Eliminação da Hanseníase / Elimination of Leprosy

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For ages hanseniasis had remained a disease with no hope, and hanseniasis control a series of frustrations. However, the situation has changed dramatically since the introduction of multidrug therapy (MDT) in the treatment of hanseniasis in the 1980s and the increasing prospects of drastic reductions in the disease prevalence as a consequence. It was primarily this success with MDT that led WHO, through a resolution of the World Health Assembly in 1991, to set the goal of eliminating hanseniasis as a public health problem by the year 2000, defining elimination as attaining a level of prevalence below one case per 10,000 population.

The Disease Burden in Hanseniasis

Hanseniasis currently occurs in significant numbers in about 55 countries or territories of Asia, Africa and Latin America. Estimates for 1997 indicate a global total of about 1.15 million cases as against 10 to 12 million in the 1970s. Approximately 0.89 million were on treatment registers by the beginning of 1997 as against 5.4 million in 1985. About 560,000 new cases are being detected annually and about 2 billion people live in countries with a hanseniasis prevalence of more than one per 10,000. In all, about two million individuals are visible disabled as a result of hanseniasis.

Of all the communicable diseases, hanseniasis is most important for its potential to cause permanent and progressive physical disability. In addition, the disease and its visible deformities, in particular, contribute to intense social stigma and social discrimination of patients.

It is estimated that, on an average, the expected healthy years of life lost is about 6.3 years per patient.

Currently the heaviest burden of hanseniasis is in the South-East Asian Region of WHO, followed by African and American Regions which have a relatively lower prevalence. (For details see Table 1). The situation in the Eastern Mediterranean and Western Pacific Regions is even more favourable. As far as Europe is concerned, hanseniasis is a relatively uncommon disease with limited foci.

The uneven distribution of the disease among countries is a marked feature of hanseniasis as shown in Table 2 and Figure 1. Only 16 countries contribute to 91% of the registered global hanseniasis prevalence of which just five countries contribute to 82%. India alone accounts for 62% of the registered global prevalence. This pattern is even more markedly seen in the distribution of new cases detected. For instance, 73% of all new cases detected in the world in 1996 came from India.

Multi-drug Therapy in Hanseniasis

Until 1980 dapsone, through domiciliary treatment of patients, was able to contribute to a limited degree of success in hanseniasis control in well-organized programmes. However, the resistance of _M.leprae_ to dapsone became widespread (1) making the treatment increasingly ineffective. In addition, the long-term and often life-long treatment required with dapsone led to poor patient compliance and ineffective disease control in general. This period of failure and frustration changed dramatically with the introduction of greatly improved treatment through the application of combinations of drugs, know as multidrug therapy (MDT), the standard regimens of which were first recommended by a WHO Study Group in 1981 (2).
Table 1: Registered cases of hanseniasis and coverage with MDT by WHO Region, 1997

<table>
<thead>
<tr>
<th>WHO REGION</th>
<th>Estimated cases</th>
<th>Registered Cases</th>
<th>Registered Prevalence per 10 000</th>
<th>Cases detected 1996</th>
<th>Detection rate per 100 000</th>
<th>Cases on MDT</th>
<th>MDT Coverage (%)</th>
<th>Cured with MDT Cumulative Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>140 000</td>
<td>82 758</td>
<td>1.39</td>
<td>46 489</td>
<td>7.80</td>
<td>81 764</td>
<td>98.8</td>
<td>507 123</td>
</tr>
<tr>
<td>Americas</td>
<td>140 000</td>
<td>127 866</td>
<td>1.63</td>
<td>43 783</td>
<td>5.59</td>
<td>121 144</td>
<td>94.7</td>
<td>235 116</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>30 000</td>
<td>13 038</td>
<td>0.28</td>
<td>5 761</td>
<td>1.25</td>
<td>12 166</td>
<td>93.3</td>
<td>58 455</td>
</tr>
<tr>
<td>Europe</td>
<td>1 000</td>
<td>732</td>
<td>0.01</td>
<td>37</td>
<td>5.11</td>
<td>726</td>
<td>99.2</td>
<td>1 945</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>800 000</td>
<td>637 413</td>
<td>4.50</td>
<td>457 921</td>
<td>32.36</td>
<td>620 798</td>
<td>97.4</td>
<td>7 377 190</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>40 000</td>
<td>26 533</td>
<td>0.16</td>
<td>12 613</td>
<td>0.77</td>
<td>26 409</td>
<td>99.5</td>
<td>236 483</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1 150 000</td>
<td>888 340</td>
<td>1.54</td>
<td>556 604</td>
<td>9.84</td>
<td>862 998</td>
<td>97.1</td>
<td>8 416 321</td>
</tr>
</tbody>
</table>

Table 2: Registered prevalence of hanseniasis, coverage with MDT and detection rate in the top 16 endemic countries*

<table>
<thead>
<tr>
<th>Country</th>
<th>Registered cases</th>
<th>Prevalence per 10000</th>
<th>Cases on MDT</th>
<th>MDT coverage %</th>
<th>Cured with MDT (cumulative total)</th>
<th>Newly detected cases</th>
<th>Detection rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>553 793</td>
<td>5.9</td>
<td>537 180</td>
<td>97.0</td>
<td>6 862 000</td>
<td>415 302</td>
<td>44.0</td>
</tr>
<tr>
<td>Brazil</td>
<td>105 744</td>
<td>6.6</td>
<td>101 000</td>
<td>95.5</td>
<td>181 763</td>
<td>39 792</td>
<td>24.7</td>
</tr>
<tr>
<td>Indonesia</td>
<td>35 739</td>
<td>1.7</td>
<td>33 739</td>
<td>100.0</td>
<td>175 104</td>
<td>15 071</td>
<td>7.5</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>13 385</td>
<td>1.1</td>
<td>13 385</td>
<td>100.0</td>
<td>70 063</td>
<td>11 225</td>
<td>9.4</td>
</tr>
<tr>
<td>Myanmar</td>
<td>18 758</td>
<td>4.1</td>
<td>18 758</td>
<td>100.0</td>
<td>148 982</td>
<td>6 935</td>
<td>15.1</td>
</tr>
<tr>
<td>Nigeria</td>
<td>14 309</td>
<td>1.2</td>
<td>14 309</td>
<td>100.0</td>
<td>45 720</td>
<td>6 871</td>
<td>8.0</td>
</tr>
<tr>
<td>Nepal</td>
<td>12 828</td>
<td>5.8</td>
<td>12 828</td>
<td>100.0</td>
<td>42 362</td>
<td>6 602</td>
<td>30.0</td>
</tr>
<tr>
<td>Zaire **</td>
<td>6 082</td>
<td>1.3</td>
<td>6 069</td>
<td>99.8</td>
<td>49 422</td>
<td>5 526</td>
<td>11.8</td>
</tr>
<tr>
<td>Mozambique</td>
<td>10 905</td>
<td>6.1</td>
<td>10 091</td>
<td>92.5</td>
<td>7 414</td>
<td>4 225</td>
<td>23.7</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>8 272</td>
<td>1.4</td>
<td>8 272</td>
<td>100.0</td>
<td>71 291</td>
<td>4 747</td>
<td>8.2</td>
</tr>
<tr>
<td>Madagascar</td>
<td>6 656</td>
<td>4.3</td>
<td>6 656</td>
<td>100.0</td>
<td>23 112</td>
<td>3 921</td>
<td>25.5</td>
</tr>
<tr>
<td>Sudan</td>
<td>3 471</td>
<td>1.3</td>
<td>3 471</td>
<td>100.0</td>
<td>8 566</td>
<td>2 126</td>
<td>7.8</td>
</tr>
<tr>
<td>Philippines</td>
<td>8 663</td>
<td>1.3</td>
<td>8 663</td>
<td>100.0</td>
<td>70 967</td>
<td>4 051</td>
<td>5.9</td>
</tr>
<tr>
<td>Cambodia</td>
<td>2 960</td>
<td>2.9</td>
<td>2 960</td>
<td>100.0</td>
<td>7 792</td>
<td>2 404</td>
<td>23.4</td>
</tr>
<tr>
<td>Tanzania</td>
<td>3 077</td>
<td>1.0</td>
<td>3 077</td>
<td>100.0</td>
<td>47 192</td>
<td>2 747</td>
<td>8.9</td>
</tr>
<tr>
<td>Guinea</td>
<td>3 732</td>
<td>5.0</td>
<td>3 732</td>
<td>100.0</td>
<td>28 127</td>
<td>3 326</td>
<td>44.2</td>
</tr>
<tr>
<td><strong>Totals:</strong></td>
<td><strong>806 374</strong></td>
<td><strong>4.3</strong></td>
<td><strong>788 190</strong></td>
<td><strong>97.4</strong></td>
<td><strong>7 839 877</strong></td>
<td><strong>534 871</strong></td>
<td><strong>28.3</strong></td>
</tr>
</tbody>
</table>

* The top sixteen endemic countries included in the table have the following characteristics: (i) they have a prevalence of more than 1 in 10,000 population, and (ii) the number of prevalent hanseniasis cases in more than 5,000, or the number of newly-detected cases in more than 2,000. Ranking of countries is based on the number of estimated cases.

** 1995 data
The standard WHO/MDT for Multibacillary (MB) Hanseniasis consists of a 24-month course of: 
**Rifampicin:** 600 mg once a month (supervised);  
**Dapsone:** 100 mg daily (self-administered);  
**Clofazimine:** 300 mg once a month (supervised) and 50 mg daily (self-administered).

The standard WHO/MDT for Paucibacillary (PB) Hanseniasis consists of rifampicin 600 mg once a month (supervised) for 6 months plus dapsone 100 mg daily (unsupervised) for the same period of six months.

What is the rationale behind multidrug therapy in hanseniasis? It is estimated that a fully-developed lepromatous hanseniasis patient harbours between $10^7$ and $10^8$ acid-fast bacilli (AFB). However, only between 1% and 5% of the organisms are considered viable on the basis of their ability to multiply in the mouse footpad. Thus the mean viable AFB population is estimated to be about $10^4$ or $10^5$ logs. This population consists of several sub-populations of drug-sensitive and naturally drug-resistant strains. It is estimated that in any wild population of *M. leprae* the number of naturally occurring rifampicin resistant mutants to be about one in $10^4$ and naturally occurring dapsone and clofazimine resistant mutants to be about one in $10^9$ each. Thus, one can expect sub-populations of 2 logs of rifampicin resistant mutants and 3 logs of dapsone and clofazimine resistant mutants in addition to about 9 logs of drug-sensitive organisms. In any monotherapy the relevant drug sensitive organisms are killed progressively depending upon the anti-bacterial activity of the drug, leaving behind the naturally occurring mutants which later multiply and result in early or late relapses. In multiple drug therapy, this problem is prevented as the second drug effectively kills the mutants to the first drug and vice versa.

The problem of anti-bacterial treatment of paucibacillary Hanseniasis is somewhat less complicated as the bacterial load is estimated to be less than $10^2$ AFB. The selection of drug-resistant mutants in this population is extremely unlikely and therefore six doses of monthly rifampicin should be sufficient to kill the organisms. However, there may be problems due to primary drug resistance, misclassification and incorrect bacterial assessment. It is because of this that a second drug along with rifampicin, such as dapsone, is necessary for the treatment of PB Hanseniasis.

Over the years MDT has demonstrated to be highly effective. It is very well received and accepted by health workers and hanseniasis patients alike and this is due to: a) the absence of treatment failures attributable to drug-resistance; b) the very low relapse rates following completion of treatment (mean cumulative risk of 1% over 9 years of follow-up) (3); c) the fixed, and relatively short duration of treatment; and d) the very low frequency of side effects contributing to better treatment compliance.

The introduction of MDT has contributed to improvements in the organization of hanseniasis control everywhere. The robustness of the treatment technology of MDT has also led to simplification of requirements for diagnosis, classification and treatment delivery. Thus it became possible to implement MDT, even where the basic health services were not so well organized, and even where conditions were less than optimal. As long as the drugs are taken in combination, MDT provides a degree of benefit even to the irregularly-treated patients. It is relevant to mention here that hanseniasis treatment is largely confined to the public health services and limiting the availability of MDT drugs to the public sector in most countries has prevented the haphazard use of the drugs in the private sector - either as monotherapy or through inappropriate combination of drugs - and thus has prevented the emergence of multidrug resistance.

Although MDT does not have any direct impact on deformities in those patients who are already deformed, it has contributed substantially to the prevention of deformities through early self-reporting and early cure. It is estimated that over the years MDT has prevented over one million persons from becoming deformed. With the increasing application of MDT and the large number of patients being discharged from registers, some programmers are increasing their focus on the management of deformed patients, whether under treatment or already cured.

**Progress made with MDT**

In terms of progress made in conquering hanseniasis over the past 10-15 years, MDT has played the central role and it continues to be the centre of the strategy.

As mentioned earlier, since 1985 hanseniasis has been reduced worldwide from around an estimated 10-12 million cases to 1.15 million cases, a reduction of about 90%. In terms of registered cases the reduction is about 84%, i.e.
from 5.4 million to 0.89 million cases. The number of cases cured through MDT since 1985 is over 8.4 million with another less than one million patients currently undergoing treatment with MDT (4). (Table 1).

In terms of implementation of MDT, the current coverage of registered cases with MDT is over 97% with variations among countries. Of the 8.4 million patients cured through MDT so far, about 7.4 million or 88% belong to the countries of the South-East Region of WHO.

Even though these figures are highly impressive all this would not have been possible without the impetus provided by MDT in reinvigorating hanseniasis programmes and in reinforcing political and professional commitment everywhere. The introduction of MDT has resulted in improved performance of hanseniasis control programmes by way of increased case-finding, organized review of hanseniasis case registers for excluding cases not needing treatment, and mobilization of community support. The encouraging results seen has also increased everywhere the motivation and enthusiasm of health workers dealing with hanseniasis. Even the donor agencies, particularly donor NGOs whose focus was more on the care of the individual patient, found the public health approach through MDT to be a very attractive social goal. This resulted in their increased support to disease control activities and support to national ministries of health.

**Elimination of Hanseniasis as Public Health Problem**

The WHO recommendation on MDT is recognized today as the chief-technological tool in the fight against hanseniasis. In the absence of any primary preventive approach to date, such as a substantially effective vaccine, MDT remains the sheet anchor of hanseniasis control. Because the hanseniasis patient is the only epidemiologically significant reservoir of infection, there is every hope that through early diagnosis and effective treatment, the transmission of the disease could be virtually stopped over a period of time.

Experience in many countries in the past 10 to 15 years has demonstrated convincingly that in well-organized hanseniasis control programmes it is possible to reduce the prevalence of registered cases up to tenfold even within a period of five years.

In several countries MDT has provided governments with opportunity to increase the priority given to hanseniasis control and to strengthen their political commitment for hanseniasis. MDT has also made possible the strengthening of health services for hanseniasis control in many countries. It cost-effectiveness and the results obtained have also contributed in to increased resources, including those from bilateral and international agencies as well as NGOs, both national and international, in a number of hanseniasis-endemic countries.

As mentioned earlier, because of the optimism that developed as a result of MDT, the Forty-fourth World Health Assembly, which met in May 1991, adopted a resolution to eliminate hanseniasis as a public health problem by the year 2000, and defined elimination as attaining a level of prevalence below one case per 10,000 population. This resolution declared WHO’s commitment to attaining global elimination, and urged the countries to increase their political commitment towards the hanseniasis elimination goal.

By establishing a target for the year 2000, the World Health Assembly drew attention to the effectiveness of the available treatment technology, the need for hanseniasis-endemic countries and donor agencies to stop regarding hanseniasis as a permanent problem and to redouble their efforts towards eliminating the disease, and to accept hanseniasis as simply another health problem with a clear solution.

The WHO-inspired goal of eliminating hanseniasis as a public health problem, in spite of attracting an overwhelmingly positive response from most people concerned with the plight of hanseniasis patients, has also generated questions among some as to its necessity and feasibility, apart from some difficulties in understanding what is elimination - and there is a need to clarify these issues (5).

It should be recognized that the tremendous physical and social burden caused by hanseniasis cannot be fully expressed just in terms of statistics. However, the most important reason why we need to eliminate hanseniasis is the unique opportunity we have now to achieve the goal. This window of opportunity is the result of a confluence of four highly favourable factors involving: (a) an epidemiological opportunity, i.e. that in many parts of the world hanseniasis is already on the retreat in terms of its secular trend; (b) a technological opportunity, i.e. that MDT is highly effective in curing the disease; c) a political opportunity, i.e. that there is good national
commitment in all major hanseniasis endemic countries, and (d) a resource opportunity, i.e. that a number of donor agencies and NGOs are currently keen to support efforts towards MDT implementation and hanseniasis elimination. Such a favourable situation may not last long. The very purpose of putting together a concerted time-bound effort is to ensure that the heavy investment during a limited period would result in sustained long-term gains.

In addition, hanseniasis as a disease offers other unique epidemiological opportunities. The very uneven distribution of the disease among and within countries makes it possible to identify and target priority areas and thus focus resources and activities more effectively. Further, the current prevalence burden in hanseniasis is a result of incident cases accumulating over several years, and even decades, with the current new cases contributing to only a small proportion of the prevalence pool. This means that through MDT a very high proportion of the disease burden can be reduced even if the new cases continue to occur in small numbers. In this connection, is should be recognized that the very long incubation period in hanseniasis makes incidence reduction in the short-term very difficult as a high proportion of new cases currently occurring are probably those that had acquired their infection several years earlier and before MDT had been introduced. Thus MDT implementation today, although capable of interrupting transmission, may not result in a dramatic reduction in incidence for many years to come due to its very long incubation period. Yet another advantage with hanseniasis is that it has no other significant reservoir of infection other than the human case and, with rifampicin capable of rendering cases practically non-infectious even with a single dose, the total infective pool can be drastically reduced even in the face of some patients not taking their treatment regularly.

In relation to the understanding of the term "elimination of hanseniasis as a public health problem", it is sometimes confused with the term "eradication". Eradication envisages total and complete interruption of transmission resulting in zero disease and also the total disappearance of the organism involved. Elimination as a public health problem is a somewhat less ambitious goal in which the disease prevalence is reduced to very low levels even if complete interruption of transmission is not possible. Further, it should be emphasized that although the World Health Assembly resolution refers to global elimination, the intention is that the goal should also be attained at the national level and for larger countries also at the first subnational level.

A question often raised is why the elimination goal is set in terms of prevalence and not incidence which is likely to be a much more sensitive indicator. The main difficulty is that incidence in hanseniasis is not easy to measure through routine reporting systems which generate information only on case detection. Hanseniasis case detection has a very low correlation with incidence in view of the prolonged delay between onset of disease and detection. Recent information indicates that backlog cases contribute to more than two-thirds of the cases detected and that the delay in detection is more than three years in a large majority of instances. Secondly, due to the long incubation period, current incidence reflects transmission that had occurred several years earlier and therefore does not indicate the effectiveness of current treatment activity.

**Strategy for Global Elimination**

Following the adoption of the WHA resolution, strategies to attain elimination have been discussed at national and regional levels, and based on these WHO has developed a global strategy for elimination of hanseniasis as a public health problem. A global strategy is essential if the envisaged goal is to be achieved. The time-limited nature of the goal warrants constant review of the progress being made and the application of flexible approaches, particularly in areas where special problems are faced. A global plan of action to implement the strategy has also been developed by WHO and endorsed at the First International Conference on Elimination of Leprosy, held at Hanoi, Viet Nam, in July 1994 (6). This was further updated and endorsed at the Second International Conference on Elimination of Leprosy, held at New Delhi, India, in October 1996(7).

Hanseniasis is a disease with a very uneven distribution among and within countries. The development of health services and their capacity to implement disease control vary widely in the different hanseniasis-endemic countries. The elimination strategy will have to take into account such variations and be adaptable to suit specific needs. Stratification, target-setting and working towards the targets are essential aspects of the elimination strategy. Capacity building, prepara-
tion of action plans and resource mobilization will be the other important elements of the strategy.

If the intensification of hanseniasis control activities through MDT continues as anticipated, the expectations are that figures for estimated prevalence, registered prevalence, estimated incidence and case-detection will approximate each other nearer the year 2000.

Future Challenges

It is clear that the treatment technology for hanseniasis through MDT is working very well with very high cure rates and very low rates of relapse. So far, there has been no significant problems with drug resistance. However, with increasing use of MDT by different sectors, and some employing injudicious drug combinations, drug resistance may emerge as a problem in the future, and better and newer MDT may become necessary. Currently, more than one new combination of drugs is already under clinical trial, providing optimism that better MDT regimes capable of dealing with drug resistance problems and of reducing the period of treatment will become available in the future.

Although MDT has contributed to a rapid reduction in prevalence, its positive impact on case-detection and incidence has been limited and in many areas not easily visible, at least during the first five years of its implementation. This appears to be largely due to the long incubation period of hanseniasis as well as operational factors such as vigorous case-finding activities. However, it is expected that over a period of 5-10 years of implementation, MDT will have an impact on incidence rates. This is already seen in a number of countries (e.g. Thailand).

However, it is not clear yet as to how soon such an impact will be seen in areas where the current intensity of the disease is very high.

Even in reasonably well organized programmes it is clear that delayed detection of new cases is an important factor in the accumulation of cases resulting in not only damage to the individual patient, but also in maintaining the infection pool in the community longer than necessary. Special initiatives are being employed through support from the community so that the disease burden can be reduced more rapidly. The special initiatives include focussed projects to reach patients from under-served communities and short-term campaign approaches to reinforce the existing approaches. While the short-term costs of campaigns are high, in the long term they may turn out to be cost-effective.

The occurrence of disability is the "raison d'être" for the concern about hanseniasis and the need to deal with the disable should not be underestimated. However, it is clear that the best way to address the problem is to prevent the occurrence of disabilities and the best way to prevent disabilities is through early diagnosis and prompt treatment with MDT. This has already happened through widespread implementation of MDT. Although early diagnosis and treatment can prevent disabilities, at the time of detection a proportion of patients will still be at risk of disability as a result of damage to the peripheral nerves and such patients will need special attention. MDT programmes should incorporate simple, targeted activities to prevent disability among such at risk" patients. In spite of this, some patients will have disabilities at the time of diagnosis and will need care to limit the disabilities and those that become handicapped will need attention and care within their families and communities. The solution has to be found for individuals with residual disability after cure within the context of community based rehabilitation (CBR). In this context it is also important to take maximum advantage of the existing internal coping mechanisms within the family and community. However, the rehabilitation issues of hanseniasis should not be confused with tasks relating to the hanseniasis elimination goal.

As we progress towards the hanseniasis elimination goal and 1000k into the future it is important to foresee new situations and challenges. For instance, there is no doubt that small numbers of cases will continue to occur for several years beyond the year 2000 resulting from infections acquired in the pre-MDT period. Even small numbers of hanseniasis endemic pockets might survive as these are the places where hanseniasis would like to retreat and retrench itself in the face of the onslaught with MDT. All these call for constant vigilance and surveillance to monitor and deal with any resurgence of the disease. However, the historic experiences with hanseniasis in the past and the epidemiology of disease as we understand it now does not suggest that hanseniasis in terms of its possible resurgence will behave in ways similar to other disease such as malaria. All the same, the elimination of hanseniasis through specific interventions like MDT - particularly in poverty
stricken situations - should be monitored carefully and special monitoring mechanisms should be developed for this purpose. It is conceivable that current research into immune response to M. leprae may yield simple tools in the near future to monitor the subclinical infection in the community in a more sensitive manner. Lastly, it is hoped that the tremendous knowledge gained in the last three to four years through the currently ongoing mapping of the genome of M. leprae so that any unforeseen problem faced with hanseniasis in the twenty-first century could be addressed effectively.

**Conclusions**

Given the available and anticipated technologies and strategies for hanseniasis control, given the political will that has been generated in recent years, and given the opportunities to raise resources through various mechanisms, the attainment of eliminating hanseniasis as a public health problem by the year 2000 - in spite of difficulties foreseen in a small number of countries - should be considered a clear possibility. However, the attainment of the goal will not come easily and it really calls for the intensified efforts of all concerned, both in terms of action and mobilization of adequate resources. Such intensification is important, particularly during the next few years. For the hanseniasis-endemic countries, it is an important opportunity to solve a major public health problem, and it cannot be missed.

**References**