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Outcomes and cost-effectiveness of an integrated holistic care package on persons affected by podoconiosis, lymphatic filariasis and leprosy and community members in north-western Ethiopia: an implementation research study

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Abstract

Background Most studies on integration of neglected tropical disease programmes have focused on mass drug administration or environmental measures rather than Disease Management, Disability and Inclusion (DMDI). The study reported here explored integration of a DMDI care package across three disabling, stigmatising neglected tropical diseases (podoconiosis, lymphatic filariasis and leprosy), across physical and mental health, and into the state health system.

Methods We conducted this pre-post study, the third phase of an implementation research project, in two predominantly rural districts in north-west Ethiopia in 2021. We assessed physical and mental health outcomes on 192 affected persons and 817 community members at baseline and 6 months after initiation of the integrated care package, implemented by nurses and health officers. Key outcomes measured were disability (using WHODAS-2.0), depression (Patient Health Questionnaire-9), discrimination (Discrimination and Stigma Scale), internalised stigma (Internalized Stigma Related to Lymphoedema), quality of life (Dermatology Life Quality Index) and social support (Oslo-3 Social Support Scale). Mixed effects linear regression models were used to estimate change in outcomes between baseline and 6 months after initiation of the care package. We also evaluated implementation feasibility and conducted cost-effectiveness analysis.

Results Among 221 patients, improvements were observed in foot (− 2.3 cm; 95% CI: − 2.2, − 1.8) and leg circumference (− 1.8 cm; − 2.0, − 1.7) and acute attacks (6.2; 0.0, 6.6); these were statistically significant at the 5% level. Reductions were seen in disability scores (− 6.5; − 7.6, − 5.5), depression (− 5.3; − 6.6, − 4.6), discrimination (− 3.3; − 4.2, − 2.3), internalised stigma (− 3.7; − 4.6, − 2.8), quality of life (− 4.0; − 4.8, − 3.2), and alcohol use (− 1.6; − 2.4, − 0.8). No notable changes were found in the presence of wounds or moss, or perceived social support. Across 817 community

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members, there was strong evidence that knowledge improved, and stigmatising attitudes and social distance reduced. The intervention was cost-effective in reducing depression and disability and improving health-related quality of life and feasible to implement.

Conclusion The integrated intervention is feasible and cost-effective even in remote areas and appears ideal for scale-up to other endemic regions in Ethiopia and other countries.

Keywords NTDs, Podoconiosis, Lymphatic filariasis, Leprosy, Mental health, Integration, Implementation research

Background

Integrated, people-centred management of neglected tropical diseases (NTDs) has long been seen as central to control or elimination of these diseases [1]. Integration (in the sense of provision of services across multiple conditions and of mainstreaming previously vertical programmes into government health systems) is advocated by the World Health Organization (WHO) 2021–2030 NTD Roadmap [2]. While a systematic review suggested that provision of services across multiple NTDs was cost-effective if based on good governance and thorough community engagement [3], most studies reviewed had integrated mass drug administration or environmental measures rather than Disease Management, Disability and Inclusion (DMDI). More recently, studies focusing on DMDI have enabled assessment of the value of integration across programmes [4] and of mainstreaming into state health systems [5].

DMDI services have been shown to be effective in mitigating the impact of podoconiosis, lymphatic filariasis (LF) and leprosy, three stigmatised skin conditions that exert considerable physical, social and economic burdens in Ethiopia [6–9]. Several studies, including randomised controlled trials, have demonstrated that encouraging simple self-care measures to promote foot hygiene can reduce limb swelling and improve quality of life [10–12]. The development of a cross-cutting sustainable DMDI programme was identified as a priority by the Ethiopian Federal Ministry of Health in 2016, with Ethiopia known to be home to an estimated 1.5 million living with podoconiosis, 5.6 million people at risk of LF, and 300,000 individuals affected by leprosy, causing significant morbidity [13]. The 'Excellence in Disability Prevention Integrated across NTDs' (EnDPoINT) project explored three dimensions of integration: across three NTDs, podoconiosis, LF and leprosy (two of which were previously managed through vertical programmes); across physical and mental health; and integration into the state health system (also termed 'mainstreaming').

The EnDPoINT project was designed in three phases, corresponding to the Medical Research Council (MRC)'s framework for the assessment of complex interventions [14]. Phase 1 involved care package development [15], Phase 2 comprised piloting and evaluation of the care package in one sub-district [16], and Phase 3 involved scaling up the care package in two districts. The full study protocol [17] and results of Phases 1 and 2 have been published elsewhere [16, 18]. In this paper we report the quantitative results of Phase 3, in which the impacts on physical and psychosocial outcomes for people affected by podoconiosis, LF, and leprosy, and on stigma outcomes amongst community members were assessed. A cost-analysis is also included.

Methods

Study setting

The study was conducted in Guangua (population 110,066) [19] and Ankesha Guagusa (population 142,947) districts of Awi zone, Amhara regional state, north-western Ethiopia, which together include 38 *kebeles* (smallest administrative units) and 10 health centres. These two districts were chosen in collaboration with the NTD department of the Federal Ministry of Health due to the lack of other DMDI programmes in the area and the co-endemicity of LF, podoconiosis and leprosy, with an estimated combined prevalence of 1% [7].

Study design

Using the Medical Research Council (MRC) Complex Intervention Framework, to develop, pilot, evaluate and implement the intervention, we conducted a pre-post study comparing physical and psychosocial characteristics of affected persons and community members at baseline and 6 months after initiation of the EnDPoINT care package.

Participants

People living with LF, podoconiosis and sequalae of leprosy in the (predominantly rural) target districts were identified from health records and were invited into the study by health extension workers (community health workers with 1 year of pre-service training). Inclusion criteria were: presence of lower limb lymphoedema (lower leg swelling) caused by one of the three diseases; age > 18 years; living in the district for more than 6 months; being willing to participate through written informed consent. Exclusion criteria were: presence of a terminal illness that prevented engagement in the care package; presence of nodules or wounds that required surgical or specialist management (those in the latter category were appropriately referred).

Community members in Guangua and Ankesha Guagusa districts were selected by allocating a sample proportional to the total population in each district and *kebele*, and selecting households within *kebeles* based on simple random sampling. We took samples from all Kebeles (sub-district) and got (villages) in the study districts. We selected samples randomly from each kebele/got proportional to population size. Inclusion criteria were resident of Guangua or Ankesha Guagusa districts ≥ 6 months; age > 18 years old; free of acute or debilitating illness; and able to communicate sufficiently in the local language.

Intervention

The EnDPoINT care package has been described elsewhere [15] and was delivered during Phase 3 between January and August 2021. In essence, the package included interventions at three levels of the health system (health organisation, facility, and community) to support limb care and mental health care appropriate to the three NTDs. At the healthcare organisation level, central coordination, supportive supervision and monitoring were introduced. At the facility level, primary care clinicians were trained in holistic management, offered simple hygiene supplies and given the skills to engage patients in self-care. At the community level, workshops were held to raise awareness and reduce stigma, community members were trained in DMDI and a Community Advisory Board was established.

Sample size calculations

For the patient cohort, the sample size calculation was based on results from EnDPoINT Phase 2 [16], with reduction in disability, as measured by the WHO Disability Assessment Schedule-2.0 (WHODAS-2.0), selected as the primary outcome measure. To detect a 3.1-point change in WHODAS-2.0 score, with 90% power at 5% significance, a one sample *t*-test of the paired differences requires 99 participants. With 13 health facilities in total, and assuming an intracluster correlation coefficient (ICC) of 0.05, the number of participants per facility needed for the analysis was 99*(1–0.05)/(13–99*0.05) = 12 per health facility, or a total of 156. Allowing for 20% attrition, the estimated total sample required was 195 participants. The community sample size calculation was based on an earlier knowledge, attitudes and practice (KAP) study in Ethiopia in which 55% of a community sample exhibited correct practice [20]. An unpaired before and after comparison would require 805 participants at each time point for 80% power at 5% significance to detect a change in correct practice from 55 to 62%. With a design effect of 1.2 the estimated sample size was 805*1.2 = 966.

Study outcomes

For affected persons, physical outcomes included: average maximum lower limb and foot circumferences in cm (measured at the widest point of the calf or foot and averaged across both legs); presence of wounds or nodules on either leg; report of ‘attacks’ of acute dermatolymphangitis in the last month (acute ‘attack’ being defined as the leg becoming hot, painful and more swollen); and signs of infection on either leg. The WHODAS-2.0, validated in Ethiopia, was used to assess disability. Scores range from 12 to 60, with higher scores reflecting greater disability [21]. Psychosocial outcomes for patients included: the Patient Health Questionnaire-9 (PHQ-9) to measure depressive symptoms [22], with total scores ranging from 0 (no depressive symptoms) to 27 (severe depressive symptoms); the Dermatology Life Quality Index (DLQI) validated in southern Ethiopia [23], with scores ranging from 0 (no effect of disease on life) to 30 (extremely large effect of disease on life); the Fast Alcohol Screening Test (FAST) to assess alcohol use disorder [24]; the discrimination section of the Discrimination and Stigma Scale (DISC)−12 [25], with modifications described in a previous Ethiopian study [26], scores ranging from 1 to 56, with higher scores reflecting more discrimination; the 11-item Internalized Stigma Related to Lymphoedema (ISRL) scale adapted from the Internalized Stigma of Mental Illness Inventory (ISMI) scale [27], scores ranging from 11 (less stigma) to 44 (more stigma); and the Oslo-3 Social Support Scale (OSSS) [28], with scores from 3 to 14, higher scores representing better support.

Amongst community members, outcomes included: access to sources of health information (five questions about frequency of exposure to sources such as magazines, radio, television, health education sessions and meetings, with total scores ranging between 5 and 15, and higher scores indicating better access to health information sources); knowledge about the causes of lymphoedema (ten indicators for podoconiosis, LF and leprosy with total scores ranging from 0 to 12, with higher scores representing better knowledge); attitudes towards persons affected by lymphoedema using an index constituting 13 negatively framed statements identified from previous reports [29, 30]; degree of closeness towards persons affected by lymphoedema using the 7-item Social Distance Scale (SDS) [31], adapted to the study context, with total scores ranging from 7 to 35 where lower scores indicated higher willingness to have social interactions.

For the cost-effectiveness analysis, data on use of healthcare services and associated costs were collected in relation to affected persons' lymphoedema, hospitalisations, medication, traditional remedies and money borrowing over the past year. We also measured the number of days completely unable to work (or go to school), and the number of days when they experienced some difficulties when working (or attending school).

Statistical analysis

All data were collected by trained field staff and transferred to an Excel data sheet for cleaning and verification, before being imported to Stata version 17 (College station, TX 77845, USA) for analysis. Mixed effects linear regression models with a random effect for participant and fixed effect for time-point were used to assess the magnitude and direction of changes as well as the statistical significance of trends in outcomes between baseline and 6 months after initiation of the care package. All models were adjusted for district, sex, religion, occupation, marital status, and relative income category. Loss in work productivity was costed using the average daily wages (Poor Persons' General consumer Price Index-Deflated Real Wages) for unskilled rural labour in Ethiopia, using figures for Amhara region in 2015 [32] and adjusting them to 2021 using purchasing power parity [33]. Costs in Ethiopian Birr (ETB) were converted to US dollars ($) using the average spot exchange rate [34] and to international dollars (I$) using purchasing power parity to reflect differences in price levels between countries [33]. Costs included cost of the EnDPoINT care package (estimated per patient in 2019 (870 ETB)[35] and adjusted to 2021 (1,028 ETB) [33] and cost of work productivity loss due to lymphoedema. For ethical reasons, we did not have a control group in this study, and all the participants were offered an intervention. In the cost-effectiveness analysis, we used the baseline data as control, or 'usual care'. Effectiveness estimates for PHQ-9, DLQI and WHODAS-2.0 were adjusted using a mixed-effects regression model with patient ID as random effect. Covariates included in the model as fixed effects were: age, gender, educational attainment, occupation, relative income, employment, and time point of data collection (baseline or 6 months).

For the incremental cost-effectiveness ratio (ICER), the difference in costs between 6 months and baseline (incremental cost) was divided by the difference in effectiveness scores between 6 months and baseline (incremental effect). The denominator was multiplied by −1 to reflect the fact that lower effectiveness scores indicate a better outcome.

$$\mathrm{ICER} = \frac{\mathrm{Cost}_{6\ \mathrm{months}} - \mathrm{Cost}_{\mathrm{baseline}}}{(\mathrm{Effect}_{6\ \mathrm{months}} - \mathrm{Effect}_{\mathrm{baseline}}) * -1}$$

Ninety-five per cent confidence levels for incremental costs and incremental effectiveness outcomes were calculated using the non-parametric bootstrap method (5000 replications). Cost-effectiveness analysis was conducted in Stata 17 (StataCorp, 2021).

Role of the funding source

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Results

Sociodemographic characteristics of patient cohort

For the patient cohort, 221 affected persons were assessed at baseline and 192 (86.9%) were followed up at endline (month 6). There were no observed differences in baseline characteristics of those lost-to-follow-up compared to those who completed follow-up. Table 1 shows their socio-demographic characteristics; most were married farmers with low levels of education who followed Orthodox Christianity.

Physical health outcomes for patient cohort

Table 2 shows the physical health characteristics of the patient cohort at baseline and endline. Six months after the care package had been initiated, there were significant reductions in limb and foot swelling, acute attack and disability.

Psychosocial outcomes for patient cohort

There were improvements between baseline and endline for depressive symptoms (− 5.3, 95% CI −6.6 to −4.6, $p <$ 0.001), discrimination (− 3.3, 95% CI −4.2 to −2.3, $p <$ 0.001), internalised stigma (− 3.7, 95% CI −4.6 to −2.8, $p < 0.001$), quality of life (− 4.0, 95% CI −4.8 to −3.2, $p =$ 0.004), and problematic alcohol use (− 1.6, 95% CI −2.4 to −0.8, $p < 0.001$); see Table 3.

Sociodemographic characteristics of community participants

Eight hundred twenty-six community members participated in the community survey at baseline, and 817 (98.9%) at endline. Table 4 shows their socio-demographic characteristics at baseline. As for the patients, most were married farmers with low levels of education who followed Orthodox Christianity.

Psychosocial outcomes for community participants

There were improvements between baseline and endline for all four community-level outcomes, i.e. for

Table 1 Sociodemographic characteristics of patient cohort

Variables	Baseline *N*	%	Lost-to-follow-up *N*	%
Age in years (mean, SD)	50.6 (SD = 13.0)		50.5 (SD = 11.3)	
Sex				
Male	108	48.9	17	58.6
Female	113	51.1	12	41.4
Total	221	100	29	100
District				
Ankesha Guagusa	112	50.7	15	51.7
Guangua	109	49.3	14	48.3
Total	221	100	29	100
Residence				
Urban	26	11.8	1	3.4
Rural	195	88.2	28	96.6
Total	221	100	29	100
Educational status				
Illiterate	142	64.3	17	58.6
No formal education	63	28.5	8	27.6
Formal education	16	7.2	4	13.8
Total	221	100	29	100
Religion				
Orthodox Christian	217	98.2	29	100
Muslim	4	1.8	0	0
Total	221	100	29	100
Marital status				
Single	6	2.7	0	0
Married	143	64.7	20	69.0
Separated/divorced	38	17.2	3	10.3
Widowed	34	15.4	6	20.7
Total	221	100	29	100
Occupation				
Merchant/petty trader	15	6.8	1	3.4
Farmer	173	78.3	28	96.6
Housewife	28	12.7	0	0
Other[a]	5	2.3	0	0
Total	221	100	29	100
Perceived relative income				
Poor	151	68.3	19	65.5
Average	66	29.9	10	34.5
Better off	4	1.8	0	0
Total	221	100	29	100
Children				
Yes	206	93.2	26	89.7
No	15	6.8	3	10.3
Total	221	100	29	100

[a] Unemployed or student

stigmatising attitudes (– 0.7, 95% CI −0.86 to −0.52), knowledge about lymphoedema (0.90, 95% CI 0.72 to 1.07), social distance (– 1.38, 95% CI −1.89 to −0.88), and source of information (– 0.10, 95% CI −0.33 to −0.02), see Table 5.

Economic analysis

Data on healthcare costs were collected for 289 participants. Average out-of-pocket expenses were 3552 ETB ($80, I$284) per year. Approximately 32% of families with affected people borrowed money from relatives or the community to meet their needs. Average amount of borrowings per year was 8911 ETB ($201, I$713) ranging from 50 to 40,000 ETB ($1–$902, I$4–I$3200). Approximately 86% of patients reported a reduction in daily activities due to their lymphoedema. They were completely unable to work or go to school on average 17.5 days per year and experienced some difficulties for an additional 12 days a year. Approximately 66% of patients required help with everyday chores on average 6 days per year. The estimated cost of work productivity loss due to lymphoedema was 1522 ETB ($34, I$122) per person per year.

Outcomes of the EnDPoINT care package used in the cost-effectiveness analysis are summarised in Appendix 1. The non-adjusted analysis is shown in Appendix 2. This analysis suggests that the EnDPoINT care package is likely to be cost-effective in reducing depression (PHQ-9) and disability (WHODAS-2.0) and improving health-related quality of life (DLQI) (Table 6). Figure 1 shows the cost-effectiveness planes generated using 5000 bootstrapped ICER estimates for EnDPoINT versus usual care. The majority of ICER estimates (92%) for the PHQ-9 (A), DLQI (B) and WHODAS 2.0 (C) fell into the lower right quadrant indicating that the EnDPoINT care package was less costly and more effective than usual care.

Discussion

The EnDPoINT study is the first to examine the impact and cost-effectiveness of the integration of a care package across three NTDs, across physical and mental health care, and into the state health system. The EnDPoINT care package was associated with significant improvements in many outcomes for people with lymphoedema caused by podoconiosis, LF, and leprosy in Awi zone, North-Western Ethiopia. Following its implementation, all patients were administering self-care, and significant improvements were noted in swelling of the feet and lower legs, signs of infection, disability, depressive symptoms, internalised stigma, perceived discrimination, quality of life, and problematic alcohol use. There was

Table 2 Physical health characteristics of patient cohort

Variables	**Baseline**		**Endline**		**χ^2 (95% CI)**	***p*-value**
	N	**%**	***N***	**%**		
Previous lymphoedema treatment					[a]	[a]
No	138	62.4	1	0.5		
Yes	83	37.7	191	99.5		
Total	221	100	192	100		
Current treatment or self-care for leg(s)					[a]	[a]
No	15	18.1	0	0		
Yes	68	81.9	191	100		
Total	83	100	191	100		
Source of treatment					0.18 (− 0.07, 0.05)	0.67
Government clinic	81	97.6	188	98.4		
Non-government clinic	2	2.4	3	1.6		
Total	83	100	191	100		
Presence of wounds					0.1 (0.001, 5.02)	0.75
No	216	97.7	187	97.4		
Yes	5	2.3	5	2.6		
Total	221	100	192	100		
Presence of Nodules					0.03 (0.001, 4.43)	0.86
No	206	93.2	175	91.1		
Yes	15	6.8	17	8.9		
Total	221	100	192	100		
Signs of infection					1.45 (0.003, 13.40)	0.23
No	213	96.4	189	98.4		
Yes	8	3.6	3	1.6		
Total	221	100	192	100		
Acute attack/reaction in the last month					6.24 (0.001, 6.64)	0.01
No	28	12.7	46	24.0		
Yes	193	87.3	146	76.0		
Total	221	100	192	100		
Mean maximum lower limb circumference (cm) (SD)	26.76 (4.8)		24.99 (4.0)		− 1.87(− 1.99, − 1.65)[b]	< 0.001
Mean maximum foot circumference (cm) (SD)	27.50 (3.1)		25.25 (3.2)		− 2.33(− 2.16, − 1.83)[b]	< 0.001
Mean WHODAS-2.0 scores (SD)	26.4 (7.1)		19.9 (5.1)		− 6.51(− 7.60, − 5.50)[b]	< 0.001

Abbreviations: *CI* Confidence interval, *SD* Standard deviation, *WHODAS-2.0* World Health Organization Disability Assessment Schedule-2.0

[a] The limited number of observations per cell (0 or 1) is too small to generate a valid *p*-value

[b] Mean (95% CI)

Table 3 Psychosocial outcomes for patient cohort: mixed effects linear regression

Variables	**Baseline**		**Endline**		**Mean change (95% CI)**	***P*-value**
	N	**Mean (SD)**	***N***	**Mean (SD)**		
Depressive symptoms (PHQ-9)	221	10.6 (5.4)	192	5.3 (5.1)	− 5.3 (− 6.6, − 4.6)	< 0.001
Discrimination (DISC)	221	8.5 (7.1)	192	5.1 (4.6)	− 3.3 (− 4.2, − 2.3)	< 0.001
Internalised stigma (ISRL)	221	27.0 (5.7)	192	23.3 (5.2)	− 3.7 (− 4.6, − 2.8)	< 0.001
Problematic alcohol use (FAST)	221	3.2 (2.4)	192	2.0 (1.9)	− 1.6 (− 2.4, − 0.8)	< 0.001
Quality of life (DLQI)	221	10.1 (4.8)	192	6.1 (3.9)	− 4.0 (− 4.8, − 3.2)	0.004
Social Support (OSSS)	221	7 (2.5)	192	6.9 (2.4)	− 0.1 (− 0.5, 0.3)	0.5

Adjusted for district, sex, religion, occupation, marital status, relative income

Abbreviations: DISC-12 Discrimination Score-12, *DLQI* Dermatology Life Quality Index, *FAST* Fast Alcohol Screening Test *ISRL* Internalized Stigma Related to Lymphoedema, *PHQ-9* Patient Health Questionnaire-9, *OSSS* Oslo Social Support Score

Table 4 Sociodemographic characteristics of community participants

Variables	***N***	**%**
Age in years, mean (SD)	**40.6 (14.7)**	
Sex		
Male	473	57.3
Female	353	42.7
Total	826	100
District		
Ankesha Guagusa	426	51.6
Guangua	400	48.4
Total	826	100
Educational status		
Illiterate	277	33.5
No formal education	254	30.8
Formal education	257	31.1
University/college diploma	38	4.6
Total	826	100
Religion		
Orthodox Christian	775	9
Protestant	1	3.8
Muslim	50	0.1
Total	826	6.1
		100
Marital status		
Single	124	15.0
Married	620	75.1
Separated/divorced	49	5.9
Widowed	33	4.0
Total	826	100
Occupation		
Merchant/petty trader	24	3.0
Farmer	610	75.3
Housewife	65	8.0
Student	88	10.9
Civil servant	7	0.9
Daily labourer	16	2.0
Total	810	100
Perceived relative income		
Poor	304	36.8
Average	337	40.8
Better off	185	22.4
Total	826	100

no improvement in perceived social support, possibly reflecting the relatively short follow-up period.

The improvement in disability for patients is in line with the preceding EnDPoINT pilot study [16], and a study in India showing significant reduction of disability scores between baseline and 24 months following simple hygiene-based lymphoedema care [36]. However, the GoLBeT pragmatic randomised controlled trial in Ethiopia was not able to demonstrate any change in disability score between the immediate treatment group and control group [37]. This difference may be explained by the emphasis on integration core to the EnDPoINT study, which included psychosocial and mental health care and engaged four levels of care (patient, community, health facility and health care organisation) in an attempt to mainstream the package. In contrast, the GoLBeT trial focused on the patient but did not engage the community or health system to any great extent. GoLBeT brought valuable evidence around the effectiveness of simple physical care but did not address the psychosocial needs of patients. The support for these needs brought by the EnDPoINT care package may have contributed to adherence to foot care, reduction of lymphoedema, and ultimately, reduction of disability. Recent comparison of counties in Liberia in which integrated DMDI was conducted compared to counties without integrated care suggested better adherence with treatment for lymphoedema and Buruli ulcer [5]. Similar to EnDPoINT, training at several levels of the health system (in Liberia, of community health workers—Community Health Volunteers or Community Health Assistants—as well as health facility staff) was considered vital to achieving these outcomes.

The improvements in psychosocial outcomes such as depressive symptoms, quality of life, internalised stigma and discrimination, are also similar to those in the EnDPoINT pilot study [16]. To our knowledge there are only two studies which have examined the impact of a hygiene and skin care-based NTD-related lymphoedema intervention on depressive symptoms, our pilot study and one in Togo where implementation of a national lymphoedema management program resulted in a significant reduction in depression [38]. In terms of quality of life, the GoLBeT trial [10], an earlier non-randomised study in southern Ethiopia [39], and a study using a hygiene and skin care regimen for persons affected by lymphoedema in Guyana in South America [40], also showed significant improvements. All these studies suggest that a hygiene and skin care-based lymphoedema management program is associated with better quality of life whether or not psychosocial and mental health needs are specifically addressed. We are not aware of any other study examining the impact of a lymphoedema care package on stigma and discrimination, making it difficult to know whether this benefit within EnDPoINT arose from engagement with the community and health system.

Our study also showed marked improvements in several community outcome measures, including a reduction in stigmatising attitudes towards affected persons,

Table 5 Psychosocial outcomes for community survey participants: mixed effects linear regression

Variables	Baseline		End-line		Mean change (95% CI)	*P*-value
	N	Mean (SD)	*N*	Mean (SD)		
Source of information	826	13.0 (1.8)	817	13.1 (1.6)	− 0.10 (− 0.33, − 0.02)	0.03
Stigmatising attitudes	826	2.9 (1.9)	817	2.2 (1.6)	− 0.70 (− 0.86, − 0.52)	< 0.001
Knowledge about lymphoedema	826	7.2 (1.8)	817	8.1 (1.6)	0.90 (0.72, 1.07)	< 0.001
Social Distance Scale	826	18.4 (6.0)	817	16.8 (5.1)	− 1.38 (− 1.89, − 0.88)	< 0.001

Adjusted for district, sex, religion, occupation, marital status, and relative income

Table 6 Summary of the cost-effectiveness analyses of EnDPoINT compared to usual care using different effectiveness outcomes

	Total cost, ETB mean (SD)	Total effect mean (SD)	Difference[a] in cost, ETB mean (95% CI)	Difference[a] in effect mean (95% CI)	ICER point estimate
PHQ-9					
EnDPoINT	3145 (1669)	5.3 (1.0)	− 279 (− 662, 104)	− 5.3 (− 5.5, − 5.1)	EnDPoINT dominates
Usual care	3424 (2272)	10.6 (1.02)			
DLQI					
EnDPoINT	3145 (1669)	6.1 (0.74)	− 279 (− 662, 104)	− 3.9 (− 4.1, − 3.8)	EnDPoINT dominates
Usual care	3424 (2272)	10.0 (0.72)			
WHODAS 2.0					
EnDPoINT	3145 (1669)	19.9 (0.91)	− 279 (− 662, 104)	− 6.5 (− 6.7, − 6.3)	EnDPoINT dominates
Usual care	3424 (2272)	26.4 (0.88)			

The costs were rounded to one ETB. The effectiveness outcomes were adjusted for covariates using a linear mixed effects model (see the "Methods" section). Lower PHQ-9, DLQI and WHODAS 2.0 scores indicate better outcome

ETB, Ethiopian Birr; *PHQ-9*, Patient Health Questionnaire 9; *DLQI*, Dermatology Life Quality Index; *WHODAS 2.0*, WHO Disability Assessment Schedule 2.0; *ICER*, incremental cost-effectiveness ratio

[a] Bootstrapped using 5000 replicates

a reduction in perceived social distance and an improvement in knowledge about lymphoedema. The community-based awareness raising and stigma reduction activities in the EnDPoINT care package seem likely to have contributed to the reduction of stigmatising attitudes, as may the healthcare professional training. We recommend that information dissemination, awareness-raising and stigma reduction activities are integral parts of DMDI for these three NTDs.

Our economic analysis suggests that the EnDPoINT care package is very likely to be cost-effective compared to "usual care" in reducing depression, disability and improving health-related quality of life. Reduction in cost was driven by lower work productivity losses in the intervention group: the number of days when participants were completely unable to work (or go to school) due to their lymphoedema fell by more than 60% following 6 months of the intervention. These results are consistent with findings from the GoLBeT study [10].

Study limitations

In keeping with most implementation research studies, we did not include a control group, because it would have been unethical to withhold knowledge of lymphoedema management techniques as recommended by WHO in endemic countries. To evaluate the effectiveness of the intervention over time, we instead compared baseline measures with endline results. Although theoretical plausibility and previous literature support a causal link [11, 12, 37], any significant trends seen over the timeframe of the study cannot be confirmed as only being due to the care package itself.

Conclusion

In conclusion, this study suggests that the integrated EnDPoINT care package is effective in improving the physical and psychosocial health of people living with podoconiosis, LF, and leprosy in north-western Ethiopia, and the knowledge and attitudes of the communities around them. This approach, which integrates across diseases, across mental and physical health and into the state health system, is feasible and cost-effective even in remote rural areas and appears ideal for scaling up to other endemic regions in Ethiopia and other countries. Certain contextual factors may have contributed to the success of this project, for example that the study districts had an organised, committed and diligent NTD

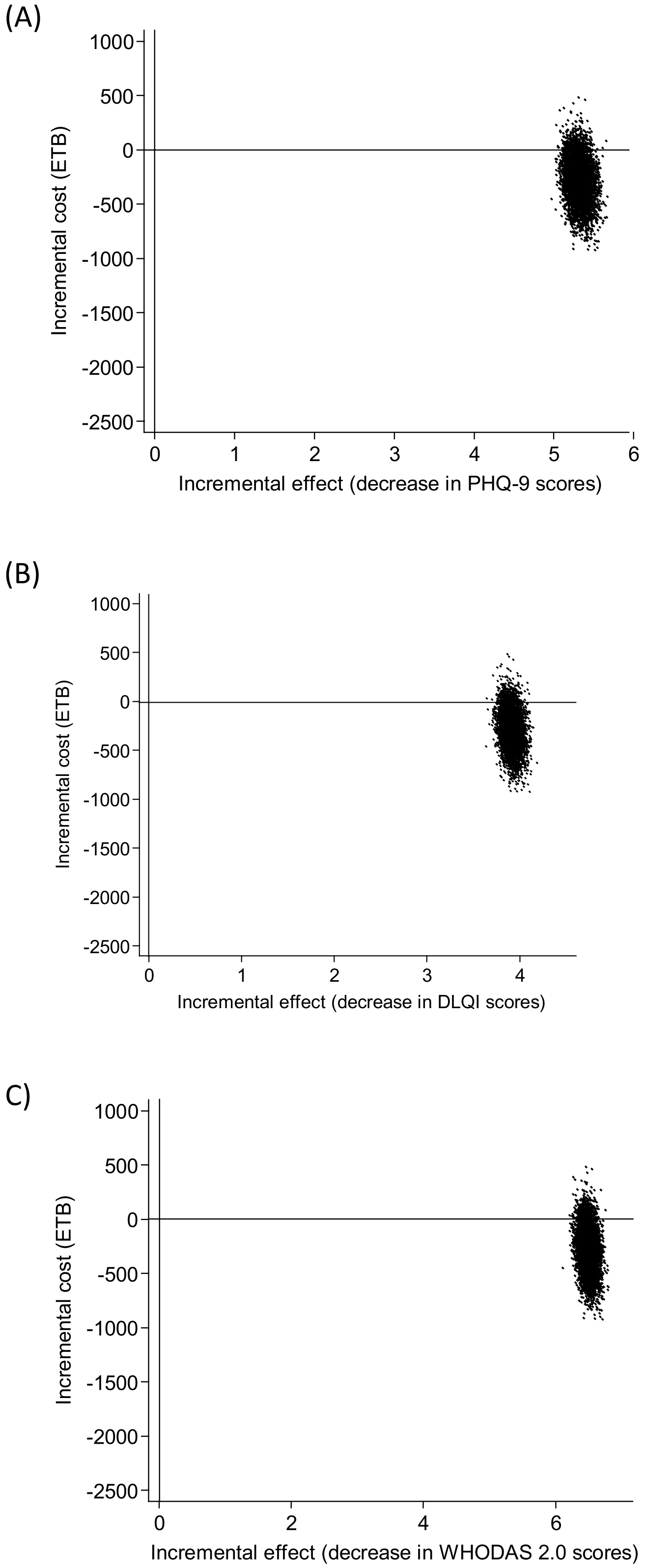

Fig. 1 Cost-effectiveness planes generated using different effectiveness outcomes: PHQ-9 (**A**), DLQI (**B**) and WHODAS-2.0 (**C**) for EnDPoINT versus usual care. The incremental effectiveness outcomes were multiplied by – 1 to reflect the fact that the lower effectiveness scores indicate better outcome. The graph shows 5000 bootstrap ICER estimates

team and health staff who supported the research team in coordinating community mobilisation, case finding, case assessment and basic lymphoedema care. Future studies should therefore confirm the transferability of the EnDPoINT care package to other settings.

Appendix 1

Table 7 Effectiveness outcomes at baseline and 6-months follow-up (non-adjusted)

Outcomes	Baseline (*n* = 221)	6 months (*n* = 192)
PHQ-9, mean (SD)	10.6 (5.4)	5.3 (5.1)
DLQI, mean (SD)	10.0 (4.8)	6.1 (3.9)
WHODAS-2.0, mean (SD)	26.4 (7.1)	19.9 (5.1)
Days unable to work/month, mean (SD)	3.0 (2.3)	2.0 (1.7)
Days with reduced activity/month, mean (SD)	2.8 (2.5)	1.5 (1.4)

PHQ-9 Patient Health Questionnaire 9, *DLQI* Dermatology Life Quality Index, *WHODAS 2.0* WHO Disability Assessment Schedule 2.0. Lower PHQ-9, DLQI and WHODAS 2.0 scores indicate a better outcomeAppendix 2

Table 8 Summary of the cost-effectiveness analyses of the EnDPoINT care package compared to usual care using various effectiveness outcomes (non-adjusted data)

	Total cost, ETB mean (SD)	Total effect mean (SD)	Difference[a] in cost, ETB mean (95% CI)	Difference[a] in effect mean (95% CI)	ICER point estimate
PHQ-9					
EnDPoINT	3145 (1669)	5.3 (5.1)	− 279 (− 658, 100)	− 5.3 (− 6.3, − 4.3)	EnDPoINT dominates
Usual care	3424 (2272)	10.6 (5.4)			
DLQI					
EnDPoINT	3145 (1669)	6.1 (3.9)	− 279 (− 658, 100)	− 3.9 (− 4,7, − 3.1)	EnDPoINT dominates
Usual care	3424 (2272)	10.0 (4.8)			
WHODAS-2.0					
EnDPoINT	3145 (1669)	19.9 (5.1)	− 279 (− 658, 100)	− 6.5 (− 7,6, − 5.3)	EnDPoINT dominates
Usual care	3424 (2272)	26.4 (7.1)			

[a] Bootstrapped using 5000 replicates. *ETB* Ethiopian Birr, *PHQ-9* Patient Health Questionnaire 9, *DLQI* Dermatology Life Quality Index, *WHODAS-2.0* WHO Disability Assessment Schedule 2.0, *ICER* Incremental cost-effectiveness ratio. The costs were rounded to one ETB. Lower PHQ-9, DLQI and WHODAS 2.0 scores indicate better outcome

Abbreviations

NTD	Neglected tropical disease
DMDI	Disease Management, Disability and Inclusion
LF	Lymphatic filariasis
WHO	World Health Organization
WHODAS	WHO Disability Assessment Schedule
DISC	Discrimination and Stigma Scale
PHQ-9	Patient Health Questionnaire-9
ISRL	Internalized Stigma Related to Lymphoedema
DLQI	Dermatology Life Quality Index
FAST	Fast Alcohol Screening Test
Oslo-3	Oslo-3 Social Support Scale
EnDPoINT	Excellence in Disability Prevention Integrated across NTDs
MRC	Medical Research Council
KAP	Knowledge, Attitudes and Practice
ETB	Ethiopian Birr

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Authors' contributions

The study was conceptualized by AF, MS and GD. AMi, OA, and NH analysed and interpreted the data, while VA and SB oversaw data management. OA prepared the initial manuscript draft under the guidance of MS, AF, and GD. AMe and MK contributed to study implementation. All authors read and approved the final manuscript.

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Data availability

The deidentified participant dataset and statistical analysis plan will be made available for 5 years following publication of the main manuscript. These will be made available after approval of a proposal and signature of a data access agreement. Proposals should be directed to globalhealth@bsms.ac.uk.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Review Board of the College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia (reference 061/18/CDT), and from the Brighton and Sussex Medical School Research Governance and Ethics Committee, Brighton, UK (reference ER/BSMS9D79/4).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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