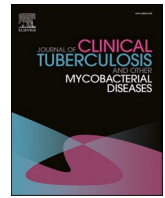




Contents lists available at ScienceDirect

Journal of Clinical Tuberculosis and Other Mycobacterial Diseases

journal homepage: www.elsevier.com/locate/jctube

Synergy between government and non-governmental organizations in health: WHO and the Union collaboration in tuberculosis control

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ARTICLE INFO

Keywords:

Tuberculosis
World Health Organization
International Union Against Tuberculosis and Lung Disease
The Union

1. Introduction, objectives and approach

The global fight against tuberculosis will not end soon despite remarkable achievements over the many past decades. Epidemiological trends worldwide tell us that, without transformational tools and innovative systems, at the current pace it will take many decades to reach the ambitious targets set within the World Health Organization (WHO) End TB Strategy endorsed by the World Health Assembly in 2014 [1]. More than ever there is a need for strong coalitions of partners working in synergy towards common aims.

With the objective of describing the collaboration to fight tuberculosis globally between key agencies over time, we have assessed the contributions of the two major global institutions that have traditionally led global efforts against this disease: the WHO on the governmental side, and the International Union against Tuberculosis and Lung Disease (The Union) on the non-governmental side. To document the work of these two organizations a thorough analysis of relevant historical documents was undertaken. The search focused, in particular, on official WHO and United Nations documents as well as the published literature. For the former, we searched through WHO, World Health Assembly (WHA) and WHO Executive Board resolutions starting in 1948 (or before for interim commissions and other earlier agencies) on the WHO dedicated web page (<https://apps.who.int/iris/handle/10665/85537/browse?type=dateissued>). For published literature, we used, as necessary, PubMed or Google Scholar with keywords such as “history of tuberculosis control”, “history of World Health Organization”, “history

of the International Union against Tuberculosis and Lung Disease” or “... of The Union”, accompanied by any other relevant keyword depending on the subject at stake and systematic (personally held) collections of periodicals (e.g. “Tuberculosis (Berlin)”, “The Bulletin of the International Union Against Tuberculosis”, and “Tubercle”).

These two institutions have been leading in formulating and implementing multiple key initiatives of both technical and strategic nature over the past and notably in collaboration during their co-existence. They have a mandate to keep sustaining the environment and encourage political will, commitment, and engagement. Their coordination role and alliance with the many partners engaged in the global campaign is critical to ensure that progress continues. In this article, therefore, we assess the historical progress in collaboration and advocate for the need of its further strengthening.

2. The beginning of an international movement driven by non-governmental organizations

The initial spark for internationalization of activities in the fight against tuberculosis might be traced to the first international medical congress in 1867 in Paris as Annik Rouillon, a scientific and executive director of the International Union Against Tuberculosis [and Lung Disease [2]], suggested [3]. Several such conferences followed, and in 1899 an international tuberculosis congress took place in Berlin which marked the first meeting at which official representatives from numerous governments and voluntary organizations took part [3,4].

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<https://doi.org/10.1016/j.jctube.2021.100251>

Available online 12 June 2021

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At the 1902 congress in Berlin the decision was made to create a Central Bureau for the Prevention of Tuberculosis in Berlin [5,6]. Its periodical “Tuberculosis” [not to be confused with the periodical by the same name, published at the same time, by the British National Association, thus quoted here for distinction as “Tuberculosis (Berlin)”] was published monthly throughout its existence that ended in 1914 with the onslaught of the First World War, also interrupting preparations for the planned conference in Bern, Switzerland, in the same year [7,8].

The last decade of the 19th and the first of the 20th century saw the foundation of multiple national tuberculosis associations, with those in Austria, France, and the United States among the first [3]. These associations were devoted to the promotion of public sensitization to the tuberculosis problem in their respective countries and to further education of the public about then concepts of prevention. The associations became later – with the foundation of The Union in 1920 – the so-called Constituent Members of the organization. In some countries, the national association, in addition to educational, advocacy work, and clinical care, also took major responsibilities in tuberculosis surveillance or assisted the government in this activity until very recent times [4,9].

The Bureau’s periodical devoted, in addition to be a place on reporting from the conferences, much space to the control of tuberculosis from both the governmental and the non-governmental side. This comprised for instance the role of the government in establishing networks of institutions (e.g., hospitals and sanatoria) for the treatment of indigent tuberculosis patients [10] or introducing mandatory notification of tuberculosis [11] or furthering progress in legislation supporting the control of tuberculosis [12]. In 1902 Gilbert Sersiron proposed the adoption of the “double-barred cross” (the Cross of Lorraine) as the international symbol for the fight against tuberculosis [13], later reaffirmed after the official creation of The Union [14], that has been retained until now.

3. Foundation of the League of Nations and The Union through the end of the Second World War

Two major historical events took place in 1920 that would shape the development of international tuberculosis control activities. On the governmental side it was the creation of the League of Nations which brought the Health Committee of the League in its wake [15]. On the non-governmental side it was the founding of The Union in Paris [3,6,16]. The Union started publication of a periodical, the Bulletin of the International Union Against Tuberculosis, with its first issue in 1924 in French and English [17]. The Bulletin became rapidly the scientific journal on tuberculosis and, as such, it soon began to regularly report on the anti-tuberculosis work of the League of Nations after a decision by its Executive Committee [18]. This was not least instigated by a preceding Union conference requesting the League of Nations to study a number of points relating to tuberculosis. These questions were wide-ranging including international standardization of tuberculin or epidemiologic information on tuberculosis mortality in various countries. Committees within The Union were set up to chair research into such questions, subsequently published in the Bulletin [19,20]. These reports were intertwined with the reports of the Health Committee of the League of Nations held at the library of the WHO (https://www.who.int/archives/fonds/collections/bytitle/fonds_3/en/, accessed 3 March 2021). Thus, the collaboration between international governmental and non-governmental tuberculosis organizations had become established.

The seizure of power by the Nazis in Germany and the resulting Second World War they unleashed disrupted any meaningful international collaboration and it also profoundly affected The Union. The Bulletin ceased its publication in mid-1940 and its Executive Committee convened again only in 1946 [16].

Overall, between the two World Wars, the League of Nations did not really attempt any significant international interventions against tuberculosis as clearly spelled out in a subsequent 1949 report by WHO explaining that, besides publication of some documents, “no practical

field work”, was undertaken by the League [21]. The same report emphasized also that the “only other international body in the tuberculosis field was the International Union against Tuberculosis with its headquarters in Paris”. However, also The Union was non-exempted from the criticism of being “largely academic in function” since its activities were mainly focused on holding conferences and publishing a quarterly bulletin [21]. On the governmental front, in 1943, a temporary agency, the United Nations Relief and Rehabilitation Administration (UNRRA), came into existence. The same 1949 WHO report noted that UNRRA’s interest in the fight against tuberculosis was “broader than that of any previous international organization”, although its assistance was limited to a list of a dozen countries that were invaded and seriously damaged [21].

4. A new beginning: United Nations and the World Health Organization

The post-war era was heralded by a renewed dedication and effort to bring people together and to overcome collectively the disaster brought upon mankind by the two World Wars with the founding of the United Nations on 24 October 1945 following the crucial United Nations Conference on International Organization (UNCIO), commonly known as the San Francisco Conference, held from 25 April 1945 to 26 June 1945 in San Francisco, California (<https://www.un.org/en/sections/history/uknited-nations-charter/1945-san-francisco-conference/index.html>, accessed 3 March 2021). The recognition of health being a key to the wellbeing of the people and stability of nations led to the establishment of the WHO in 1948 as a specialized agency of the United Nations.

The new agency recognized the importance of tuberculosis already before being launched. In April 1947, there had been a key meeting of the Committee on Priorities set up by the Interim Commission of the future WHO. The Committee was chaired by Manuel Martínez Baez from Mexico and included highly influential people such as Karl Evang from Norway, one of the fathers of WHO who launched the idea of a new health agency during the San Francisco Conference, and George Brock Chisholm from Canada, who a year later became the first Director-General of WHO [22]. That Committee reported back to the Interim Commission identifying those priorities “requiring immediate setting-up of machinery during the interim period” by “forming an Expert Committee”. The three recommended Expert Committees included one on Biological Standardization, another on International Pharmacopeia and one on tuberculosis [23].

WHO had its own periodical, the Bulletin of the World Health Organization, right from the beginning. In the first issue it published the report of the Expert Committee on Tuberculosis, resulting from the latter’s first session in 1947 [24,25]. Johannes Holm from the Statens Serum Institut of Denmark (who later became the Tuberculosis Section Chief of WHO and in 1961 Executive Director of The Union) had been elected to chair the committee. Surveillance to describe the magnitude of the tuberculosis problem was identified as the first priority. The evaluation of chemotherapeutic agents such as the recently discovered streptomycin [26,27] were high but not yet on top of the agenda. John B McDougall, Chief Medical Officer for tuberculosis at WHO, published in the same year the priority list of the three top diseases ranked by their epidemiologic importance for WHO to target, i.e. malaria, tuberculosis, and venereal diseases [28]. One priority action he pointed out was that “the closest liaison be maintained with other international organizations – governmental or voluntary – which have an interest in tuberculosis”. The same was recommended in the Report of the first Expert Committee itself: “The committee has been informed that the International Union against Tuberculosis is about to establish a branch office in Geneva. It is urged that liaison be established at once between WHO and The Union in order that their several activities go forward in unison” [24]. It is therefore not surprising that the Executive Board of WHO agreed in October 1948 to establish relationship with nine non-governmental organizations in various fields of health, and among them was The Union

as the representative of non-governmental entities fighting tuberculosis [29]. Its functions were defined later and included promotion of tuberculosis control, studies and dissemination of information, training and engagement in WHO technical meetings. At the Second World Health Assembly in June 1949, McDougall informed the Committee that WHO had been in “constant contact” with The Union “with which liaison had been established in accordance with the Executive Board’s decision” [30].

From 1951 through 1974 WHO published a series of crucial technical reports prepared by the Expert Committee on Tuberculosis [31–35]. Representatives of The Union’s network of associations and individual members were well represented in all the technical committees. The recommendations of the Expert Committee had global impact on setting priorities in tuberculosis control. In hindsight some recommendations may be disputable, such as the Eighth Report on chemotherapy allowing for monotherapy with isoniazid in the continuation phase [34]. Yet, these recommendations were made by the then top experts in the fields, likely a result of compromises between forces from different fractions as is in the nature of such committees. Here specifically, the lessons from Crofton, a key researcher in the development of anti-tuberculosis regimens from Edinburgh, about the curability of tuberculosis through proper chemotherapy [36] lost against the opinion of McDermot, the editor of the American Review of Tuberculosis, that there was no evidence for supporting the view of curability of tuberculosis nor the need for triple chemotherapy [37].

From 1948 to 1963 WHO and the international expert community placed emphasis on so-called vertical programs [25] to address specifically defined communicable diseases responsible for a high burden of public health importance. From 1964 to 1976, the global health community shifted the attention towards integrating service delivery, recognizing the specific needs and capabilities of low-income countries [25]. This approach was built up and culminated in the conference at and declaration of Alma-Ata in 1978 [38]. The underlying logic supporting the promotion of primary health care is straight forward and clear: there cannot be effective disease control without having a basic functional infrastructure. Isolated disease-specific programs without such a basis are bound to fail in absence of a general health structure to support them. However, it was soon noted that success with integrated programs was at best patchy [39]. While successes with integration were observed in immunization, logistics, and laboratory services [25], Pio and Raviglione noted that these were overshadowed by “... failures in key areas of tuberculosis control in many less-developed countries” [25]. In 1978 the WHO Tuberculosis Unit was transformed into a Tuberculosis and Respiratory Diseases Unit with additional tasks but without a commensurate increase in staff and funding. Yet, at the same time falls the production by WHO of the undisputedly most outstanding technical book on tuberculosis ever written, Toman’s “Case-finding and chemotherapy. Questions and answers” [40]. It is a collection of key questions in tuberculosis control activities as asked during meetings and conferences that were answered by the most prominent experts in tuberculosis at the time. The answers in the book were based on these responses; for each a meticulous search was undertaken and referenced from the evidence base in the published scientific literature. The Union provided substantial technical assistance towards the realization of this WHO project and translated the book into French and Spanish. The book hasn’t lost anything of its relevance until today and was updated by WHO in 2004 [41], again in collaboration with experts from The Union (the original can be downloaded from https://www.tbrieder.org/publications/books_english/books_english.html).

5. The Union’s hour and its collaborative tuberculosis model programs

The slow decade-long demise of the pre-eminence in tuberculosis leadership at WHO resulted in the simultaneous establishment of a much stronger international guidance function by The Union. What should

rightly be WHO duties, such as the strategic and technical assistance to governments in building up national tuberculosis programs, was largely taken over by The Union that intensified its collaboration with specific countries becoming responsible for a service not any longer provided by WHO. As a prelude to The Union’s reorientation of what had been called the “Mutual assistance programs” since 1961 [16], four national tuberculosis associations under the joint auspices of The Union and WHO established the Tuberculosis Surveillance and Research Unit (TSRU) in 1965, generously provided housing on the premises of the Royal Netherlands Tuberculosis Association (KNCV) [42]. While the focus of the TSRU at the outset was on studying various aspects of tuberculosis diagnosis, epidemiology, interventions, and surveillance in low-incidence countries, it was understood that the research should be planned in such a way as to have relevance on implications for high-incidence and resource-constrained settings [42]. The occasion to put that vision of transfer into practice of what became the “IUATLD Collaborative National Tuberculosis Programmes” from 1976 onward [43,44] arose with the sequence of events that began with a meeting in Arusha, Tanzania, in 1977 [45,46]. The Tanzania government decided to launch a program that combined tuberculosis and leprosy control on the entire territory of the country. As the international technical advisor to the tuberculosis component The Union was invited and Karel Styblo, TSRU director and Director of Scientific Activities of The Union, was entrusted with the coordination of all Union responsibilities. The bulk of financing the program lay with the Tanzania government in providing the health infrastructure and the personal staffing for the program at all three levels. Support from European governments and non-governmental organizations was mustered to provide funding for diagnostics, medications, training, and means of transport for both leprosy and tuberculosis. The national program brought existing elements and scientific results from research together [47] and offered innovative implementation of various standardized components, e.g. diagnostic case definitions based on bacteriology with an emphasis on sputum smear microscopy, application of standardized treatment regimens in a cascade of regimens, recording and reporting, and most importantly evaluation of program performance indicators such as the proportion of cured. These principles had been described in the 1973 WHO 9th Expert Committee but never implemented in the field. Most notably Styblo’s innovation included the requirement to report treatment outcome in predefined categories among successive cohorts of patients enrolled on treatment at a point in time when they could have completed treatment (so-called “cohort analysis”) [44,45,48–50]. The first-line regimen used was strictly based on a clinical trial evaluated on the continent jointly by the British Medical Research Council and regional research councils. Initially, in 1977 [51] the 12-month regimen with isoniazid plus thioacetazone throughout, supplemented by streptomycin during the first two months, was chosen [52]. This regimen had demonstrated clinical trial efficacy, was affordable and paid for by the Tanzania government. Because effectiveness was evaluated continuously, it soon emerged that the outcome results with this regimen were poor (50% success). As a result, it was thus decided to pilot-test the 8-month regimen [53] with a 2-month intensive phase consisting of isoniazid, rifampicin, pyrazinamide plus streptomycin, given daily under direct observation during hospitalization, followed by a 6-month continuation consisting of daily thioacetazone plus isoniazid, supplied monthly for self-administered treatment [54]. The regimen’s trial efficacy was also reflected in a high field effectiveness (success approaching 80%) and implementation was gradually expanded [55] to all of the entire program. The regimen costs (\$US 50) exceeded the budget of Tanzania. For bacteriological, epidemiologic, and logistic reasons the indication for the new regimen was initially limited to sputum smear microscopy-confirmed and clinically severe cases. It required increased funding by the external governmental donor that could be negotiated and was channeled through The Union for direct purchase of the medications.

6. WHO takes the lead in global tuberculosis control

While the unprecedented success of the Tanzania model program initially found seemingly little echo internationally beyond “insiders”, a first breakthrough for recognition came with a change at WHO in 1988 after headquarters tuberculosis staff had shrunk to two professionals [25]. A new leadership took over – and it was largely “naïve” to tuberculosis. Arata Kochi, chief of the Tuberculosis Unit, went along with Styblo on a routine evaluation of the Tanzanian program, recognizing its potential for scalability. Simultaneously, the World Bank’s “Health Sector Priorities Review” brought The Union’s model to the forefront. The report utilizing data from the Tanzanian and other Union collaborative programs modeled among these lines was first presented at the Union conference in Boston [56]. More prominently for the scientifically oriented audience was the report the following year, identifying chemotherapy of sputum smear-positive tuberculosis as one of the most cost-effective interventions in health in terms of costs per death averted and per disability-adjusted life years saved [57,58]. In the same year, WHO announced in a seminal editorial its new control strategy [59,60]. Subsequently, the World Bank published its historical 1993 World Development Report “Investing in health” fully devoted to health and its economic implications [57]. This remarkable document reiterated the concept of cost-effectiveness of “Tuberculosis chemotherapy” making it well-known outside of the tuberculosis community and among financial decision-makers and public health stakeholders. This was a milestone in the global fight against tuberculosis: it was the result of a fruitful collaboration between a non-governmental organization such as The Union that operationalized and evaluated a public health approach in the field, WHO that recognized its value and promoted it making it policy, and the World Bank that acknowledged its cost-effectiveness value.

Three years later, the strategic WHO document “Framework for effective tuberculosis control” stood [61], matching the basic principles of the “Tanzania model program” formulated in The Union’s “orange guide” [48,62,63], that had been operationalizing the Ninth Report of the WHO Expert Committee [35]. By then, Styblo had retired from The Union and the TSRU, serving now as a technical adviser to WHO, collaborating among other things with an unprecedented World Bank-supported project in China. The first highly successful results with the new WHO strategy were published in a prominent journal already in 1996 [64]. International tuberculosis control leadership and policy formulation was now where it should have been in the first place, at WHO headquarters [65].

What WHO branded in 1995 as the “DOTS Strategy” was an extraordinary success in penetrating the ministries of health across the globe. The key ingredient of this simplified and standardized strategy was not technical but political commitment [44,66]. Lip service was initially perhaps often commonplace, yet the technical results were measurable and tangible and national leaders could be held accountable [67]. The challenges emerged with implementation progress. The discourse intensified with the setting of the 2005 targets [68,69], yet the success with the progress of the implementation strategy in India [70] heralded optimism for an entirely new era of efficacious, effective, and efficient global tuberculosis control.

The technical key to the success of tuberculosis control was an appropriate standard chemotherapy regimen. The international community differed in the approach to chemotherapy: in high-income countries a six-month, rifampicin-throughout regimen, first established in Singapore [71], became with minor modifications [72] the standard first-line regimen after the usual quibbles [73,74]. In contrast, in Union collaborative programs, prioritizing the protection of rifampicin against acquisition of drug resistance the choice fell on a “cascade of regimens”, i.e. a rifampicin-throughout regimen was kept as the “fall-back” treatment in case of failure of an 8-month regimen using rifampicin only in the intensive phase [50]. The discourse on differences in the approach was also reflected in the development of WHO treatment

guidelines. In 2003, the two approaches still lived in parallel as “legitimate” alternatives until a clinical trial conducted by the Union showed unequivocally that the WHO-recommended regimen [75] was associated with a lower risk of relapse and failure [76]. Yet, introducing the rifampicin-throughout regimen came at the cost of rendering obsolete the then recommended retreatment regimen also based on the “core drug” [77] rifampicin undermining the concept of the cascade of regimens [50]. An alternative “fall-back” regimen for treatment failure due to rifampicin-resistant tuberculosis based on another core drug was urgently required.

7. The start of the partnership era

In the late 1990s, establishing formal global and public health agency coalitions to target complex health problems became fashionable [78]. New partnerships were formed as a “key strategic component of health development” with the aim of attracting support for a specific challenge from as many sectors as possible within the health world and beyond. WHO underwent a complex process of reform of organizational, cultural and operational nature to align with the new global health vision. In this context, the then Global Tuberculosis Programme decided to lead the establishment of one of the first prominent partnerships: the Stop TB Partnership [79]. The natural key ally in this new coalition to fight tuberculosis globally was The Union, with which closer collaboration was sought from the start of the partnership discussion. Other agencies were strongly involved from the start including the Dutch KNCV Tuberculosis Foundation, the US Centers for Disease Control and Prevention, the Rockefeller Foundation, the World Bank and a few donors such as USAID, and the Canadian, British, and Dutch bilateral cooperation agencies. This new partnership became soon a consensus building entity working in harmony with WHO and functioning as a conduit towards any partners engaged in the global fight against tuberculosis. It played an important role in deciding strategically what to do and how to do it synergistically to accelerate progress against the disease. WHO hosted the Partnership for many years and The Union was the agency that strongly supported it to the point of mobilizing during transition periods its own Executive Director, Nils E Billo, who spent time in Geneva to lead the Partnership while WHO was selecting the new Executive Secretary. This new political dimension of joint work cemented a half-a-century long collaboration that was originally focused on technical and strategic issues.

Advocacy to make the tuberculosis cause more visible at political level was one of the fundamental functions of the newly established partnerships. Events such as World Tuberculosis Day celebrations were an example of collaborative work. This activity had already been the result of the collaboration between WHO and The Union since the late 1990s. Inspired by a World Antituberculosis Day proposed by the Belgian member of the International Tuberculosis Association, the date to be determined at the planned 1914 conference in Bern [80], The Union celebrated in 1982 the centennial of Robert Koch’s historical discovery of the tubercle bacillus by launching the idea of a World Tuberculosis Day. This idea was then made reality when WHO in 1997 proclaimed 24 March as World Tuberculosis Day in commemoration of the day of announcement of Koch’s discovery [81].

Collaboration between WHO and The Union, however, continued also on a more technical ground. During the 1990s, with the dismantling of the former USSR, tuberculosis experts and responsible ministerial authorities from the European countries – finally re-united as a cohesive continent – realized the need for harmonization of surveillance and control practices throughout the region. This sentiment brought WHO and The Union, under the leadership of KNCV, to conceive regular technical workshops to discuss new policies and guidance for European countries at large. These workshops were originally held in the small village of Wolfheze in the rural Gelderland province of the Netherlands. Wolfheze soon became synonymous with sound standard norms and guidelines valid throughout Europe. Their importance in building

commitment of European governments to standardize surveillance definitions and control practices allowing for the first time in the history of tuberculosis comparison of performance across borders cannot be emphasized enough. As described in a paper summarizing the history of the Wolfheze workshops, “they have been and still are an essential platform for this exchange of experiences, promoting common approaches” [82].

Several other key activities have characterized the fruitful collaboration between WHO and The Union during the recent two decades. Seminal work was jointly done to look at the interaction between smoking and tuberculosis [83], and to prepare roadmaps addressing the neglected issues of childhood tuberculosis [84] and zoonotic tuberculosis [85,86]. Finally, both agencies have been strong supporters of KNCV and other partners in the USAID-funded tuberculosis control programmes that were implemented in many countries between 2001 and 2019: starting from the TB Coalition for Technical Assistance (TBCTA), to TB Control Assistance Program (TB CAP), TB CARE and Challenge TB (<https://www.challengetb.org/about>).

8. The new challenge: emergence of rifampicin resistance and new chemotherapy regimens

However, not in every scientific debate there was an immediate agreement between the two agencies. One remarkable example is that of the design of an optimal regimen to face multidrug-resistant (MDR) tuberculosis. The emergence of drug resistance as a key threat to effective tuberculosis control had long been recognized and the joint project by WHO and The Union for its surveillance produced its first report in 1997 [87]. It virtually coincided with the WHO guidelines produced by Crofton and collaborators on treatment of drug-resistant tuberculosis [88]. Based on these guidelines, Van Deun and collaborators initiated a treatment program in the Damien Foundation projects in Bangladesh for “failures of failures”, i.e. for patients who had been treated with the “cascade approach” and who had also failed on the rifampicin throughout re-treatment regimen. These patients had proven rifampicin- plus isoniazid-resistant (i.e. MDR) tuberculosis. In a sequentially adapted series of seven regimens, a nine-month regimen based on the core fluoroquinolone drug gatifloxacin emerged as a highly efficacious and effective MDR regimen with results on par with first-line regimens for drug-susceptible tuberculosis [89,90]. The results of this observational study with over 500 patients were later replicated among over 1000 patients in nine francophone countries [91,92]. They were also confirmed for efficacy in a randomized clinical trial by The Union in four countries [93]. The programmatic effectiveness and trial efficacy exceeded that obtained with the 21-month regimen [94], largely because of better tolerance and lesser loss from follow-up [95]. Given the differences in assessment and background of experience, it is remarkable that finally a consensus that reasonably took not just the evidence but also the different interpretation thereof into account was finally reached in 2016 after multiple consultations by WHO of different stakeholders and interest groups [96]. This was amended as a result of new evidence from the then only clinical trial on the shorter regimen [93] in 2018 [97]. A subsequent analysis by the trial group showed the substantial reduction in health-system cost of the shorter MDR treatment regimen [98]. The contribution of The Union through systematic research, both operationally for effectiveness among over 2000 patients in Africa and Asia and conducting the relevant respective clinical trial evaluating on a large scale also the efficacy of the shorter regimen, supplemented by active collaboration in guideline development had enhanced the collaborative spirit between WHO and The Union in the challenging topic of the response to MDR tuberculosis.

9. Has the WHO / Union collaboration over 73 years been effective?

From the very early days of WHO, collaboration with The Union, the

entity representing the national anti-tuberculosis associations, has been overall very fruitful, showing how synergy between governmental and non-governmental organizations in global health responses is crucial. If one attempts to assess the achievements of this synergy then multiple areas come to mind. First, WHO and The Union have jointly developed key scientific research that resulted in milestone publications and technical advice to the world, including at joint events at the fifty-one annual World Conferences on tuberculosis that The Union has been organizing since 1920. Second, The Union’s control strategy has been the basis for the game changing global strategy promoted by WHO since 1995 as the DOTS strategy which has remained the core of tuberculosis control. Third, countries have benefitted from training and technical support provided by the agencies. Fourth, the TSRU joint initiative has been the think tank of surveillance and control interventions over decades. Fifth, building on the work by the Laboratory Section of the Union, then directed by Adalbert Laszlo, WHO and The Union could start and nurture the Global Drug Resistance Surveillance network that, over the past 25 years, has allowed – unprecedented for any infectious disease – a precise understanding of the global threat posed by drug resistance. Sixth, the Wolfheze workshops, organized jointly with KNCV, have been fundamental to allow harmonization of definitions and practices in Europe. Seventh, previously neglected aspects of tuberculosis control, such as the interaction with tobacco smoking, childhood and zoonotic tuberculosis have been faced effectively by engaging sectors and experts not always involved previously. Finally, joint advocacy efforts including World Tuberculosis Day events and press conferences have helped disseminate information and raise political attention that are key components of advocacy for increased investments and mobilization of resources at all levels.

10. Conclusions

From our analysis some principles emerge clearly. The global fight against tuberculosis needs both governmental and non-governmental forces to succeed. The former needs the latter and *vice versa*. This principle, that is well demonstrated by the successes jointly achieved in the fight against tuberculosis, applies to any global health challenge, including the current COVID-19 pandemic. Coordinated scientific and research efforts, bold policies by governments promoted by competent non-governmental entities, joint support to country implementation with community engagement are key elements of successful containment of any high-burden disease.

Towards this aim, WHO is and should remain responsible for the coordination of the global response by its Member States to epidemic and endemic threats and provide the necessary stewardship role through the ministries of health that form the Organization itself. Non-governmental organizations such as The Union have another fundamental role to play to support global and country efforts. In global tuberculosis control, The Union with its political independence and technical and scientific capacity is the global face of national anti-tuberculosis associations and other non-state entities strongly engaged in care, prevention and control of tuberculosis. To accomplish its aims, The Union needs to consolidate its well-recognized independent scientific role and technical support competence especially in those countries where WHO’s technical advice is hampered by its nature of a member state organization. In simple words, The Union must re-gain its function of the umbrella organization under which non-governmental entities can sit together, coordinate their efforts and synergize with WHO to ensure that country governments continue progressing worldwide. At the same time, both The Union and WHO need to keep engaging with the scientific community that can provide those transformational tools and system innovations to be assessed under operational conditions, made policy and practice on a large scale, and ultimately allow accelerated progress worldwide.

The two agencies have a responsibility and should be accountable for it while working to ensure that all involved in activities against

tuberculosis respond in a proper and coordinated manner. The collaboration between WHO and The Union over the past 73 years of co-existence has not always been smooth but has proven fundamental especially at times when WHO had temporarily withdrawn from its leadership and guidance role. The importance of keeping momentum in the global fight against tuberculosis is expressed in a statement made by Jaap F Broekmans, then Executive Director of KNCV Tuberculosis Foundation, during the 2000 Amsterdam Ministerial Conference organized by KNCV on behalf of the Stop TB Initiative. As the incoming WHO Director-General dismantled the WHO's Global Tuberculosis Programme in 1998, thus depriving the world of the necessary tuberculosis lighthouse, he remarked "Tuberculosis is too important a global challenge to depend only on the mood of the Director-General of WHO" (MCR, personal communication). Indeed, to eliminate tuberculosis as a public health threat, a strong coalition between governmental and non-governmental organizations and partners at all levels, from the international to the community one, is indispensable and a *sine qua non*.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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