

Policies and strategies formoving from malaria control to elimination require adequate planning to account for transmission levels and for the structure of health and social systems. Identification of asymptomatic and imported cases are key elements for malaria control planning. Assessing surveillance capacity and selecting relevant indicators for surveillance and monitoring are key preparatory issues that help to understand how the health and social systems function in a given place. In addition, countries must work in redefine and unified clinical malarial guidelines and protocols for

malaria transfusion at both rural and urban areas. It is important establish algorithms and diagnose criteria between semi immune population and immune populations from non-endemic and endemic regions. The impact and cost of malaria treatments due to inadequate management and implementation could be reduced by additional research to identify state of drug resistance and permanent sentinel surveillance systems(44), (45).

The monitoring and evaluation of strategies of malaria elimination must be permanent. Definition of indicators for program managers at administrative level as well as lab and clinics places would contribute to forecast outbreaks and epidemics. The early detection of clinical failures in treatments will reduce the cost of changing treatments.

In Latin America, has recorded contrasting evidence about the association of malaria and fever as a main symptom(17, 23). In similar regions, authors present contradictory results about the prevalence of asymptomatic infections, ranging from 4.2% to 96% (18), (19), (21), (22),(46). In Colombia, two studies conducted in Choco and Cordoba showed similar trends to those mentioned above. The study in Quibdo, highly endemic for *P.falciparum*, showed the absence of asymptomatic cases among school children(47). Meanwhile in Tierralta, an area endemic for *P.vivax*, the study found 14.6% of cases were asymptomatic (23). These findings coincide with our results, showing exposure differences by sex and age, as well as the different symptomatic behavior patterns of the two species *P.falciparum* and *P.vivax*. Therefore, the differences in age and sex between the febrile and afebrile cases cannot be just a chance finding and merits further exploration.

Despite these findings, the precision of estimates presented in this study suffers from the low number of cases and from the limited access to populations and population groups in the conflict zones. These results are consistent with previous findings from other authors on the same region(48), (11), (49). However, it must be noted that the proportion of fever attributable to malaria appears stable at around 39-42%. The degree of self-medication in some areas remains an important and big challenge to national efforts towards developing effective national surveillance systems and to the National Institute for Food and Drug Surveillance(INVIMA).

The findings of this study have implications for malaria surveillance systems and malaria control and elimination programs. Currently, a malaria case is defined as any case that tests positive for parasites by thick blood smear and/or RDT. Presently, clinical cases are detected by passive case detection (PCD). Active case detection has been reduced due to costs, such as those associated with transport to endemic areas. In Colombia, the priorities are: (i) to develop strategies for surveillance-response systems adapted to a given endemic area and (ii) to develop new strategies for primary and secondary preventive actions that also include different actors of the conflict, as well as active participation of the displaced Afro-Colombian and indigenous populations. Some of the cases detected came from those in the military; Colombia faces the task of reforming strategies in a way that allows young people to reflect more on their future and roles in society.

The systematic narrative study and fieldwork show how the evidence between countries varies. There is not enough temporal and spatial information to indicate the real status of malaria elimination and pre elimination efforts in Latin America, mainly in the Amazon region. Any attempts to discuss progress towards malaria elimination will first have to elucidate and define parameters for statistically significant comparisons. Mathematical models offer a way to predict the value of progress indicators, while related informatics systems can help to evaluate the impact of elimination and control efforts considering variables of place, time and person. Tracking these epidemiological markers from infection to illness, plus setting a new threshold of fever, must be evaluated in both the short- and long-term to really have an impact on the malaria elimination strategy and redefine new programs. Finally, a sentinel surveillance system to measure and establish the state of native cases versus imported is also required between countries. The weekly report must be mandatory to forecast epidemics and prevent early presence of imported cases and avoid the malaria reintroduction in areas with Reproductive Rate close to Zero.

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Chapter V. Historical Review of the current sanitary policy of goiter elimination in Colombia, 1990-2012

Título: Revisión de políticas sanitarias y situación actual del Bocio Endémico: El caso de Colombia.

Título en Inglés: Revision of the sanitary politics and current situation of goiter: the case of Colombia.

Título abreviado: Bocio endémico en Colombia.

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5.1 Resumen

Introducción: En la actualidad el bocio endémico es considerado uno de los desórdenes producidos por la deficiencia de yodo. Su prevalencia en distintas regiones a nivel mundial, llevó a que algunos países declararan que estos desórdenes constituyen un problema de salud pública, no solo por las consecuencias directas en la salud de grupos vulnerables como las mujeres embarazadas y los niños en edad escolar sino por su impacto negativo en el desarrollo de las comunidades afectadas. En Colombia, se adoptó la yodización universal de la sal como principal estrategia para el control de estos desórdenes declarándose su eliminación a finales del siglo pasado. **Objetivo:** establecer la evidencia sobre el estado de las políticas y la prevalencia de bocio endémico y el estado nutricional del yodo medido por la determinación de la yoduria en algunas regiones del país. **Metodología:** realizar una revisión histórica de la literatura científica para Colombia y el estado de la eliminación de una patología que fue considerada endémica como es el Bocio. **Uso de meta buscadores:** de la Universidad Nacional de Colombia. **Conclusiones:** Se requiere atención por parte de las autoridades sanitarias no solo por la persistencia de los desórdenes por deficiencia de yodo sino por el riesgo de enfermedades tiroideas por la ingesta excesiva de yodo en algunas regiones del país. Actualmente no hay política por que el país fue declarado libre de Bocio en 1990. Es necesario la organización del Sistema de Salud y la Política de Control Enfermedad Tiroidea.

Palabras clave: Deficiencia de Yodo; Bocio endémico; Política de Salud; Glándula Tiroides; Colombia; Prevalencia (*Fuente BIREME*)

5.2 Abstract

Introduction: Goiter Syndrome is currently considered one of the iodine deficiency disorders (thyroids diseases). The prevalence of this made it some countries to declare this disorders as a public health problem, not just because of its direct health consequences on vulnerable groups like pregnant women and scholar children but its negative impact on the develop of the affected communities. **Objective:** To establish in Colombia, impact of the universal salt iodization adopted as the main strategy to control these disorders, and the state of declaration of its elimination at the end of the past century. **Methods:** Narrative review of the scientific publication. **Conclusions:** Some subsequent reports had shown that goiter prevalence and iodine nutritional state measured by urinary iodine in some regions of the country requires the attention of the sanitary authorities not just for the persistence of this iodine deficiency disorders but also for the risk of thyroid diseases caused by excessive intake of iodine in some regions of the country. Exist and urgent need to include again the sanitary policy and surveillance the thyroid diseases.

Keywords: Iodine Deficiency; Goiter; Endemic; Health Policy; Thyroid Gland; Colombia; Prevalence (*Fuente BIREME, MeSH*)

Revisión de políticas sanitarias y situación actual del Bocio Endémico: El caso de Colombia

5.3 Introducción

Los *desórdenes por deficiencia de yodo*(1) son un conjunto de entidades patológicas que reflejan un estado de disfunción tiroidea ocasionado principalmente por el aporte insuficiente de yodo a la dieta. Aunque el entendimiento sobre su fisiopatología ha sido un gran avance para la medicina en el diseño de programas destinados al aumento del aporte de yodo a las poblaciones, en la actualidad estos desórdenes son un problema de salud pública en 54 países del mundo y se considera que a nivel global 225 millones de escolares tienen una ingesta insuficiente de yodo (2). Respecto a esto, Colombia implementó la política de *yodización universal de la sal* (YUS) y fue declarada en 1998 libre de los DDY. Sin embargo, se ha observado que algunos de los países que previamente habían alcanzado este logro han venido presentando prevalencias de bocio endémico y cifras de yoduria en escolares que demuestran que no se ha sostenido esta eliminación (3). Por esta razón, la tendencia mundial está dirigida al reconocimiento que los programas de control y eliminación de estos desordenes deben contar con al menos dos características fundamentales que les permitan lograr y sostener los resultados, la primera es el establecimiento de alianzas eficaces entre el sector sanitario, el académico y el industrial en la que se asegure el cumplimiento de los estándares establecidos en los procesos de yodización de la sal y la segunda es el uso

reflexivo de indicadores de impacto y sostenibilidad cuya finalidad radica en el seguimiento del estado nutricional del yodo en la población.

5.4 Breve historia del Bocio Endémico

El bocio endémico parece haber acompañado a la humanidad desde siglos pasados. Existen documentos que muestran que en la cultura china, en el siglo XXIX a. C ya se conocían distintas clases de tumores de cuello. Estos tumores también aparecen registrados en documentos Egipcios e Hindúes del siglo XVI a.C.En el siglo XVIII a.C., en el “Tratado sobre aguas y tierras” se asoció la presencia de bocio con el agua de ciertas regiones geográficas montañosas. Esta misma observación aparece en Roma entre los siglos I a.C. y I d.C. así como la descripción de lo que parece concordar con lo que hoy conocemos como cretinismo “existen aguas que tienen el poder no solo de cambiar el cuerpo sino también la mente” (4). En América, antes de la conquista, algunos autores mencionan el uso del términocoto o *ccotto* por los nativos (5)mientras que otros opinan que en la región no había bocio hasta el siglo XVIII y XIX(6).

Aunque en el siglo XVI las características geográficas propias de las regiones con presencia de bocio que incluían regiones montañosas, llanuras aluviales a altura considerable y distantes del mar, con el correr de los años, estas características dejaron de ser relativamente exclusivas y se encontró que había deficiencia “significativa de yodo” en áreas costeras, ciudades y países desarrollados(3).

En cuanto a la historia del tratamiento de esta patología, en China en los años 400-500 d.C algunos médicos chinos utilizaron *Sargassum* y *Laminaria Japonica* e incluso glándulas tiroides animales. Sin embargo, en los siglos previos existe evidencia de que los egipcios practicaban tratamiento quirúrgico a este tipo de tumores. Estas prácticas permanecieron aún hasta el siglo XV(7). David Marine se considera uno de los pioneros en la profilaxis masiva del bocio endémico “el bocio simple es la enfermedad prevenible más sencilla... debe ser excluida de la lista de enfermedades humanas tan pronto como la sociedad determine hacer el esfuerzo” (8).

En 1950, durante la Tercera Asamblea Mundial de la Salud se recomendó a los países que estudiaran la magnitud del bocio endémico en sus territorios y en 1958 la Organización Mundial de la Salud(9) publicó un conjunto de seis revisiones que pretendían aportar un enfoque a los trabajadores de salud pública de los países para el abordaje de la enfermedad.

En 1960 la OMS reconoció que el esfuerzo por prevenir el bocio endémico todavía no había sido hecho debido a que las autoridades sanitarias no estaban convencidas de su inclusión dentro de los problemas de salud pública, de la eficiencia y seguridad de las medidas profilácticas y de la factibilidad de superación de las dificultades técnicas de las intervenciones(7).

5.5 DEFINICIÓN DE LOS DESORDENES POR DEFICIENCIA DE YODO

El único papel confirmado del yodo en el cuerpo humano es aquel relacionado con la síntesis de hormonas tiroideas **(10)**. Los DDY son definidos por la Organización Mundial de la Salud (9) como las consecuencias de la deficiencia de yodo en una población que podrían ser prevenidas si esta tuviera una adecuada ingesta de yodo **(3)**. Se considera como un “fenómeno ecológico natural” en ciertas regiones del mundo, en las que existe pérdida de yodo del suelo debido a erosión, pérdida de vegetación y labores de pastoreo excesivas.

En el cuadro 1 se muestran las dosis de yodo recomendadas en la dieta por la UNICEF, el ICCIDD y la OMS, que varían de acuerdo a la edad y estado fisiológico.

Cuadro 1. Requerimientos de yodo en la dieta recomendados actualmente

Rango de edad	Dosis recomendada
Niños preescolares (0-59 meses)	90 µg
Niños escolares (6-12 años)	120 µg
Adolescentes y adultos	150 µg
Mujeres embarazadas y lactando	250 µg

Fuente:**(3)**. Adaptada por los autores.

Los DDY son considerados una amenaza a la salud pública en países en los cuales la mediana del yodo urinario es menor a 100µg/L **(2)**, pues afecta especialmente la salud de los niños preescolares y de las mujeres embarazadas y el desarrollo de las poblaciones **(2)(10)**. El espectro de DDY abarca el desarrollo de bocio, hipotiroidismo, anomalías congénitas, mortalidad perinatal e infantil, cretinismo, hipertiroidismo inducido por yodo, entre otros. Debido a la incorporación de yodo y la producción de hormonas tiroideas en el feto en formación el periodo más crítico abarca desde el segundo trimestre de embarazo hasta el tercer año posterior al nacimiento **(3)**. Actualmente se considera que la deficiencia de yodo es la causa prevenible más importante de daño cerebral **(3)** y el principal motivo detrás de los programas de eliminación de los DDY **(10)**. La deficiencia de yodo también tiene un impacto grave a nivel colectivo pues produce alteración en el desarrollo físico y mental de las poblaciones con distintos grados de severidad, de modo que se ha reportado que las personas que viven en áreas afectadas por deficiencia severa de yodo pueden tener un coeficiente de inteligencia de 13.5 puntos menos que grupos control **(11)**.

5.5.1 Factores que influyen en la aparición de bocio

El principal factor responsable de la deficiencia de yodo en el mundo es la baja ingesta de yodo en la dieta **(10)**. Aparte de la deficiencia de yodo en la aparición de bocio endémico existen algunos factores etiológicos como los alimentos (mandioca, maíz, batatas, brotes de bambú, nabos, coles,

casaba,leches (Finlandia y Tasmania), ajo, cebolla, etc. La acción antitiroidea de los bociógenos se relaciona con la presencia de tiocianatos que inhiben el transporte del yoduro y a altas dosis compiten con el yoduro en la síntesis de hormonas tiroideas. El potencial de desarrollo de bocio (“goitrogenicity” en inglés) está determinado por el balance entre los aportes de yodo y de tiocianatos cuando la razón yoduria (μg): tiocianato (mg) cae por debajo de 3” (10).Otros factores incluyen alteraciones nutricionales, factores genéticos, minerales presentes en fuentes hídricas (dureza del agua, concentraciones elevadas de calcio, magnesio y flúor y disminuidas de selenio y zinc), contaminación de las aguas de consumo humano y animal, presencia elevada de yoduros naturales en los ecosistemas de algunas regiones del mundo (Isla de Hokkaido en Japón y en la región de Salt Lake City), origen geológico de los suelos (12).

5.6 SITUACIÓN DE LOS DDY EN EL MUNDO Y POLITICAS SANITARIAS ACTUALES

En el año 1990, en la Cumbre Mundial para los Niños de las Naciones Unidas se reconoció la deficiencia de yodo como un problema de salud pública por lo que en 1991 se adoptó la meta de su eliminación en la Asamblea Mundial de la Salud y fue reafirmada en 1992 en la Conferencia Internacional de Nutrición. En 1993 la OMS y la UNICEF recomendaron como principal medida para el logro de esta meta la “*yodización universal de la sal*”.En el 2005 la Asamblea Mundial de la Salud adoptó el compromiso de reportar la situación global de los desórdenes por deficiencia de yodo cada tres años(3).

En 1993 la OMS reportó el estado mundial de los desordenes por deficiencia de yodo basándose en la prevalencia de bocio endémico en los países. Posteriormente, ya que muchos países habían iniciado programas de eliminación de los DDY, la OMS volvió a analizar el estado nutricional de estos países mediante la medición de la yoduria y la prevalencia de bocio endémico con el fin de comparar los resultados de la década pasada. Para esto recogió los datos de estudios nacionales y subnacionales realizados en distintos países del mundo entre 1993 y 2003 y evaluó la prevalencia total de bocio y la mediana del yodo urinario. Estos resultados se publicaron en el año 2005(2) y mostraron que la deficiencia de yodo era considerada aún un problema de salud pública en 54 países del mundo y el 36.5% de los escolares del mundo (285 millones) pertenecían al grupo de ingesta insuficiente de yodo, al extrapolar este resultado a la población general se estima que cerca de dos billones de individuos tienen una ingesta insuficiente de yodo. En cuanto a la proporción de escolares con un estado nutricional deficiente de yodo este porcentaje varió entre un 10.1% en la Región de las Américas y un 59.9% en la Región Europea. En el Sureste Asiático el porcentaje fue de 39.9% y en el Pacífico Occidental de 26.2%. Con relación a la prevalencia total de bocio (PTB) en la población general, se estima que en el mundo la prevalencia es del 15.8%, variando entre un 4.7% para las Américas y un 28.3% en África y en comparación con los datos del año 1993, la PTB aumento en un 31.7% a nivel global, a excepción de las Américas y el Pacífico Occidental en donde se presentó un descenso en la PTB en un 46% y 32.2% respectivamente. Sin

embargo, la TPB encontrada no es consistente con el estado nutricional del yodo actual, que se puede explicar por el retardo en los cambios en la TPB con relación al momento de implementación de la yodización de la sal. También se encontró que el número de países en los que la deficiencia de yodo representa un problema de salud pública disminuyó de 110 en 1993 (medida por la PTB) a 54 (medida por el yodo urinario), en 43 países la nutrición con yodo es óptima, en 54 es inadecuada y en 29 países la ingesta de yodo es más que adecuada o excesiva. Asimismo, estos hallazgos por regiones se correlacionan con el hecho de que las Américas sea la región en la que hay una mayor proporción de hogares que consumen sal yodada (90%) en comparación con Europa que alcanza solo el 27%.

5.6.1 La yodación de la sal como principal herramienta

En la actualidad se reconocen diversas fuentes de aporte de yodo al ser humano, por ejemplo, en las zonas que no son endémicas de bocio se encuentran concentraciones de yodo en el agua de 5µg/L y en las endémicas de 1µg/L. El aporte de yodo en el agua es de 10µg/L. En el aire la presencia de yodo se relaciona con la contaminación atmosférica, en una región contaminada la atmósfera contiene hasta 1µg/m³ de yodo para un aporte diario de 10 a 20µg/día (12). Sin embargo, la yodización de la sal es actualmente la estrategia más usada para el control y la eliminación de los DDY. La yodización universal de la sal es definida por la OMS como la yodización de la sal para consumo humano y animal por encima de unos niveles fijados internacionalmente (>90% de los hogares) (3). Además de la cobertura de este tipo de sal a la población afectada, la OMS llama la atención sobre la necesidad de vigilar la calidad del proceso de yodización y distribución de la misma, lo que requiere la colaboración de los sectores públicos y privados. Aparte de la yodización de la sal existen casos en los que es necesario el aporte de suplementos de yodo a las mujeres embarazadas y niños menores de 2 años (13).

5.6.2 Necesidad de seguimiento a los programas (Cuadro 2)

Al existir distintos estados nutricionales de yodo en los países del mundo, la OMS ha reconocido que es necesario fortalecer el seguimiento a las políticas de yodización de la sal para asegurar que estas tienen el impacto deseado, así como para “identificar poblaciones en riesgo y asegurar una prevención y control sostenible de los desórdenes por deficiencia de yodo” (2). Esto también debido a que la ingesta excesiva de yodo puede producir hipertiroidismo y enfermedades tiroideas autoinmunes (14).

Hasta los años 90 la prevalencia total de bocio era utilizada como el principal indicador de la deficiencia de yodo en las poblaciones sin embargo lleva muchos años el cambio en la prevalencia de bocio una vez instauradas las medidas de yodización. La OMS recomienda el estudio en niños preescolares por su fácil acceso y porque son una representación adecuada del estado nutricional de la población general, sin embargo para monitorizar el impacto de los programas de yodización de la sal deben incluir a otros grupos vulnerables incluyendo a las mujeres embarazadas (2).

Cuadro 2. Consecuencias en la salud por deficiencia y exceso en la ingesta de yodo.

Grupos etarios	Deficiencia de yodo	Exceso de yodo
Todas las edades	Bocio Hipotiroidismo Aumento en la susceptibilidad de la glándula tiroides a la radiación nuclear	Hipertiroidismo Tiroiditis autoinmune
Feto	Abortos Anomalías congénitas Aumento en la mortalidad perinatal	
Neonatos	Cretinismo endémico Aumento en la mortalidad infantil	
Niñez y adolescencia	Alteraciones en la función mental Retraso en el desarrollo físico Hipertiroidismo inducido por yodo	
Adultez	Alteraciones en la función mental Hipertiroidismo inducido por yodo Disminución en la fertilidad	Bocio inducido por yodo

Fuente: (3) y (10) Adaptado por los autores.

Para ello se han ideado distintas formas de seguimiento a los programas de yodización de la sal, de su impacto en la prevalencia de bocio endémico y otros desordenes por deficiencia de yodo y de su sostenibilidad una vez implementados los programas. En los cuadros 3-5 se enumeran los criterios epidemiológicos para evaluar el estado nutricional de los escolares, por medio de la mediana de la yoduria, así como la clasificación clínica del bocio recomendada actualmente por la OMS y la interpretación sobre su prevalencia para un territorio dado.

5.6.3 Indicadores del proceso de yodización de la sal:

La legislación apropiada y las regulaciones que apoyen los procesos son las piedras angulares de los programas de yodización de sal en los países. Una de estas regulaciones es aquella que especifica el contenido de yodo en la sal de consumo humano y animal en los sitios de producción. La OMS actualmente recomienda el método de titulación o sus equivalentes, asimismo se recomienda el uso de yodato de potasio en preferencia al yoduro por ser su mayor estabilidad (3). Dentro de los factores que determinan el contenido de yodo en la sal al nivel del consumidor se encuentran:

Diferencias en la cantidad de yodo agregado a la sal, contenido diferente de yodo en un mismo lote o por bolsas de sal debido a fallas en el proceso de mezcla, falta de control de la humedad a lo largo del proceso de producción (con pérdidas de yodo aproximadas entre el 30 y el 80%), pérdida de yodo debido a impurezas de la sal, o por los procesos de lavado o cocción a nivel domiciliario, y disponibilidad de fuentes de sal no yodadas para el consumidor (3). Estos escenarios de pérdida

potencial del contenido requerido de yodo en la sal indican la importancia de la evaluación de los procesos desde la producción, el empaquetamiento y distribución de la sal hasta el nivel del consumidor final.

La OMS, UNICEF y el ICCIDD recomiendan que “considerando que bajo las condiciones habituales existe una pérdida del 20% del contenido de yodo desde el productor hasta el consumidor, otro 20% en los procesos de cocción previas al consumo, que en promedio una persona ingiere 10g de sal al día, se recomienda un contenido de yodo en la sal en el sitio de producción de 20-40 mg de yodo por kg de sal (20-40 ppm) para proveer 150 µg de yodo al día. Para las comidas procesadas se debe utilizar sal con un contenido de yodo cercano al rango inferior recomendado **(3)**.

Sin embargo además del monitoreo del contenido de yodo en la sal es necesario determinar la yoduria en muestras representativas a nivel nacional, siendo el rango recomendado de 100-199 µg/L en la población general y 150-249 µg/L en las mujeres embarazadas **(3)**. A partir de los resultados de la población, la OMS recomienda considerar los determinantes del consumo de yodo, como son:

- El porcentaje de casas que utilizan sal adecuadamente yodada.
- Calidad en el sitio y procesos de producción, empaquetamiento, distribución.
- Hábitos alimentarios con relación al consumo y uso de la sal.

5.6.4 Indicadores de impacto:

El yodo urinario se prefiere como indicador de impacto de los programas de control de los DDY porque refleja la ingesta actual de yodo y responde relativamente rápido a la corrección de la deficiencia**(10)**. La OMS recomienda que los estudios de deficiencia de yodo se hagan en escolares entre 6-12 años de edad**(2)**. A pesar del desfase en los cambios de la PTB y el estado nutricional del yodo, la PTB es considerada un indicador práctico de evaluación de base en áreas donde la deficiencia de yodo es severa**(2)**.

Cuadro 3. Criterios Epidemiológicos para evaluar el estado nutricional del yodo en escolares (mayores a 6 años) y en mujeres embarazadas por medio de la concentración urinaria de yodo.

Grupo poblacional	Yoduria (µg/L)*	Ingesta de yodo	Estado del yodo
Niños escolares >6 años.	<20	Insuficiente	Deficiencia de yodo severa
	20-49	Insuficiente	Deficiencia de yodo moderada
	50-99	Insuficiente	Deficiencia de yodo leve
	100-199	Adecuada	Nutrición adecuada de yodo
	200-299	Por encima de los requerimientos	Es posible que provea una adecuada ingesta a las mujeres embarazadas o lactando, pero

	≥300	Excesiva	representa un posible riesgo para la población general†. Riesgo de consecuencias adversas para la salud ‡
Mujeres embarazadas	<150	Insuficiente	
	150-249	Adecuada	
	250-499	Por encima de los requerimientos	
	≥500	Excesiva	
Mujeres lactando y niños < 2 años.	100	Adecuada	

Fuente: (3)y(10)(2)Adaptado por los autores.

*Como la distribución del yodo urinario no es normal, el punto de corte es definido en la base de valores de mediana(10).

† Riesgo de hipertiroidismo inducido por yodo posterior a la introducción de yodización de la sal en grupos susceptibles(2).

‡ Hipertiroidismo inducido por yodo, tiroiditis autoinmune

Cuadro 4. Clasificación simplificada del bocio por palpación

Grado 0	Bocio no palpable ni visible
Grado 1	Bocio palpable pero no visible cuando el cuello está en posición normal, incluyendo nódulos tiroideos en una tiroides no aumentada de tamaño.
Grado 2	Bocio claramente visible cuando el cuello está en posición normal, consistente con un aumento del tamaño de la tiroides a la palpación.

Fuente: (3)Adaptado por los autores.

Cuadro 5. Severidad de los DDY según criterios epidemiológicos

	Grado de los DDY, expresados como porcentaje del total de escolares evaluados			
	Ninguno	Leve	Moderado	Severo
Total goitrate				
Prevalencia de bocio	0.0-4.9%	5.0-19.9%	20.0-29.9%	≥30%

Fuente: (3) y (10)Adaptado por los autores.

5.7 EL CASO DE COLOMBIA. HISTORIA DE LAS POLITICAS SANITARIASY SITUACION DE LOS DDY EN COLOMBIA

En Colombia entre los siglos XVI y XVIII cronistas como Fray Pedro Aguado reportaron la prevalencia de bocio en distintas regiones. Francisco José de Caldas también registro la enfermedad que se presentaba “a lo largo del Rio Magdalena hasta la confluencia del Rio Cauca” **(15)**. En 1832 el francés Boussingault recomendó el consumo de sal procedente de fuentes yodadas para la prevención del bocio en Colombia y en 1857 el Congreso de la República convocó a los científicos de la época para que investigaran en la prevención y tratamiento del bocio. Sin embargo, solo hasta la primera mitad del siglo pasado se conoció la magnitud y gravedad del problema del bocio endémico en Colombia gracias a la Encuesta Nacional de Bocio, realizada entre 1945 a 1948. Esta encuesta estudió 183.243 escolares de ambos sexos, correspondientes a 385 municipios del país. Esta encuesta mostró una prevalencia de bocio de 52,6 %, siendo los Departamentos más afectados los de Caldas, Cauca, Huila, Tolima y Boyacá.

En 1947 se aprobó la Ley 44 por medio de la cual se creó el antiguo Instituto Nacional de Nutrición, como dependencia del Ministerio de Higiene, y se determinó la yodación de la sal.

En 1950 la Concesión de Salinas del Banco de la República inició la producción de 300 toneladas mensuales de sal yodada con 50 ppm de yodo. Gran parte de esta sal se distribuyó en siete municipios del Departamento de Caldas que previamente habían sido seleccionados debido a que su prevalencia superaba ampliamente el promedio nacional. A los dos años el Instituto Nacional de Nutrición realizó una nueva encuesta en los escolares de estos municipios para determinar la efectividad de las medidas de yodación de la sal en la prevención del bocio endémico. Esta nueva encuesta mostró una reducción acentuada en la prevalencia del bocio endémico general para los siete municipios de 83,1% a 33,9%” **(15)**.

El Decreto Legislativo 0591 de 1955 estableció la yodación de la sal para consumo humano y animal, de acuerdo con las normas de la OMS (50-100 ppm de yodo) y en 1959 la Concesión de Salinas construyó una refinería moderna para este fin **(15)**. En 1959 el Ministerio de Salud Pública “encarga al Instituto Nacional de Nutrición de efectuar el control y la supervisión de la yodación de la sal” en el país y tres años después mediante la Ley 14 y el Decreto Reglamentario 1908 se establece que la Concesión Salinas transfiera a esta entidad 2 centavos por cada libra de sal yodada en Colombia **(12)**.

En 1960 la Encuesta de Nutrición de Colombia encontró que la prevalencia de bocio endémico era de 41% en los niños menores de 15 años. En Colombia, la explotación de las salinas marítimas y terrestres fue contratada por el Gobierno con el Banco de la República desde 1931 bajo la Concesión de Salinas. Para 1965 se explotaban las salinas terrestres de Zipaquirá en el interior del país y las marítimas de Manaure y Galerazamba sobre el Mar Caribe” **(15)**.

En 1959 la yodación cubrió el 48 % de la sal producida en el país; en 1964 este porcentaje subió al 76 %, y en 1966 se calcula que el 55 % de la sal producida en Colombia se encontraba yodada. El

15% restante corresponde a sal marina, utilizada en su mayoría para consumo animal y uso industrial. “El control efectivo de la yodación de la sal en Colombia se inició en 1963, después de la creación del nuevo Instituto Nacional de Nutrición” **(15)**.

Para la evaluación de estas medidas a escala nacional se realizaron encuestas nacionales en escolares, una de ellas se limitó a los siete municipios del Departamento de Caldas mientras que otra se diseñó en dos etapas: la primera de ellas limitada a los Departamentos que habían presentado una prevalencia de bocio mayor del 50% en la encuesta nacional (Boyacá, Caldas, Cauca, Huila, Tolima y Valle). En 1968 la Ley 75 responsabiliza al Instituto Colombiano de Bienestar Familiar del control de la yodación de la sal y se aumenta en cinco centavos el aporte por libra de sal yodada vendida. Luego la Ley 27 de 1974 establece la participación del ICBF en el 12% del precio oficial de la sal **(12)**.

Al finalizar la década de los años 70, la Ley 09 de 1979 determina “que la sal para consumo humano se considere un alimento” **(12)** y en los años posteriores se dictan decretos reglamentarios de esta Ley que establecen entre otras el control del reempaque de la sal yodada. Durante el periodo 1947 – 1983 las muestras analizadas de sal yodada en el país no solo eran menores al número mínimo analizable por ley sino que no cumplían con los requisitos mínimos de contenido de yodo establecido por la OMS. Para este periodo, Carrillo muestra que de las 9000 muestras analizables mínimas por ley esperadas, solo se analizó un número de 2462, de las cuales 429 tenían un contenido de yodo entre 50-100 ppm, 1967 tenían menos de 50 ppm y 66 tenían más de 100 ppm para un promedio del contenido de yodo de 14.2 ppm **(12)**. En 1992 el Decreto 6568 “crea el Comité Interinstitucional para la vigilancia de los desórdenes por deficiencia de yodo, flúor y el control de la calidad de la sal para el consumo humano” **(12)**. En 1998 el 91% de la sal para consumo humano estaba correctamente yodada y la prevalencia de bocio en escolares era del 7% por lo que el país fue declarado libre de Desórdenes por Deficiencia de Yodo. Entre 1994 y 1996 se realizó un estudio de prevalencia de DDY Instituto Nacional de Salud en 74 municipios de 32 departamentos. Este estudio mostró una prevalencia de bocio del 7 % en una muestra de 15 807 escolares y una deficiencia de yodo en cerca de 6000 muestras de yoduria. Sobre esa base, los expertos de la Organización Panamericana de la Salud, UNICEF e ICCDDI que visitaron a Colombia recomendaron mejorar la organización y vigilancia, para asegurar sostenibilidad del programa **(14)**.

ESTUDIOS EN COLOMBIA (Cuadro 2)

Cuadro 6. Estudios encontrados en la literatura sobre la prevalencia del bocio endémico en Colombia y políticas sanitarias de yodación para cada periodo*

Periodo de estudio	Política Nacional	Tipo de Estudio	Métodos de medición	Área geográfica	Muestra	Prevalencia del BE	Observaciones	Fuente
1942					153.000 personas para el servicio militar	10%		(16)
1945-1948	Ley 44 de 1944 para Yodación de la sal.	Transversal. Encuesta Nacional de Bocio	Presencia de bocio clínico	385 municipios en 14 departamentos.	183.243 escolares a nivel nacional.	52.62% (96.435 casos)	En 8.062 escolares de 7 municipios de Caldas prevalencia del 83.1% de bocio	(17)
1952		Tranversal. Encuesta.	Presencia de bocio clínico	7 municipios de Caldas	6.511 escolares	33.9%	Reducción del 83.1% al 33.9% posterior al suministro de sal yodada.	(18)
1960	Decreto Legislativo 591 de 1955 Control efectivo de la yodación	Transversal. Encuesta de Nutrición de Colombia	Presencia de bocio clínico por criterios de la OMS.		Menores de 15 años	41%		
1965			Presencia de bocio clínico por criterios combinados uno es de la OMS.	7 municipios de Caldas	2166 escolares	1.8% y 0.8% según clasificación antigua y nueva respectivamente.		(19)
1978								(20)

1994-1996			74 municipios de 32 Departamentos	15.807 escolares, 5971 muestras de yoduria	7% bocio endémico, 92.8% Deficiencia de yodo.		(21)
2006-2007	Descriptivo transversal.	Yoduria (método Sandell-Kolthkoff modificado)	Quindío (6 municipios)	444 escolares (8-18 años)	28.8% Déficit de yodo (11.5% déficit severo, 12.6% déficit moderado, 4.7% déficit leve).	59.3% Ingesta excesiva de yodo. Diferencia significativa de deficiencia entre los estratos, procedencia rural o urbana y municipio.	(14)

* Posterior a la política de yodización universal de la sal en el país y de acuerdo con los parámetros recomendados por la OMS para el seguimiento de los programas**(3)**, al comparar la prevalencia de bocio endémico en cada periodo debe considerarse que solo representa una proporción de los DDY y que en la actualidad su presencia no refleja con exactitud el estado de ingesta de yodo de la población general.

5.8 DISCUSIÓN SOBRE EL SEGUIMIENTO EN COLOMBIA

En el cuadro 7 se muestra los indicadores recomendados por la OMS para la evaluación en los países con programas de control y eliminación de los DDY, las entidades en Colombia encargadas de estas mediciones y las observaciones de los autores sobre la situación del país respecto a cada uno de ellos.

Cuadro 7. Indicadores utilizados en los programas de control de los DDY*.

Tipo de Indicador	Objetivo	Medidas empleadas	Sectores Responsables	Observaciones
Indicadores de proceso	Monitoreo y evaluación de los procesos de yodización de sal	Contenido de yodo en sal en procesos de producción, importación, en hogares y en la industria alimenticia.	INVIMA	
Indicadores de impacto	Evaluación del estado del yodo en la población y el impacto de los programas de yodización de la sal.	La principal es la mediana de yodo urinario. Determinación de bocio por palpación o ultrasonido. TSH en neonatos y tiroglobulina en escolares como indicadores de función tiroidea.	INS, ICBF	Una vez implementada la yodización de sal los cambios en la prevalencia de bocio no reflejan con exactitud el estado de ingesta de yodo de la población.
Indicadores de sostenibilidad	Evaluación de la eliminación de los DDY y de la sostenibilidad de los programas.	Mediana de yodo urinario en la población (100-199ug/L) y en mujeres embarazadas (150-249 ug/L) Disponibilidad de sal yodada en los hogares (>90%) y logro de 8 de 10 indicadores programáticos.	INS	Ultimo estudio disponible de yoduria es del 2007. Plan Estratégico Nacional 2007-2010.

***Abreviaturas utilizadas en la tabla:** DDY Desórdenes por deficiencia de yodo.

Fuente: (3) Adaptado por los autores.

La eliminación de los DDY se logra cuando la yodización de la sal puede ser sostenida. Esto implica que una vez que se logra este reconocimiento los países deben asegurarse del mantenimiento de estos logros mediante un sistema adecuado de monitoreo y evaluación que parta desde un nivel regional y nacional **(3)**. La importancia de alcanzar la eliminación de estos desórdenes radica en su afectación a las poblaciones de distintos grupos de edad, con un alto impacto en el desarrollo infantil, no solo en cuanto a la presencia de formas severas de alteraciones cognitivas sino en el desarrollo de formas leves que alcanzan mayor distribución. Por lo anterior, el seguimiento activo a estos programas no solo es beneficioso para las poblaciones desde el punto de vista de salud pública sino que trasciende al impacto de estas medidas en el desarrollo económico de las mismas **(3)**. Esto es importante si se tiene que la falta de sostenimiento de las medidas de control y vigilancia ha llevado a un retroceso en áreas que previamente habían logrado la eliminación. En Colombia, Gallego y cols. en un estudio reciente en la población de Quindío sugieren que la presencia de DDY podría estar ligada a las políticas de seguridad alimentaria **(14)**. Asimismo, las condiciones propias de las distintas áreas rurales o urbanas y de los estratos socioeconómicos con relación a las fuentes de acceso a alimentos asociados a la presencia de desnutrición en estas poblaciones se reflejan también en que existan áreas donde el problema no sea la deficiencia sino el exceso de yodo. Aunque el presente estudio no cuenta aun con datos y aportes de las entidades encargadas oficialmente del monitoreo del programa de eliminación de los DDY en su fase de seguimiento y sostenibilidad, los resultados preliminares de la revisión indican por lo menos tres conclusiones preliminares de la situación del bocio endémico en el país y sus políticas sanitarias:

1. No se conoce con exactitud datos reales sobre la carga de los DDY en el país, ni su distribución por regiones, estratos socioeconómicos, y grupos poblacionales.
2. Falta información sobre los indicadores del proceso de yodización de la sal periódicos y accesibles a la comunidad académica.
3. Sin los datos anteriores no se puede establecer la efectividad de los programas actuales, la situación real del bocio y de otros DDY en el país así como tampoco su comportamiento en respuesta a las medidas de control implementadas.

Debido a lo anterior, consideramos necesario el establecimiento de encuestas regionales con muestras significativas, de escolares, mujeres embarazadas y otros grupos poblacionales cuyo objetivo sea la determinación de la situación nutricional de yodo de los individuos, la prevalencia de bocio endémico y la carga de los DDY en el país. En la actualidad el uso de software especializados permiten el diseño de mapas que ayuden en la identificación de prioridades en salud pública y orienten en la planeación de programas y posterior seguimiento. Asimismo, consideramos que esta información requiere ser relacionada con los estudios de contenido y estabilidad del yodo en la sal en los distintos niveles de proceso de producción así como la investigación de los determinantes culturales y socioeconómicos que influyen en el acceso y consumo de la sal en las distintas regiones del país. Consideramos que este análisis podrá ser útil a las autoridades sanitarias en la evaluación de la yodización de la sal, su

impacto real en la salud de la población y la investigación en otras estrategias que permitan aportar este micronutriente a los grupos con requerimientos especiales.

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5.11 Declaración de Conflictos de Interés

Las declaraciones y afirmaciones realizadas en este artículo comprometen a sus autores y no a la Universidad Nacional de Colombia. Los autores declaramos no tener ningún conflicto de interés.

5.12 References

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CHAPTER VI. GENERAL DISCUSSION and RECOMMENDATIONS

This thesis explores the challenges and opportunities for controlling and eliminating diseases of poverty and neglected tropical diseases (NTDs)(1), using malaria as a case study and focusing on the Latin American context, yet drawing out generalizable lessons for all endemic areas. Diseases of poverty and NTDs continue to be a major public health burden in tropical areas, especially in resources constrained countries. Some disease areas, like smallpox, have surpassed the goal of elimination to achieve eradication while others, like goiter, have rolled back to a state of re-emergence in some developing countries (2), (3), (4),(5, 6), (7), (8). Impact indicators at both local and global levels can be affected by population and microorganism dynamics. In addition, health systems and stakeholders cannot forecast uncertainties such as natural disasters, outbreaks, epidemics and sudden budget constraints. These are among the structural determinants and barriers to completing the process of elimination and eradication, from a public policy and planning perspective.

In this chapter, we discuss possible limitations of the study and draw some mid-level conclusions that may allow for public health action as well as process of planning in health services.

This study was conducted in a representative sample of people affected by malaria and other infectious diseases of poverty. Given the magnitude of the population at risk, additional studies must be conducted in order to establish the goals achieved in terms of the direct relation investment and malaria indicators of elimination. However, the variables included in the analyses represent common risk factors for endemic areas in Colombia. The Caribbean and Pacific coastal regions account for around 70% of all malaria cases in the country. Agriculture and mining are the core economic activities in these two natural regions. The population in these regions are disproportionately affected by conditions of poverty, political unrest, and the presence of illegal economies —all known determinants of malaria persistence and resurgence (9, 10). When these factors are compared to those in other endemic countries, the similarity is considerable. For instance, colonization of the Brazilian Amazon region can explain the persistent conditions of poverty and the prevalence of endemic and epidemic infectious diseases like malaria and tuberculosis in the Amazon region. The “garimpeiros” — the migrants that went to the region to exploit its natural resources for short periods — dominated the region. The intense migratory movement of people without immunity, in and out of a malaria endemic region, created the epidemiological conditions for maintaining malaria transmission, in our case of study, however the health indicators such as maternal and infant mortality are not in better conditions. Malaria

situations are related to social, economic and cultural determinants and the trend of the disease is strongly associated to them. These basic characterization allow to extrapolate from our findings and make generalizations for areas with similar eco epidemiological conditions. Thus, the pilot model of pre-elimination or elimination developed in Colombia can be adapted and implemented in other endemic areas of the Amazon region. In fact, the RAVREDA group has been working along those lines, unfortunately with limited results up to now. There is an urgent need to compile and organize all the evidence on the elimination experience so far in order to make further informed decisions.

Unfortunately, collaborative projects between national and regional health authorities tend to exclude the academic and private sectors. The problem is exacerbated by limited funding for developing field research and by the minimal interest in amalgamating actors and research evidence (11-13).

The information provided by national and local health authorities were often incomplete or unavailable due to laws protecting personal data (*habeas data*) and other issues of confidentiality. The literature review shows that statistics on and reports of malaria interventions in Colombia and Latin America were not very well updated in libraries or on the web pages of various health institutions. In most cases, when a report refers to a particular year, the figures correspond to data collected two or three years before. The International Health authority in charge of compiling information for Colombia, both WHO and PAHO did not provide the original information. And the differences from WHO-RBM reports and local secondary information are not correlated.

6.1. From elimination to equity and community empowerment

This study comprised qualitative and quantitative investigation, fieldwork, systematic literature reviews and special surveys. Thus, the findings are based on triangulation of information from three kinds of sources, which show that there are enormous differences between endemic and non-endemic areas in terms of health coverage, education indicators and development models. More specifically, rural and urban populations differ, not only in epidemiological and demographic aspects but also as regards equity, gender and ethnic considerations. Tracing the historic development of micro and macro structures in these endemic regions permits an understanding of how the towns, villages, and populations improved welfare. Those societal structures, from individual to community level that are well organised and permit entitlements and active participation in democracy, coincide with communities that have overcome the public health challenges associated with diseases of poverty. On the contrary, groups with low levels of empowerment maintain high rates of infant and maternal deaths and experience most of the burden of infectious diseases (14), (15-17)

The effort to control and hence reduce the impact and cost of infectious diseases has been a high priority since the mid-1950s(18), (19). Well-known challenges have been encountered, not only in setting an international agenda but also in transforming the health and education sectors. When reviewing the history from the inception of tropical medicine in 1951 to the more recent concept of international and global health, it becomes clear that improved sanitary conditions and better living conditions contributed to reducing mortality as well as the burden of infectious diseases (20).

The historical transformation of disease concepts is closely related to epidemiological and demographic transitions, and to transformations of structures and control policies. Public health programs have succeeded in reducing transmissible diseases in some endemic regions with historical evidence of outbreaks and epidemics. Control, elimination or the complete eradication of infectious diseases such as smallpox (21, 22) are evidence of the nature and impact of country successes. Currently, the global agenda promotes the strengthening of health systems as well as well-built control programs with adequately trained human resources and high level technology to improve action towards elimination and eradication of diseases in poor areas of the world.

The design and implementation of this study considered many factors, including migration, access to health services, natural disasters, political unrest, poverty, and illegal economies. The main challenges, however, come from the limited efforts by networks and researchers in consolidating findings and making this information available not only to other partners but also to civil society and political decision makers. In Colombia and other countries in the region, public policies and plans of actions are poorly articulated, with absent processes for monitoring and evaluation between different sectors.

The first conclusion of the investigation is the urgent need to recognize the other players and actors within the same society, as well as the innovate effective harmonization strategies among different levels of organization to ensure that results generated through research and/or public health actions are available and accessible. This in turn will allow any citizen to exercise her/his rights to be informed and make decisions according to information resulting from different scenarios into the system. Communities will not be empowered or be able to participate designing health and education plans if access to information is limited. In that sense, Sen has referred to the freedom for development and entitlement and how greater participation and communication strengthen democracy. Martha Nussbaum complements the idea by discussing the relevance of participation of minorities and considering the social determinants of particular vulnerable groups(23), (24), (25, 26).

The main challenges of validating and using results and evidence on experience/concepts of elimination of diseases of poverty in Colombia and Latin America was the limited capacity of the author to consolidate information from a wide range of sources with more holistic approaches. Here, the analyses are focused on how to collect the results of malaria control or elimination and comparing the trends in terms of improving or maintaining control policies. It also compares and establishes time-space relations and the experience of convergent and divergent trends in relation to elimination and control of common epidemiological patterns, taking into full consideration of a given the socio-cultural and socioecological situation and history of each region(27), (28). The agencies responsible of elimination at the state and MoH, were reluctant to provide information which will to correlate investment, plans of action and both mortality and morbidity of malaria.

The secondary sources allow suggesting that Colombia and its neighbouring countries intend to make use of concerted efforts and inter-sectoral collaboration to eliminate and reduce to zero not only malaria, but also NTDs such as leprosy, American Trypanosomiasis, Leishmaniasis, dengue, goiter diseases, and infant mortality. Unfortunately, the presence of the new epidemics of Zika and chikungunya confirm that vector-borne programs and policies are not yet well articulated. For example, only the number of Zika cases, till 16 week 2016, is > 40,000 cases and we regularly face isolated outbreaks of dengue. Or, the malaria day, past 25th of April, Choco department had recorded 19'915 cases of malaria caused by *Plasmodium falciparum*, and 30 deaths (www.elcolombiano.com, www.defensoriadelpueblo.org; accessed 1st May 2016).

During the last 20 years, Latin America has maintained similar epidemiological patterns, with diseases of poverty and NTDs remaining unstable and very difficult to control. Countries in and out of the Amazon region have been challenged by outbreaks of dengue, malaria, and recently by Zika and Chikungunya viruses(28), (29). Fortunately, most epidemiological alerts coincide with international tournaments. For instance, in 2007, Brazil celebrated the Pan Americans Games and faced the challenge of controlling a dengue epidemic. In 2015, Chile fought against a Chikungunya epidemic during the Americas Football Cup, and now the big challenge will be guaranteeing safety conditions due to the Zika epidemic affecting Brazil and Colombia, with the Olympic games scheduled to take place in Brazil in August 2016. Health authorities and sport players alike are concerned about the risk and sanitary conditions. The actions implemented are not permanent and structural. Instead, most of them are for a short period and limited in coverage. So it is quite probably that Latin America, will attend more epidemics and emerging diseases.

These epidemiological markers and the magnitude of the affected population offer evidence to public health programs, States and society of the relevance of inter sectoral cooperation and of the urgent need to strength surveillance systems and weekly reporting.

6.2 General considerations on the elimination of NTDs

Analyses of elimination programs in Latin America and the rest of the world are focused on malaria. Colombia maintains similar policies of control and indicators do not show considerable changes in favour of reduction of transmission. The agreements between countries' health actors are mainly to support partnerships and accomplish the goals fixed by PAHO and WHO (30, 31), (32, 33). If tasks go well, the question will be how close programs and institutions are to keeping malaria incidence close or equal to zero and how sustainable are the results in the long term?

With regards to NTDs, leprosy in Colombia is an interesting example. Leprosy is a very limited problem and affects no more than six municipalities (N=1.101). The annual incidence is very low, with 0.89 cases among 100,000 inhabitants, i.e. around 300 new cases each year (34). Unfortunately, the number of relapses is almost 12% and 30% of patients (3/10) are handicapped at level 2. Fixed dose multidrug regimens have been implemented since 1985 and led to major improvements. In 2005, there was a slight increase of the number of cases, most probably due to problems with the surveillance program. We are now at the point of needing more applied research projects to evaluate the state of drug resistance as well as the effectiveness of the surveillance system, including the level of community participation throughout the programme. The stigmatization and occupational incapacity are truly compelling reasons to aim for elimination, which will improve the quality of life and well-being of those most at risk. In addition, the failure to inform and educate the community or to include them in surveillance approaches have been revealed as key problems of the National Leprosy Elimination program (35, 36). Interestingly, in the same region, Brazil is the country that has still not achieved the elimination goal owing to a series of socio-cultural factors and inadequate information and surveillance approaches leading to early diagnosis and prompt treatment in the health system (37).

Another example among the NTDs is the attempt to eliminate Chagas' disease. The scenario in the region shows substantial differences in control and elimination strategies within and between countries. Countries with rigid structures of planning and control at different levels present better results(38). Argentina has a Federal Plan of Health, Brazil has decreed a Social Invest Fund, Bolivia has the Chagas Law, however Uruguay is the country with the most commitment elimination and better results. Uruguay focused on eliminating the vector through structural household improvements in rural areas, serology to detect vertical transmission and rigorous surveillance of all blood derivatives in haematological centres(39). The most successful strategies consider multilevel participation, integrated interventions targeting host, parasite, and vector, and better living conditions. The screening of pregnant women for Chagas' disease is a priority only in Uruguay and Bolivia. In Colombia, vector control with insecticide spray exists, but young patients have limited

access to treatment. In areas with intense conflict, access to radical treatment is not possible and most patients do not complete treatment.

These two examples are correlated with the results obtained almost 15 years after goiter disease elimination in Colombia. Sustainability of both control or elimination programs must be considered in the plans, which are implemented for ten years at a time without indicators for monitoring and evaluation. When designing programs, stakeholders and communities are strongly advised to include interim evaluations that consider not only impact indicators of diseases and mortality but also societal and economic risk factors, which clearly influence final results and may even lead to other public health actions.

Common determinants for these endemic diseases are poverty and the vulnerable conditions of children and pregnant women, who are the most affected but neglected populations in their state.

Colombia was declared free of goiter disease by 1990. Our findings show clearly how for different conditions and diseases entities the same risk groups are identified (7). The goiter problem is an example of a clearly multi factorial disease problem. Besides autoimmune factors, diet and consumption of iodized salt is also implicated. The reintroduction of this public health problem is explained by low and high ingestion of iodized salt. Unfortunately, the macro determinants are inadequate diets in children and pregnant women as a consequence of the globalization of nutrition conditions on the one hand, and the weak food and drug surveillance system to guarantee the quality of salt for human consumption on the other. The consequences of food globalization and resulting feeding habits are well known, including its effect on the new pandemic of type II diabetes plus obesity (40).

The control or elimination of other infectious diseases related to poverty, like malaria, HIV/AIDS and TB, or NTDs, are governed mainly by social determinants. The low success rates of control and elimination efforts are strongly associated with low levels of community empowerment and high levels of inequity. In countries with better indicators of health and education, public health policy design often considers the local condition and encourages active participation of the population in solving the problem. Countries with a limited public policy impact often show both weak governance and limited transparency in its processes. Colombia started decentralizing its health services in 1986 (Law 12). However, given the low administrative levels of less developed municipalities it introduced Law 715 in 2004 in order to exempt rural areas from the decentralization process, bringing these responsibilities once again to administrative departments in the capital, where the budget in different contexts leads to different outcomes compared to the real costs encountered / budgeted for a given subnational level. When analyses are conducted to compare the Internal

Gross Product, some countries like Mexico, Colombia and Bolivia show an improvement of their economies. This does not mean that communities, families and individuals receive better incomes or salaries. The illegal economies in the region have been reduced considerably due to legal actions and international partnerships but, unfortunately, the number of people of productive age employed in the informal sector has increased or remained stable(41, 42).

Data from occupation risk databases show that only 6 million workers are formally linked to institutions. Equity indicators like the Ginni Coefficient in countries like Bolivia or Colombia do not reflect this social injustice. However, poverty conditions and misery remain stable in numbers. To achieve many of the goals proposed in the new agenda, the conditions of living, household, employment, social security affiliation and alleviation of climate change must be included in a decennial plan, with indicators of process, outcome and results.

6.3 Elimination of malaria in Colombia: How far is it?

Recent publications have analysed the distribution of malaria cases for endemic countries in Latin America(43), (44), (45). The distribution and frequency of the disease suggest some considerable changes in patterns of transmission. There is an agreement that malaria morbidity due to *Plasmodium falciparum* was considerably reduced and mortality attributed to this species is considerably low. However, the long series of data are not consistent with a real trend of reduced morbidity rates. There are considerable variations and peaks, which suggest instability within the programs and maybe also budget constraints to implementing sustainable programs towards elimination. The incidence and prevalence estimation could coincide at times with elimination (epidemiological periods close to zero), however sudden epidemics or deaths are still possible, which can be forecast and avoided with preventive actions from the public and private health sector(46), (47).In Colombia, the number of deaths associated with malaria is unclear. Some authors have referred to underreporting and low coverage of the surveillance system; hence the analyses of malaria trends under this scenario risks possible biases. The field study conducted in Tumaco, Montelibano, Puerto Libertador and Bocas de Satinga showed evidence of asymptomatic cases in urban areas, through active case detection (48). The surveillance system is the responsibility of the National Health Institute, SIVIGILA, but the stability of human resources and the capacity of health institutions to systematically capture and analyse field information is not assured and partly unknown. The municipalities, in most of cases, do not have computer equipment or secure access to big cities. For reasons mentioned above, a combination of factors contributes to the persistence of malaria and other infectious diseases.

Finally, sentinel surveillance to follow-up treatment failures, the development of resistance against anti-malarials, treatment adherence, self-medication and monitoring of vector insecticide resistance, is absent in endemic areas.

Malaria is concentrated in municipalities and villages where more than 80% of the population has unmet basic needs. In these areas, the right to health for the population must be upheld by authorities. They must guarantee access to water and food, and education and health. The infant mortality rates in Colombia vary widely. In the Andean region, rates are 20/1000, while the Pacific Coast experiences rates similar to Africa of 80/ 1000. The first one shows a pattern of epidemiological and demographic transition, while regions like the Pacific, Caribbean, Amazon and Orinoquia have a pyramidal shaped population structure. African descendants and indigenous groups are the ethnic minorities. The African descendants are mainly located on the Pacific Coast where malaria falciparum cases and other transmissible diseases are prevalent. Indigenous populations are mostly found in the Caribbean, Amazon and Orinoquia regions, where the *P.vivax* cases are more frequent and hepatitis, tuberculosis and serious malnutrition form a great burden(14, 17, 49-51).

Under these variations, evident through data analyses, with unstable trends, peaks of new cases in inter years and intrinsic and extrinsic factors affecting the dynamics of transmission and sources of information, it is quite difficult to assume that the programs are on their way to or are achieving elimination. Consequently, the basic determinants of malaria transmission persist as a common factor within and between the 21 Latin American countries reporting malaria cases.

6.4. Recommendations for further research and public health action

6.4.1 Further research to be undertaken:

Field research conducted in two natural regions of Colombia, with eco-epidemiological conditions for vector borne disease transmission as well as the presence of socio-economic indicators of poverty, suggest that additional operational research is needed. During the elaboration of this thesis, several outbreaks and epidemics were reported. The frequency and distribution of malaria, dengue, Chikungunya and Zika, in areas under 2000 m above sea level, require characterization of the risk factors and of the main social, political, cultural and economic determinants associated with the persistence and re-emergence of these kinds of communicable diseases. The first question is a socio demographic one and requires establishing the degree of relational transmission vs. transmission due to migration and forced displacement. In a globalized world, where several regions and countries are used as a corridor to finding better options in life, Colombia is not an exception. Migrant populations from Africa, Asia and the Caribbean Islands, pass through Colombia

and contribute to spreading diseases not only transmitted by direct contact but also by arthropods like *Anopheles* spp. and *Aedes* spp when people arrive infected from their place of origin. The policy of migration and the International Sanitary Code must be updated to reflect these new epidemiological conditions and to guarantee minimal risk for both the receiving population as well as the migrants themselves(9).

Colombia and Latin America did not achieve the MDG related to alleviating climate change(52). Most of these pathologies, where a vector is involved, are strongly associated with extreme changes in temperatures and rain fall. The current evidence is not sufficient for evaluating the integration and adaption of vectors to higher levels above the sea. Future research should examine how these arthropods adapt to survive and subsequently change the patterns of transmission. Studies about vector genetics and patterns of adaptability to new ecosystems should be linked to studies on transmission capability and its impact on control measures and re orientation of programs.

Few studies related to primary productive systems have been carried out (53), (54), (55) . There is a positive correlation between primary structures of society and malaria persistence and resurgence. The poverty and poor models of development associated with illegal economies and displacement are among the main determinants. The difficulties of eliminating and eradicating infectious diseases from endemic regions in Colombia and Latin America can be traced back to those structures(48, 56, 57).

Our field work identified barriers to accessing health services. First geographical barriers (distance) and the cost of transportation are important causes of late diagnosis and inadequate treatment. Thus, febrile patients usually consume herbal and bark infusions, i.e. cinchona bark . In addition, the living conditions —unprotected houses, without potable water— are another risk factor for malaria transmission (48, 58). Considerable resources have been invested in researching treatments and insecticides and many studies of RDT have been published. There is no evidence that eradication of any vectors is possible and/or feasible. What is the magnitude of the impact on malaria risk reduction when living conditions are improved? In Colombia and Latin America, financial resources are used only to support the biological model perspective and the triadic: mosquito, parasite, host. However, innovation based on biological, social and social science models are less frequent. If the number of cases has been reduced to the levels reported by health authorities, then why not re-orient part of the budget to improve the quality of houses and provide adequate latrines to reduce the impact on the environment? Studies, since 1900 have suggested the benefits of re-designing places for living (59). The explanation is simple: the purpose of the primary prevention is to reduce incidence. This decrease is given by the fact that risk factors and

host contact almost disappeared. The number of new cases starts to decline and the chain of transmission is blocked. The modification of domiciliary and peri-domiciliary characteristics could consider the participation of community and local authorities.

Control, elimination, and eradication are arts and depend on the capability and articulation at all levels, from the individual, family, and community to actors in health systems and the State; all must work as an artificial open system, where the parts depend on the whole and vice versa. The system must be dynamic and modifiable depending on society's needs. Furthermore, cause and effect is not direct, it works in both directions i.e. malaria eradication leads to better productive system and quality of life; better productive system and quality of life contributes to malaria eradication.

6.4.2 Recommendation for public health action

The information obtained in this study and the analyses conducted at different levels and correlated to other sources and findings allow some basic recommendations that can be implemented at three levels: health system and legal regulation, social justice and equity, and community and other sectoral participation.

6.4.2.1. Health System and Legal Regulation

- a. The Ministry of Health at the legislative level is directly responsible for new health system reforms and for designing action plans according to the structural organization of departmental and municipal health services. The redirection of responsibilities call on both public and private sector to strengthen strategies for active and passive case detection, and to focus on early diagnosis and prompt treatment. In rural and remotes areas, human resource and infrastructure must be a priority.
- b. The National Institute of Health at the executive level requires financing to innovate surveillance systems, including forecasting of epidemics and outbreaks, sentinel surveillance of parasite drug resistance and vector insecticide resistance, as well as clinical studies in vivo, and adherence to treatment by infected patients. New techniques are also needed to detect self-medication. The INVIMA, Institute for food and drug surveillance, implement adequate control and supervision in rural areas regarding distribution and sale of antimalarial medications
- c. Primary Health Care programs require adaptation according to local needs in all institutions. In addition, financial resources could be directed to diagnose the health situation and update clinical guidelines
- d. Health promotion and disease prevention in rural areas affected by malaria must be incorporated at local health programs along with monitoring and evaluation indicators to reflect activity plans and budget.
- e. Academy and National Department of Investigation: organise and define priority areas of research with budget assigned from state with transdisciplinary participation of research groups

d. Malaria research funding distributed on equity principles

6.4.2.2 Social Justice and Equity

The main social determinants of malaria persistence that jeopardize elimination or reduction to zero in Colombia and countries in the Andean region, is poverty and inequities in access to health and education.

- a. Children and pregnant women need to be included in special programs of control, Decennial Public Health Plan should include an specific chapter with actions and result indicators
- b. Programs for vulnerable minorities and populations from primary productive sectors in endemic areas identified; priority health care attention to reducing geographical barriers and other factors that delay diagnosis and adequate treatment; and education of patients for treatment adhesion and not self-medication
- c. Investment of resources to improve health infrastructure in rural areas
- d. Reduce the inequities between rural and urban populations: primary productive sectors, politics to alleviate climatic change and natural disaster

6.4.2.3 Community Education and Empowerment

The structure of the society, and the active participation of its members is crucial. This calls for the development of community surveillance and control actions that the community itself can implement and thus will to contribute and complement to health authorities' integrated control plans.

- a. Organise communities in groups according to roles in their community and levels of risk
- b. Participation of educational sector is fundamental to training and teaching children who can translate those experiences to their families, given that in these areas many parents are illiterate
- c. Colombia is a country with one of the highest rates of dysfunctional families. Due to the war, mothers are in charge of children and also find formal or informal employees to guarantee social security and incomes for the family. Mother and caregiver must be trained and offer welfare conditions to contribute to infectious disease reduction; they and their children must be visible to society and to the health and education sectors. A network of community surveillance with a bonus could help to update information and forecast and prevent outbreaks.

6.5 Do we need vaccines?

The effective use of mass vaccination has shown to be useful in controlling infectious diseases. Polio and measles are only two examples of vaccine benefit for non-immune

populations. The implementation of a malaria vaccine requires some specific conditions: it must be low cost, require a maximum of 2 doses, and achieve efficacy around 90%. All the vaccines introduced into the Expanded Immunization Programme should guarantee full protection and also herd immunity. It is compulsory that the candidate vaccine demonstrate protective immune response and a wide range of coverage give the variety of strains. Finally, we all recognize that a vaccine will surely be a great achievement, but it is even greater to see a vaccine to become an effective complement of the already existing tools for control and elimination.

On this century, health efforts are concentrated on vaccines, drugs and technology innovation. Only 10% of those technology and therapies for humans are being used. The spray of resources for health effective interventions and the considerable number of agencies, NGOs, reflect the absent of policies and programs for International Health Authorities.

Famines, increased number of refugees, climatic change, and epidemics are telling more than we can understand and suggest the need of a new and re-structured global agenda: multilevel and inclusive.

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Políticas sanitarias y situación actual del Bocio Endémico: El caso de Colombia

*Sanitary policy and current situation of Goiter Syndrome:
Colombia Case*

María Victoria Valero- Bernall • Roberto Franco Vega • Angélica María Chaves • Juan Sebastián Montero

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| Resumen |

La deficiencia de yodo tiene muchos efectos adversos, sobre la Salud Humana. Se considera la deficiencia de yodo, como la principal causa de discapacidad humana prevenible, se estima que más de 800'000.000 de personas están en riesgo; 190'000.000 afectados con bocio y más de 3'000.000 pueden presentar cretinismo.

El bocio endémico es considerado uno de los desórdenes producidos por la deficiencia de yodo. Su alta prevalencia en distintas regiones a nivel mundial, llevó a que la OMS declarara durante muchas décadas problema de salud pública, debido a las consecuencias directas en la salud de grupos vulnerables como las mujeres embarazadas y los niños en edad escolar sino por su impacto negativo en el desarrollo de las comunidades afectadas. En Colombia, se adoptó la yodización universal de la sal como principal estrategia para el control de estos desórdenes declarándose su eliminación a finales del siglo pasado. Sin embargo, algunos reportes posteriores han mostrado que la prevalencia de bocio endémico y el estado nutricional del yodo medido por la determinación de la

yoduria en algunas regiones del país requieren atención por parte de las autoridades sanitarias no solo por la persistencia de los desórdenes por deficiencia de yodo sino por el riesgo de enfermedades tiroideas por la ingesta excesiva de yodo en algunas regiones del país.

Palabras clave: Deficiencia de Yodo; Bocio endémico; Política de Salud; Glándula Tiroides; Colombia; Prevalencia (DeCS).

Valero M. V., Franco R., Chaves A. M., Montero J. S. Políticas sanitarias y situación actual del Bocio Endémico: El caso de Colombia. Rev Fac Med. 2012; 60: 303-311.

Abstract

Iodine deficiency leads to many adverse effects concerning human health. Iodine deficiency has been considered the leading cause of preventable human disability; it has been estimated that more than 800 million of the world's population are at risk, 190 million are affected by goitre and more than 3 million may be suffering from cretinism.

Endemic goitre is considered to be one of the disorders caused by iodine deficiency. Its continued high prevalence around the world has led to the WHO declaring it to be a public health problem for many decades now due to its direct impact on the health of vulnerable groups, such as pregnant women and school-aged children, and its negative impact on the affected communities' development. Universal salt iodisation (USI) was adopted in Colombia as the main strategy for controlling such disorders; it was declared that they had been eliminated

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at the end of the last century. However, subsequent reports have shown that the prevalence of endemic goitre and iodine nutritional status (measured by determining urinary iodine in some areas of Colombia) requires the pertinent health authorities' attention due to the persistence of iodine deficiency disorders and the risk of thyroid disease caused by excessive iodine intake in some regions of Colombia.

Keywords: Iodine Deficiency; Goiter; Endemic; Health Policy; Thyroid Gland; Colombia; Prevalence (MeSH).

Valero M. V., Franco R., Chaves A. M., Montero J. S. Sanitary policy and current situation of Goiter Syndrome: Colombia Case Rev Fac Med. 2012; 60: 303-311.

Introducción

Los desórdenes por deficiencia de yodo (DDY) son un conjunto de entidades patológicas que reflejan un estado de disfunción tiroidea ocasionado principalmente por el aporte insuficiente de yodo a la dieta. Aunque el entendimiento sobre su fisiopatología ha sido un gran avance para la medicina en el diseño de programas destinados al aumento del aporte de yodo a las poblaciones, en la actualidad estos desórdenes son un problema de salud pública en 54 países del mundo y se considera que a nivel global 225 millones de escolares tienen una ingesta insuficiente de yodo (1,2). Respecto a esto, Colombia implementó la política de yodación universal de la sal (YUS) y fue declarada en 1998 libre de los DDY. Sin embargo, se ha observado que algunos de los países que previamente habían alcanzado este logro han venido presentando prevalencias de bocio endémico y cifras de yoduria en escolares que demuestran que no se ha sostenido esta eliminación (3,4). Por esta razón, la tendencia mundial está dirigida al reconocimiento que los programas de control y eliminación de estos desórdenes deben contar con al menos dos características fundamentales que les permitan lograr y sostener los resultados, la primera es el establecimiento de alianzas eficaces entre el sector sanitario, el académico y el industrial en la que se asegure el cumplimiento de los estándares establecidos en los procesos de yodación de la sal y la segunda es el uso reflexivo de indicadores de impacto y sostenibilidad cuya finalidad radica en el seguimiento del estado nutricional del yodo en la población.

Breve historia del Bocio Endémico

El bocio endémico parece haber acompañado a la humanidad desde siglos pasados. Existen documentos que muestran que en la cultura china, en el siglo XXIX a. C ya se conocían distintas clases de tumores de cuello. Estos tumores también aparecen registrados en documentos egipcios e indios del siglo

XVI a.C. En el siglo XVIII a.C., en el "Tratado sobre aguas y tierras" se asoció la presencia de bocio con el agua de ciertas regiones geográficas montañosas. Esta misma observación aparece en Roma entre los siglos I a.C. y I d.C. Así como la descripción de lo que parece concordar con lo que hoy conocemos como cretinismo "existen aguas que tienen el poder no solo de cambiar el cuerpo sino también la mente" (5). En América, antes de la conquista, algunos autores mencionan el uso del término coto o cotto por los nativos (5) mientras que otros opinan que en la región no había bocio hasta el siglo XVIII y XIX (6).

Aunque en el siglo XVI las características geográficas propias de las regiones con presencia de bocio que incluían regiones montañosas, llanuras aluviales a altura considerable y distantes del mar, con el correr de los años, estas características dejaron de ser relativamente exclusivas y se encontró que había deficiencia "significativa de yodo" en áreas costeras, ciudades y países desarrollados (2).

En cuanto a la historia del tratamiento de esta patología, en China en los años 400-500 d.C algunos médicos chinos utilizaron Sargassum y Laminaria Japónica e incluso glándulas tiroideas animales. Sin embargo, en los siglos previos existe evidencia de que los egipcios practicaban tratamiento quirúrgico a este tipo de tumores. Estas prácticas permanecieron aún hasta el siglo XV (7). David Marine se considera uno de los pioneros en la profilaxis masiva del bocio endémico "el bocio simple es la enfermedad prevenible más sencilla, debe ser excluida de la lista de enfermedades humanas tan pronto como la sociedad determine hacer el esfuerzo" (7).

En 1950, durante la Tercera Asamblea Mundial de la Salud se recomendó a los países que estudiaran la magnitud del bocio endémico en sus territorios y en 1958 la Organización Mundial de la Salud (OMS) publicó un conjunto de seis revisiones que pretendían aportar un enfoque a los trabajadores de salud pública de los países para el abordaje de la enfermedad.

En 1960 la OMS reconoció que el esfuerzo por prevenir el bocio endémico todavía no había sido hecho debido a que las autoridades sanitarias no estaban convencidas de su inclusión dentro de los problemas de salud pública, de la eficiencia y seguridad de las medidas profilácticas y de la factibilidad de superación de las dificultades técnicas de las intervenciones (8).

Definición de los desórdenes por deficiencia de yodo

El único papel confirmado del yodo en el cuerpo humano es aquel relacionado con la síntesis de hormonas tiroideas (9-11). Los DDY son definidos por la Organización Mundial de la Salud (OMS) como las consecuencias de la deficiencia de yodo

en una población que podrían ser prevenidas si esta tuviera una adecuada ingesta de yodo (2, 12,13). Se considera como un “fenómeno ecológico natural” en ciertas regiones del mundo, en las que existe pérdida de yodo del suelo debido a erosión, pérdida de vegetación y labores de pastoreo excesivas (14).

En el cuadro 1 se muestran las dosis de yodo recomendadas en la dieta por la UNICEF, el ICCIDD y la OMS, que varían de acuerdo a la edad y estado fisiológico, ver cuadro 1.

Cuadro 1. Requerimientos de yodo en la dieta recomendados actuales.

Rango de edad	Dosis recomendada
Niños preescolares (0-59 meses)	90 µg
Niños escolares (6-12 años)	120 µg
Adolescentes y adultos	150 µg
Mujeres embarazadas y lactando	250 µg

Fuente: (4). Adaptada por los autores.

Los DDY son considerados una amenaza a la salud pública en países en los cuales la mediana del yodo urinario es menor a 100µg/L (1), pues afecta especialmente la salud de los niños preescolares y de las mujeres embarazadas y el desarrollo de las poblaciones (1,12,13,15). El espectro de DDY abarca el desarrollo de bocio, hipotiroidismo, anomalías congénitas, mortalidad perinatal e infantil, cretinismo, hipertiroidismo inducido por yodo, entre otros. Debido a la incorporación de yodo y la producción de hormonas tiroideas en el feto en formación el periodo más crítico abarca desde el segundo trimestre de embarazo hasta el tercer año posterior al nacimiento (2,15). Actualmente se considera que la deficiencia de yodo es la causa prevenible más importante de daño cerebral (2, 12,16-19) y el principal motivo detrás de los programas de eliminación de los DDY (8). La deficiencia de yodo también tiene un impacto grave a nivel colectivo pues produce alteración en el desarrollo físico y mental de las poblaciones con distintos grados de severidad, de modo que se ha reportado que las personas que viven en áreas afectadas por deficiencia severa de yodo pueden tener un coeficiente de inteligencia de 13.5 puntos menos que grupos control (18,19,20).

Factores que influyen en la aparición de bocio

El principal factor responsable de la deficiencia de yodo en el mundo es la baja ingesta de yodo en la dieta (2,3). Aparte de la deficiencia de yodo en la aparición de bocio endémico existen algunos factores etiológicos como los alimentos (mandioca, maíz, batatas, brotes de bambú, nabos, coles, casaba, leches (Finlandia y Tasmania), ajo, cebolla, etc. La acción antitiroidea de los bo-

ciógenos se relaciona con la presencia de tiocianatos que inhiben el transporte del yoduro y a altas dosis compiten con el yoduro en la síntesis de hormonas tiroideas (21,22,23). El potencial de desarrollo de bocio (“goitrogenicity” en inglés) está determinado por el balance entre los aportes de yodo y de tiocianatos cuando la razón yoduria (µg): tiocianato (mg) cae por debajo de 3” (22). Otros factores incluyen alteraciones nutricionales, factores genéticos, minerales presentes en fuentes hídricas (dureza del agua, concentraciones elevadas de calcio, magnesio y flúor y disminuidas de selenio y zinc), contaminación de las aguas de consumo humano y animal, presencia elevada de yoduros naturales en los ecosistemas de algunas regiones del mundo (Isla de Hokkaido en Japón y en la región de Salt Lake City), origen geológico de los suelos (14,24,25).

Situación de los DDY en el mundo y políticas sanitarias actuales

En el año 1990, en la Cumbre Mundial para los Niños de las Naciones Unidas se reconoció la deficiencia de yodo como un problema de salud pública, por lo que en 1991 se adoptó la meta de su eliminación en la Asamblea Mundial de la Salud y fue reafirmada en 1992 en la Conferencia Internacional de Nutrición. En 1993 la OMS y la UNICEF recomendaron como principal medida para el logro de esta meta la “yodación universal de la sal”. En el 2005 la Asamblea Mundial de la Salud adoptó el compromiso de reportar la situación global de los desórdenes por deficiencia de yodo cada tres años (26-28).

En 1993 la OMS reportó el estado mundial de los desórdenes por deficiencia de yodo basándose en la prevalencia de bocio endémico en los países. Posteriormente, ya que muchos países habían iniciado programas de eliminación de los DDY, la OMS volvió a analizar el estado nutricional de estos países mediante la medición de la yoduria y la prevalencia de bocio endémico con el fin de comparar los resultados de la década pasada (29,30). Para esto recogió los datos de estudios nacionales y sub-nacionales realizados en distintos países del mundo entre 1993 y 2003 y evaluó la prevalencia total de bocio y la mediana del yodo urinario. Estos resultados se publicaron en el año 2005 (1,28,30) y mostraron que la deficiencia de yodo era considerada aún un problema de salud pública en 54 países del mundo y el 36.5% de los escolares del mundo (285 millones) pertenecían al grupo de ingesta insuficiente de yodo, al extrapolar este resultado a la población general se estima que cerca de dos billones de individuos tienen una ingesta insuficiente de yodo. En cuanto a la proporción de escolares con un estado nutricional deficiente de yodo este porcentaje varío entre un 10.1% en la Región de las Américas y un 59.9% en la Región Europea. En el Sureste Asiático el porcentaje fue de 39.9% y en el Pacífico Occidental de 26.2%. Con relación a la prevalencia total de bocio (PTB) en la población general, se estima que en el mundo la prevalencia es del 15.8%, variando entre un 4.7% para las Américas y un 28.3% en África y en comparación con los

datos del año 1993, la PTB aumento en un 31.7% a nivel global, a excepción de las Américas y el Pacífico Occidental en donde se presentó un descenso en la PTB en un 46% y 32.2% respectivamente. Sin embargo, la TPB encontrada no es consistente con el estado nutricional del yodo actual, que se puede explicar por el retardo en los cambios en la TPB con relación al momento de implementación de la yodación de la sal. También se encontró que el número de países en los que la deficiencia de yodo representa un problema de salud pública disminuyó de 110 en 1993 (medida por la PTB) a 54 (medida por el yodo urinario), en 43 países la nutrición con yodo es óptima, en 54 es inadecuada y en 29 países la ingesta de yodo es más que adecuada o excesiva. Asimismo, estos hallazgos por regiones se correlacionan con el hecho de que las Américas sea la región en la que hay una mayor proporción de hogares que consumen sal yodada (90%) en comparación con Europa que alcanza solo el 27%.

La yodación de la sal como principal herramienta

En la actualidad se reconocen diversas fuentes de aporte de yodo al ser humano, por ejemplo, en las zonas que no son endémicas de bocio se encuentran concentraciones de yodo en el agua de 5 µg/L y en las endémicas de 1 µg/L. El aporte de yodo en el agua es de 10 µg/L. En el aire la presencia de yodo se relaciona con la contaminación atmosférica, en una región contaminada la atmósfera

contiene hasta 1 µg/m³ de yodo para un aporte diario de 10 a 20 µg/día (31). Sin embargo, la yodación de la sal es actualmente la estrategia más usada para el control y la eliminación de los DDY. La yodación universal de la sal es definida por la OMS como la yodación de la sal para consumo humano y animal por encima de unos niveles fijados internacionalmente (>90% de los hogares) (31,32). Además de la cobertura de este tipo de sal a la población afectada, la OMS llama la atención sobre la necesidad de vigilar la calidad del proceso de yodación y distribución de la misma, lo que requiere la colaboración de los sectores públicos y privados. Aparte de la yodación de la sal existen casos en los que es necesario el aporte de suplementos de yodo a las mujeres embarazadas y niños menores de 2 años (31-33).

Necesidad de seguimiento a los programas (Cuadro 2)

Al existir distintos estados nutricionales de yodo en los países del mundo, la OMS ha reconocido que es necesario fortalecer el seguimiento a las políticas de yodación de la sal para asegurar que estas tienen el impacto deseado, así como para "identificar poblaciones en riesgo y asegurar una prevención y control sostenible de los desórdenes por deficiencia de yodo" (1). Esto también debido a que la ingesta excesiva de yodo puede producir hipertiroidismo y enfermedades tiroideas autoinmunes (34-37).

Cuadro 2. Consecuencias en la salud por deficiencia y exceso en la ingesta de yodo.

Grupos etarios	Deficiencia de yodo	Exceso de yodo
Todas las edades	Bocio Hipotiroidismo Aumento en la susceptibilidad de la glándula tiroides a la radiación nuclear	Hipertiroidismo Tiroiditis autoinmune
Feto	Abortos Anomalías congénitas Aumento en la mortalidad perinatal	
Neonatos	Cretinismo endémico Aumento en la mortalidad infantil	
Niñez y adolescencia	Alteraciones en la función mental Retraso en el desarrollo físico Hipertiroidismo inducido por yodo	
Adulthood	Alteraciones en la función mental Hipertiroidismo inducido por yodo Disminución en la fertilidad	Bocio inducido por yodo

Fuente: (4) y (32) Adaptado por los autores.

Hasta los años 90 la prevalencia total de bocio era utilizada como el principal indicador de la deficiencia de yodo en las poblaciones sin embargo lleva muchos años el cambio en la prevalencia de bocio una vez instauradas las medidas de yodación. La OMS recomienda el estudio en niños preescolares por su fácil acceso y porque son una representación adecuada del estado nutricional de la población general, sin embargo para monitorizar el impacto de los programas de yodación de la sal deben incluir a otros grupos vulnerables incluyendo a las mujeres embarazadas (1).

Para ello se han ideado distintas formas de seguimiento a los programas de yodación de la sal, de su impacto en la prevalencia de bocio endémico y otros desordenes por deficiencia de yodo y de su sostenibilidad una vez implementados los programas. En los cuadros 3-5 se enumeran los criterios epidemiológicos para evaluar el estado nutricional de los escolares, por medio de la mediana de la yoduria, así como la clasificación clínica del bocio recomendada actualmente por la OMS y la interpretación sobre su prevalencia para un territorio dado (38,39).

Indicadores del proceso de yodación de la sal:

La legislación apropiada y las regulaciones que apoyen los procesos son las piedras angulares de los programas de yodación de sal en los países. Una de estas regulaciones es aquella que especifica el contenido de yodo en la sal de consumo humano y animal en los sitios de producción. La OMS actualmente recomienda el método de titulación o sus equivalentes, asimismo se recomienda el uso de yodato de potasio en preferencia al yoduro por ser su mayor estabilidad (39). Dentro de los factores que determinan el contenido de yodo en la sal al nivel del consumidor se encuentran: Diferencias en la cantidad de yodo agregado a la sal, contenido diferente de yodo en un mismo lote o por bolsas de sal debido a fallas en el proceso de mezcla, falta de control de la humedad a lo largo del proceso de producción (con pérdidas de yodo aproximadas entre el 30 y el 80%), pérdida de yodo debido a impurezas de la sal, o por los procesos de lavado o cocción a nivel domiciliario, y disponibilidad de fuentes de sal no yodadas para el consumidor (39,40). Estos escenarios de pérdida potencial del contenido requerido de yodo en la sal indican la importancia de la evaluación de los procesos desde la producción, el empaquetamiento y distribución de la sal hasta el nivel del consumidor final.

La OMS, UNICEF y el ICCIDD recomiendan que “considerando que bajo las condiciones habituales existe una pérdida del 20% del contenido de yodo desde el productor hasta el consumidor, otro 20% en los procesos de cocción previas al consumo, que en promedio una persona ingiere 10g de sal al

día, se recomienda un contenido de yodo en la sal en el sitio de producción de 20-40 mg de yodo por kg de sal (20-40 ppm) para proveer 150 µg de yodo al día. Para las comidas procesadas se debe utilizar sal con un contenido de yodo cercano al rango inferior recomendado (38,39,41).

Sin embargo además del monitoreo del contenido de yodo en la sal es necesario determinar la yoduria en muestras representativas a nivel nacional, siendo el rango recomendado de 100-199 µg/L en la población general y 150-249 µg/L en las mujeres embarazadas (2,20,29,30). A partir de los resultados de la población, la OMS recomienda considerar los determinantes del consumo de yodo, como son: el porcentaje de casas que utilizan sal adecuadamente yodada, la calidad en el sitio y procesos de producción, empaquetamiento, distribución y los hábitos alimentarios con relación al consumo y uso de la sal.

Indicadores de impacto:

El yodo urinario se prefiere como indicador de impacto de los programas de control de los DDY porque refleja la ingesta actual de yodo y responde relativamente rápido a la corrección de la deficiencia (30-32). La OMS recomienda que los estudios de deficiencia de yodo se hagan en escolares entre 6-12 años de edad (1). A pesar del desfase en los cambios de la PTB y el estado nutricional del yodo, la PTB es considerada un indicador práctico de evaluación de base en áreas donde la deficiencia de yodo es severa (1).

El caso de Colombia historia de las políticas sanitarias y situación de los ddy en Colombia

En Colombia entre los siglos XVI y XVIII cronistas como Fray Pedro Aguado reportaron la prevalencia de bocio en distintas regiones. Francisco José de Caldas también registro la enfermedad que se presentaba “a lo largo del Rio Magdalena hasta la confluencia del Rio Cauca” (42). En 1832 el francés Boussingault recomendó el consumo de sal procedente de fuentes yodadas para la prevención del coto en Colombia y en 1857 el Congreso de la República convocó a los científicos de la época para que investigaran en la prevención y tratamiento del bocio. Sin embargo, solo hasta la primera mitad del siglo pasado se conoció la magnitud y gravedad del problema del bocio endémico en Colombia gracias a la Encuesta Nacional de Bocio, realizada entre 1945 a 1948. Esta encuesta estudió 183.243 escolares de ambos sexos, correspondientes a 385 municipios del país. Esta encuesta mostró una prevalencia de bocio de 52,6 %, siendo los Departamentos más afectados los de Caldas, Cauca, Huila, Tolima y Boyacá.

En 1947 se aprobó la Ley 44 por medio de la cual se creó el antiguo Instituto Nacional de Nutrición, como dependencia del Ministerio de Higiene, y se determinó la yodación de la sal.

En 1950 la Concesión de Salinas del Banco de la República inició la producción de 300 toneladas mensuales de sal yodada con 50 ppm de yodo. Gran parte de esta sal se distribuyó en siete municipios del Departamento de Caldas que previamente habían sido seleccionados debido a que su prevalencia superaba ampliamente el promedio nacional. A los dos años el Instituto Nacional de Nutrición realizó una nueva encuesta en los escolares de estos municipios para determinar la efectividad de las medidas de yodación de la sal en la prevención del bocio endémico. Esta nueva encuesta mostró una reducción acentuada en la prevalencia del bocio endémico general para los siete municipios de 83,1% a 33,9%” (42-44).

El Decreto Legislativo 0591 de 1955 estableció la yodación de la sal para consumo humano y animal, de acuerdo con las normas de la OMS (50-100 ppm de yodo) y en 1959 la Concesión de Salinas construyó una refinería moderna para este fin (42). En 1959 el Ministerio de Salud Pública “encarga al Instituto Nacional de Nutrición de efectuar el control y la supervisión de la yodación de la sal” en el país y tres años después mediante la Ley 14 y el Decreto Reglamentario 1908 se establece que la Concesión Salinas transfiera a esta entidad 2 centavos por cada libra de sal yodada en Colombia (45,46).

En 1960 la Encuesta de Nutrición de Colombia encontró que la prevalencia de bocio endémico era de 41% en los niños menores de 15 años. En Colombia, la explotación de las salinas marítimas y terrestres fue contratada por el Gobierno con el Banco de la República desde 1931 bajo la Concesión de Salinas. Para 1965 se explotaban las salinas terrestres de Zipaquirá en el interior del país y las marítimas de Manaure y Galerazamba sobre el Mar Caribe” (42,45,46).

En 1959 la yodación cubrió el 48 % de la sal producida en el país; en 1964 este porcentaje subió al 76 %, y en 1966 se calcula que el 55 % de la sal producida en Colombia se encontraba yodada. El 15% restante corresponde a sal marina, utilizada en su mayoría para consumo animal y uso industrial. “El control efectivo de la yodación de la sal en Colombia se inició en 1963, después de la creación del nuevo Instituto Nacional de Nutrición” (42,45,46).

Para la evaluación de estas medidas a escala nacional se realizaron encuestas nacionales en escolares, una de ellas se limitó a los siete municipios del Departamento de Caldas mientras que otra se diseñó en dos etapas: la primera de ellas limitada a los Departamentos que habían presentado una prevalencia de bocio mayor del 50% en la encuesta nacional (Boyacá, Caldas, Cauca, Huila, Tolima y Valle). En 1968 la Ley 75 responsabiliza al Instituto Colombiano de Bienestar Familiar del control de la yodación de la sal y se aumenta

en cinco centavos el aporte por libra de sal yodada vendida. Luego la Ley 27 de 1974 establece la participación del ICBF en el 12% del precio oficial de la sal (42).

Al finalizar la década de los años 70, la Ley 09 de 1979 determina “que la sal para consumo humano se considere un alimento” (42-,47) y en los años posteriores se dictan decretos reglamentarios de esta Ley que establecen entre otras el control del reempaque de la sal yodada. Durante el periodo 1947 – 1983 las muestras analizadas de sal yodada en el país no solo eran menores al número mínimo analizable por ley sino que no cumplían con los requisitos mínimos de contenido de yodo establecido por la OMS. Para este periodo, Carrillo muestra que de las 9000 muestras analizables mínimas por ley esperadas, solo se analizó un número de 2462, de las cuales 429 tenían un contenido de yodo entre 50-100 ppm, 1967 tenían menos de 50 ppm y 66 tenían más de 100 ppm para un promedio del contenido de yodo de 14.2 ppm (48). En 1992 el Decreto 6568 “crea el Comité Interinstitucional para la vigilancia de los desórdenes por deficiencia de yodo, flúor y el control de la calidad de la sal para el consumo humano” (48). En 1998 el 91% de la sal para consumo humano estaba correctamente yodada y la prevalencia de bocio en escolares era del 7% por lo que el país fue declarado libre de Desórdenes por Deficiencia de Yodo. Entre 1994 y 1996 se realizó un estudio de prevalencia de DDY Instituto Nacional de Salud en 74 municipios de 32 departamentos. Este estudio mostró una prevalencia de bocio del 7 % en una muestra de 15 807 escolares y una deficiencia de yodo en cerca de 6000 muestras de yoduria. Sobre esa base, los expertos de la Organización Panamericana de la Salud, UNICEF e ICCDDI que visitaron a Colombia recomendaron mejorar la organización y vigilancia, para asegurar sostenibilidad del programa (12).

Discusión sobre el seguimiento en Colombia

En el cuadro 7 se muestra los indicadores recomendados por la OMS para la evaluación en los países con programas de control y eliminación de los DDY, las entidades en Colombia encargadas de estas mediciones y las observaciones de los autores sobre la situación del país respecto a cada uno de ellos.

La eliminación de los DDY se logra cuando la yodación de la sal puede ser sostenida. Esto implica que una vez que se logra este reconocimiento los países deben asegurarse del mantenimiento de estos logros mediante un sistema adecuado de monitoreo y evaluación que parta desde un nivel regional y nacional (4). La importancia de alcanzar la eliminación de estos desórdenes radica en su afectación a las poblaciones de distintos grupos de edad, con un alto impacto en el desarrollo infantil, no solo en cuanto a la presencia de formas severas de alteraciones cognitivas sino en el desarrollo de formas leves

que alcanzan mayor distribución. Por lo anterior, el seguimiento activo a estos programas no solo es beneficioso para las poblaciones desde el punto de vista de salud pública sino que trasciende al impacto de estas medidas en el desarrollo económico de las mismas (4). Esto es importante si se tiene que la falta de sostenimiento de las medidas de control y vigilancia ha llevado a un retroceso en áreas que previamente habían logrado la eliminación. En Colombia, Gallego y cols. en un estudio reciente en la población de Quindío sugieren que la presencia de DDY podría estar ligada a las políticas de seguridad alimentaria (50). Asimismo, las condiciones propias de las distintas áreas rurales o urbanas y de los estratos socioeconómicos con relación a las fuentes de acceso a alimentos asociados a la presencia de desnutrición en estas poblaciones se reflejan también en que existan áreas donde el problema no sea la deficiencia sino el exceso de yodo. Adicionalmente, Lastra y Colaboradores, llaman la atención sobre posible prevalencia aumentada de enfermedad tiroidea autoinmune, que puede estar relacionada con exceso en la ingesta de yodo en algunas regiones (51)

Aunque el presente estudio no cuenta aún con datos y aportes de las entidades encargadas oficialmente del monitoreo del programa de eliminación de los DDY en su fase de seguimiento y sostenibilidad, los resultados preliminares de la revisión indican por lo menos tres conclusiones preliminares de la situación del bocio endémico en el país y sus políticas sanitarias: 1. No se conoce con exactitud datos reales sobre la carga de los DDY en el país, ni su distribución por regiones, estratos socioeconómicos, y grupos poblacionales, 2. Falta información sobre los indicadores del proceso de yodación de la sal periódico y accesible a la comunidad académica y 3. Sin los datos anteriores no se puede establecer la efectividad de los programas actuales, la situación real del bocio y de otros DDY en el país así como tampoco su comportamiento en respuesta a las medidas de control implementadas.

Debido a lo anterior, consideramos necesario el establecimiento de encuestas regionales con muestras significativas, de escolares, mujeres embarazadas y otros grupos poblacionales cuyo objetivo sea la determinación de la situación nutricional de yodo de los individuos, la prevalencia de bocio endémico y la carga de los DDY en el país. En la actualidad el uso de software especializado permite el diseño de mapas que ayuden en la identificación de prioridades en salud pública y orienten en la planeación de programas y posterior seguimiento. Asimismo, consideramos que esta información requiere ser relacionada con los estudios de contenido y estabilidad del yodo en la sal en los distintos niveles de proceso de producción así como la investigación de los determinantes culturales y socioeconómicos que influyen en el acceso y consumo de la sal en las distintas regiones del país. Consideramos que este análisis podrá ser útil a las autoridades sanitarias en la

evaluación de la yodación de la sal, su impacto real en la salud de la población y la investigación en otras estrategias que permitan aportar este micronutriente a los grupos con requerimientos especiales.

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Declaración de Conflictos de Interés

Las declaraciones y afirmaciones realizadas en este artículo comprometen a sus autores y no a la Universidad Nacional de Colombia. Los autores declaramos no tener ningún conflicto de interés.

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