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Prevention, control, and elimination of neglected diseases in the Americas: Pathways to integrated, inter-programmatic, inter-sectoral action for health and development
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General Notes on the Revised Ms.: We believe we have responded to all of the reviewer’s comments and suggestions (which were excellent). Some general comments on the changes made are:

1. Both reviewers recommended shortening the first two sections dealing with background information, including the section “Background: Multiple Dimensions of Global Poverty” and “Discussion: The Case for a Different Approach”. The specific changes we have made are described in detail in the point-by-point responses to reviewer’s section that immediately follows these general notes.
2. We have added the references that the reviewer suggested as they all helped to strengthen the paper. We specified these below in the minor and discretionary revision sections. We also deleted some of the original references in order to shorten certain sections, which required us to renumber most of the references.
3. We have also reduced the spaces between the bullet points in the paper to make the spacing between bullets consistent throughout the paper.
4. We have replaced the word percent with % throughout the paper.

Point-by-Point Responses to Reviewer’s (Dr. Juerg Utzinger) Comments:

General Appraisal of the Work:

1. The reviewer recommended that some sections be shortened considerably, specifically the section titled “Background: Multiple Dimensions of Global Poverty”.
   a) We deleted the title of the first section “Unmet Challenges” and replaced it with “Broader Understanding of Poverty.
   b) We deleted the first and third paragraph of the paper on former page 4 and 5.
   c) We shortened the quote taken from the Global Poverty Report on former page 4.
   d) We deleted the first paragraph under the “Poverty and Conflict” section.
   e) We deleted the quote from the second paragraph under the “Poverty and Conflict” section including former reference 9.
f) We deleted the last line in the second paragraph (and removed former reference 16) and the quote in the third paragraph from the “Poverty and Conflict” section.
g) We deleted the first two lines of the first paragraph under the section titled “The Final Straw: Disease”.
h) We changed the last line of the first paragraph under the section “Neglected Diseases” to read as follows: The NDs also contribute to the overall burden of communicable diseases in the region.
i) We shortened the first line of the second paragraph under “Neglected Diseases” on new page 5 to the following: Although medically diverse, NDs share features that allow them to persist in conditions of poverty where they frequently overlap [20].
j) We deleted the words “prevent, control and eliminate” and replaced them with “control” in the second paragraph under “Neglected Diseases”.
k) We reworded the sentence in the first paragraph under “Neglected Populations” to read as follows: In some areas women and children may be considered neglected populations due to their limited access to health and social support services.
l) We deleted the first paragraph under “Millennium Development Goals”
m) We deleted the first two lines of the third paragraph under “Millennium Development Goals”.
n) We reworded the last line in the third paragraph under “Millennium Development Goals” to read as follows: An integrated strategy which includes the NDs supports all eight of the MDGs including ten out of the eighteen Millennium Declaration targets.
o) We condensed the box of “Examples of How to Integrated ND Control Supports the MDGs” which is on new page 6 by deleting some extraneous text within each bullet point. It now reads as follows:

- De-worming cost-effectively improves the nutritional status of poor children, contributing to the goal of **Eradication of Hunger (MDG-1)** [22, 23, 24, 25], and combines well with vitamin A supplementation.
- De-worming improves school attendance and thus increases the chances of completing primary education, contributing to the goal of **Primary Education (MDG-2)** [22, 23, 26]
- Promoting income-generating activities such as micro-enterprises for poor women to produce insecticide-treated bed nets, combined with educating mothers in child care and health skills contributes to the **Empowerment of Women (MDG-3)** [27].
- Reducing the combined burden of multiple parasitic diseases (poly-parasitism) [28] and micronutrient deficiencies contributes to the **Reduction of Child Mortality (MDG-4)**.
- Controlling iron deficiency and anemia due to hookworm results in the **Improvement of Maternal Health (MDG-5)** [29].
- Combating NDs contributes to the goal of **Combating HIV, Malaria and other Diseases (MDG-6)** [30] especially where co-
infection compounds the health problems of AIDS and malaria victims.

- Implementing environmental sanitation (safe excreta and wastewater disposal) reduces fecal contamination of soil, water, and irrigated crops, contributing to Ensuring Environmental Sustainability (MDG-7).
- Inter-sectoral approaches to ND prevention and control involve establishing extended partnerships compatible with the goal of Global Partnerships for Development (MDG-8) [31].

p) We deleted the paragraph under the box of “Examples of How to Integrated ND Control Supports the MDGs”.

q) We deleted part of the first line of the first bullet under the box of “Examples of How to Integrated ND Control Supports the MDGs” so that it now reads as follows: How can an integrated ND agenda provide entry points to unify and coordinate the various programs and sectoral agencies involved?

r) We deleted part of the second line of the first paragraph under “Rationale for an Integrated Approach” so that it now reads as follows: The introduction of basic public health measures in communities would significantly reduce the burden of a number of diseases where these elements play an important role.

s) We deleted the last line of the first paragraph under “Rationale for an Integrated Approach” on former page 9.

t) We deleted the second, third, fourth, and sixth line of the second paragraph under “Rationale for an Integrated Approach” (on former page 9) as well as revised some of the language used so that it now reads as follows:

i. There exists an urgent need to develop innovative tools to combat NDs, particularly ones that move away from a single disease-centered approach to those that focus on a population health approach. The population approach encompasses a broader notion of health which recognizes the range of social, economic and physical environmental determinants that contribute to health. By providing opportunities for integrative solutions to health conditions, and by fostering participatory approaches at the local level, these neglected populations will be better equipped to identify determinants that contribute to poor health, thereby allowing them to exercise their basic human rights, and ultimately break out of the cycle of poverty and illness.

u) We combined the paragraphs discussing integrated, inter-programmatic, and inter-sectoral approaches under “Integrated, Inter-Programmatic, and Inter-sectoral Approaches”.

v) We reworded the second line of the second paragraph on new page 8 discussing the word “integrated” so that it now reads as follows: These interacting elements may be assessed by examining the available resources within an equity framework.
w) We deleted the last line of the second bullet under “Integrated, Inter-
Programmatic, and Inter-sectoral Approaches” on former page 10.

x) We reworded the first sentence of the first paragraph under “Integrated,
Inter-Programmatic, and Inter-sectoral Approaches” so that it now reads as
follows: Many complex issues, such as housing for the urban poor and
local economic development require a wide range of resources and
abilities that integration, inter-programmatic and inter-sectoral efforts are
the only viable approaches to effectively address them over the long-term
and help to reduce the duplication of activities.

y) We revised the fifth paragraph under “Integrated, Inter-Programmatic, and
Inter-sectoral Approaches” so that it now reads as follows: The
combination of these approaches are emerging as an increasingly
important development strategy. Current trends in the LAC region include
a decline in international development funding, the slow decentralization
or devolution of national government power and function to municipal and
local entities, heightened involvement of the private sector in social issues,
and an increasing number of civil society actors [37]. This implies the
need for more effective coordination among government programs,
increased transparency through participatory approaches and increased
access to better information for all stakeholders.

z) We deleted the last paragraph under “Integrated, Inter-Programmatic, and
Inter-sectoral Approaches” on former page 11.

Minor Essential Revisions:

1. Additions made as suggested by reviewer. We have explained why we use the
term “neglected diseases” instead of “neglected tropical diseases” on new page 5,
paragraph 4.

2. Changes made as suggested by reviewer. We have summarized the bullet points
in tabular form, as well as added a line to the first bullet addressing the number of
people in the Latin America and Caribbean region that live on less than $1 and $2
a day.

3. Changes made as suggested by reviewer. We have consulted Hotez’s list of 13
neglected tropical diseases and added Buruli ulcer to the list, as well as replaced
intestinal worms with soil-transmitted helminthes and ascariasis, trichuriasis and
hookworm infection. We have not included all 13 because all of them are not
relevant to the Latin America and Caribbean region.

4. Changes made as suggested by reviewer. We have included the reference
(Brooker et al. 2006, Int J of Parasitol); see new reference number 20 (cited on
new page 5). This article is a useful reference on multiple species parasitic
infections in the Latin American and Caribbean region.

5. Changes made as suggested by reviewer. We have cross-referenced both articles
the reviewer mentioned (Lancet Editorial, 4 December 2004; WHO 2005
Deworming for Health and Development); see new reference number 22 (cited on
page 6) and 23 (cited on page 6). The box as well as the paragraph preceding the
Changes made as suggested by reviewer. We have included the reference (Ezeamama et al JID, 2005); see new reference number 28 (cited on new page 6).

Changes made as suggested by reviewer. We have included the two references (Hotez et al, PloS Med, 2006; Lammie et al, Trends in Parasitol, 2006); see new reference numbers 34 and 35 (cited on new page 8). We have also removed the words “innovative and cost effective” before solutions, as more work needs to be done to establish this as the case. We also added lymphatic filariasis to the list of diseases.

Changes made as suggested by reviewer. The word “seven” was replaced by “eight”, as there are actually eight initiatives.

Changes made as suggested by reviewer. The words “human rights” were taken out as it is mentioned twice, and the full phrase was substituted by the abbreviation “STIs”.

Changes made as suggested by reviewer. We added malaria to the list of parasitic diseases that increase due to microdams and irrigation projects. We have cross-referenced the article the reviewer suggested (Keiser et al, 2005, Amer J Trop Med & Hyg); see new reference number 50 (cited on page 13). To address the comment that there is a paucity of studies examining the effect of small dams on schistosomiasis and malaria we have revised the text as follows:

Similar to the case of large dams, research in several countries examining the impact of microdams and irrigation projects has shown that these projects can contribute to an increase in favorable environmental conditions for the transmission of parasitic diseases during the dry season, specifically schistosomiasis, intestinal helminths and malaria.

Changes made as suggested by reviewer. We have included the reference (Keiser et al J Am Mosq Control Assoc, 2002); see new reference number 53 (cited on new page 13).

Changes made as suggested by reviewer. We have included the reference (de Castro PNAS, 2006); see new reference number 56 (cited on new page 14). We have revised the text as follows:

As these geographical areas are further developed, strategies to control malaria and other diseases require a combination of preventive and curative methods well as close collaboration between the health and agricultural sectors [56].

Changes made as suggested by reviewer. Both terms were replaced by Trichuris trichiura, and Schistosoma mansoni as suggested.

Changes made as suggested by reviewer. We have revised text as follows:

By supporting programs to strengthen the environmental health agenda, PAHO also sought to strengthen the leadership and advisory capabilities of the region’s health ministries and improve community mobilization and inter-sectoral coordination.

Changes made as suggested by reviewer. Term was replaced by schistosomiasis japonica.
16. Changes made as suggested by reviewer. We have consulted the articles the reviewer mentioned and included text about the “one health” concept on new page 26 paragraph 5 and included both of them as references, (Schelling et al, BMJ 2005; Zinsstag et al, Lancet 2005); see new reference number 95,96 (cited on new page 26). We have added the following sentence, which describes the “one health” concept in relation to mobile communities:

Per the “one health” concept, an integrated human and animal-health system for specific mobile and remote sedentary populations enhances zoonoses detection and control, and offers a novel perspective for strengthening and shaping health systems in hard-to-reach rural communities [95, 96].

Discretionary Revisions

1. Changes made as suggested by reviewer. Word “disastrous” was deleted.
2. Changes made as suggested by reviewer. We have revised the text as follows and moved it to the section “Millennium Development Goals” on new page 6 paragraph 3:

   Among this agenda are the explicit goals of eradicating extreme poverty and hunger (MDG #1), and ensuring environmental sustainability (MDG #7).

3. Changes made as suggested by reviewer. We have replaced “towards” with “toward” to be consistent with US English on new page 4 paragraph 1.
4. Changes made as suggested by reviewer. We have replaced “primary” with “school-age” on new page 4 in the box.
5. Changes made as suggested by reviewer. We have added a hyphen to “poverty-related” on new page 4 in the box.
6. Changes made as suggested by reviewer. We have replaced “con-infection” with “co-infection” on new page 7 in the box.
7. Changes made as suggested by reviewer. We have replaced “the perfect” with “an ideal” on new page 7 paragraph 2.
8. Changes made as suggested by reviewer. We have included a sentence discussing the concept of economies of scale, and added the reference (Utzinger & De Savigny, PloS Med 2006); see new reference number 32 (cited on new page 7).

   It is now an opportune time to link an integrated ND strategy with the newly emerging global partnerships addressing HIV/AIDS, tuberculosis and malaria, in order to take advantage of the economies of scale that occur during the scaling up process of these global initiatives [32].

9. Changes made as suggested by reviewer. We have replaced the word “factors” twice with “determinants” on new page 7, paragraph 3.
10. Changes made as suggested by reviewer. We deleted the words “proper assessment” on new page 8, paragraph 2 and revised the text as follows:

    These interacting elements may be assessed by examining the available resources within an equity framework.

11. Changes made as suggested by reviewer. We have made the letters in “Inter-Sectoral Partnerships” lower case, as well as removed the abbreviation “ISP”, 
because there is no reference to this abbreviation anywhere else in the paper, nor
does it appear in the list of abbreviations section.

12. Changes made as suggested by reviewer. We have spelled out the abbreviation
NGOs on new page 8 paragraph 2.

13. Changes made as suggested by reviewer. We have made certain to abbreviate
“Latin America and the Caribbean” to “LAC” in every instance, subsequent to its
introduction on new page 4 in the box.

14. Changes made as suggested by reviewer. We decided to include alcohol abuse as
a factor that increases the burden of disease in indigenous populations on new
page 9 in paragraph 1 of the section titled “Health of the Indigenous Peoples of
the Americas Program”.

15. Changes made as suggested by reviewer. We have added behavioral to the types
of factors that influence the transmission of NDs on new page 10 paragraph 3.

16. Changes made as suggested by reviewer. We have added a period to the last time
of paragraph 3 on new page 10.

17. Changes made as suggested by reviewer. We have replaced “clean safe water”
with “clean water” in paragraph 4 on new page 10.

18. Changes made as suggested by reviewer. In order to capture the point that
aquaculture and other water resource projects may be a risk factor in spreading
disease we have added the following sentence to paragraph 1 on new page 11:

Though natural resource development projects have sometimes been
linked to the spread or intensification of some parasitic diseases, well-
planned development projects which involve local communities in
planning and implementation can prove beneficial [42].

We have added the reference (Keiser & Utzinger EID 2005); see new reference
number 42. We have removed the example of aquaculture microenterprise in
paragraph 1 on new page 14.

19. Changes made as suggested by reviewer. We have replaced “addressing” with
“achieving” in paragraph 3 on new page 11.

20. Changes made as suggested by reviewer. We revised the text by giving a
definition of poverty and changing the number of the rural poor from 63% to
64%. We replaced the reference with IFAD Strategy for Rural Poverty Reduction,
2002; see new reference 45 in paragraph 2 on new page 12. It now reads as
follows:

Poverty rates in rural areas are far higher than in the urban areas, with
64% of the rural population living below the poverty line [45]. The
poverty line is calculated according to a ‘basic basket’ of goods and
services that take into account prevailing wage and price structures [45].

21. Changes made as suggested by reviewer. We have replaced geohelminth with
soil-transmitted helminth in paragraph 1 on new page 14.

22. Changes made as suggested by reviewer. We replaced DEC with
diethylcarbamazine, followed by its abbreviation in box on new page 14.

23. Changes made as suggested by reviewer. We replaced “Agenda” with “agenda”
in line 10 from the bottom, on new page 15.
24. Changes made as suggested by reviewer. We added more details with regard to "periodic chemotherapy" starting on line 5 on new page 19. The revised text is as follows:

The strategy is based upon the integration and inter-sectoral efforts to deliver periodic chemotherapy (once or twice a year depending upon the prevalence and worm burden in the area) to schoolchildren in high-risk areas, intense health and hygiene education, and improvement of sanitation and a safe water supply.

25. Changes made as suggested by reviewer. We replaced “dictate” with “govern” in paragraph 2 on new page 19.

26. Changes made as suggested by reviewer. We abbreviated MDGs in paragraph 2 on new page 20, as well as every other instance subsequent to its introduction.

27. Changes made as suggested by reviewer. We have replaced the word “percent” with “%” throughout the paper.

28. Changes made as suggested by reviewer. We replaced “adequate safe water” with “clean water” in paragraph 2 on new page 23.

29. Changes made as suggested by reviewer. We replaced “seventies” with “1970s” in paragraph 3 on new page 23.

30. Changes made as suggested by reviewer. We changed 178 to 179, as that is the exact number of governments that adopted Agenda 21 in paragraph 5 on new page 23.

31. Changes made as suggested by reviewer. We replaced “lower the prevalence of NDs” with “lower the burden due to NDs” in paragraph 2 on new page 24.

32. Changes made as suggested by reviewer. We replaced “neglected diseases” with “NDs” in the last paragraph on the new page 27, and in every other instance in the paper where it appears subsequent to its introduction.

33. Changes made as suggested by reviewer. We replaced JE with JPE and SA with SKA in the Acknowledgements section as well as in the Author’s contributions section.

34. Changes made as suggested by reviewer. We have abbreviated all journal titles in the references section. We changed the former reference 28 which is now new reference 33 to read “WHO Tech Rep Ser, No. 912”. We corrected the spelling of Parassitologia in former reference 41, which is now new reference 51.

Dr. Carlos Franco-Paredes’ Discretionary Revisions

1. Changes made as suggested by reviewer. We have shortened the first two sections as recommended. The details on the edits can be found above under the Point-by-point responses to Dr. Juerg Utzinger’s comments on page 1.