PLOS Neglected Tropical Diseases

Economic performance and cost-effectiveness of using a DEC-salt social enterprise for eliminating the major neglected tropical disease, lymphatic filariasis

--Manuscript Draft--

Manuscript Number:	PNTD-D-18-01969R1
Full Title:	Economic performance and cost-effectiveness of using a DEC-salt social enterprise for eliminating the major neglected tropical disease, lymphatic filariasis
Short Title:	Performance and effectiveness of using a DEC-salt social enterprise for LF elimination
Article Type:	Research Article
Keywords:	Mosquito-borne neglected tropical diseases; lymphatic filariasis; DEC-medicated salt; cost-revenue analysis; financial forecasting, net cash flow; break-even; data-driven parasite transmission modeling; Mass Drug Administration; cost-effectiveness analysis.
Corresponding Author:	Edwin Michael, Ph.D. University of Notre Dame Notre Dame, Indiana UNITED STATES
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	University of Notre Dame
Corresponding Author's Secondary Institution:	
First Author:	Swarnali Sharma
First Author Secondary Information:	
Order of Authors:	Swarnali Sharma
	Morgan E. Smith
	James Reimer
	David B. O'Brien
	Jean M. Brissau
	Marie C. Donahue
	Clarence E. Carter
	Edwin Michael, Ph.D.
Order of Authors Secondary Information:	
Abstract:	Background Salt fortified with the drug, diethylcarbamazine (DEC), and introduced into a competitive market has the potential to overcome the obstacles associated with tablet-based Lymphatic Filariasis (LF) elimination programs. Questions remain, however, regarding the economic viability, production capacity, and effectiveness of this strategy as a sustainable means to bring about LF elimination in resource poor settings. Methodology and Principal Findings We evaluated the performance and effectiveness of a novel social enterprise-based approach developed and tested in Léogâne, Haiti, as a strategy to sustainably and cost-efficiently distribute DEC-medicated salt into a competitive market at quantities sufficient to bring about the elimination of LF. We undertook a cost-revenue analysis to evaluate the production capability and financial feasibility of the developed DEC salt social enterprise, and a modeling study centered on applying a dynamic mathematical model localized to reflect local LF transmission dynamics to evaluate the cost-

effectiveness of using this intervention versus standard annual Mass Drug Administration (MDA) for eliminating LF in Léogâne. We show that the salt enterprise because of its mixed product business strategy may have already reached the production capacity for delivering sufficient quantities of edible DEC-medicated salt to bring about LF transmission in the Léogâne study setting. Due to increasing revenues obtained from the sale of DEC salt over time, expansion of its delivery in the population, and greater cumulative impact on the survival of worms, this strategy could also represent a significantly more cost-effective option than annual DEC tablet-based MDA for accomplishing LF elimination.

Significance

 A social enterprise approach can offer an innovative market-based strategy by which edible salt fortified with DEC could be distributed to communities both on a financially sustainable basis and at sufficient quantity to eliminate LF. Deployment of similarly fashioned intervention strategies would improve current efforts to successfully accomplish the goal of LF elimination, particularly in difficult-to-control settings.

Suggested Reviewers:	Eric Ottesen, PhD Director, The Task Force for Global Health eottesen@taskforce.org Dr Ottesen is an expert on NTDs, particularly with respect to the epidemiology, immunology and control of LF. He was also instrumental in developing the global strategy to eliminate LF. Given this research, programmatic, and policy backgrounds, he is eminently suited to review the present work.
	Frank O Richards, PhD Director, Carter Center frank.richards@cartercenter.org Dr Richards has long expert experience with developing evidence-based policy and interventions for controlling LF and other NTDs. Given his clinical and epidemiological training and expertise in evaluating best options for eliminating LF, he will be particularly suited to appraising the validity of the methods used in this paper, including the economic methodology applied.
	James W Kazura, PhD Distinguished University Professor, Case Western Reserve University School of Medicine jxk14@case.edu Prof. Kazura is a world expert on the epidemiology and control of LF and other vectorborne diseases, and will provide an informed assessment of the present work and its value in current attempts to develop the intervention arsenal against LF.
	Moses J Bockarie, PhD Head Africa Office, European and Developing Countries Clinical Trials Partnership bockarie@edctp.org Works on field trials and evaluations of interventions against lymphatic filariasis, and development of LF policy at DfiD, EU and WHO. Will thus provide a fair assessment of the value of the social enterprise as a strategy for LF elimination.
Opposed Reviewers:	
Additional Information:	
Question	Response
Financial Disclosure Enter a financial disclosure statement that describes the sources of funding for the work included in this submission. Review the submission guidelines for detailed requirements. View published research articles from PLOS NTDs for specific examples.	The author(s) received no specific funding for this work.

This statement is required for submission and **will appear in the published article** if the submission is accepted. Please make sure it is accurate.

Unfunded studies

Enter: *The author(s) received no specific funding for this work.*

Funded studies

Enter a statement with the following details:
- Initials of the authors who received each award
- Grant numbers awarded to each author
- The full name of each funder
- URL of each funder website
- Did the sponsors or funders play any role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript?
- **NO** - Include this sentence at the end of your statement: *The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*
- **YES** - Specify the role(s) played.

* typeset

Competing Interests	The authors have declared that no competing interests exist.
Use the instructions below to enter a competing interest statement for this submission. On behalf of all authors, disclose any competing interests that could be perceived to bias this work—acknowledging all financial support and any other relevant financial or non-financial competing interests.	

This statement **will appear in the published article** if the submission is accepted. Please make sure it is accurate. View published research articles from *PLOS NTDs* for specific examples.

* typeset

Data Availability

Authors are required to make all data underlying the findings described fully available, without restriction, and from the time of publication. PLOS allows rare exceptions to address legal and ethical concerns. See the PLOS Data Policy and FAQ for detailed information.

A Data Availability Statement describing where the data can be found is required at submission. Your answers to this question constitute the Data Availability Statement and **will be published in the article**, if

Yes - all data are fully available without restriction

accepted.

Do the authors confirm that all data underlying the findings described in their manuscript are fully available without restriction?

Describe where the data may be found in full sentences. If you are copying our sample text, replace any instances of XXX with the appropriate details.

- If the data are **held or will be held in a public repository**, include URLs, accession numbers or DOIs. If this information will only be available after acceptance, indicate this by ticking the box below. For example: *All XXX files are available from the XXX database (accession number(s) XXX, XXX.).*
- If the data are all contained **within the manuscript and/or Supporting Information files**, enter the following: *All relevant data are within the manuscript and its Supporting Information files.*
- If neither of these applies but you are able to provide **details of access elsewhere**, with or without limitations, please do so. For example:

  Data cannot be shared publicly because of [XXX]. Data are available from the XXX Institutional Data Access / Ethics Committee (contact via XXX) for researchers who meet the criteria for access to confidential data.

All relevant data is provided in the manuscript. The codes used in this paper are freely available on Github. https://github.com/EdwinMichaelLab/DEC_Salt_Haiti_LF.git

The data underlying the results presented in the study are available from (include the name of the third party and contact information or URL). • This text is appropriate if the data are owned by a third party and authors do not have permission to share the data. * typeset	
Additional data availability information:	Tick here if the URLs/accession numbers/DOIs will be available only after acceptance of the manuscript for publication so that we can ensure their inclusion before publication.

Dear Editor,

We would like to submit our paper "Economic performance and cost-effectiveness of using a DEC-salt social enterprise for eliminating the major neglected tropical disease, lymphatic filariasis" for consideration as a research article in PLoS Neglected Tropical Diseases.

The manuscript undertakes an economic, financial and modelling-based evaluation of the performance of a novel social enterprise-based project developed in Haiti for marketing DEC-fortified salt in endemic communities as an economically and operationally feasible strategy for achieving the long-term elimination of the major vector-borne macroparasitic disease, Lymphatic Filariasis (LF). Our analysis of the economic and social effectiveness of the enterprise indicates that the entity because of its innovative business strategy has already achieved sufficient financial viability and production capacity to significantly and positively affect the prospects of achieving LF elimination in the study setting of Léogâne compared to standard tablet-based drug programs. Results from the break-even projections carried out in this study indicate that the strategy may break-even in the near future, and could even have the potential to achieve zero elimination costs for societies once it attains profitability (i.e., results in a positive cash-flow). Finally, our simulation-based cost-effectiveness study indicates that because of: 1) increasing revenue from the sale of the DEC salt obtained over time, 2) expansion of its delivery in the population, and 3) the adverse effect of continuous consumption of the drug on worms, the delivery of DEC through the present Haiti salt enterprise represents a significantly more cost-effective option than annual DEC tablet-based MDA for accomplishing LF elimination in Léogâne arrondissement. With less than three years remaining for meeting the 2020 target set by WHO for accomplishing the global elimination of LF, the present results indicate that development of policy and strategies for possible deployment of similarly-fashioned salt enterprises in socially-challenging environments, similar to Haiti, possibly following the example of universal iodization via the salt industry, would provide a new sustainable and economically efficient tool that could greatly enhance our current efforts for meeting the exacting goal of accomplishing global LF elimination successfully.

The results presented in this paper, we believe, will be of major interest to not only public health officials, funders, agencies, and policy makers engaged with national and global LF elimination, but also to epidemiologists, parasitologists, medical researchers and health economists working on the design and management of programs aiming to control or eliminate neglected tropical diseases from the poor communities in the regions of the world where these diseases occur. They will also help to motivate further work on how social enterprises could offer a strategy to overcome current obstacles facing health system-led mass drug programs for accomplishing parasite elimination, including achieving the financial viability and operational sustainability required to maintain the long-term interventions needed for breaking the transmission of these diseases effectively.

We declare that we have no competing interests related to this article. We also confirm that all authors approved the manuscript for submission and that the content has not been published or submitted for publication elsewhere.

We thank you for your time and consideration.

With kind regards,

Swarnali Sharma

Edwin Michael*

*Corresponding author (Department of Biological Sciences, University of Notre Dame, Notre Dame, IN 46556, USA, Edwin.Michael.18@nd.edu)

1

2

Economic performance and cost-effectiveness of using a DEC-salt social enterprise for eliminating the major neglected tropical disease, lymphatic filariasis

6

7

Swarnali Sharma[1], Morgan E. Smith[1], James Reimer[2], David B. O'Brien[3], Jean M. Brissau[4], Marie C. Donahue[5], Clarence E. Carter[6], Edwin Michael[1*]

[1]Department of Biological Sciences, University of Notre Dame, Galvin Life Science Center, Notre Dame, IN 46556, USA

[2]1071 Devonshire Road, Grosse Pointe Park, MI 48230, USA

[3]10720 Serenbe Lane, Chattahoochee Hills, GA 30268, USA

[4] College of Science, University of Notre Dame, Notre Dame, IN 46556, USA

[5]Eck Institute of Global Health, University of Notre Dame, 305 Brownson Hall, Notre Dame, IN 46556, USA

[6] College of Science, 215 Jordon Hall of Science, University of Notre Dame, Notre Dame, IN 46556, USA

21

22

23

*Corresponding author

E-mail: Edwin.Michael.18@nd.edu (EM)

26

Abstract

Background

Salt fortified with the drug, diethylcarbamazine (DEC), and introduced into a competitive market has the potential to overcome the obstacles associated with tablet-based Lymphatic Filariasis (LF) elimination programs. Questions remain, however, regarding the economic viability, production capacity, and effectiveness of this strategy as a sustainable means to bring about LF elimination in resource poor settings.

Methodology and Principal Findings

We evaluated the performance and effectiveness of a novel social enterprise-based approach developed and tested in Léogâne, Haiti, as a strategy to sustainably and cost-efficiently distribute DEC-medicated salt into a competitive market at quantities sufficient to bring about the elimination of LF. We undertook a cost-revenue analysis to evaluate the production capability and financial feasibility of the developed DEC salt social enterprise, and a modeling study centered on applying a dynamic mathematical model localized to reflect local LF transmission dynamics to evaluate the cost-effectiveness of using this intervention versus standard annual Mass Drug Administration (MDA) for eliminating LF in Léogâne. We show that the salt enterprise because of its mixed product business strategy may have already reached the production capacity for delivering sufficient quantities of edible DEC-medicated salt to bring about LF transmission in the Léogâne study setting. Due to increasing revenues obtained from the sale of DEC salt over time, expansion of its delivery in the population, and greater cumulative impact on the survival of worms leading to shorter timelines to extinction, this

48   strategy could also represent a significantly more cost-effective option than annual DEC tablet-

49   based MDA for accomplishing LF elimination.

50   **Significance**

51   A social enterprise approach can offer an innovative market-based strategy by which

52   edible salt fortified with DEC could be distributed to communities both on a financially

53   sustainable basis and at sufficient quantity to eliminate LF. Deployment of similarly fashioned

54   intervention strategies would improve current efforts to successfully accomplish the goal of LF

55   elimination, particularly in difficult-to-control settings.

Author summary

With less than three years remaining for meeting the 2020 target set by WHO for accomplishing the global elimination of Lymphatic Filariasis (LF), concerns are emerging regarding the feasibility of meeting this goal using the current tablet-based Mass Drug Administration strategy. Salt fortified with the antifilarial drug, diethylcarbamazine (DEC), could offer an intervention that avoids many of the barriers connected with tablet-based elimination programs. We analyzed the economic performance and cost-effectiveness of a novel DEC-salt social enterprise developed and tested in Léogâne arrondissement, Haiti, as a particularly significant strategy for accomplishing sustainable LF elimination in such complex settings. We show that because of increasing revenue from the sale of the DEC salt over time, expansion of its delivery in the population, and the adverse effect of continuous consumption of the drug on worms, the delivery of DEC through a salt enterprise can represent a significantly more cost-effective option than annual DEC tablet-based MDA for accomplishing LF elimination in settings, like Léogâne. We indicate that development of policy and research into how to deploy similarly-fashioned interventions, or work with the salt industry to increase population use of medicated salt, would improve present efforts to successfully accomplish the elimination of LF.

Introduction

Lymphatic filariasis (LF), a mosquito-borne neglected tropical disease (NTD), commonly known as elephantiasis, is one of only parasitic six diseases currently targeted for potential global eradication by 2020 using preventive mass chemotherapy [1-3]. Despite the impressive expansion of a WHO-led elimination program aimed toward the meeting of this goal in all endemic countries since 2000, stakeholders committed to global LF elimination have recognized that the current tablet-based mass drug intervention is resource-intensive, can face significant compliance issues with time, and may be difficult to implement in remote or socio-ecologically complex areas, such as urban and socio-politically unstable settings, hampering foreseen elimination goals [4-8]. These difficulties have heightened interest in investigating the impacts of either approaches aimed at scaling-up treatment strategies or inclusion of preventive activities into drug programs (such as supplemental vector control), or evaluation of novel intervention technologies, that can effectively overcome current barriers in order to accelerate parasite elimination [9-11].

Salt fortified with the anti-filarial drug, diethylcarbamazine (DEC), could offer an intervention that avoids many of the above issues connected with tablet-based elimination programs [18]. Indeed, DEC-salt has played a major role in the elimination of LF in a number of pilot and region-wide settings in Africa, Central America, and Asia [5,12-17]. The low dose of DEC (0.1-0.6% [w/w]) used in these studies and programs was well tolerated and rarely associated with adverse reactions. It also has the potential to be more effective than tablet-based Mass Drug Administration (MDA) programs via reduction of the durations of intervention required to interrupt parasite transmission [18]. Moreover, fortified salt can also be provided to a

97   population without developing a dedicated public distribution system, overcoming the need for

98   developing an effective health infrastructure capable of distributing anti-filarial drugs at the high

99   coverages needed for achieving elimination [5,7,8].

100   Haiti is one of only four countries remaining in the Americas where LF is still endemic

101   [8,19]. MDA using DEC first started in the country under the National Program to Eliminate LF

102   (NPELF) in 2000, and by 2005 had expanded to mass treatment of some 1.6 million people at

103   least once in 24 of the initially endemic 120 communes of the country ([8]. However, following

104   funding, sociopolitical and natural disaster-based challenges to further scaling up, the program

105   realized full national coverage of all the endemic communes in the country only by 2012

106   [5,7,8,20]. This delay together with the technical challenge of interrupting transmission in areas

107   of highest prevalence even with high levels of coverage using the suggested five successive years

108   of annual MDA [5,7,8,20], indicate that it is unlikely that NPELF will meet the goal of

109   accomplishing LF elimination in the country by the target year of 2020. In 2006, partly to

110   overcome the above issues, a project was initiated with the collaboration of Congregation de

111   Sainte Croix, the Notre Dame Haiti Program, and the Ministry of Public Health and the

112   Population (MSPP), focused on the local processing and marketing of DEC-mediated salt co-

113   fortified with potassium iodate as an alternative means to facilitate the elimination of LF (and

114   prevention of iodine deficiency disorders) in Haiti [8]. Based on the principle of employing a

115   social enterprise framework for providing goods and services in an entrepreneurial and

116   innovative fashion to solve social problems [21-23], this project purchases both local and

117   imported raw salt which are then cleaned, sized, fortified and packaged for sale in the local

118   market as food-grade co-fortified salt, raising the potential of using a business-based approach to

119 delivering DEC-medicated salt as a sustainable means to accomplish LF elimination in settings,

120 such as Haiti.

121   Here, our major aim was to examine the economic performance and effectiveness of

122 using the Haitian social enterprise-based framework for producing and marketing DEC-fortified

123 salt as a sustainable, cost-effective, model for achieving the long-term elimination of LF,

124 focusing on Léogâne arrondissement, Haiti. A cost-revenue analysis combined with a

125 mathematical modeling-based evaluation of the cost-effectiveness of the DEC salt social

126 enterprise compared to standard MDA was carried out to undertake this analysis. Specifically,

127 we evaluated the economic performance and social value of the enterprise by assessing: 1) the

128 growth in salt production, costs of resources consumed, and revenues from sales gained to

129 determine break-even points, 2) the impact of the product-mix used for realizing the socially-

130 relevant sale price of the salt, and 3) its cost-effectiveness compared to tablet-based MDA for

131 accomplishing LF elimination in the study setting of Léogâne arrondissement, Haiti. We discuss

132 the results in terms of how using a social enterprise can offer a sustainable and innovative

133 strategy for accomplishing LF elimination in Haiti, and similarly resource-constrained settings,

134 that face both programmatic and social difficulties in delivering long-term tablet-based LF

135 MDAs.

136 **Methods**

137 **Overview**

138   We carried out a cost-revenue analysis to evaluate the production capability and financial

139 feasibility of the developed DEC salt social enterprise via assessment of the relationship between

140 fixed and variable costs versus the revenue received [24,27] and a modeling study centered on

141   applying a dynamic transmission model to evaluate the cost-effectiveness of using this

142   intervention versus standard annual MDA for eliminating LF in Léogâne arrondissement, where

143   the salt enterprise operates [28-31]. The cost-revenue analysis was based on costs and revenue

144   data contained in financial accounts during the production phase of the salt enterprise from 2013

145   to 2018, while the break-even analysis was carried out over a time horizon that ranged between

146   2013 to the year when the break-even point was attained. The predicted timelines to LF

147   elimination along with the costs of annual MDA versus the net cost of supplying DEC-fortified

148   salt until elimination was achieved were used to carry out the cost-effectiveness modeling study.

149   **Cost-revenue and break-even analyses**

150   **Cost estimation**

151   From the operational perspective, these included periodic financial investments primarily

152   used for purchasing large equipment; fixed costs (administrative, marketing, maintenance, and

153   leasing costs) and variable costs (costs of raw salt, salt packaging, custom fees, labor,

154   transportation, and drug supplies). As the salt enterprise used a product-mix business strategy of

155   producing three different types of salt to meet demands and application in different market

156   segments, viz. industrial – untreated salt processed to meet the requirements of various industrial

157   applications, coarse and fine single-fortified salt (treated with 40 ppm of potassium iodate only)

158   and double-fortified salt (treated with both 40 ppm of potassium iodate and 0.32% DEC [w/w]),

159   to assure price competitiveness of the double-fortified salt with the local table salt in the market

160   and to meet customer preference for either coarse or fine edible salt, we additionally estimated

161   the variable costs of the two fortified salt types. At the project level, we multiplied the unit cost

162   with the unit quantity of each cost item consumed on a yearly basis to obtain the annual total cost

163   of producing all three types of salt.

Revenue estimation

165   The unit sale price was multiplied by the unit quantity sold per year to quantify the

166   annual revenue obtained by the sale of each salt type. Total revenue was simply the sum of

167   revenues obtained from the sale of each salt type.

Forecasting break-even time points

169   This was conducted by projecting forward the total costs (investment + fixed + variable

170   costs) and total revenues from the sale of all three types of salt estimated for different periods

171   between 2013 to 2018 until the point at which cash flow from the project (total revenue – total

172   cost) becomes zero or the break-even for the enterprise is attained [24-27]. Simple linear forward

173   projections were used to make these calculations. Costs and revenues (both in US$) were used

174   undiscounted in this study.

Cost-effectiveness modeling

Overview of the LF transmission model

177   We extended the data-driven Monte Carlo population-based EPIFIL model for predicting

178   local LF infections [32-36] to include comparative costs and simulations of the effectiveness of

179   the standard two-drug (DEC plus Albendazole (ALB)) tablet-based MDA used in Haiti versus

180   consumption of double-fortified salt sold by the salt enterprise to perform this analysis. We used

181   a data-model assimilation technique based on the Bayesian Melding (BM) algorithm to calibrate

182   the LF model to the microfilariae (mf) prevalence data observed in our Léogâne endemic setting

183   [28-31], and used the localized model to simulate the impact of either intervention on timelines

184   required to the decrease the community-level mf prevalence below the WHO-mandated

185   elimination threshold of 1% mf [1,2]. Modeling of the impacts of MDA using DEC+ALB and

186   DEC-medicated salt followed our previous methods published in detail in Smith et al [18].

187   **Input epidemiological data**

188   The data sources used for calibrating the LF model were collected from Léogâne

189   commune, Haiti [28-31]. The epidemiological data inputs encompassed information on baseline

190   community-level mf prevalence (15.5%), the annual biting rate (ABR) estimated inversely by

191   model fitting to mf prevalence data [39], and details regarding the dominant mosquito genus

192   (*Culex quinquefasciatus)*. Published details of the MDA interventions, including the relevant

193   drug regimen, carried out in this setting during 2000-2008 were also assembled and used as

194   required [20,28-31]. All model parameters, functions, and fitting procedures specific to this work

195   are given in detail in S1 Supporting Information.

196   **Cost-effectiveness analysis**

197   This was carried out by comparing the costs and effectiveness achieved by the production

198   and sale of DEC-fortified salt versus implementation of the annual tablet-based DEC/ALB MDA

199   for accomplishing LF elimination in Léogâne (as measured by the times by which the initially

200   observed baseline pre-control mf prevalence in this setting reach below the WHO-recommended

201   1% mf prevalence threshold [1,2]). Timelines taken by each intervention to reduce the initial

202   prevalence to below the 1% mf threshold were quantified by simulating trends in infection

203   prevalence due to these interventions using the Monte Carlo-based EPIFIL model localized to

204   reflect LF transmission in Léogâne as described above. The impact of the annual tablet-based

205   MDAs was studied by running the model at 65% and 80% population coverages, while we

206   simulated the effect of the produced DEC salt using 65%, 80% and the actual population

207   coverages given in Table 4.

208   The economic cost for carrying out annual MDA was fixed conservatively at US$0.64

209   per person inclusive of drug cost, given the finding that this represented the average cost of

210   treating an individual in Haiti once initial costs stabilized [29,37], while the cost of delivering

211   DEC-medicated salt per person per year was estimated from the difference between the costs of

212   production and the revenues gained from sales of the salt. Simulations of cost-effectiveness were

213   carried out by fixing the Léogâne arrondissement population at 500,000 [38]. All costs are

214   calculated from the perspective of the financial costs of delivering either DEC tables or fortified

215   salt.

216

217   **Results**

218   **Costs and production of salt**

219   Table 1 summarizes the investment, fixed and variable costs incurred in establishing and

220   operating the Léogâne DEC salt enterprise. These costs are presented for the years between

221   2013-2018 when production of food-grade fortified salt began (following an experimental phase

222   which addressed technical issues in the fortifying of salt with DEC) along with corresponding

223   data on the quantity of the three different types of salt (industrial, coarse and fine single-fortified,

224   coarse and fine double-fortified) produced and sold. Note that investments occurred periodically

225   during different expansion phases (2013, 2014, and 2017), and were primarily used to acquire

226   capital items either from the US or from within Haiti. These were recorded as fixed assets, and

227   comprised factory items, such as different types of pumps, screens, control systems, hoppers,

228   sealers, storage tanks, generators, and office equipment. Fixed costs, i.e., costs that remain the

229   same whatever the level of output produced or products sold included operating expenses, while

230   variable costs comprised costs of items which scaled with production volume [24,25]. Examples

231   of components of the latter two cost types incurred are given in Methods.

232 **Table 1. Cost (investment, fixed cost and variable cost (in US$)) and summary of all types of salt (industrial salt, coarse and**
233 **fine single-fortified salt, and coarse and fine double-fortified salt) produced (tons) from 2013-2018.**

234

Year	Cost (US$)			Salt Production (Tons)				
	Investment	Fixed Cost	Variable Cost	Industrial	Single-fortified		Double-fortified	
					Coarse	Fine	Coarse	Fine
2013 (Jan-Dec)	98,418	36,612	75,176	10	0	0	230	0
2014 (Jan-Dec)	397,249	180,589	120,296	272	1	5	470	0
2015 (Jan-Dec)	0	275,495	225,367	557	146	33	334	7
2016 (Jan-Dec)	0	275,495	392,882	2140	452	206	479	61
2017 (Jan-Dec)	49,280	558,904	601,308	2811	648	308	979	91
2018 (Jan-Dec)	23,000	352,000	800,000	2431	1013	527	1841	33

235

236   The data on salt production show that initial output was low (e.g., 10 metric tons of

237   industrial salt and 230 tons of coarse double-fortified salt in 2013, compared to 272, 6, and 470

238   tons of industrial, single-fortified, and double-fortified salt respectively in 2014). To increase

239   production, a three phase expansion of the project was introduced beginning in the year 2013.

240   Phase 1 focused on installing higher capacity processing equipment (January 2013-March 2014),

241   while Phase 2 aimed to expand processing capacity by adding bulk storage and extension of the

242   brine-washing system (May 2014-March 2015), and Phase 3 further expanded these washing,

243   processing and storage capacities (January 2017-June 2018). These expansion phases meant that

244   both the fixed and variable costs of salt production varied over time (Table 1), but in general, and

245   as expected, as production expanded the variable costs increased proportionately while the fixed

246   costs simply reflected increases in capital investments. By contrast, the production figures show

247   that the manufacture and sale of each type of salt increased steadily, with industrial salt

248   dominating production particularly toward the later years followed by double-fortified (i.e., DEC

249   and iodine medicated) and single-fortified (iodine-medicated only) coarse salts. Given the

250   population preference for coarse edible salt in Léogâne (and Haiti in general), fine salt

251   production and sale lagged behind in volume (Table 1). The figures, however, demonstrate that

252   with expansion in capacity the enterprise was able to achieve significant production volumes for

253   the double-fortified salt by year 2018 (1841 metric tons recorded for the coarse variety).

254   **Net cash flow and break-even forecasting**

255   The total annual costs of salt production (= Investment + Fixed Costs + Variable Costs)

256   and revenues attained from the sale of all three types of salt are given in Table 2. Total annual

257   costs increased as production expanded (Table 1) from US$210,206 in 2013 to US$1,175,000 in

14

258   2018 – i.e., approximately five times – but the figures show that revenue increased even faster,

259   up to 17 times that obtained initially in 2013 (US$61,636) to close to cost of production by 2018

260   (US$1,064,000). The net cash flow [24-27] figures in the Table, which represent the difference

261   between total production cost and total revenue, although being negative for all the years from

262   2013-2018, capture this increasing revenue returns (as reflected by the declining negative trend

263   in the net cash flow) towards the later years, suggesting that the project is close to achieving

264   break-even or profitability in the near future. To estimate the exact time point when the

265   enterprise is likely to break-even (i.e., the time point when the total program cost is equal to the

266   total revenue), we employed a simple linear model to project forward the total project costs and

267   revenues calculated for 2013-2018. Fig 1(a) shows that if we use the full data on annual costs

268   and revenues obtained for the whole 2013-2018 period, the project will break-even in 2027.

269   However, if we use the data from 2016-2018, when total salt production had reached significant

270   levels (Table 1), to predict the time point at which the break-even point will be achieved, this

271   will occur earlier by year 2022 (Fig 1(b)).

Table 2. Year wise details of total cost, total revenue and net cash flow attained by the Haiti salt enterprise between 2013 to 2018. The total costs shown are calculated using the cost data for the production of all three types of salt, while total revenue is calculated using the revenue data from the sale of all three types of salt for each year.

Year	Total Cost (US$)	Total Revenue (US$)	Net Cash Flow
2013	210,206	61,636	-148,570
2014	698,134	118,583	-579,551
2015	448,168	175,629	-272,539
2016	721,070	512,588	-208,482
2017	1,209,492	832,285	-377,207
2018	1,175,000	1,064,000	-111,000

Fig 1. Forecasts of the break-even years of the salt enterprise. Results are shown from using a simple linear model to project forward the total project costs and revenues (in US$). **(a)** Forecast of break-even year using total cost and total revenue data calculated for 2013-2018 given in Table 2. **(b)** Forecast of break-even year using total cost and total revenue data calculated for 2016-2018 given in Table 2. The red dotted line indicates the break-even point for each scenario.

Fig 2 depicts the per ton revenues from sales and costs of producing the three different types of salts for the years 2013-2018. The results show that for all salt types, while initially there was a large difference between the production cost and revenue per ton (i.e., a large negative cash-flow), this difference decreased for each salt category with time. This occurred faster, however, in the case of the industrial and single-fortified salt, such that break-even was achieved by 2018. By contrast, the cash-flow from the production and sale of the double-fortified salt was still negative (lower revenue compared to production costs) at the end of the present study period of 2018. This result shows, first, that the overall break-even estimated in this study (Fig 1) for the project is due to the delay in reaching the break-even year for double-fortified salt. Second, it also highlights how the mixed product strategy of producing different types of salt targeting different market sectors can allow the more profitable products (industrial, single-

16

293   fortified salt) to subsidize the sale of a product (double-fortified salt) whose cost (approximately

294   US$200 per ton (Fig 2)) needs to be kept competitive with other edible salt sold (retailed at

295     $US265 per ton in Haiti (James Reimer, personal communication)) in the local market.

296   **Fig 2. Revenue and production cost for industrial, single-fortified and double-fortified salt.**
297   Both revenue and production cost (in US$) for each salt are shown per ton.

298   **Marginal cost of manufacturing DEC-medicated salt**

299   This was evaluated by analysis of the difference in the variable costs of producing the

300   single-fortified (which included only potassium iodate) versus the double-fortified (both

301   potassium iodate and DEC included) salt types, given that the investment and fixed costs going

302   into manufacturing all salt types were shared equally between each type. The variable costs per

303   ton for producing the single-fortified (coarse and fine) and double-fortified (coarse and fine) salt

304   for two types of bags/bales (25.0-kg bags and 12.5-kg bales) are provided in Table 3 for the

305   years 2014-2018 when both salt products were produced (note that production of single-fortified

306   salt began only in 2014 (Table 1)). Analysis of the difference in the variable costs for producing

307   the single-fortified versus the double-fortified salt indicate that this was consistently about

308   US$70 per metric ton, irrespective of which type - coarse or fine variety - or types of bags/bales

309   were produced (Table 3). Given that the cost of DEC, as delivered by Syntholab Chemicals to

310   the project was US$21.60 per kg (James Reimer, personal communication), and DEC salt in this

311   project was fortified with 0.32% DEC by weight or with 3.2kg of DEC/ton, it can be seen that

312   the cost of producing one metric ton of DEC salt works to be US$ 69.12/ton (i.e., 3.2 kg DEC x

313   US$21.60 per kg). This result indicates that the marginal cost, or difference in the variable cost,

314   of adding DEC to single-fortified salt (US$70; Table 3) was simply due to the purchase cost of

315   DEC.

Table 3. Marginal cost of manufacturing DEC-medicated salt. This was evaluated by analysis of the difference in the variable costs of producing the single-fortified (which included only potassium iodate) versus the double-fortified (both potassium iodate and DEC included) salt types, given that the investment and fixed costs going into manufacturing all salt types were shared equally between each type.

Year	Types of Bags/Bales	Variable cost of Coarse Salt (US$/Ton)			Variable cost of Fine Salt (US$/Ton)		
		Single-fortified	Double-fortified	Difference	Single-fortified	Double-fortified	Difference
2014	25.0-kg Bags	150	220	70	160	230	70
	12.5-kg Bales	190	260	70	200	270	70
2015	25.0-kg Bags	145	215	70	155	225	70
	12.5-kg Bales	185	255	70	195	265	70
2016	25.0-kg Bags	145	215	70	155	225	70
	12.5-kg Bales	185	255	70	195	165	70
2017	25.0-kg Bags	135	205	70	145	215	70
	12.5-kg Bales	175	245	70	185	255	70
2018	25.0-kg Bags	135	205	70	145	215	70
	12.5-kg Bales	175	245	70	185	255	70

Population coverage attained by the DEC salt enterprise

Table 4 shows the potential increase in demand for salt in the Léogâne arrondissement calculated as a function of changes in population size from 2013 to 2018. It also presents the potential DEC-fortified salt coverage which may be achieved in the setting by increasing sale of the double-fortified salt produced over this period. The annual population size estimates from 2013 onwards were predicted using a growth rate of 1.28% [38], whereas the yearly population demand for edible salt was calculated by assuming that the daily salt consumption per person is 15gm (average of the reported daily per-capita consumption in Haiti of 10gm and 19gm [5,40]). Assuming that the sale of double-fortified salt is widespread in the community (i.e., not targeted towards one segment of the population), coverage of DEC salt in Léogâne can then be roughly estimated simply by dividing the quantity of salt produced over the estimated demand. The

18

334   results from this calculation, listed in the last column of Table 4, shows that as production

335   increased rapidly from 2013 to 2018, this could increase potential population coverage achieved

336   by sales of the DEC-medicated salt from as low as 8.45% in 2013 to approximately 65% in 2018.

Table 4. Details of production of double-fortified (DEC-medicated) salt (tons), its potential demand/year, and coverage in Léogâne Arrondissement.

Year	Quantity of double-fortified (DEC-medicated) salt (Tons)	Population of Léogâne Arrondissement*	Potential Demand of salt/year (Tons)**	Coverage (%)
2013	230	497,274	2,723	8.45
2014	470	503,241	2,755	17.06
2015	341	509,280	2,788	12.23
2016	540	515,799	2,824	19.12
2017	1070	522,401	2,860	37.41
2018	1874	529,088	2,897	64.69

*Population growth rate of Haiti is 1.28% [38]

**Assuming that the salt consumption rate per person per day is 15gm [5,40]

Cost-effectiveness modeling

Fig 3 portrays the predicted timelines to LF elimination in Léogâne under each of the

MDA and salt interventions investigated. For MDA, the depicted simulations indicate that it

would take up to 7 years at 65% coverage, and 5 years at 80% coverage, respectively, to reach

the 1% mf threshold. By contrast, the model predictions show that it will take just 1 year at 65%

coverage, 5 months at 80% coverage, and 3 years if actual population coverage (Table 4) are

used to reduce the pre-control prevalence to below this threshold via consumption of the traded

DEC salt (Fig 3). This highlights the dramatic effect that daily consumption of DEC-medicated

salt even at low dosages (0.32% w/w) would have compared to annual intake of a higher dosages

of DEC (and ALB) as provided by tablet-based MDA for eliminating LF infection in an endemic

setting [12,15-18]. Note that the actual DEC salt population coverages (Table 4) used in this

analysis assume that salt supply occurred uniformly and sale was restricted to Léogâne

arrondissement only. Any changes in these parameters would mean attaining lower annual

population coverages than shown in Table 4; however, a sensitivity analysis using coverage

values 15-20% lower than those depicted in the Table did not affect the above timelines

significantly (data not shown).

**Fig 3. Timelines to reach the WHO recommended 1% mf threshold for MDA implanted at
65% and 80% coverage and DEC-medicated salt at 65%, 80%, and actual population
coverages.** The median model predicted trajectory is shown for each intervention strategy. The
black dotted horizontal line indicates WHO recommended 1% mf prevalence threshold. The
blue, red, orange, purple and green dotted vertical lines indicate the time points to reach 1% mf
threshold using either MDA at 65% and 80% coverages or DEC Salt at 65%, 80%, and actual
coverage respectively.

The comparative costs of carrying out annual MDA versus supplying DEC-medicated

salt are shown in Table 5. These show that while the total cost of delivering annual MDA (here

369   fixed at US$0.64 per person, inclusive of the cost of the drug [29,37]), simply scaled with

370   population growth, and will continue to be substantial on a yearly basis until LF elimination is

371   achieved, the net cost of supplying DEC-fortified salt through the social business model will

372   decline dramatically with time as production costs decrease and revenues begin to increase over

373   time (Fig 2). Indeed, projection forward of the net or revenue - production cost data collected

374   during the years 2013-2018 indicates that the total and per capita net costs of DEC salt provided

375   through the present social enterprise could potentially even become zero at the time point (2027)

376   when the project breaks even (Fig 1(a)).

Table 5. Forecast of the population of Léogâne, annual cost of supplying double- fortified (DEC-medicated) salt per person per year, and total costs of treatment with DEC-medicated salt and MDA respectively for the years 2013-2027. The population growth rate for Haiti estimated in year 2015 (1.28%) was used in making the population size estimations shown in the Table, whereas a simple linear model based on the cost and revenue data connected with DEC-medicated salt production and sale (both fine- and coarse salt types) for the years 2013-2018 (Fig 2) was used to forecast the annual cost of salt-based DEC treatments per person and for the total population between 2019-2027.

Year	Population of Léogâne*	Annual Cost for Double fortified (DEC-medicated) salt per person (US$)	Total cost for treating with DEC-medicated salt (US$)	Total cost for MDA (US$)**
2013	497,274	3.38	1,680,786	318,255
2014	503,241	4.27	2,148,839	322,074
2015	509,280	0.94	478,723	325,939
2016	515,799	0.97	500,325	330,111
2017	522,401	1.01	527,625	334,337
2018	529,088	0.58	306,871	338,616
2019	535,860	0.61	329,018	342,950
2020	542,719	0.51	276,787	347,340
2021	549,666	0.41	223,164	351,786
2022	556,702	0.30	168,124	356,289
2023	563,827	0.20	111,638	360,849
2024	571,044	0.09	53,678	365,468
2025	578,353	0.01	5,783	370,146
2026	585,757	0.001	586	374,884
2027	593,254	0	0	379,683

*Population growth rate of Haiti is 1.28% [38]

**Using cost for annual MDA as US$0.64 per person/year [37]

We used the total costs of implementing each strategy until LF elimination (crossing below the 1% mf threshold) is achieved to investigate the cost effectiveness of either strategy. The total costs and effectiveness of using MDA at 65% and 80% coverages and supplying DEC salt at 65%, 80% and the actual coverages given in Table 4, were evaluated and compared via calculations of the average cost effectiveness ratio [10,41-47]. With respect to DEC salt, we also conducted the analysis using three different net costs of salt production per person per year as

23

395   recorded in Table 5: (i) average of the net cost of salt produced per person calculated for the

396   years 2018-2020, i.e., US$0.57 per person/year, (ii) average of the net cost of salt per person for

397   the years 2021-2023, i.e., US$0.3 per person/year, and (iii) average of the net cost of salt per

398   person for the years 2025-2027, i.e., US$0.025 per person/year. This was performed to assess the

399   sensitivity of the present results to changes in the steeply declining net cost of salt production

400   over time observed in this study.

401   The results from this exercise are shown in Table 6, and indicate, principally, that

402   irrespective of coverage, the costs of using MDA are significantly greater than those arising from

403   using the salt strategies, primarily because of its lesser effectiveness as well as higher and

404   stationary unit cost. Among the three salt scenarios, costs for eliminating LF, as expected,

405   declined with decreasing net cost of production over time with scenario three showing the lowest

406   costs. However, for all strategies, while the most effective strategy is to deliver MDA or salt at

407   80% coverage, the most cost-effective option (in terms of minimizing the cost-effectiveness

408   ratio) occurred at either 65% drug coverage for MDA or at the lower actual coverages recorded

409   for DEC salt (Table 6). This suggests the existence of a trade-off between cost and effectiveness

410   (in terms of duration of interventions required to achieve elimination) in the case of these

411   strategies, i.e., obtaining a higher coverage for accomplishing earlier LF elimination comes with

412   heightened costs. Overall, however, the results indicate that because of: 1) decreasing net cost of

413   DEC salt production over time, and 2) expansion of its coverage in the population leading to

414   significantly reduced elimination timelines, the delivery of DEC through a salt enterprise may be

415   significantly more cost-effective than annual DEC tablet-based MDA for accomplishing LF

416   elimination in the Léogâne arrondissement setting. It is also to be appreciated that we used a

417   conservative treatment cost of $0.64 per person for modeling the cost-effectiveness of the tablet-

418   based MDA program in this study. This represented a best-case scenario for the MDA program

419   implemented in Léogâne given that the actual economic costs, i.e., inclusive of the cost of

420   donated drugs, started out higher (US$1.84 over the first 3 MDAs) before approaching the

421   stabilized value used in our analysis as the program became more efficient [29,37]. Indeed, a

422   recent systematic review indicated that MDA program costs can vary substantially between

423   settings, with an average economic cost that could reach as high as US$1.32 [48]. Use of such

424   values or inclusion of the actual change observed in the per person treatment cost over time in

425   Léogâne in the present analysis would clearly further increase the cost of MDA over that

426   presented in Table 5, which in turn would lead to an even higher cost-effectiveness ratio for

427   MDA compared to those estimated for DEC salt in this study (Table 6).

Table 6. Comparison of total costs and CE ratios of population treatment using MDA versus supply of DEC-medicated salt for different drug coverages and DEC salt costs.

Treatment Method	Coverage	No. of years to reach 1% mf threshold	Total Cost (US$)	CE ratio
Annual MDA*	65%	7.00	1,456,000	208,000
	80%	5.00	1,280,000	256,000
DEC salt[1]	65%	1.00	185,250	185,250
	80%	0.42	95,760	228,000
	Actual†	3.00	105,450	35,150
DEC salt[2]	65%	1.00	97,500	97,500
	80%	0.42	50,400	120,000
	Actual†	3.00	55,500	18,500
DEC salt[3]	65%	1.00	8,125	8,125
	80%	0.42	4,200	10,000
	Actual†	3.00	4,625	1,542

*Using cost for annual MDA as US$0.64 per person/year [37], and total population of Léogâne arrondissement 500,000 (fixed).

†Actual coverage of DEC-medicated salt given in Table 4.

[1]Average of the net cost of DEC salt produced per person calculated for the years 2018-2020 given in Table 5, i.e., US$0.57 per person/year.

[2]Average of the net cost of DEC salt produced per person calculated for the years 2021-2023 given in Table 5, i.e., US$0.3 per person/year.

[3]Average of the net cost of DEC salt produced per person calculated for the years 2025-2027 given in Table 5, i.e., US$0.025 per person/year.

Discussion

In this study, we have undertaken a performance assessment of a novel social enterprise developed through a collaboration between Haitian and international partners engaged with LF control in the country, as a means to enhance the delivery of anti-filarial drugs to populations through the trading of salt co-fortified with DEC. Although DEC-fortified salt has been used previously in both pilot and region-wide LF intervention programs in a variety of global regions, ranging from Brazil, Tanzania, India and China to effectively control or eliminate LF [5,12-17], it is to be noted that the developed Haiti salt enterprise is the first attempt anywhere in the world to apply the principles of social entrepreneurship for delivering such an intervention. Recent work has highlighted how such social enterprises – that is, a social mission-driven organization that trades in goods or services for a social purpose – are emerging as a potentially effective supply side solution to the provision of cost-efficient public services in response to government failures, business that seek to extract maximal returns on investment, and unstable non-profit organizations [21-23]. In particular, this work has shown how these business entities can solve social problems via their potential to deliver greater responsiveness, efficiency and cost-effectiveness, through an explicit focus on meeting specific social goals while operating with the financial discipline and innovation of a private-sector business [21-23,49,50].

Although there is continuing debate as to how best to evaluate the performance of social enterprises, it is clear that at least two basic components related to the bottom line of these entities require assessment [21,23]. These primarily include: the economic-financial component for measuring overall organizational efficiency, profitability and hence sustainability, and the social effectiveness of the enterprise [21-23]. Here, we have combined the tools of financial

463   accounting and modeling of cost-effectiveness to measure these components in order to present a

464   first analysis of the utility of using the developed Haitian DEC salt enterprise as a sustainable

465   and economically efficient strategy to bring about LF elimination in programmatically difficult-

466   to-control settings, like the arrondissement of Léogâne, Haiti [10,41-47].

467   Our analysis of the performance of the present salt enterprise for creating social value

468   first focused on the question of capacity to economically produce sufficient amounts of DEC-

469   fortified salt for significantly affecting the elimination of LF in the study setting. The production

470   figures shown in Table 1 indicate, firstly, that while initial production of all types of salt were

471   low during the initial years of operation, by 2018, and just 5 years after processing began in

472   2013, the enterprise had reached high levels of both total (5,845 metric tons) and DEC-fortified

473   salt (1,841 metric tons) production, respectively (Table 1). Our analysis of the population

474   coverage that the sale of DEC salt could provide demonstrate that the amounts produced could

475   have potentially resulted in a coverage rate of 65% by 2018 (Table 4), which our previous

476   modeling study [18] and the present cost-effectiveness exercise (Fig 3 and Table 6) indicate is

477   sufficient to accelerate the achievement of LF elimination in the Léogâne setting. These findings

478   suggest that as the result of the expansion phases carried out through new capital investments

479   (Table 1), the current DEC salt project may have reached the production capacity required to

480   achieve its stated social mission of using a market-based approach for delivering sufficient edible

481   DEC-medicated salt as a means to bring about efficient LF transmission interruption in the

482   present study setting.

483   Assessment of the economic and financial performance of the salt enterprise carried out

484   in this study using cost-revenue analysis and financial forecasting has provided further insights

485   regarding the organization efforts used to reach economic equilibrium and hence trading

486   viability. This is an important consideration for evaluating the performance of social enterprises

487   because first and foremost these entities are enterprises, and therefore their social goals can be

488   pursued only by ensuring economic and financial fidelity [21-23]. Our major result in this area is

489   providing clarity regarding how the enterprise's achieved outputs in salt production and sale may

490   affect its potential to reach break-even points (Fig 1). Specifically, we show that given the

491   observed trends in production costs and revenue to 2018 (Table 2), the present salt enterprise

492   may either break-even by 2027 (if we forecast linearly using all the data from 2013 to 2018), or

493   as early as by 2022 (if we use data collected during 2016-2018 after the project had significantly

494   expanded capacity). This result is clearly dependent on assuming that capacity to produce the

495   increased amount of salt to meet either break-even points is available within the enterprise

496   without any further expansion, and demand for the produced salt in all sectors (industrial to

497   edible salt markets) will also expand commensurately. Nonetheless, the finding that it might be

498   possible to reach the break-even point by 2022 (i.e., over the next 4 years) is encouraging, and

499   suggests that the enterprise is likely to be self-sustaining and could become profitable in the very

500   near future. Indeed, analysis of trends in costs of production and revenues gained per ton of each

501   category of salt (Fig 2) indicate that both the industrial and single-fortified salt categories may

502   already have reached their individual break-even points in 2018, and that the delay for achieving

503   break-even status by the social enterprise is primarily due to the lag experienced by the

504   production and sale of the double-fortified salt. Although the per ton production cost of the latter

505   salt declined as significantly over time as the other two salt categories (Fig 2), indicating the

506   achievement of considerable economics of scale, the need to keep the price of the DEC salt

507   below the marginal cost of adding the drug ($70/metric ton (see Table 3)) to compete with

508   untreated local edible salt in the market means that either: 1) the current market price of the

509   double-fortified DEC salt needs to be revised upwards, or 2) further economies of scale need to

510   be found to bring down production costs, or 3) cross-subsidy from the more profitable categories

511   of salt produced will be required in order to continue with the processing of DEC salt in this

512   setting. While on the one hand, such a capacity to use a product mix strategy innovatively as a

513   means to subsidize the marketing of a product for meeting a social need is a feature of using an

514   enterprise model, note that this may be a particular effect of developing markets in settings, such

515   as Léogâne and Haiti in general, where a strong market-based economy is only just evolving. For

516   other LF endemic settings with stronger market economies and established salt industries, the

517   need for such subsides may be significantly lower meaning that the sale of DEC salt could occur

518   at nearer the true marginal cost of production, i.e., at the actual cost of purchasing the drug itself.

519   Note also that our present forecasts do not fully consider the likely impacts of key swing factors

520   that may significantly affect the profitability of the salt social enterprise, such as enforcement of

521   the 2017 law requiring all food salt in Haiti to be fortified, further progress on market

522   segmentation and the resulting product mix, and significant weather events similar to Hurricane

523   Michael in 2016. Positive changes in the first two factors will clearly enhance the enterprise's

524   ability to break-even faster and hence attain profitability sooner than predicted in this work.

525   The cost-effectiveness modeling exercise carried out in this study showed that apart from

526   the efficiency of the business model used for achieving economic and financial sustainability, the

527   salt enterprise may also be more cost-effective than the standard tablet-based annual MDA

528   program for accomplishing LF elimination in Léogâne (Table 6). This is because not only will

529   the population coverage that can be potentially attained by sale of the DEC salt (Table 4) be

530   sufficient to make this strategy more effective than annual MDA in reducing the number of years

531 (3 versus 7 years) required for achieving LF elimination (as defined by reducing mf prevalence

532 below the WHO threshold of 1% [2]), the total overall costs involved - due to both decreasing

533 net cost of production and the need for shorter durations of control - for using the salt approach

534 are also significantly lower than those which will be incurred in running the MDA program.

535 Indeed, this greater social impact of using the present social salt enterprise compared to annual

536 MDA was found to be a general outcome, irrespective of the other intervention coverages

537 investigated (i.e., at 65% coverage – the often normal coverage obtained by MDA programs - or

538 at the recommended optimal coverage of 80% [2]) (Table 6). These results add to our recent

539 modeling work, which highlighted how the continuous consumption of the drug, even at low

540 daily per capita dosages, by resulting in a cumulative impact on the survival of worms and mf

541 which is significantly higher than that afforded by the higher-dosed annual MDA treatment,

542 make DEC medicated interventions, even when delivered at moderate population coverages, a

543 markedly potent strategy for interrupting LF transmission [18]. Finally, an intriguing

544 possibility highlighted by the break-even analysis and the cost forecasting results shown in

545 Fig 1 and Table 5 is that using a social enterprise strategy for delivering DEC through

546 marketing of medicated salt could in principle also lead to zero disease elimination cost for

547 the community once the social business attains profitability (i.e., return a positive cash-flow).

548 This is an important result, and demonstrates how using a social enterprise that pursues a

549 social goal by production of services and goods whilst respecting economic efficiency may

550 offer an effective, financially sustainable, intervention strategy in settings facing major fiscal,

551 infrastructural and logistical barriers to carrying out tablet-based programs aiming to control

552 or eliminate parasitic infections.

553   The present performance evaluation primarily focused on internal (labor, capital,

554   income and taxes) and external (goods and services bought outside the company)

555   expenses/resources related to the economic viability of the salt enterprise [21]. However,

556   estimation of the full social value of a sustainable health social enterprise must also consider,

557   apart from the social benefits accruing from reducing disease only, the wider consequences

558   for a community [21]. Benefits here could be via the choice and use of resources that further

559   address the community interest, such as choosing local salt suppliers to favor short supply

560   chains, choosing socially certified suppliers, adopting a regime of decent work conditions and

561   even giving employment to workers coming from disadvantaged backgrounds [21]. Such

562   analysis must also include calculation of the larger social benefit associated with the potential

563   for the double-fortified salt to additionally and simultaneously reduce the impacts of iodine

564   deficiency in the population [5]. Note, additionally, that the present salt enterprise represents

565   the first attempt to build industrial-scale capacity on the island for processing large volumes

566   of salt to meet various local needs, which apart from providing a market for local raw salt

567   producers can also act as means to significantly stabilize the price of salt sold in the local

568   markets. These benefits, however, must be contrasted against potential adverse effects, such

569   as domination of the market by the growing enterprise, requiring an analysis of how best to

570   compensate for such loses. Recent developments in applying Social Returns on Investment

571   (SROI) approaches for comparing the full monetized social costs of a program with the full

572   monetized social benefits of achieving a health outcome (or set of outcomes) may offer a

573   means for undertaking this fuller analysis [22,51].

574   We have also used rough first calculations of the population coverages that could be

575   obtained with the expansion of salt production in the present cost-effectiveness modelling

576   study. Field studies to assess the actual household coverage achieved through the enterprise

577   will be critical for not only more realistically quantifying its effectiveness for accomplishing

578   LF transmission interruption in a community, but also for identifying better marketing

579   strategies to achieve good population coverage.

580   In conclusion, we have presented an economic and financial analysis of the Haitian

581   salt social enterprise, which indicates that it may present a sustainable and socially-

582   responsible strategy for aiding the elimination of LF via the marketing of DEC-medicated salt

583   in settings facing fiscal, infrastructural and logistical challenges for delivering tablet-based

584   elimination programs. Results from the break-even projections carried out in this study

585   indicate that the strategy may even have the potential to achieve zero societal costs once it

586   attains profitability (i.e., results in a positive cash-flow). This study further has shown that the

587   Haitian salt enterprise may have already reached production and sales levels that could result

588   in the coverage of the Léogâne study population at proportions sufficient enough to break LF

589   transmission. Finally, our simulation-based cost-effectiveness study has indicated that because

590   of: 1) increasing revenue from the sale of the DEC salt obtained over time, 2) expansion of its

591   delivery in the population, and 3) the effect of continuous consumption of the drug, even at

592   low daily per capita dosages, leading to a cumulative impact on the survival of worms and mf

593   higher than that afforded by the higher-dosed annual MDA treatment [18], the delivery of

594   DEC through the present Haiti salt enterprise may represent a significantly more cost-

595   effective option than annual DEC tablet-based MDA for accomplishing LF elimination. While

596   these are encouraging first results and highlight both the economic viability and social

597   effectiveness of using a salt enterprise in the fight against LF, it is clear that efforts to more

598   fully quantify the social value and strategies for developing similar salt social enterprises

599 elsewhere in other endemic settings with different market structures than those of Haiti are

600 now required if the comparative or joint utility of the approach among the current arsenal of

601 LF intervention strategies is to be fully appraised and understood. We note that the means by

602 which the global iodization of edible salt has been accomplished successfully over the past

603 two decades may offer a particularly apt model for building and sustaining the present

604 intervention globally, and suggest that similar tactics used in that program based on

605 introducing DEC medication into prevailing salt production and distribution systems,

606 collaboration with the national and regional salt industries, and engagement with the

607 government sector, civic society and the general public [52], could also make the universal

608 deployment of DEC-medicated salt eminently possible. With less than three years remaining

609 for meeting the 2020 target set by WHO for accomplishing the global elimination of LF, the

610 present results indicate that these appraisals and development of policies and strategies for

611 delivery of DEC-salt, either via deployment of similarly-fashioned salt enterprises, such as the

612 present, or through mobilization of existing salt industries, perhaps along with health system-

613 led MDA and vector-control programs, in socially-challenging environments, like Haiti,

614 would improve our current efforts for meeting this laudable but exacting goal successfully.

Acknowledgements

615

References

1. World Health Organization. Global programme to eliminate lymphatic filariasis. WHO. Wkly Epidemiol Rec. 2007;82(42):361-380.

2. World Health Organization. Monitoring and epidemiological assessment of mass drug administration in the global programme to eliminate lymphatic filariasis: a manual for national elimination programmes. WHO, 2011.

3. World Health Organization. Elimination of Lymphatic Filariasis as a public health problem-Resolution of the Executive Board of the WHO (WHA50.29). Fifth World Health Assembly, Geneva, Switzerland. WHO, 1997.

4. Bockarie MJ, Kelly-Hope LA, Rebollo M, Molyneux DH. Preventive chemotherapy as a strategy for elimination of neglected tropical parasitic diseases: endgame challenges. Phil Trans R Soc B. 2013;368(1623):20120144.

5. Freeman AR, Lammie PJ, Houston R, LaPointe MD, Streit TG, Jooste PL, et al. A community-based trial for the control of lymphatic filariasis and iodine deficiency using salt fortified with diethylcarbamazine and iodine. Am J Trop Med Hyg. 2001;65(6):865-871.

6. Klepac P, Metcalf CJE, McLean AR, Hampson K. Towards the endgame and beyond: complexities and challenges for the elimination of infectious diseases. Phil Trans R Soc B. 2013;368(1623): 20120137.

7. Lammie P, Milner T, Houston R. Unfulfilled potential. Using diethylcarbamazine-fortified salt to eliminate lymphatic filariasis. Bull World Health Organ. 2007;85:545-549.

8. Oscar R, Lemoine JF, Direny AN, Desir L, de Rochars VEMB, Poirier MJ, et al. Haiti National Program for the Elimination of Lymphatic Filariasis: A Model of Success in the Face of Adversity. PLoS Negl Trop Dis. 2014;8(7):e2915.

9. Irvine MA, Stolk WA, Smith ME, Subramanian S, Singh BK, Weil GJ, et al. Effectiveness of a triple-drug regimen for global elimination of lymphatic filariasis: a modelling study. Lancet Infect Dis. 2017;17(4):451-458.

10. Kastner RJ, Stone CM, Steinmann P, Tanner M, Tediosi F. What is needed to eradicate lymphatic filariasis? A model-based assessment on the impact of scaling up mass drug administration programs. PLoS Negl Trop Dis. 2015;9(10):e0004147.

11. Michael E, Singh BK. Heterogeneous dynamics, robustness/fragility trade-offs, and the eradication of the macroparasitic disease, lymphatic filariasis. BMC Med. 2016;14(1):14.

12. Fan P. Eradication of bancroftian filariasis by diethylcarbamazine-medicated common salt on Little Kinmen (Liehyu District), Kinmen (Quemoy) Islands, Republic of China. Ann Trop Med Parasitol. 1990;84(1):25-33.

669 13. Meyrowitsch D, Simonsen P, Makunde W. Bancroftian filariasis: analysis of infection and
670   disease in five endemic communities of north-eastern Tanzania. Ann Trop Med Parasitol.
671   1995;89(6):653-663.
672
673 14. Meyrowitsch D, Simonsen P, Makunde W. Mass DEC chemotherapy for control of bancroftian
674   filariasis: comparative efficacy of four strategies two years after start of treatment. Trans R Soc
675   Trop Med Hyg. 1996;90(4):423-428.
676
677 15. Narasimham M, Sharma S, Sundaram R, Reddy G, Raina V, Sambasivam V, et al. Control of
678   bancroftian filariasis by diethylcarbamazine medicated common salt in Karaikal, Pondicherry,
679   India. J Infect Dis. 1989;21(3):157-170.
680
681 16. Rao C, Panduranga R, Russel S. Control of bancroftian filariasis with common salt medicated
682   with diethylcarbamazine in Lakshadweep. Indian J Med Res. 1981;73:865-873.
683
684 17. Reddy GS, Venkateswaralu N. Mass administration of DEC-medicated salt for filariasis control
685   in the endemic population of Karaikal, south India: implementation and impact assessment. Bull
686   World Health Organ. 1996;74(1):85.
687
688 18. Smith ME, Singh BK, Michael E. Assessing endgame strategies for the elimination of lymphatic
689   filariasis: A model-based evaluation of the impact of DEC-medicated salt. Sci Rep.
690   2017;7(1):7386.
691
692 19. World Health Organization. Global programme to eliminate Lymphatic Filariasis. WHO. Wkly
693   Epidemiol Rec. 2010;365-372.
694
695 20. Grady CA, De Rochars MB, Direny AN, Orelus JN, Wendt J, Radday J, et al. Endpoints for
696   lymphatic filariasis programs. Emerg Infect Dis. 2007;13(4):608.
697
698 21. Bagnoli L, Megali C. Measuring performance in social enterprises. Nonprofit Volunt Sect Q.
699   2011;40(1):149-165.
700
701 22. Millar R, Hall K. Social return on investment (SROI) and performance measurement: The
702   opportunities and barriers for social enterprises in health and social care. Public Adm Rev.
703   2013;15(6):923-941.
704
705 23. Yang CL, Huang RH, Lee YC. Building a performance assessment model for social enterprises-
706   views on social value creation. Sci J Bus Manag. 2014;2(1):1-9.
707
708 24. Kang HY, Schoenung JM. Economic analysis of electronic waste recycling: modeling the cost
709   and revenue of a materials recovery facility in California. Environ Sci Technol. 2006;40(5):1672-
710   1680.
711
712 25. Collis J, Hussey R. Break-even Analysis. In: Cost and Management Accounting. London:
713   Springer; 1999. p.129-139.
714
715 26. Bierman Jr H, Smidt S. The capital budgeting decision: economic analysis of investment projects.
716   9th ed. London: Routledge; 2012.
717
718 27. Samonas M. Financial Forecasting, Analysis, and Modelling: A Framework for Long-term
719   Forecasting. New York: John Wiley & Sons; 2015.

720

721   28.   Boyd A, Won KY, McClintock SK, Donovan CV, Laney SJ, Williams SA, et al. A community-
722   based study of factors associated with continuing transmission of lymphatic filariasis in Leogane,
723   Haiti. PLoS Negl Trop Dis. 2010;4(3):e640.
724

725   29.   De Rochars MB, Kanjilal S, Direny AN, Radday J, Lafontant JG, Mathieu E, et al. The Leogane,
726   Haiti demonstration project: decreased microfilaremia and program costs after three years of mass
727   drug administration. Am J Trop Med Hyg. 2005;73(5):888-894.
728

729   30.   Mathieu E, Deming M, Lammie PJ, McLaughlin SI, Beach MJ, Deodat DJ, et al. Comparison of
730   methods for estimating drug coverage for filariasis elimination, Leogane Commune, Haiti. Trans
731   R Soc Trop Med Hyg. 2003;97(5):501-505.
732

733   31.   Mathieu E, Direny AN, De Rochars MB, Streit TG, Addiss DG, Lammie PJ. Participation in
734   three consecutive mass drug administrations in Leogane, Haiti. Trop Med Int Health.
735   2006;11(6):862-868.
736

737   32.   Michael E, Malecela MN, Zervos M, Kazura JW. Global eradication of lymphatic filariasis: the
738   value of chronic disease control in parasite elimination programmes. PLoS One. 2008;3(8):e2936.
739

740   33.   Michael E, Malecela-Lazaro MN, Maegga BT, Fischer P, Kazura JW. Mathematical models and
741   lymphatic filariasis control: monitoring and evaluating interventions. Trends Parasitol.
742   2006;22(11):529-535.
743

744   34.   Michael E, Malecela-Lazaro MN, Simonsen PE, Pedersen EM, Barker G, Kumar A, et al.
745   Mathematical modelling and the control of lymphatic filariasis. Lancet Infect Dis. 2004;4(4):223-
746   234.
747

748   35.   Singh BK, Bockarie MJ, Gambhir M, Siba PM, Tisch DJ, Kazura J, et al. Sequential modelling of
749   the effects of mass drug treatments on anopheline-mediated lymphatic filariasis infection in
750   Papua New Guinea. PLoS One. 2013;8(6):e67004.
751

752   36.   Singh BK, Michael E. Bayesian calibration of simulation models for supporting management of
753   the elimination of the macroparasitic disease, lymphatic filariasis. Parasit Vectors. 2015;8(1):522.
754

755   37.   Goldman AS, Brady MA, Direny A, Desir L, Oscard R, Vely J-F, et al. Costs of integrated mass
756   drug administration for neglected tropical diseases in Haiti. Am J Trop Med Hyg.
757   2011;85(5):826-833.
758

759   38.   DSDS: Population Totale, Population de 18 ans et Plus Menages et Densites Estimes en 2015.
760   Institut Haïtien de Statistique et d'Informatique (IHSI), Minstere de L'Economie et des Finances
761   (MEF), Republique d'Haiti, 2015.
762

763   39.   Michael E, Singh BK, Mayala BK, Smith ME, Hampton S, Nabrzyski J. Continental-scale, data-
764   driven predictive assessment of eliminating the vector-borne disease, lymphatic filariasis, in sub-
765   Saharan Africa by 2020. BMC Med. 2017;15(1):176.
766

767

768   40.   USAID: The Haitian sea salt industry: a commercialisation strategy. TechnoServe, March 2012.
769

770 41. Baltussen RM, Adam T, Tan-Torres Edejer T, Hutubessy RC, Acharya A, Evans DB, et al.
771   Making choices in health: WHO guide to cost-effectiveness analysis. WHO, Geneva 2003.
772
773 42. Guyatt H. Different approaches to modelling the cost-effectiveness of schistosomiasis control.
774   Mem Inst Oswaldo Cruz. 1998;93:75-84.
775
776 43. Hall A, Horton S, de Silva N. The costs and cost-effectiveness of mass treatment for intestinal
777   nematode worm infections using different treatment thresholds. PLoS Negl Trop Dis.
778   2009;3(3):e402.
779
780 44. Kim YE, Sicuri E, Tediosi F. Financial and economic costs of the elimination and eradication of
781   onchocerciasis (River Blindness) in Africa. PLoS Negl Trop Dis. 2015;9(9):e0004056.
782
783 45. Lee BY, Bartsch SM, Gorham KM. Economic and financial evaluation of neglected tropical
784   diseases. Adv Parasitol. 2015;87:329-417.
785
786 46. Lo NC, Bogoch II, Blackburn BG, Raso G, N'Goran EK, Coulibaly JT, et al. Comparison of
787   community-wide, integrated mass drug administration strategies for schistosomiasis and soil-
788   transmitted helminthiasis: a cost-effectiveness modelling study. Lancet Glob Health.
789   2015;3(10):e629-e638.
790
791 47. Turner HC, Truscott JE, Fleming FM, Hollingsworth TD, Brooker SJ, Anderson RM. Cost-
792   effectiveness of scaling up mass drug administration for the control of soil-transmitted helminths:
793   a comparison of cost function and constant costs analyses. Lancet Infect Dis. 2016;16(7):838-
794   846.
795
796 48. Gedge LM, Bettis AA, Bradley MH, Hollingsworth TD, Turner HC. Economic evaluations of
797   lymphatic filariasis interventions: a systematic review and research needs. Parasit Vectors.
798   2018;11(1):75.
799
800 49. Cordes JJ. Using cost-benefit analysis and social return on investment to evaluate the impact of
801   social enterprise: Promises, implementation, and limitations. Eval Program Plann. 2017;64:98-
802   104.
803
804 50. Manetti G. The role of blended value accounting in the evaluation of socio-economic impact of
805   social enterprises. Voluntas. 2014;25(2):443-464.
806
807 51. Banke-Thomas AO, Madaj B, Charles A, van den Broek N. Social Return on Investment (SROI)
808   methodology to account for value for money of public health interventions: a systematic review.
809   BMC Pub Health. 2015;15(1):582.
810
811 52. Mannar MV. Making salt iodization truly universal by 2020. IDD Newsl. 2014;42:12-15.
812
813

814 **Supporting Information**

815 **S1 Supporting Information. Lymphatic Filariasis model descriptions.**
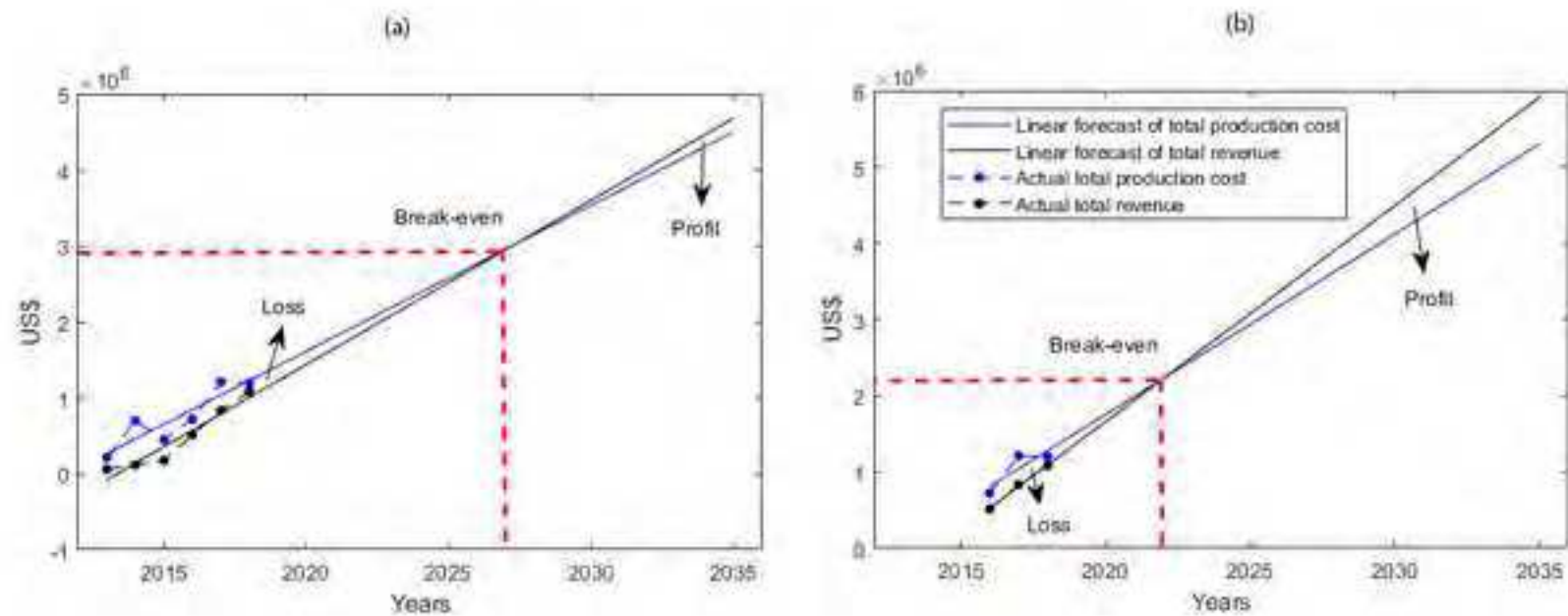
816

Figure 1

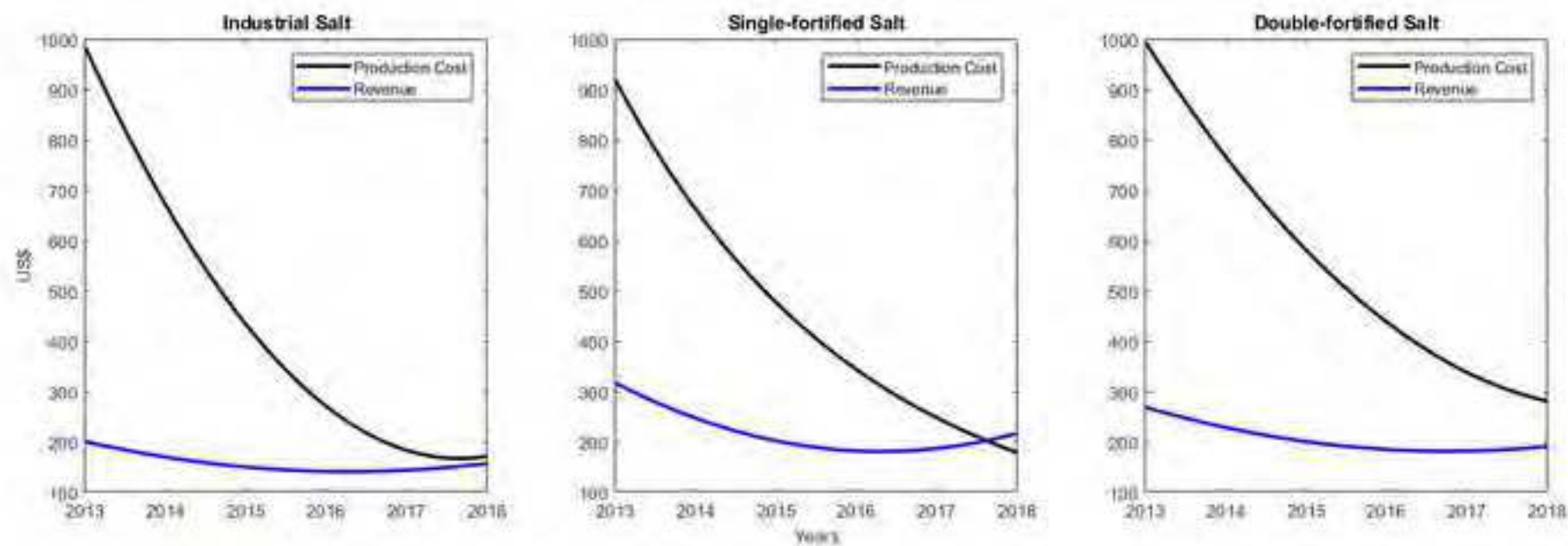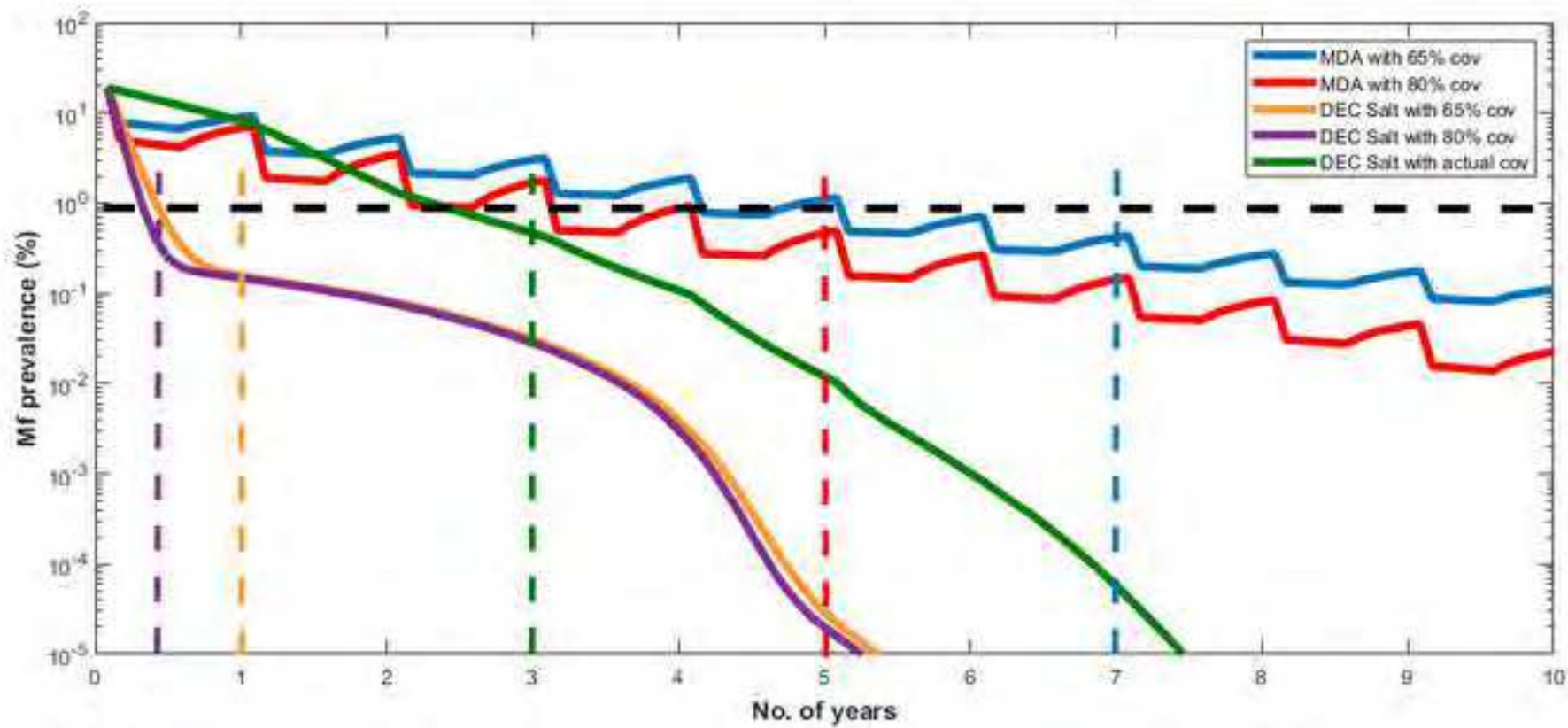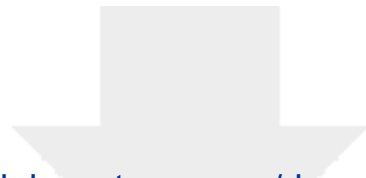Click here to access/download;Figure;Fig1.tif ⬇
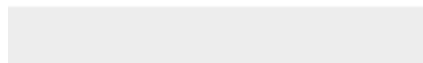

(a)

(b)

Figure 2

Figure 3

Click here to access/download

Supporting Information

S1_Supporting_information.docx

Deputy Editors,

Plos NTDs

Dear Deputy Editors,

Thank you for your email of Feb 1 2019 asking us to modify our manuscript" "Economic performance and cost-effectiveness of using a DEC-salt social enterprise for eliminating the major neglected tropical disease, lymphatic filariasis" (#PNTD-D-18-01969), according to reviewer comments. We are glad that the reviewers appreciated the attention to the important topic addressed by our paper, and provide below our itemized responses to each reviewer comments. Note we refer to new additions to text based on the tracked version of the revised ms.

We want to thank both reviewers for their comments, which has allowed us to clarify issues raised better.

Our itemized responses:

Reviewer #1: Overall this is a well written and interesting analysis of an important topic. In particular, I found the discussion well rounded and comprehensive.

The authors: We are pleased that the Reviewer found the paper well written and an interesting analysis of an important topic. Also that our discussion is well rounded and comprehensive.

Major comments

I think what you mean by social enterprise framework and how the salt is sold (and costs recovered) needs to be defined very clearer in the introduction or in a Box. Although this may seem like a minor comment, the paper is much harder to follow without this.

The authors: We thank the reviewer for bringing this need for clarity to our attention. We had given the definition of the framework of a social enterprise as it pertains to this work in lines 112-116, but also elsewhere (lines 447-455). However, we have amended the text in the revised version (lines 114-116) to clarify the business model behind the Haitian salt enterprise so as to define and describe it better.

The sensitivity analysis of the coverage achieved with DEC salt also needs to consider a much lower range (such as a 20% coverage).

The authors: For the sensitivity analysis with DEC salt, we have considered three different scenarios: (i) 65% coverage, (ii) 80% coverage, and (iii) actual coverage (8.45%, 17.06%, 12.23%, 19.12%, 37.41%, and 64.69% (Table 4)). Thus, the actual coverages modelled in (iii) already reflect a much lower range in the initial 5 years of the intervention. Also, as we explained on p. 21, a sensitivity analysis using coverage values 15-20% lower than those depicted in the Table did not affect the predicted timelines significantly.

Are the costs being discounted or adjusted for inflation at all? For the costs what is the base year of the analysis?

The authors: The costs (and outcomes) were not discounted or adjusted for inflation as we conveyed on p. 9. For the costs the base year of analysis is 2013.

The outcomes of the cost-effectiveness modelling and the analysis perspective should be defined in the methods.

The authors: We thank the Reviewer for these suggestions. The outcomes were originally defined in the 1st para of the Cost-Effectiveness modelling results section (p. 20 of the original ms). We agree with the Reviewer, however, that this should be placed in the Methods in a new section termed Cost-effectiveness analysis following the subsection labeled as Input Epidemiological Data (new pages 10-11). This has now been done. We have also included text to note that the analysis is from the perspective of the financial costs of a neglected tropical diseases treatment programe (p. 11).

Table 6: I don't think a CR ratio makes sense for this analysis. Comparing the Programme duration and cost is enough.

The authors: We are not sure what the Reviewer means. The CE ratio is calculated here is a standard method that compares the costs and effectiveness (duration of interventions until 1% mf prevalence) of different strategies to determine the greater (or not) benefit per cost unit of one strategy to another.

Minor comments

Please clarify how the compliance of MDA and DEC Salt was modelled (was any systematic non-compliance accounted for).

The author: This is a good point, but given our deterministic model as we have described previously, we model MDA coverage simply as a random proportion (of various coverages) of the total population given the drugs/consume the drugs.

Line 93 (and other places) what does the "[w/w]" mean.

The authors:"[w/w]" is a standard unit of concentration representing weight of DEC per weight of the salt mixture. Simply put, DEC (0.1-0.6%[w/w]) means that a given salt mix contains 0.1-0.6g of DEC in 100g of salt.

Line 152: I found "segments, viz. industrial" unclear.

The authors: Here we have described the three different types of salt, namely, industrial, coarse and fine single fortified and double fortified salt. Market segments refer to these the three salt types produced to serve each of the corresponding consumers.

Line 345-347: Unclear you are referring to DEC salt.

The authors: We apologize for this missing reference. We have changed the text in line 347/348 to rectify this mistake.

Lines 504-506: I think these are important points. Could you expand slightly? For example,

when you say the "current market price needs to be revised upwards", are you referring to the DEC salt or non-DEC salt.

The authors: Here we are referring the current market price of DEC salt which needs to be revised upwards to fully reflect the true marginal cost of adding DEC to untreated salt. As noted on p. 29, currently cross-subsidy from the sale of the more profitable industrial salt is used to keep the price of the DEC salt below the marginal cost of adding the drug to compete with untreated local edible salt. If we want to reach a faster breakeven point for DEC salt similar to industrial and single-fortified salt then we need to pursue the 3 strategies described on p. 30, one of which is to revise its price upwards. We have made this explicit now by indicating that it is the current market price of DEC salt needs to be revised upwards (p. 30). We thank the Review for pointing to the need to clarify this point better.

Figures 1 and 3. I don't think these having the 10^-x best scale to use. Why not put the cost (in millions) or the % value? It will be more understandable/accessible to non-mathematicians.

The authors: The scales were used in this format to better depict the results as otherwise the large numerical differences would compress the results and make the results different to discern. It is also a more natural depiction of timelines and break-even trajectories than using % values, particularly in the case of Fig 3.

Reviewer #2: Abstract:
•   Please provide clear results in rather than making conclusion. I would expect cost and effectiveness ratios in the abstract, before the authors concluded that the strategy is cost-effective option than annual DEC tablet-based MDA.

        The authors: We agree with the reviewer's comment, and indeed did provide the reasons why the DEC salt enterprise is a more cost-effective option than annual DEC tablet-based MDA, viz: (lines 45-49): "Due to increasing revenues obtained from the sale of DEC salt over time, expansion of its delivery in the population, and greater cumulative impact on the survival of worms, this strategy could also represent a significantly more cost-effective option than annual DEC tablet-based MDA for accomplishing LF elimination"

        However to better clarify why it is more cost-effective we have explicitly also included the following text (line 47): "....survival of worms leading to shorter timelines to extinction, this strategy...".

Introduction
•   Please provide clear status of the LF programme in Haiti, how many district/IU are endemic, how long has the treatment been given. How many district are still endemic, this will give clear relevance of the suggested intervention provision approach.

The authors: We did provide text (original lines 100-108) regarding the history and current status of the LF programme in Haiti. Following the Reviewer's suggestion, we have now provided further information on the programme in lines 102-105, together with the relevant references to provide a clearer picture of the programme.

•   If the programme achieved geographical coverage in 2012, what is the problem for not

achieving 2020 goal? This should be clearly described to bring the readers into the national context.

The authors: Geographic coverage simply means whether that the LF programme managed to treat all endemic communes. This is only one component for achieving elimination. As we noted (lines 106-109), despite achieving full geographic coverage by 2012, it is unlikely that national elimination will be achieved in 8 years due to the impact of high prevalence areas and the technical challenges commonly faced by long-term MDA programs (ex. sustained coverage, compliance, and resources). Also, while the WHO guidelines suggest that 4-6 years of MDA treatment at >65% coverage of a community could be enough to interrupt transmission, field and modelling evidence suggests achieving this 2nd criterion also may not produce this outcome similarly everywhere and additional rounds may be necessary in difficult areas (see references given line 108, plus our previous publications – refs 11 & 36 in particular).

Methods
•   The authors should do sensitivity analysis how the cost and effectiveness change based on change on the model assumptions.

The authors: We have done sensitivity analyses on cost and effectiveness based on variations that might be expected (see our response to Reviewer 1 above). Note we used models calibrated to local data to carry out the effectiveness simulations that accounted for variations in best-fitting parameters automatically (lines 180-189, with details provided in refs 32-36 on how our data-driven Monte Carlo model uses data to capture this model heterogeneity).


Results and discussion
•   It is important that authors bring the discussion with the actual current status of LF in Haiti.

The authors: We did provide information on the current status of LF originally and in response to the Reviewer's comments have clarified the situation further in lines 102 to 106. This is the published information currently available to us.

Yours sincerely

Edwin Michael
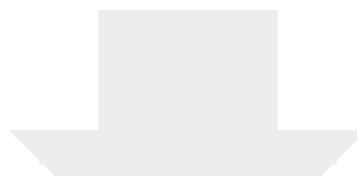
Click here to access/download
Revised Article with Changes Highlighted
economic analysis_DECSalt_revised_tracked.docx