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Directives for Schistosomiasis Control in Endemic Areas of Brazil

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1. Introduction

The World Health Organization (WHO, 2010) estimates that 7.1 million people are infected with Schistosoma mansoni in the Americas, 95% of which in Brazil. Resolution CD49.R19 of the Pan American Health Organization (PAHO, 2009) urged Member States to commit themselves to eliminate or reduce neglected diseases and other infections related to poverty for which tools exist, to levels so that these diseases are no longer considered public health problems by year 2015. The resolution considered schistosomiasis as one of the diseases whose prevalence can be drastically reduced in the Americas with available cost-effective interventions, and approved goals and strategies to be adopted by the countries according to their health policies, epidemiological situation and health service structure.

The present chapter firstly compares similarities and differences in the main goals and primary strategies between the current recommendations of the Brazilian Schistomiasis Control Programme (PCE), Ministry of Health (MS), and those of CD49.R19, with particular emphasis on improving coverage of diagnosis and treatment. Secondly, it examines data from a representative endemic area to provide evidence that an approach including school-based diagnosis and treatment would enable short-term improved access to and coverage of the control actions targeted at the school-aged group. Thirdly, it applies spatial analysis to evaluate baseline and post-treatment prevalence data from an endemic locality to show the feasibility of mapping re-infection risk areas based on the identified “hot spots”, thus contributing to improve preventive measures such as environmental sanitation and snail control. Finally, it will be argued that the current MS strategy can be further improved towards the goal of drastically reducing prevalence in the foreseeable future taking into account the epidemiological situation and health service structure without compromising the country’s health policies.

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2. Directives for schistosomiasis control

The MS (1998, 2008) current strategy for schistosomiasis control in endemic areas focus on periodical stool surveys of whole populations through active case detection followed by prompt treatment of the egg-positives at the municipal primary health care level, together with preventive measures such as environmental sanitation and health education. It is envisaged that early, regular detection and treatment of the positives would avoid increasing morbidity and transmission among all age-groups. The main goals are to prevent the occurrence of severe forms of the disease and to reduce prevalence to less than 25% at the community level. This strategy has contributed to decrease the country-wide percentage of egg-positives from 10.4% in 1997 (290,031 positives out of 2,791,831 examined) to 5.2% in 2009 (68,952 positives out of 1,329,585 examined), confirming a downward trend observed since the mid-1990s (Coura & Amaral, 2004; Amaral et al., 2006); however, it has yielded unsatisfactory results in highly endemic areas mainly due to low population coverage (Favre et al., 2006a). Therefore, it has been advocated that control activities in such problematic areas should focus on high-risk groups like school-aged children rather than whole populations (Favre et al., 2009).

The PAHO Resolution CD49.R19 proposes that the main goal for drastically reducing schistosomiasis in the Americas is to decrease prevalence and parasite load in high transmission areas; the primary strategies are (i) regular administration of chemotherapy irrespective of infection status to at least 75% of school-aged children that live in at-risk areas, defined by a prevalence over 10% in school-aged children, (ii) improved excreta disposal systems and access to drinking water and (iii) health education. This strategy of preventive chemotherapy has been established in accordance with the WHO (2002) recommendations of targeting treatment to high risk groups without prior diagnosis in preference to the previously advocated community-wide approach. The main differences in control strategy between PAHO/WHO and the MS are summarized in Table 1 and briefly discussed below.

2.1 Diagnosis

Kato-Katz (KK) thick smears remain the method of choice for diagnosing egg-positive individuals in schistosomiasis control actions aimed at whole populations and high-risk groups from endemic areas of Brazil (MS, 2008). At present, KK kits are provided by the Immunobiological Technology Institute (Bio-Manguinhos/Fiocruz) at a cost of US$ 0.41 per exam. A single KK slide (one exam) is recommended for active-search surveys due to its operational cost-effectiveness, as increasing the number of slides or stool samples significantly increases the diagnosis sensitivity only in cases of light-intensity infections (less than 100 eggs per gram of faeces, or epg) (Rabello, 1992).

2.2 Prevalence classes

The PCE/MS recommends a cut-off value of 5% for the lower prevalence class, instead of 10% as suggested by PAHO/WHO, to compensate for the low sensitivity of one single KK slide used in stool surveys. A study from a low prevalence area in Brazil showed that screening a population with one KK slide missed 61.1% of the egg-positive individuals compared with a gold standard, indicating a sensitivity of 38.9% (Enk et al., 2008). According to this estimation, a prevalence of 5% based on one KK slide would correspond to an actual prevalence of 12.8%, whereas 10% would correspond to 25.7%. As the majority
of severe forms usually occur in areas with prevalence above 25% (Coura & Amaral, 2004), the cut-off value of 5% based on one KK slide is a more cautious approach than 10% for the low-prevalence class. Accordingly, the MS sets the cut-off value of 25% as a prevalence level from which the control measures should be intensified at the community level in order to prevent the occurrence of severe forms of the disease.

The cut-off value of 50% for the higher prevalence class based on a single KK slide implies that, in endemic localities with prevalence ≥ 50%, practically all individuals are egg-positive. Furthermore, as a significant, positive relationship between prevalence and intensity of infection is usually found in endemic areas, a prevalence of 50% or more may correspond to a geometric mean of 200 or more eggs per gram of faeces (epg) (Rabello et al., 2008). This is regarded as moderate-to-heavy intensity of infection (WHO, 2002), which requires urgent control actions.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Prevalence</th>
<th>Endemic localities</th>
</tr>
</thead>
</table>
|       | ≥ 50%      | Annual screening and treatment of all population
|       |            | Health education and environmental sanitation |
| MS (1998, 2008) | From 25% to < 50% | Biennial screening of all population followed by treatment of the positives and their household cohabitants
|       |            | Health education and environmental sanitation |
|       | From 5% to < 25% | Biennial screening of all population followed by treatment of the positives
|       |            | Health education and environmental sanitation |
|       | < 5%        | Passive case detection and treatment
|       |            | Health education and environmental sanitation |

Table 1. Strategies for schistosomiasis control recommended by the Brazilian Ministry of Health (MS) and the Pan American Health Organization (PAHO/WHO) in endemic areas.

2.3 Stool surveys
The PCE/MS currently recommends regular household stool surveys of whole populations for actively searching for infection carriers in endemic areas. The suggested survey periodicity varies according to the local prevalence class: annual for high prevalence and biennial for moderate prevalence. Passive case detection is only recommended for the low prevalence class. However, as pointed out by Favre et al. (2006a), the municipal primary
health care services of endemic areas have already reached their maximum capacity due to the overload of duties and are unable to sustain community-wide stool surveys at a regular basis. As a result, the targets agreed upon by the municipalities to fulfil the MS recommendations in those areas are far from being accomplished (Favre et al 2009).

The PAHO/WHO strategy involves stool surveys only to collect baseline data of the community prevalence prior to intervention and to follow-up its impact. Samples of 200-250 school-aged children from each ecologically homogeneous area are used for parasitological monitoring just before treatment and at 2-3 years thereafter (Montresor et al., 2002).

2.4 Treatment

Praziquantel (PZQ) is the drug of choice for treating egg-positive individuals in the course of schistosomiasis control actions. At present, it is provided by the Medicines and Drugs Technology Institute (Far-Manguinhos/Fiocruz) as 600 mg tablets at a cost of U$ 0.15 per tablet. The PCE/MS recommends a single oral dose of 60mg/kg for children of 2-15 years and 50 mg/kg for older children and adults (MS, 2008). Following official advice by the Federal Council of Medicine (CFM), treatment without prior diagnosis is not currently recommended. The only exceptions are: (i) treatment of all population in areas of prevalence ≥ 50% assessed through annual screening, which is accepted by the CFM, and (ii) treatment of household cohabitants of egg-positive individuals in areas of prevalence between 25% and 50% assessed through biennial screening.

The PAHO/WHO strategy involves school-based and community-based treatment targeted at school-aged children and other high-risks groups without prior diagnosis, as well as treatment of egg-positives following passive-case detection. The periodicity of school-based treatment varies according to the prevalence class: annual for high prevalence, biennial for moderate prevalence and twice during elementary schooling (on entry and on leaving) for low prevalence. This strategy of targeted preventive chemotherapy is viewed by the MS as a step backward for the Americas, as studies conducted in Brazil had shown that mass chemotherapy had only a transitory effect on schistosomiasis indicators (Coura & Conceição, 2010); instead, the focus should be on strengthening capacity for diagnosis and treatment of infection carriers at the primary care level and on improving environmental sanitation (PAHO, 2009). As pointed out by Rabello & Enk (2006), targeted treatment irrespective of infection status has the following implications: (i) risk of increasing drug resistance; (ii) relative high cost and low sustainability as compared to individual treatment integrated into the primary health care system; (iii) ethical requirement of informing the patient about the risks and benefits of unnecessary treatment and the right to refuse it without positive diagnosis.

Table 2 shows parasitological data from a school-based stool survey followed by treatment of egg-positives in order to illustrate the issues involved in targeting preventive chemotherapy at school-aged children from a municipality with moderate prevalence in an endemic area of Brazil. Both stool survey and treatment were performed by the municipal primary health care team. A total of 2,625 school-aged children (6-15 years) were examined in 11 schools, and all 676 (25.8%) egg-positives were treated with 60 mg/kg PZQ. If all 2,625 children were given PZQ irrespective of infection status, 1,949 (73.9%) of them would take the drug unnecessarily. Moreover, in five schools more than 80% of the children would be treated with negative diagnosis.

It is noteworthy that, although the side effects of PZQ are considered to be mild and transient (Coura & Conceição, 2010), they are a major factor discouraging people from taking the drug (Fleming et al., 2009; Garba et al., 2009; Souza-Figueiredo et al., 2010). A
Table 2. Differences in treatment delivery to school-aged children between selective (positive only) and targeted (positive and negative) chemotherapy. The data are from school-based diagnosis followed by treatment of egg-positives carried out at the primary health care service from the municipality of Araçoiaba, North-east Brazil.
recent multi-country randomized controlled clinical trial on the efficacy and safety of single
dose PZQ 40-60 mg/kg among adolescents (10-19 years) has shown that overall 78% of the
patients reported adverse events up to four hours post-treatment; the most frequent were
abdominal pain (40.4%), diarrhoea (17.5%), headache (10.7%), nausea (9.9%), vomiting (9.0)
and dizziness (8.0%) (Olliaro et al., 2011). It is also worth mentioning that the bitter, disgusting
taste of PZQ tablets is a major drawback for its administration among school-aged children
(Meyer et al., 2009). Further evidence is needed to evaluate whether the bitter taste and side
effects of PZQ can lower compliance, particularly in the absence of positive diagnosis.

2.5 Integrated measures
Some countries in sub-Saharan Africa have been successful in drastically reducing
schistosomiasis infection using mass treatment with PZQ among school-aged children in
high prevalence areas (Kabatereine et al., 2006; Kolaczinski et al., 2007; Touré et al., 2008;
Tohon et al., 2008). However, to obtain sustained, satisfactory results mass treatment
coverage should be kept around 90%, which has proven challenging over the years. In
Brazil, selective treatment has reduced prevalence of infection in the short-term and
morbidity in medium to long-term periods, but has not been sufficient to control disease
transmission (Coura & Conceição, 2010). Studies from different endemic areas have shown
that treatment strategies should be accompanied by auxiliary measures according to the
epidemiological and geographical settings of each region (Guo et al., 2005; Wang et al., 2009;
Sarvel et al., 2011). Accordingly, the MS advocates integrated measures combining selective
treatment with environmental sanitation and health education incorporated into the
primary health care system, as follows:

Recommended environmental sanitation measures include safe-water supply, adequate
sewage collection and disposal, proper land use and occupation, soil drainage and control of
intermediate snail hosts. Large-scale measures may be covenant between the municipal
and state level according to specific epidemiological requisites and complying with the
environmental legislation. Local, small-scale measures to control intermediate host snails
may include drainage, removal of vegetation and debris in habitats such as waste-water
ditches and streams; methods aimed at direct elimination of snails such as molluscicide
application are acceptable only under exceptional circumstances (MS, 2007)

Strategies of information, education, and communication (IEC) are also given special emphasis
by the MS. A new approach to health education is recommended, involving interdisciplinary
actions both in the school setting and in the community. As proposed by Massara & Schall
(2004), the education process is seen not only as the acquisition of abilities but also as the
building of affective and social relationships as well as environmental awareness.

As pointed out by Pieri & Favre (2007), an integrated approach aimed at improving
coverage of both diagnosis and treatment and intensifying the use of auxiliary preventive
measures is of paramount importance for scaling up the Brazilian schistosomiasis control
programme within the Unified Health System (SUS). As the current directives of the MS and
PAHO/WHO are not without drawbacks, an alternative strategy may be proposed to offset
the issues raised.

3. An alternative strategy
An alternative strategy aiming to improve the MS current directives by further integrating
the control actions into the primary health care system and involving diagnosis and
selective treatment of school-aged children in the school setting is given in Table 3. It takes into account the operational difficulties faced by the most troubled municipalities without compromising the programme main goals. Thus, stool surveys are targeted at school-aged children as their prevalence is a suitable indicator of the community prevalence level (Guyatt et al 1999; Rodrigues et al 2000; Pereira et al 2010). Treatment is indicated in case of egg-positive diagnosis in conformity with prescribed indications and contraindications. Community-wide mass treatment is only considered if prevalence among school-aged children is more than 50%; treatment of cohabitants without prior diagnosis is not indicated.

### Table 3. An alternative strategy for schistosomiasis control in endemic areas of Brazil.

In endemic areas of Brazil for which there are reliable estimates of infection at the locality level, most prevalence levels are between 5% and 50% (Favre et al 2006b; Barbosa et al 2006). This situation is exemplified in Table 4 showing baseline parasitological data from stool surveys carried out in representative localities of an endemic area of Pernambuco, extracted from Pereira et al (2010). Those data may be used to compare the three strategies shown here as regards diagnosis and treatment.

According to the MS directives, in the locality of Paroés (prevalence 5%) only passive case detection should be carried out, as a part of the primary health care routine; in the eight localities with prevalence from 5% to 50%, all 4,934 residents should be screened and the 694 egg-positives, treated; in the five localities with prevalence from 25% to 50%, all 3,141 residents should be screened, and the 1,012 egg-positives and their 1,815 cohabitants (not in the table), treated; in the locality of Araújo (prevalence ≥50%), all 181 residents should be screened and treated. Overall 8,256 exams and 3,702 treatments should be performed.

In contrast, according to PAHO/WHO recommendations, all children aged 6-15 years should be screened except in Caricé and Sotave (where a representative sample of 250 children would be selected in each), totalling 1,447 exams and 2,088 treatments. It is of concern that this strategy would result in at 1,553 (74.4%) school-aged children being treated without positive diagnosis.

According to the proposed alternative strategy, in the locality of Paroés (prevalence 5%) only passive case detection should be carried out, as a part of the primary health care routine; in the 13 localities with prevalence from 5% to 50%, all 1,983 school-aged children should be screened and the 487 egg-positives, treated; in the locality of Araújo (prevalence ≥50%), all 68 school-aged children should be screened and all 181 residents, treated. On the whole, 2,051 exams and 668 treatments would be performed. It should be noted that none of the 1,553 school-aged children without positive diagnosis would receive treatment.
<table>
<thead>
<tr>
<th>Locality</th>
<th>Number residents</th>
<th>Number examined</th>
<th>Number positives</th>
<th>% positives</th>
<th>Number residents</th>
<th>Number examined</th>
<th>Number positives</th>
<th>% positives</th>
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<td>68</td>
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<td>40.2</td>
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<td>409</td>
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Table 4. Parasitological data from whole populations and school-aged children in representative localities of an endemic area of schistosomiasis in Brazil. The data were extracted from Pereira et al (2010)

It must be borne in mind that population coverage of 75.3%, as observed in the given example, is rarely achieved by the health teams in the endemic areas. In fact, stool surveys of whole populations in the highly endemic Rainforest Zone of Pernambuco from 2003 to 2006 reached 19.7% of the population at risk (Favre et al, 2009); more recently, from 2007 to 2010, the coverage in the same zone was increased by only 4 percentage points to 23.7% (MS, 2011). This low coverage is due to the fact that the municipal authorities annually set covenanted quantitative targets for population diagnosis and treatment in line with the Priority Action Plan in Health Surveillance (PAP-VS) adjusted to the availability of personnel and financial resources. In the Rainforest Zone of Pernambuco the average target for 2006-2007 has been only 13.7% of the population at risk (Table 5).

It has been argued that the PAP-VS target for diagnosis and treatment set by the most troubled municipalities from endemic areas may be better accomplished if it is applied to school-aged children (Pieri & Favre, 2007). Firstly, school-aged children are particularly vulnerable to schistosomiasis and play an important role in maintaining transmission. Secondly, school-aged children are accessible and generally show good compliance. Thirdly, school-based actions involving teachers and children’s families may help the health teams to scale up control actions as needed. Fourthly, detecting and treating infection in school-aged children prevent infection from increasing as they reach the pre-adult stage. Fifthly, the focus on school-aged children is a more realistic, feasible strategy to accomplish the PAP-VS target; as it can be seen in Table 5, the total target of 172,500 exams set for 2006-2007 would exceed in 3.6% the population in that age-group.
<table>
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TOTAL 12.2 1,262,455 222,002 172,500 13.7 103.6

(* Source: Brazilian Institute of Geography and Statistics (IBGE)
(**) Source: State Health Secretariat of Pernambuco (SES-PE).

Table 5. Prevalence of schistosomiasis, population data* and number of stool exams targeted for 2006-2007 by the Priority Action Plan in Health Surveillance (PAP-VS)** for the municipalities of the Rainforest Zone of Pernambuco state. The percentages of 2006-2007 PAP-VS target for all ages and school-aged children (7-14 yrs) are also given.

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It must be stressed that the proposed alternative of targeting diagnosis and treatment at school-aged children aims to assist the municipalities that do not have enough resources to follow the current MS recommendations of covering whole populations, as is the case of Araçoiaba (Table 6).

- **Geographic coordinates**: 07° 47' 24" S 35° 05' 27" W
- **Area**: 92 km²
- **Main economic activity**: cash-crop agriculture for the production of alcohol and sugar.
- **Population (2009)**:
  - Total: 17,484
  - Municipal Human Development Index (IDH-M): 0.637;
  - Basic Education Index (IDEB): 2.8
- **Schistosomiasis status**
  - Covenanted target: (2005 – 2009): 7,346 exams (42% of the population)
  - Diagnosis coverage (2005 -2009): 6,070 exams (34.7% of the population)
  - Treatment compliance (2005 - 2009): 1,320 patients (75.9% of the positives)
  - Reasons for no treatment: absence (18.1%), contraindication (6.0%)
  - Prevalence: 40.9% (2005), 32.2% (2006), 30.2% (2007), 19.8% (2009)
- **School-aged children (6 -15 yrs)**:
  - Total: 3,418;
  - Enrolled: 3,273 (95.8%);
  - Drop-out: 13.6%
  - Elementary schools: 11

Table 6. Demographic and parasitological data of Araçoiaba, a municipality from the endemic area of North-east Brazil.

That municipality holds a relatively low index of human development (0.637) in the endemic area of schistosomiasis in Pernambuco. The covenanted target for schistosomiasis diagnosis between 2005 and 2009 was only 42% of the population at risk, but the actual cumulative coverage was even lower, 34.7%. Of the 6,070 exams carried out during that period, 1,739 (28.6%) were positive. It can be argued from the data on school-aged children that the elementary schools would provide a satisfactory setting for implementing control actions in the municipality. Thus, 95.8% of the school-aged children are enrolled at school and the drop-outs are negligible (13.6%) may be reached out from the school records. According to the MS (2011), only two of the 99 endemic municipalities surveyed in Pernambuco between 2005 and 2009 had higher prevalence than Araçoiaba, namely, Escada (33.1%) and João Alfredo (47.3%). It is of note that treatment compliance was satisfactory (75.9% of the egg-positives), the main reason for non-treatment being absence (18.1%). As the contraindication cases were considerable (105 out of 1739), the importance of well-trained health staff during this phase cannot be underestimated.

4. Spatial analysis

Spatial analysis and Geographic Information Systems (GIS) are important tools that can be used for identifying environmental risk factors and delimiting risk areas of schistosomiasis, leading to optimization of resources and improvement of actions for the specific conditions.
Fig. 1. Kernel intensity estimates of egg-positive subjects at baseline (Day 0), 21 days, 180 days and 360 days after treatment with PZQ 40 mg/kg or PZQ 60 mg/kg. The vertical bars indicate the kernel intensity scale. The original data are from Galvão et al., 2010.
of the disease (Bergquist, 2002). Thus, the MS recommends that data from stool surveys should include the geographic coordinates of the households obtained by a Global Positioning System (GPS) receptor for later insertion on a digitized map and a georeferenced database. As egg-positive households tend to cluster within communities due to focal characteristics of risk factors and transmission, kernel density exploratory analysis has been of help to assess differences in their spatial distribution patterns and to relate them to potential sources of risk in endemic areas of schistosomiasis in Brazil (Gazzinelli et al., 2006; Araújo et al., 2007; Galvão et al., 2010; Cardin et al., 2011) and China (Zhang et al., 2009).

Figure 1 illustrates the use of kernel density estimator for visually identifying risk areas and comparing the magnitude of spatial clustering in individual infection before and up to one year after treatment with either 40mg/kg or 60mg/kg PZQ single dose. A bandwidth of 75 meters was used, and the colour pattern of the intensity scale varied from white (lowest intensity kernel) to red (highest intensity kernel). The data are from Galvão et al. (2010). Before treatment (D0) the clusters of egg-positives were similar with respect to intensity and extent, as the individuals were randomly assigned to each treatment group. The area-wide white seen at D21 reflects the fact that all individuals became egg-negative at 21 days after treatment. The highest kernel intensity and extent of clusters in the group of 40 mg/kg than in the 60 mg/kg, both at 180 and 360 days, indicate that reversion of individuals to egg-positive up to one year after treatment was higher in the lower-dose group. Figure 1 also indicates that infection tended to return to the pre-treatment level, although they might take longer among the patients who received the higher PZQ dose.

Based on this information, it can be recommended that primary health care teams should carry out snail surveys to identify potential transmission foci and implement local environmental sanitation and other preventive measures as appropriate.

5. Concluding remarks

It is clear from the above explanation that the current MS strategy for schistosomiasis control can be further improved without compromising the country’s health policies, especially as regards the ethical requirement of delivering treatment only to egg-positive diagnosis. It is expected that the health authorities will incorporate sustained school-based actions for scaling up coverage and achieving rapid impact on schistosomiasis, particularly in the most troubled municipalities. However, the primary health care teams should include community-wide control actions as soon as the critical situation is overcome.

6. References


Oliaro, P. L.; Vaillant, M. T.; Belizario, V. J.; Lwambo, N. J. S.; Ouldabdallahi, M.; Pieri, O. S.; Amarillo, M. L.; Kaatano, G. M.; Diaw, M.; Domingues, A. L. C.; Favre, T. C.; Lapujade, O.; Alves, F. & Chitsulo, L. (2011). A multicentre randomized controlled trial of the efficacy and safety of single-dose praziquantel at 40 mg/kg vs. 60 mg/kg for treating intestinal schistosomiasis in the Philippines, Mauritania,


In the wake of the invitation by InTech, this book was written by a number of prominent researchers in the field. It is set to present a compendium of all necessary and up-to-date data to all who are interested. Schistosomiasis or blood fluke disease, also known as Bilharziasis, is a parasitic disease caused by helminths from a genus of trematodes entitled Schistosoma. It is a snail-borne trematode infection. The disease is among the Neglected Tropical Diseases, catalogued by the Global Plan to combat Neglected Tropical Diseases, 2008-2015 and is considered by the World Health Organization (WHO) to be the second most socioeconomically devastating parasitic disease, next to malaria. WHO demonstrates that schistosomiasis affects at least 200 million people worldwide, more than 700 million people live in endemic areas, and more than 200,000 deaths are reported annually. It leads to the loss of about 4.5 million disability-adjusted life years (DALYs).

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