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## PODOCONIOSIS IN ETHIOPIA: FROM NEGLECT TO PRIORITY PUBLIC HEALTH PROBLEM

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### ABSTRACT

*Podoconiosis is a geochemical disease occurring in individuals exposed to red clay soil of volcanic origin. This Neglected Tropical Disease (NTD) is highly prevalent in Ethiopia. According to the nationwide mapping in 2013, the disease is endemic in 345 districts, where an estimated 35 million people live. The government of Ethiopia prioritized podoconiosis as one of eight priority NTDs and included it in the national integrated master plan for NTDs. An integrated lymphoedema management guideline has been developed. Service expansion has continued in the last few years and lymphoedema management services have been expanded to over one hundred endemic districts. The last few years have been critical in generating evidence about the distribution, burden and effective interventions for podoconiosis in Ethiopia. Although the extent of the problem within Ethiopia is considerable, the country is well positioned to now scale-up elimination efforts. Given the extraordinary progress of the past ten years and the current commitment of government, private and third sectors, Ethiopia seems to be on course for the elimination of podoconiosis in our lifetime. We need continued strong partner commitment, evidence-building, and scale-up of activities to accomplish this.*

**Key words:** NTDs, Podoconiosis, Ethiopia.

### INTRODUCTION

Podoconiosis (endemic non-filarial elephantiasis) is a geochemical disease occurring in individuals exposed to red clay soil of volcanic origin (1). The disease causes bilateral, but asymmetrical swelling almost invariably of the lower legs (2). Although the etiology is not fully understood, existing scientific evidence suggests the important role of exposure to irritant red clay soil in endemic areas as well as the effect of genetic susceptibility (3,4). Globally, the disease occurs in highland areas of tropical Africa, Central America and northwest India and is related to poverty. Studies have also indicated that podoconiosis exists in areas where the altitude is above 1000meters above sea level and annual rainfall above 1000 millimeters. About 4 million people are said to be affected by the disease worldwide and it is deemed a serious public health problem in at least 10 African countries (1).

The disease impinges on affected individuals' health, social and economic wellbeing. For example, a study in Wolaita in southern Ethiopia has indicated the total direct costs of podoconiosis amounted to the equivalent of US\$ 143 per patient per year with a productivity loss amounting to 45% of working days per year per patient. In a zone with 1.5 million population, the overall cost of podoconiosis exceeds US\$ 16 million per year (5), primarily from acute dermatolymphangioadenitis (ADLA) 'acute attacks' which are recurrent painful episodes of inflammatory swelling of the lymphedematous legs. Acute attacks are common and disabling complications of podoconiosis lymphoedema. Studies have documented that most patients on average experience five or more episodes of acute attacks per year and spend a total of 90 days per year incapacitated by ADLA resulting in a loss of productive days (6). In filarial lymphoedema (LF), episodes of ADLA have been shown to accelerate damage to peripheral lymphatic vessels and to lead to fibrosis (7). Podoconiosis is also associated with serious social consequences (8-10).

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**The Ethiopian Context:** The rise of podoconiosis from neglect to priority public health problem is no small feat. Over the past few decades, new and emerging diseases as well as the Millennium Development Goals (MDGs) have led to multiple health policies yielding positive results in Ethiopia. Unfortunately, until 2013 none of these policies have mentioned or prioritized podoconiosis or other tropical diseases. Podoconiosis was particularly neglected because it was found to be non-communicable and to overwhelmingly cause morbidity rather than mortality. Following the pioneering work of Ernest Price in the 1970s (1) and his death in 1990, there was little discernible pattern of interaction between research and policy. Soon after his death, podoconiosis entered a “dark age” for over a decade. However, its revival began with the Ethiopian millennium, with initiation of podoconiosis research in Addis Ababa University, School of Public Health. Over the past 14 years, the interplay between scientific research and international partnerships on podoconiosis brought podoconiosis to the policy arena. A trans-disciplinary approach to podoconiosis research was applied (11), and a series of pioneering studies were conducted.

Early studies explored disease prevalence (12), disease burden (6,13,14), economic burden, disease staging, genetics and research ethics (3-5,15,16). In addition studies on the social consequences such as quality of life, stigma and mental distress (8,17,18) were conducted. The validation of important tools such as the Dermatology Life Quality Index (19), ethical issues in approaching podoconiosis patients and communities in which they live (16), and the identification of individual correlates and minerals that trigger podoconiosis were all important (20,21). A recent study mapped podoconiosis nationally and showed that the disease is endemic in 345 districts and had a prevalence of 4% nationally (22-24). In addition, 34.9% (43.8%) of the Ethiopian population lives in an environment conducive for podoconiosis (23). Another important ongoing study is a randomised controlled trial in northern Ethiopia investigating the effectiveness of lymphoedema management in podoconiosis. The study is the first fully controlled, pragmatic trial of the intervention and the evidence is highly likely to inform the implementation of podoconiosis control interventions in a new master plan for integrated control of neglected tropical diseases (NTDs) (25).

Building scientific evidence and advocacy has improved the awareness of diseases and resulted in improved knowledge and documented best practices for planning of the treatment and prevention needs of podoconiosis patients. These have led to a clear sense of urgency among the government of Ethiopia, Universities, research institutes, funders, and non-governmental organizations to forge a partnership against NTDs and, in particular, on LF and podoconiosis (26). Effective advocacy and international partnerships led to significant progress, most notably, the World Health Organization’s inclusion of podoconiosis into its official list of NTDs (27,28) and the National Master Plan for NTDs (29). This heralded the dawn of a new era for podoconiosis and other NTDs. A few non-governmental organizations (NGOs) have led efforts implementing podoconiosis intervention programs in Ethiopia. They were jointly able to reach only 3% of the estimated cases, covering 12% of the endemic districts. The umbrella organization for NGOs working on podoconiosis treatment and prevention, the National Podoconiosis Action Network (NaPAN), was founded with the objective of helping these organizations share experience and translate research into practice towards the ultimate goal of providing treatment services to all patients and preventing new cases in endemic areas (27). Accordingly, through grants to NaPAN from partners for podoconiosis prevention and treatment activities, the number of successfully managed cases has risen steadily, reaching 6% (26).

Podoconiosis is an entirely preventable non-communicable disease. It has been eradicated from countries in northern Africa and Europe since footwear use has become standard (2), demonstrating that elimination can be achieved in Ethiopia. Although the Ethiopian Federal Ministry of Health has prioritized podoconiosis for elimination by 2020, the national program is faced with significant challenges to stay on track for the 2020 target (26). The purpose of this special issue is, therefore, to offer a comprehensive picture of the journey of podoconiosis in Ethiopia from neglect to priority public health problem and now to look ahead to the 2020 target of elimination of NTDs in Ethiopia. In the following sections, we review the social and economic burden of podoconiosis; operational and basic research gaps: epidemiology and distribution mapping, program implementation, scale up, partnerships and challenges and future prospects.

**Burden of disease:** Podoconiosis is widely distributed in selected countries in Africa, South America, and Asia (1). At least ten African countries have highland areas where podoconiosis is endemic. In Ethiopia, past studies in different regions of the country have documented prevalence estimates ranging from 2.8% to 7.4% (11). Most recently, a large integrated mapping of podoconiosis and lymphatic filariasis was conducted to estimate the geo-

graphical distribution of podoconiosis at national level. A total of 775 districts were surveyed from all nine regional states and two city administration. Podoconiosis was most common in the central highlands of Ethiopia, in Amhara, Oromia, and Southern Nations, Nationalities, and Peoples Region (SNNPR) regional states. Regression modelling showed that the probability of podoconiosis increased with increasing altitude, precipitation, and silt fraction of soil and decreased with population density and clay content. Based on this model, researchers estimated that 43.8% of Ethiopia's national population lived in areas environmentally suitable for the occurrence of podoconiosis in 2010.

The recent mapping in Ethiopia showed that podoconiosis is widespread in the country. According to the national map of podoconiosis (23), there are 345 districts with a prevalence >1% (see Table 1). Most of these districts are found in Oromia, Amhara and SNNPR regional States. In total, 35 million people live in these districts where podoconiosis is endemic. Podoconiosis is widespread in six Regional States in the country (Amhara, Benishangul Gumuz, Oromia, SNNPR, Somali and Tigray) (23)

Table 1. Classification of prevalence of podoconiosis among adults  $\geq 15$  years old in Ethiopia, by region

Region	Podoconiosis prevalence category (%)						Total	$\leq 1\%$	$> 1\%$
	0	0.01-1	1.01-5	5.01-10	10.1-15	$> 15$			
Addis Ababa	4	0	0	0	0	0	4	4	0
Afar	32	0	0	0	0	0	32	32	0
Amhara	55	25	40	6	7	11	144	80	64
Benishangul Gumuz	16	1	3	1	0	0	21	17	4
Dire Dawa	7	0	0	0	0	0	7	7	0
Gambella	10	0	0	0	0	0	10	10	0
Harari	8	1	0	0	0	0	9	9	0
Oromia	104	50	76	32	15	21	298	154	144
SNNPR	21	6	39	40	24	25	155	27	128
Somali	38	10	1	0	0	0	49	48	1
Tigray	30	12	4	0	0	0	46	42	4
Total	325	105	163	79	46	57	775	430	345

**Social burden:** The social burden podoconiosis imposes is immense. Podoconiosis is a poorly understood disease and this has led to widespread misconceptions about the causes, prevention and treatment. Although it is rarely a cause of mortality, podoconiosis is a disabling and highly disfiguring condition which places a large psychosocial burden on individual patients. Understanding the socio-cultural milieu in which podoconiosis patients live and the consequences they face as a result of the disease is of paramount importance for the implementation of disease prevention strategies and programs.

Podoconiosis patients face significant stigma from their communities. Earlier qualitative work suggested that the familial tendency of the disease contributes to the social burden it imposes[30]. Subsequent studies in Ethiopia have also described a similar manifestation of intense podoconiosis-related stigma. For example, a study in southern Ethiopia identified the following podoconiosis-related social phenomenon: unwillingness to marry a diseased person or anyone from a podoconiosis-affected family; shunning of patients and family members; avoiding physical contact with patients; excluding patients from social events like weddings and funerals; spitting on patients; pinching nose when walking past patients at a distance; unwillingness of classmates to sit with patients at the same desk in school; and unwillingness of unaffected family members to approach an affected household member (8,30). Podoconiosis was derogatorily termed *gediyakita*, which means leg swelling (16).

In another study by Molla et al. in Northern Ethiopia, approximately 13% of patients mentioned that they had experienced one or more forms of social stigmatization at school, church, or in the market place including school dropout, forced exclusion, not buying products from them, shunning, pointing at them, nose pinching and insulting

(31). Similarly, a study on the extent of stigma in southern Ethiopia showed that over half of affected patients in endemic areas reported significant levels of stigma (32). In general, podoconiosis patients are stigmatized by communities in which they live as well as by health professionals including social isolation, differential treatment at social events such as funerals and weddings, discrimination in marriage, leadership roles and decision-making roles in community affairs (9,10,31).

People with podoconiosis were also found to have higher mental distress than healthy controls, suggesting that podoconiosis is associated with reduced quality of life and depression (33,34). These will undoubtedly lead patients to resort to coping strategies that could be positive or negative. For example, avoidant behaviors were described in a study in Southern Ethiopia including avoiding participation in church, school, funerals and weddings; avoiding marriage to non-patients; taking actions like abduction, changing place of residence and premarital sex during mate selection; divorce; and in extreme cases, suicidal ideation (8) as well as avoid seeking treatment (31). The social burden also extends to family members through perceptions of fear of public identification of the familial nature of the disease and costs associated with care (8). Based on these findings, the integration of psychosocial care and stigma reduction strategies into current morbidity management of podoconiosis is essential (32,34).

**Economic burden:** As a chronic and debilitating condition, podoconiosis has had a large economic impact on affected areas. A study by Tekola *et al.* found that the total direct costs of podoconiosis were approximately 143 US dollars per patient per year (5). The productivity loss per patient was estimated at 45% of all working days in a year. In Wolaita Zone with a population of 1.5 million people in Southern Ethiopia, the overall cost of podoconiosis was more than 15 million US dollars per year (5). Studies in Western and Southern Ethiopia found that 76-100% of podoconiosis patients were in the economically productive age groups of 15-64 years (5,13,14). Concerns have also been raised about the economic sustainability and scale-up of podoconiosis treatment activities. However, a study by Tamiru *et al.* found that most patients were willing to pay for podoconiosis treatment services, suggesting that a subsidized cost-recovery system could be used to increase podoconiosis treatment utilization and sustainability of efforts (35).

**Control strategies:** The key strategies for podoconiosis control are prevention of contact with irritant soil (primary prevention) and lymphoedema morbidity management (secondary and tertiary prevention) (36) (Figure 1). The primary prevention of podoconiosis includes using footwear, regular foot hygiene and covering the house floor. These measures will prevent contact between the foot and the minerals triggering the inflammatory process. Secondary and tertiary prevention of the disease are based on lymphoedema management which consists of foot hygiene, foot care, wound care, compression, exercises and elevation, treatment of acute attack and use of shoes and socks to reduce further exposure to the irritant soil. In some cases with nodules, surgical excision of the nodules may be recommended. Price described the objectives of secondary and tertiary prevention as (37):

- To arrest progress of early disease
- To reduce the frequency of acute attack
- To reduce the swelling of the limbs, and
- To maintain reduction of the swelling

The first proof-of-concept study of podoconiosis lymphoedema morbidity management indicated modest clinical improvement and significant improvements in quality of life(38). Currently, there is an ongoing Randomized Controlled Trial (RCT) which is aimed at measuring the effectiveness and cost-effectiveness of morbidity management (25).

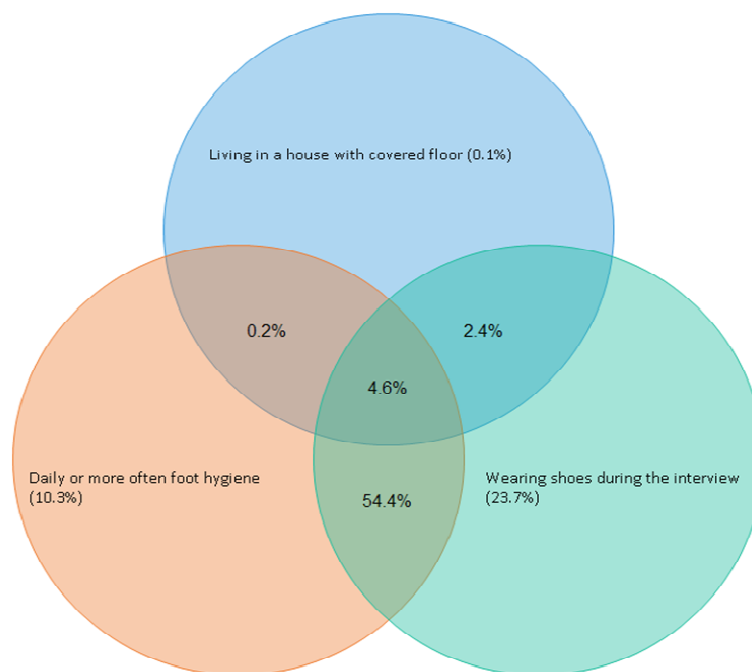


Figure 1. Overlap between the three key prevention practices for podoconiosis.

The blue circle shows that 7.3% of patients live in houses with covered floors. The green circle shows that 85.1% of those interviewed wore shoes during the interview. The orange circle shows that 69.5% of patients interviewed wash their feet daily or more often. The overlapping sections indicate the intersections of these three podoconiosis preventive practices.

Accurate diagnosis of podoconiosis is important for case management, surveillance, and research. The diagnosis of podoconiosis is established clinically. There is no gold standard point-of-care diagnostic tool. Although lymphoedema of the lower leg in endemic areas is highly suggestive, no clinical signs of disease are pathognomonic for podoconiosis. Currently, podoconiosis is a diagnosis of clinical exclusion based on history, physical examination and certain disease-specific tests to exclude common differential diagnoses. Several studies have shown that 30–40% of podoconiosis patients report having affected blood relatives (6,13,14,39,40). Therefore, enquiring about family history may also assist as a pointer towards the diagnosis of podoconiosis. Although shared risks of LF might also result in clustering of LF cases within a household.

The common differential diagnoses of podoconiosis are filarial elephantiasis, lymphoedema of systemic disease and leprotic lymphoedema. Although there are point-of-care diagnostic tests for lymphatic filariasis infection, these are not very sensitive in establishing filarial infection among advanced cases. The differentiation of podoconiosis from filarial elephantiasis uses a panel approach, including clinical history, physical examination, antigen and antibody tests. The swelling of podoconiosis starts in the foot and progresses upwards (1), whereas the swelling in filarial elephantiasis starts elsewhere in the leg. Podoconiosis lymphoedema is bilateral, asymmetric, usually confined to below the level of the knees, and unlikely to involve the groin (2). In contrast, filarial elephantiasis is commonly unilateral and extends above the knee, usually with groin involvement. In addition to the clinical history and physical examination, an antigen-based ICT test (the Binax©NowFilaria ICT) can also help to further distinguish between the two lymphoedemas, although the majority of filarial elephantiasis patients are also negative for the antigen-based test.

The other important differential diagnosis is leprotic lymphoedema. In podoconiosis patients, sensory perception of the peripheral nerves is intact in the toes and forefoot, and there are no neurotrophic ulcers or thickened nerves (2). Onchocerciasis also has clear clinical features which can easily be distinguished from podoconiosis. Systemic causes of lymphoedema can be ruled out by examination of other organ systems. Some hereditary lymphoedemas can be excluded since they occur at birth or immediately after birth, whereas podoconiosis requires extended exposure to red clay soil.

**Program implementation:** Podoconiosis program implementation activities have been carried out over the past 10 years in three regions of the country. Four NGOs lead these efforts including Action against Podoconiosis Association (APA), Ethiopian Catholic Secretariat Social and Development Commission (ECC-SDCO), International Orthodox Christian Charities (IOCC), and Mossy Foot International (MFI). These organizations have pioneered podoconiosis implementation activities and demonstrated the effectiveness of activities such as lymphedema management and awareness creation. The management includes patient counselling, foot hygiene, bandaging, skin care with ointment or emollients, elevation and exercise, footwear, wound care and management of acute attack. However, they face challenges related to lack of resources and are only able to offer activities with limited geographic scope, reaching only 12% of endemic districts and 3% of total cases.

In 2011, the National Podoconiosis Action Network (NaPAN) was established with major funding from POMS Shoes to coordinate the work of these four implementing NGOs, to standardize interventions, mobilize resources, create awareness about the disease at the national level and organize a learning forum among partners. In 2013, the BIG Lottery Fund provided a grant to the National Podoconiosis Action Network (NaPAN) through Brighton and Sussex Medical School for podoconiosis prevention and treatment, which raised the number of managed cases to 6%. Through this funding, podoconiosis interventions were scaled up to 18 districts through the four implementing NGOs. Through the same funding, NaPAN worked with the Ethiopian Federal Ministry of Health (FMOH) to integrate podoconiosis lymphedema management services into 40 government health centers in Amhara and SNNP regional states for the first time. In order to integrate podoconiosis morbidity management with lymphatic filariasis in co-endemic districts, NaPAN secured additional resources from the UK government through Liverpool School of Tropical Medicine. Through this funding, integrated LF and podoconiosis lymphedema morbidity management services were initiated in 13 government health centers. Two health professionals from these health centers were trained on an integrated LF and podoconiosis morbidity management approach.

In line with this, the FMOH has given due attention to scaling up podoconiosis interventions in Ethiopia. The FMOH has included podoconiosis as one of the eight neglected tropical diseases in the master plan, developed an integrated LF and podoconiosis morbidity management guideline and included an indicator for podoconiosis management in the national Health Management Information System (HMIS). Ethiopia is pioneering podoconiosis control, which will be an example for other podoconiosis-endemic countries on how to target and address podoconiosis. In total, through the expansion of podoconiosis services integrated with government health facilities, an additional 60 districts have been reached for a total of 100 countrywide (29% of endemic districts).

The development of integrated morbidity management of lymphatic filariasis and podoconiosis and teaching tools such as a video on morbidity management could lead to further expansion of services to other endemic districts. The implementation of podoconiosis interventions needs strong partnerships between different stakeholders and a multisectoral approach. Treatment can easily be provided at primary level, but the availability of supplies for treatment should be ensured through the pharmaceutical fund and supply agency (PFSA). In the national NTD master plan, there is a plan to expand services to all endemic districts by 2020 and eliminate podoconiosis as a public health problem from the country by 2030. To achieve this goal as stated in the NTD master plan, the scale-up of services is critical.

**Basic and implementation research gaps:** The aetiology of podoconiosis is not yet completely understood. Based on existing evidence, the most accepted cause of podoconiosis is an inorganic particle-induced inflammatory response on a background of genetic susceptibility (2). Mineral particles, absorbed through the skin of the foot, are taken up by macrophages in the lower limb lymphatics and induce an inflammatory response in the lymphatic vessels, leading to fibrosis and obstruction of the vessel lumen. This leads initially to oedema of the foot and the lower leg, which progresses to elephantiasis: gross lymphedema with mossy and nodular changes of the skin (41). Price indicated that silicate particles cause subendothelial oedema, endolymphangitis, collagenisation and obliteration of the lymphatic lumen (41). Biopsies from inguinal and femoral lymph nodes of affected individuals have shown the presence of birefringent particles and foreign body granulomata (42). Electron microscopy of the lymph node biopsy and micro-analysis showed that the particles are found inside the macrophages and consist dominantly of silica with varying amount of aluminium, titanium and iron oxide (43). Histological examination of the lymphedematous skin shows epidermal hyperkeratosis, acanthosis and hypergranulosis, with dilated blood vessels with surrounding fibrosis. This may be a consequence of growth factors released by the inflammatory cells, which are attracted to the irritant. The presence of dilated blood vessels with surrounding fibrosis mimics the findings of stasis. This feature, together with dermal sclerosis, contributes to the hardness and irreversibility of lesions (44).

Several studies showed high heritability and a strong genetic basis of podoconiosis (3,4). A pedigree study showed that the sibling recurrence risk ratio is 5.07 (i.e., the sibling of an affected person is at five times increased risk of developing podoconiosis when compared to a person in the general population) and the estimated heritability is 0.629 (i.e., 63% of the variation in development of podoconiosis is accounted for by genetic factors). The most parsimonious model revealed the contribution of a major gene, and the roles of age, and history of use of footwear as environmental covariates (3). A genome-wide association study validated with family-based association testing and high resolution sequence-based HLA typing found that class II HLA genes namely *HLA-DQA1*, *HLA-DRB1*, and *HLA-DQB1* are podoconiosis genetic susceptibility loci. These findings suggest that podoconiosis is a T-cell mediated inflammatory condition (4). Further studies to discern the causal genetic variants, the immunologic and pathologic mechanisms are underway. Oxidative stress biomarkers and pro-fibrotic TGF $\beta$ 1 may also modulate the inflammatory response in podoconiosis (45). The skin of podoconiosis patients has poor stratum corneum hydration, suggesting increased risk of cracking, susceptibility to infection, and lymphedema (46). Further studies are needed to understand the role of genetics, host immunity, and microbes in the progression of podoconiosis from the early reversible stage to the more advanced disease stages.

Currently, podoconiosis is a disease of exclusion and the diagnosis is clinical. Point of care diagnosis is important for the expansion of services and achieving the elimination target by 2030. Studies on a clinical algorithm and clinical biomarkers are important. Scaling-up the morbidity management and disability prevention of podoconiosis requires implementation research to test the best approach for service delivery and integration. Social mobilization approaches should be tested to dispel the barefoot tradition and make shoe-wearing consistent and universal.

**Challenges:** Despite the significant achievements in podoconiosis research and control seen in the last decade, there are several important challenges that still exist. Podoconiosis management services are still not offered in more than 70% of endemic districts and approximately 90% of cases have yet to be addressed. Resource constraints continue to be a large barrier. Resources are required to train health providers, obtain necessary treatment supplies and expand critical services to all endemic districts. More training of health providers at the pre-service level is needed and inclusion of podoconiosis in the curriculum of health workers at all levels is important to increase the index of suspicion among clinicians while treating patients. Continued advocacy is needed for increased NTD funding for podoconiosis and the development of a global strategy for podoconiosis elimination. Second, widespread barefoot practice continues to be a major impediment to the implementation of podoconiosis prevention. Countrywide, social transformation to dispel widespread misconceptions about shoe wearing needs to be encouraged.

**Prospects:** There have been enormous and positive changes in the way that podoconiosis has been viewed within Ethiopia in the past ten years. In 2006, the condition appeared in no health curriculum or policy and was frequently confused with lymphatic filariasis. However, robust nationwide mapping(20)has now clearly defined the burden and distribution of podoconiosis, and has, thus, revolutionized the way podoconiosis is viewed. Inclusion of podoconiosis into the National Master Plan for NTDs (29) in 2013 has increased awareness of the condition as a priority public health problem through the NTD community and beyond.

Research within Ethiopia has had global impact (47), drawing in new research funding from a range of international bodies and catalysing research on podoconiosis in other endemic countries in Africa and central America. Further basic, applied and implementation research is necessary if elimination of podoconiosis is to be achieved within our lifetimes. Important research gaps for Ethiopia include a point-of-care diagnostic test, treatment to reverse advanced stage disease, and strategies to best deliver integrated care.

On the basis of more than 5 years of experience, Ethiopian teams have led training of health workers in podoconiosis prevention and treatment in Cameroon in 2014 and Uganda in 2015. In terms of advocacy, the Ethiopian National Podoconiosis Action Network (NaPAN) and Footwork, the International Podoconiosis Initiative (27), have led calls for elimination of podoconiosis. Again, Ethiopian research lies behind the arguments for global elimination of podoconiosis (48) and defines what elimination should include (49). Elimination of podoconiosis is achievable because no biological agent or vector involved in podoconiosis has been identified, the global scale of the problem is relatively small, the means for podoconiosis prevention and control are safe, and societal commitment towards elimination is growing.

What shape might podoconiosis control within Ethiopia take? Current projects funded by national and international non-government organizations[36,50] must be used as centres of excellence for training of government health workers, coordinated by NaPAN. An integrated care package that includes podoconiosis care with that of other foot-related Neglected Tropical Diseases such as leprosy and lymphatic filariasis must be developed. Care for the social (18,32) and mental health (18,34,51) consequences of podoconiosis must be essential components to this package. This package must be harmonized and included in the state health system and backed by robust public health policies, sustainable resource allocation, and the revision of education curricula for health professionals. Creative public-private partnerships must be developed so as to match public resources (including the state health system and research institutions) with private financial investments.

**Conclusion:** The last few years have been critical in generating evidence about the distribution, burden and effective interventions for podoconiosis in Ethiopia. Although the scale of the problem within Ethiopia is considerable, the country is well-equipped to now scale-up elimination efforts. Given the extraordinary progress of the past ten years and the current commitment of government, private and third sectors, Ethiopia seems to be on course for the elimination of podoconiosis in our lifetime. We need continued strong partner commitment, evidence-building, and scale-up of activities to accomplish this.

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## REFERENCES

1. Price E. Podoconiosis: Non-filarial Elephantiasis. Oxford Medical Publications, Oxford. 1990.
2. Davey G, Tekola F, Newport MJ. Podoconiosis: non-infectious geochemical elephantiasis. *Trans R Soc Trop Med Hyg.* 2007;101(12):1175-80.
3. Davey G, GebreHanna E, Adeyemo A, Rotimi C, Newport M, Desta K. Podoconiosis: a Tropical Model for gene-environment interactions? . *Trans R Soc Trop Med Hyg.* 2007;101(1):91-6.
4. Tekola Ayele F, Adeyemo A, Finan C, et al. HLA class II locus and susceptibility to podoconiosis. *N Engl J Med* 2012;366(13):1200-8.
5. Tekola F, Mariam DH, Davey G. Economic costs of endemic non-filarial elephantiasis in Wolaita Zone, Ethiopia. *Trop Med Int Health.* 2006;11(7):1136-44.
6. Molla YB, Tomczyk S, Amberbir T, Tamiru A, Davey G. Podoconiosis in East and West Gojam zones, Northern Ethiopia. *PLoS Negl Trop Dis.* 2012;6(7):e1744.
7. Addiss DG. Global elimination of Lymphatic Filariasis: Addressing the public health problem. *PLoS Negl Trop Dis.* 2010;4(6):e741.
8. Tora A, Davey G, Tadele G. A qualitative study on stigma and coping strategies of patients with podoconiosis in Wolaita zone, Southern Ethiopia. *Int Health.* 2011;3(3):176-81.
9. Yakob B, Deribe K, Davey G. High levels of misconceptions and stigma in a community highly endemic for podoconiosis in southern Ethiopia. *Trans R Soc Trop Med Hyg.* 2008;102(5):439-44.
10. Yakob B, Deribe K, Davey G. Health professionals' attitudes and misconceptions regarding podoconiosis: potential impact on integration of care in southern Ethiopia. *Trans R Soc Trop Med Hyg.* 2010;104(1):42-7.
11. Deribe K, Tomczyk S, Tekola-Ayele F. Ten years of podoconiosis research in Ethiopia. *PLoS Negl Trop Dis.* 2013;7(10):e2301.
12. Desta K, Ashine M, Davey G. Prevalence of podoconiosis (endemic non-filarial elephantiasis) in Wolaitta, Southern Ethiopia. *Tropical Doctor.* 2003;33(4):217-20.
13. Alemu G, Tekola Ayele F, Daniel T, Ahrens C, Davey G. Burden of podoconiosis in poor rural communities in Gulliso woreda, West Ethiopia. *PLoS Negl Trop Dis.* 2011;5(6):e1184.
14. Tekola Ayele F, Alemu G, Davey G, Ahrens C. Community-based survey of podoconiosis in Bedele Zuria woreda, southwest Ethiopia. *Int Health.* 2013; 5(2):119-25.

15. Tekola F, Ayele Z, Mariam DH, Fuller C, Davey G. Development and testing of a de novo clinical staging system for podoconiosis (endemic non-filarial elephantiasis). *Trop Med Int Health*. 2008;13(10):1277-83.
16. Tekola F, Bull S, Farsides B, et al. Impact of social stigma on the process of obtaining informed consent for genetic research on podoconiosis: a qualitative study. *BMC Med Ethics*. 2009;10:13(13).
17. Deribe K, Tomczyk S, Mousley E, Tamiru A, Davey G. Stigma towards a Neglected Tropical Disease: Felt and enacted Stigma Scores among Podoconiosis Patients in Northern Ethiopia. *BMC Public Health*. 2013;13(1178).
18. Mousley E, Deribe K, Tamiru A, Davey G. The impact of podoconiosis on quality of life in Northern Ethiopia. *Health Qual Life Outcomes*. 2013;11(122).
19. Legesse H, Davey G. Validation of the Dermatology Life Quality Index among patients with podoconiosis in southern Ethiopia. *British Journal of Dermatology*. 2008;159(4):903-6.
20. Deribe K, Brooker SJ, Pullan RL, et al. Epidemiology and individual, household and geographical risk factors of podoconiosis in Ethiopia: results from the first nationwide mapping. *Am J Trop Med Hyg*. 2014;In press.
21. Molla YB, Wardrop NA, Le Blond JS, et al. Modeling environmental factors correlated with podoconiosis. *Int J Health Geogr*. 2014;13(1):24.
22. Deribe K, Brooker SJ, Pullan RL, et al. Epidemiology and individual, household and geographical risk factors of podoconiosis in Ethiopia: results from the first nationwide mapping. *Am J Trop Med Hyg*. 2015;92(1):148-58.
23. Deribe K, Cano J, Newport MJ, et al. Mapping and modeling the geographical distribution and environmental limits of podoconiosis in Ethiopia. *PLoS Negl Trop Dis* 2015;9(7):e0003946.
24. Sime H, Deribe K, Assefa A, et al. Integrated mapping of lymphatic Filariasis and podoconiosis: lessons learnt from Ethiopia. *Parasit Vectors*. 2014;7(1):397.
25. Negussie H, Kassahun MM, Fegan G, et al. Podoconiosis treatment in northern Ethiopia (GoLBet): study protocol for a randomised controlled trial. *Trials*. 2015;16(16):307.
26. Mengitsu B, Shafi O, Kebede B, et al. Ethiopia and its steps to mobilize resources to achieve 2020 elimination and control goals for neglected tropical diseases: Spider webs joined can tie a lion. *International Health* 2016;8:I34-I52.
27. Davey G, Bockarie M, Wanji S AD, et al. Launch of the International Podoconiosis Initiative. *Lancet*. 2012;379 (9820):1004.
28. Davey G, Newport M. Podoconiosis: the most neglected tropical disease? . *Lancet*. 2007;369:888-9.
29. Federal Democratic Republic of Ethiopia Ministry of Health. Ethiopia National Master Plan For Neglected Tropical Diseases. Available at [http://ntdenvision.org/resource/ethiopia\\_national\\_master\\_plan\\_for\\_neglected\\_tropical\\_diseases](http://ntdenvision.org/resource/ethiopia_national_master_plan_for_neglected_tropical_diseases) Accessed on 03-04-2014. 2013.
30. Gebrehanna E. The social burden of podoconiosis in Wolaita zone. Addis Ababa: Addis Ababa University; 2005.
31. Molla YB, Tomczyk S, Amberbir T, Tamiru A, Davey G. Patients' perceptions of podoconiosis causes, prevention and consequences in East and West Gojam, Northern Ethiopia. *BMC Public Health*. 2012;12:828.
32. Tora A, Franklin H, Deribe K, Reda AA, Davey G. Extent of podoconiosis-related stigma in Wolaita Zone, Southern Ethiopia: a cross-sectional study. *Springerplus* 2014;3:647.
33. Henok L, Davey G. Validation of the Dermatology Life Quality Index among patients with podoconiosis in southern Ethiopia. *Br J Dermatol*. 2008;159(4):903-6.
34. Mousley E, Deribe K, Tamiru A, Tomczyk S, Hanlon C, Davey G. Mental distress and podoconiosis in Northern Ethiopia: a comparative cross-sectional study. *Int Health*. 2015;7(1):16-25.
35. Tamiru A, Tsegay G, Wubie M, Gedefaw M, Tomczyk S, Tekola-Ayele F. Podoconiosis patients' willingness to pay for treatment services in Northwest Ethiopia: potential for cost recovery. *BMC Public Health*. 2014;14:259.
36. Davey G, Burrridge E. Community-based control of a neglected tropical disease: the mossy foot treatment and prevention association. *PLoS Negl Trop Dis*. 2009;3(5):e424.
37. Price EW. The management of endemic (non-filarial) elephantiasis of the lower legs *Trop Doct* 1975;5:70-5.
38. Sikorski C, Ashine M, Zeleke Z, Davey G. Effectiveness of a simple lymphoedema treatment regimen in podoconiosis management in southern Ethiopia: one year follow-up. *PLoS Negl Trop Dis*. 2010;4(11):e902.
39. Geshere Oli G, Tekola Ayele F, Petros B. Parasitological, serological, and clinical evidence for high prevalence of podoconiosis (non-filarial elephantiasis) in Midakegn district, central Ethiopia. *Trop Med Int Health*. 2012;17(6):722-6. doi: 10.1111/j.1365-3156.2012.02978.
40. Kloos H, Kello AB, Addus A. Podoconiosis (endemic non-filarial elephantiasis) in two resettlement schemes

- in western Ethiopia. *Tropical Doctor*. 1992; 22(3):109-12.
41. Price E. The association of endemic elephantiasis of the lower legs in East Africa with soil derived from volcanic rocks. *Trans R Soc Trop Med Hyg*. 1976;4:288- 95.
  42. Price EW. The pathology of non-filarial elephantiasis of the lower legs. *Trans R Soc Trop Med Hyg* 1972;66(1):150-9.
  43. Price EW, Henderson WJ. The elemental content of lymphatic tissues of barefooted people in Ethiopia, with reference to endemic elephantiasis of the lower legs. *Trans R Soc Trop Med Hyg* 1978;72(2): 132-6.
  44. Wendemagegn E, Tirumalae R, Böer-Auer A. Histopathological and immunohistochemical features of nodular podoconiosis. *J Cutan Pathol*. 2015;42(3):178-81.
  45. Addisu S, El-Metwally TH, Davey G, Worku Y, Titheradge MA. The role of transforming growth factor-beta1 and oxidative stress in podoconiosis pathogenesis. *Br J Dermatol*. 2010;162(5):998-1003.
  46. Ferguson JS, Yeshanehe WE, Matts PJ, Davey G, Mortimer PS, Fuller LC. Assessment of skin barrier function in podoconiosis: measurement of stratum corneum hydration and transepidermal water loss. *Br J Dermatol*. 2013;168(3):550-5544.
  47. Davey G. Podoconiosis: Let Ethiopia lead the way. *Ethiopian Journal of Health Development* 2008;22:1-2.
  48. Deribe K, Wanji S, Shafi O, et al. The feasibility of eliminating podoconiosis. *Bull World Health Organ*. 2015;93(10):712-8.
  49. Deribe K, Wanji S, Shafi O, et al. Measuring elimination of podoconiosis, endemicity classifications, case definition and targets: an international Delphi exercise. *Int Health*. 7(5):306-16.
  50. Tomczyk S, Tamiru A, Davey G. Addressing the neglected tropical disease podoconiosis in Northern Ethiopia: lessons learned from a new community podoconiosis program. *PLoS Negl Trop Dis*. 2012;6(3):e1560.
  51. Bartlett J, Deribe K, Tamiru A, et al. Depression and disability in people with podoconiosis: a comparative cross-sectional study in rural Northern Ethiopia. *Int Health*. 2016;8(2):124-31.