

Impact of Anthelmintic Price Increases on Practice Patterns of Healthcare Providers Caring for Immigrant and Refugee Populations in the United States

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Abstract. In the United States, prices of long-established, generic anthelmintic medications have markedly risen. In the past decade, albendazole and mebendazole have increased in price by > 8,000%, whereas praziquantel has increased by > 500%. To determine the effect of these price increases on the practice patterns of healthcare providers, we conducted a cross-sectional electronic survey of clinics in the United States that primarily care for immigrant and refugee patient populations. Among 32 clinics, 53.1% reported that price increases impacted how providers diagnosed and treated helminth infections. A third (34.4%) of clinics reported that price increases have left them unable to treat known helminth infections. Other ways in which price increases impacted practice patterns included prescribing anthelmintics other than albendazole, mebendazole, or praziquantel when possible (34.4%); avoiding screening asymptomatic patients for helminth infections (15.6%); advising patients to acquire medications from another country (15.6%) or the patient's home country (9.4%); reducing anthelmintic dosing regimens to fewer pills (9.4%); and advising patients to purchase medications on the Internet (6.3%). These findings suggest price increases have negatively impacted the diagnosis and treatment of helminth infections in this population, and have resulted in the inability to treat known helminth infections. These findings have significant implications for the morbidity and mortality of infected individuals, as well as for public health in the United States.

INTRODUCTION

Over the past several years, there have been numerous examples of significant price increases affecting long-used drugs for neglected conditions.^{1–4} One category of generic drugs that has seen marked price increases is anthelmintics, medications used to treat parasitic worm infections. In the United States, the prices of many prescription anthelmintic agents—which can often be acquired for a few dollars or less in many other countries—have skyrocketed in the past decade. Albendazole, a benzimidazole that is the drug of choice for soil-transmitted helminths such as *Ascaris lumbricoides*, hookworms, and whipworm, increased in price by > 8,000%, from \$2.96 per 200 mg tablet in 2010 to \$241.1 per tablet in 2018 (average wholesale price).⁵ Currently, on GoodRx, a website some patients and clinicians use to obtain discount coupons for cash payment of medications at retail pharmacies, the cost for two 200 mg tablets of albendazole is more than \$120 at most pharmacies (thus, a standard 3-day course would still cost more than \$360).⁶ Mebendazole, another benzimidazole used to treat soil-transmitted helminths, also increased in price by > 8,000%, from \$5.82 per 100 mg tablet in 2010 to \$508.07 per 100 mg tablet in 2019,⁵ and is not currently available on GoodRx. Praziquantel, which treats both fluke and tapeworm infections and is the only medication approved by the United States Food and Drug Administration (FDA) for treatment of schistosomiasis, increased in price > 500%, from \$15.02 per 600 mg tablet in 2011 to \$99.6 per tablet in 2015.⁵ On GoodRx, the lowest available price for a standard 1-day course of praziquantel therapy for

schistosomiasis (two 600 mg tablets three times in 1 day) is \$168, with most pharmacies charging more than \$200.⁷ For certain helminth diseases, such as cystic echinococcosis, and cysticercosis, treatment often must be given for weeks, driving the treatment cost into the thousands. Although many factors contribute to price increases affecting generic drugs, limited manufacturer competition due to the small U.S. market for these drugs has allowed manufacturers to set high prices, and contributes to the lack of downward pressure.^{8–10}

Untreated helminth infections can cause significant morbidity and mortality to children and adults.^{11–14} Immigrants and refugees in the United States are more greatly affected by parasitic helminth infections than individuals born in the United States. These patients may encounter barriers such as limited healthcare access, communication difficulties, or lack of insurance. To date, no studies have directly assessed how anthelmintic price increases have affected healthcare provider practices when caring for these patients. We hypothesized that price increases have negatively impacted the diagnosis and treatment of helminth infections in this patient population. Thus, the goal of this study was to evaluate the impact of anthelmintic drug price increases on practice patterns of providers caring for immigrant and refugee patient populations in the United States.

METHODS

We conducted a cross-sectional electronic survey of healthcare clinics in the United States that primarily care for immigrant and refugee patient populations. Target clinics were identified through email listservs and electronic directories at the Society of Refugee Healthcare Providers, Association of Refugee Health Coordinators, American Committee on Clinical Tropical Medicine and Traveler's Health (ASTMH Clinical Group), American Academy of

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TABLE 1
Characteristics of the patient populations seen in the queried clinics

	Average	Median	Range	SD (STDA)
Number of patients seen annually per clinic	6,961	1,498	100–85,000	16,436.4
Percent of patients from specific geographical regions				
United States	22.5	5.0	0–86.0	29.5
Central America, Caribbean, and South America	24.6	13.0	0–100	27.5
Europe, Canada, and Australia	0.4	0.0	0–5.0	1.0
West Africa	2.8	2.0	0–10.0	3.4
East Africa	10.4	5.0	0–35.0	11.2
Central and South Africa	7.8	5.0	0–49.0	11.3
North Africa and Middle East	15.5	5.0	0–70.0	20.8
Central Asia	0.7	0.0	0–6.0	1.40
South and east Asia	5.6	2.0	0–40.0	9.1
Southeast Asia and South Pacific	10.1	4.1	0–44.0	12.1
Percent of patients with a given immigration status				
U.S.-born	29.0	7.5	0–98	34.2
Undocumented immigrants	16.3	3.5	0–99	26.2
Total documented immigrants				
Refugees	32.7	20.7	0–99	32.2
International adoptees	0.0	0.0	0–1	0.2
Other documented immigrants	10.9	10.0	0–30	11.1
Percent of patients with insurance	75.8	92.5	0–100	35.3

One clinic did not provide geographic regions of origin and was excluded.

Pediatrics Section of International Child Health, and the Refugee and International Health Program at the Minnesota Department of Health.

The survey was designed to be completed within 30 minutes. Survey data were collected and managed using REDCap electronic data capture tools hosted at the University of Minnesota. The survey comprised 12 multiple-choice questions and 13 short answer questions. Questions primarily addressed patient demographic information, helminth infections diagnosed in the clinic, use of anthelmintics, impacts of anthelmintic price increases, use of patient assistance programs (PAPs), and experience with presumptive treatment programs. The survey was distributed through email listservs and forums, with a request for one survey to be filled out per clinic. Survey responses were collected from May 2018 through October 2018.

The inclusion criteria for surveys consisted of a history of prescribing anthelmintics (albendazole, mebendazole, praziquantel, or ivermectin) in the clinic and completion of $\geq 95\%$ of the survey.

The survey was voluntary, and the names of the respondents were not requested. The study was reviewed and approved by the Institutional Review Board at the University of Minnesota and assigned a determination of Not Human Research (STUDY00003341).

Analysis. Demographic data provided in Table 1 were averaged across clinics, irrespective of the size of each clinic population, to determine averages on a per-clinic basis. For the data in Tables 2 and 3, affirmative responses were tallied and expressed as a percentage of clinics. The number of prescriptions, as well as the number of prescriptions per 100 patients, was determined for each clinic and subsequently averaged across clinics (Table 4).

RESULTS

We received a total of 50 survey responses, of which 32 responses met the inclusion criteria. All of the excluded responses were due to incomplete surveys. Among the 32

responses that met the inclusion criteria, 47% of survey respondents identified themselves as the medical director, supervisor, or coordinator of the responding clinic. The remainder identified themselves as providers. The responses came from clinics across 13 states: Colorado (2), Indiana (1), Kentucky (1), Maryland (1), Massachusetts (1), Minnesota (2), New Hampshire (1), New York (2), Pennsylvania (1), Texas (9), Vermont (1), Virginia (1), and Washington (1). For eight of the clinics, the state was indeterminable.

Demographics. Table 1 demonstrates the demographics of the clinics' patient population, including geographic region of origin, immigration status, and health insurance status. The median number of patients seen annually across clinics was 1,498. The average was notably higher (6,961) because of five outlier clinics that reported annual patient populations of 15,000–85,000. Averaged across clinics, the most common regions of origin were Central America, the Caribbean, South America (24.6%), and the United States (22.5%). Other well-represented regions included North Africa, the Middle East (15.5%), East Africa (10.1%), and Southeast Asia, South

TABLE 2
Number of clinics reporting diagnoses of helminth infections in the past year

Helminth infection	N	%
<i>Strongyloides stercoralis</i>	18/32	56.3
Schistosomiasis	17/32	53.1
Pinworm (<i>Enterobius vermicularis</i>)	15/32	46.9
<i>Ascaris lumbricoides</i>	14/32	43.8
Neurocysticercosis (<i>T. solium</i> larval stage)	11/32	34.4
<i>Hymenolepis nana</i>	9/32	28.1
Whipworm (<i>Trichuris trichiura</i>)	8/32	25.0
Hookworm (<i>Ancylostoma duodenale</i> and <i>Necator americanus</i>)	7/32	21.9
<i>Taenia solium</i>	7/32	21.9
Filariae (lymphatic filariasis, onchocerciasis, and <i>Loa loa</i>)	5/32	15.6
<i>Taenia saginata</i>	5/32	15.6

TABLE 3

Impacts of anthelmintic price increases on practice patterns		
Impact of anthelmintic price increases practice patterns	N	%
Unable to treat known helminth infections	11/32	34.4
Try to prescribe anthelmintics other than albendazole, mebendazole, or praziquantel when possible	11/32	34.4
Avoid screening patients who are asymptomatic	5/32	15.6
Advise patients to acquire medications from another country	5/32	15.6
Advise patients to acquire medications from their home country	3/32	9.4
Change the dosing regimen to fewer pills	3/32	9.4
Advise patients to purchase medications off of the Internet	2/32	6.3
Other (see text)	5/32	15.6

Pacific (10.1%). On average, the patient population comprised refugees (32.7%), U.S.-born individuals (29.0%), undocumented immigrants (16.3%), and documented immigrants (10.9%). The median percent of patients with insurance was 92.5%. The average was notably lower (75.8%) because of four outlier clinics that reported that $\leq 5\%$ of their patients have insurance.

Helminth infections. Ninety percent (90.6%) of clinics reported diagnosing a helminth infection within the past year. The three clinics that did not report diagnosing any helminth infections within the past year did report prescribing anthelmintic medications. One of these clinics wrote: "Our patients do not have the resources to pay for stool studies or serologies."

Strongyloidiasis and schistosomiasis were the most common infections diagnosed in the past year across clinics, with 56.3% and 53.1% of clinics reporting these infections, respectively. Other prominent helminth infections included pinworm (*Enterobius vermicularis*) (46.9%), *A. lumbricoides* (43.8%), neurocysticercosis (*Taenia solium* larval stage) (34.4%), *Hymenolepis nana* (28.1%), whipworm (*Trichuris trichiura*) (25.0%), hookworm (*Ancylostoma duodenale* and *Necator americanus*) (21.9%), *T. solium* (21.9%), filariae (lymphatic filariasis, onchocerciasis, and *Loa loa*) (15.6%), and *Taenia saginata* (15.6%) (Table 2).

Impact of price increases on clinical practice. Ninety percent (90.6%) of clinics reported they were aware of the recent price increases affecting common anthelmintics. Half (53.1%) of the clinics reported that price increases impacted how providers prescribed anthelmintics. A third (34.4%) of clinics reported that price increases have left them unable to treat known helminth infections among their patients. The 11 clinics that reported this, on average, were unable to treat known helminth infections 31.4% of the time (median 25%, range 5–100%, SD 27.1).

Clinics reported that anthelmintic price increases have caused a number of changes in practice patterns. These changes include prescribing anthelmintics other than albendazole, mebendazole, or praziquantel when possible (34.4% of clinics reported this practice); avoiding screening asymptomatic patients for helminth infections (15.6%); advising patients to acquire medications from another country (15.6%) or the patient's home country (9.4%); reducing anthelmintic dosing regimens to fewer pills (9.4%); and advising patients to purchase medications on the Internet (6.3%) (Table 3).

The survey offered respondents the opportunity to write in other impacts price increases have caused in how healthcare providers care for their patients. One clinic wrote that they "submit for prior [authorization], and when denied, [the] clinic pays for albendazole." Other clinics wrote that they "work with funding agencies to get prescriptions at cheaper prices" and "find funding or get prior authorizations to cover [the] cost." Another provider wrote "I test instead of treat for patients without insurance because we can cover tests with charity care."

All clinics (100%) reported that if albendazole, mebendazole, and/or praziquantel were made available at no or low cost in the United States, then they would access the medications. All clinics reported that they thought this would benefit their patients.

Number of prescriptions per year. Clinics reported substantial use of anthelmintics (Table 4). Albendazole was commonly prescribed, with an average of 132 total prescriptions per clinic in the past year and an average of 11 prescriptions per 100 patients. Ivermectin was prescribed at similar rates, with an average of 133 total prescriptions per clinic in the past year and 13 prescriptions per 100 patients. Praziquantel and mebendazole were prescribed at lower rates, with an average of 17 and three prescriptions total per clinic in the past year, respectively.

Patient assistance programs. Approximately one-third (31.3%) of the clinics reported recommending charitable access programs or PAPs to their patients for the acquisition of anthelmintics. Of the 10 clinics that have tried using charitable access programs or PAPs, 50.0% have experienced denial by the pharmaceutical company at least once. Clinics reported that other reasons that PAPs have failed include that the patient's immigration status was prohibitive, and "difficulty with follow-up." One clinic commented that the delay involved when using PAPs results in barriers to treatment of patients (Table 5). Only 30.0% of clinics that have used charitable access programs or PAPs have found them to be an efficient and timely option for acquiring medications.

Presumptive treatment. Twenty-three clinics (71.9%) reported seeing patients who were part of the U.S. Refugee Resettlement Program who received predeparture presumptive treatment for helminth infections. Four (12.5%) clinics reported it was unknown to them whether they had seen these patients. To gain a sense of how predeparture presumptive treatment has impacted clinics and their patients, the survey included a free text response section for clinics to report their experience with such programs. Many clinics wrote that predeparture presumptive treatment was

TABLE 4

Approximate number of prescriptions of anthelmintics prescribed in the past year

	Average	Median	Range	SD
Number of prescriptions prescribed by clinics in the past year				
Albendazole	132.2	21.0	1–1,011	239.6
Mebendazole	2.9	0.0	0–20	6.0
Praziquantel	16.5	5.0	0–77	20.0
Ivermectin	133.0	20.0	0–1,051	275.8
Number of prescriptions prescribed per 100 patients in the past year				
Albendazole	11.4	1.2	0–80.1	19.6
Mebendazole	0.3	0.0	0–6.7	1.2
Praziquantel	1.8	0.5	0–15.6	3.2
Ivermectin	12.7	1.3	0–55.4	21.2

One clinic did not provide prescription counts and was excluded.

TABLE 5
Open answer on the impact of anthelmintic price increases

- “Our patients simply cannot afford these medications. We see newly arrived children who have crossed the border and who are at high risk for infection. We encourage them to find other ways to get presumptive treatment. We are a free clinic and suggest that they go to a (Federally Qualified Health Center), but many will not do it due to language barriers, limited clinic hours, long waits, and fear of authorities. Most people have to figure out a way to get medication from another country. We stopped trying PAP because they always wanted Social Security number for the patients.”
- “Due to the variability and lack of medical support for our patient populations, we may have one opportunity to treat the patients. Working with PAPs takes a long time to obtain the medication, in which case we may have lost contact with the patient. Thus, patients continue with untreated helminth infections.”
- “We had an asylee client who did not receive parasite treatment overseas. He also was not eligible for Medicaid without refugee status. So the albendazole and ivermectin prescriptions we gave him would have cost him \$1,500 out of pocket. He could not afford that, so did not fill his prescriptions. He contacted us several months later after seeing worms in his stool. We worked with our state Newcomer Health Program to get him proper parasite treatment meds at no cost to him.”
- “Before knowing about the price changes, when it wasn’t making headlines, I had sent all members of a symptomatic family for albendazole. I had prescribed it when volunteering in Mexico and it cost less than \$1 per 400 mg treatment. I was called by the Walmart pharmacy saying it was hundreds of dollars and I laughed and thought the pharmacist had made a mistake or Walmart didn’t sell much so had priced it funny. So I sent them to another pharmacy and was called with the same info. I recommended that they have it sent from their home country which I assumed that they did, though I wasn’t able to follow-up.”

PAP = patient assistance program.

helpful, reduced screening of asymptomatic patients, and reduced the need to treat (whether empiric or not). However, one clinic reported diagnosing patients with multiple parasitic infections despite documentation that patients had received treatment overseas.

Open answer. The survey included an open answer section to describe any other ways in which anthelmintic price increases have impacted their clinic, patients, or diagnosis and treatment of helminth infections. Representative responses are included in Table 5.

Many clinics made references to the array of challenges their patients face, such as a language barrier, financial burden, diminished access to health care, and difficulty with follow-up. Two clinics referenced the 340B Drug Pricing Program, a federal program that allows eligible hospitals and clinics caring for underserved populations to purchase prescription medications at a reduced price. These two clinics indicated this program allowed patients to obtain medications at a reasonable cost, thereby facilitating their treatment.

DISCUSSION

Findings. The results of this cross-sectional survey demonstrate that price increases of anthelmintic drugs have had a substantial impact on the practice patterns of healthcare providers caring for immigrant and refugee patient populations in the United States. The survey sampled the intended audience, as demonstrated by the immigration status of patients, the clinics’ substantial use of anthelmintics, and the helminth infections diagnosed in these clinics. A key finding is that a third (34.4%) of responding clinics reported being unable to treat known helminth infections because of anthelmintic price increases. On average, these clinics estimate they are unable to treat known helminth infections approximately one-third (31.4%) of the time.

Other important ways in which practice patterns have been impacted by anthelmintic price increases include reducing helminth screening of asymptomatic patients, advising patients to acquire medications from another country or the patient’s home country, reducing anthelmintic dosing regimens to fewer

pills, and advising patients to purchase medications from the Internet.

All of the clinics reported that if anthelmintics were made available at no or low cost in the United States, they would access the medications to the benefit of their patients.

Implications. The findings of this study have implications for both individual and public health in the United States. With regard to individual health, leaving helminth infections untreated engenders significant morbidity and mortality. Children are a particularly vulnerable population, as intestinal helminth infections can cause anemia, anorexia, and malabsorption, with impacts on growth, academic achievement, and quality of life.^{11–13} The two most common helminths reported by clinics in this study, *Strongyloides* and *Schistosoma* spp., can both cause severe and even life-threatening diseases. In particular, individuals infected with *Strongyloides stercoralis* can harbor the infection for life and are at risk of death by hyperinfection syndrome if given corticosteroids or other immunosuppressive medications.¹⁴

Untreated helminth infections can also have important public health implications. Endemic transmission of soil-transmitted helminth infections in the United States has been poorly characterized, with few surveillance studies since the 1980s. However, active disease has been demonstrated in communities in the United States, and large regions in this country have conditions that would facilitate transmission.^{15–17} Insufficient treatment of known helminth infections increases the likelihood of autochthonous transmission of these parasites in the United States. Transmission of certain parasitic helminths, such as pinworm, *H. nana*, and *T. solium*, has little dependence on specific environmental conditions and thus these infections have the potential for transmission anywhere in the United States.

Several clinics reported that adequate follow-up is a challenge. Given this, it is likely that untreated helminth infections are under-recognized. If a provider only has one opportunity to see and treat a patient, then they may not be aware that a patient was unable to fill a prescription.

Many of the providers acknowledged in the open answer section that their patients are unable to afford anthelmintics. These providers are placed in the difficult position of finding mitigating strategies. Some clinics (15.6%) reported avoiding screening patients who are asymptomatic because of price

increases. This is notable, given that most of the helminth infections are asymptomatic, and yet these subclinical infections can still carry morbidity and mortality risks, as well as contribute to endemic transmission. The practice of avoiding certain anthelmintics (albendazole, mebendazole, and praziquantel) or reducing dosing regimens to fewer pills introduces the possibility that patients receiving suboptimal treatment may not have eradication of their infection. In this way, these price increases are impacting prescribing behavior, access to medications, and best practice care for this population.

Some pharmaceutical companies offer charitable access programs or PAPs after substantially raising prices on previously inexpensive generic anthelmintics. Of the clinics that have tried these programs, half report experiencing failure to acquire medications at least once, and the majority did not feel these were an efficient option for acquiring treatment. This is understandable, particularly when considering some providers may have limited opportunities for follow-up. The PAP process is complex, time consuming, and resource intensive, often requiring the involvement of a pharmacist or social worker,^{18–20} and may be particularly difficult to navigate for non-English speakers. The eligibility criteria often lack transparency,²¹ with some requiring U.S. citizenship.²² The application typically requires substantial personal information and documentation, such as tax returns.²³ Historically, there has been little evidence for their effectiveness.²⁴

The majority (72%) of clinics have cared for patients who were part of the U.S. Refugee Resettlement Program and received predeparture presumptive treatment. Although we did not collect quantitative data on this subject, many clinics provided free text responses that indicated this program is having an overall positive impact by reducing the need to screen asymptomatic patients and decreasing overall need to treat helminth infections. These survey results are consistent with a recent report suggesting that an overseas presumptive treatment program of albendazole and ivermectin may be the most cost-effective intervention for management of helminth infections in refugee populations, particularly when compared with domestic screening and treatment.²⁵

Summary of studies that look at drug pricing effects on prescribing practices. Multiple studies have evaluated the impact that disproportionate price increases of established generic drugs have on medication use by patients. Prevalent strategies used by patients to reduce prescription drug costs include asking their physician for a less expensive medication, not taking their medication as prescribed (e.g., skipping doses and delaying filling a prescription), using alternative therapies, and purchasing medications from another country.^{26–28} A quarter (25.5%) of patients in one clinic reported that the cost of insulin has caused them to underuse insulin (e.g., take less than prescribed, “stretch out” their insulin, stop using insulin, and not fill a prescription).²⁹ Similar strategies have been reported in cancer patients.^{30,31} Many of these studies have also demonstrated that behaviors of nonadherence or altering medication courses are more common with patients of lower socioeconomic status.

Given the high cost of anthelmintic medications, it is likely that the populations cared for by the clinics surveyed in this study also alter medication use because of high prices. Not only are immigrant and refugee populations typically of lower socioeconomic status but also they must contend with language barriers, diminished access to health care, and, in some

cases, fear of authorities. Although we did not directly survey the patients themselves in this study, the fact that providers are unable to treat known helminth infections because of high drug prices strongly suggests that many patients provided with anthelmintic prescriptions may forgo filling them in favor of paying for more pressing needs.

Currently, the few publications that have evaluated the impacts of price increases on provider practices have shown mixed findings with regard to the impact of price increases on the use of a medication. Intramuscular adrenocorticotrophic hormone, the preferred treatment for infantile spasm, is an older, niche medication which has also undergone disproportionate price increases. Wray et al.³² reported that following price increases, patients with infantile spasm at one institution were more likely to be treated with oral antiepileptic medications rather than adrenocorticotrophic hormone, correlating with longer inpatient admissions. However, with regard to oral doxycycline hyclate undergoing marked price increases, Barbieri et al.³³ found that providers did not alter prescribing practices for the treatment of acne.

Study limitations. This study had a range of significant limitations. The survey was intended to have a low barrier to completion, with a manageable number of questions. Although some respondents provided precise numbers, suggesting they obtained their data from formal and accurate databases, other data were likely estimations, subject to bias and inaccuracies. Moreover, we anticipate a significant selection bias, as providers who have observed impact from anthelmintic price increases may be more inclined to respond to the survey. Given the lack of a standardized registry of all clinics that predominantly see immigrant and refugee patients, we do not know what percentage of such clinics we were able to survey, and were unable to calculate a response rate. Creation of a registry of clinics in the United States that predominantly care for refugees and immigrants would be potentially useful for evaluating and addressing issues in these patient populations.

CONCLUSION

Despite the limitations of the cross-sectional survey design of this study, the findings strongly suggest that recent anthelmintic price increases are having a markedly negative effect on the screening and treatment of helminth infections in immigrant and refugee populations in the United States. Inability to treat helminth infections, alternative dosing strategies, and reduced screening can all be expected to increase the prevalence of helminth infections in these populations, ultimately causing increased morbidity to infected individuals and increasing public health risks for the population at large. Policy solutions are urgently needed and have been discussed in the literature. These might include enforcement of current existing anticompetitive laws and regulations, and new legislative efforts; facilitating public-private partnerships or nonprofits; and support for the importation of drugs.^{8,34} Future research is needed to further characterize the effect of extreme drug pricing and its impact on factors such as patient outcomes, added healthcare costs (both direct drug cost and costs incurred because of resulting lack of access to care), and potential marginalization of the FDA through pursuit of non-FDA-approved medications from sources such as personal importation and via the Internet.

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