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Working Papers Series

UMR 6031 TREE

Transitions Energétiques et Environnementales

TREE WP No. 12
December 2022

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Worms or sugar? Mass deworming treatment doubles the probability to suffer from diabetes ten to fifteen years later.*

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December 1, 2022

Abstract

Mass deworming has long been promoted as a cost-effective device to improve health status and educational attainment of children. Recent contributions suggest that they would in addition increase lifetime earnings of individuals. However, recent medical research emphasizes the role played by the gut microbiome and helminths in particular – colloquially termed worms – on the prevention of metabolic syndromes and inflammatory diseases including Type-2 diabetes. We use publicly available data from the Kenya Life Panel Survey (rounds 2 and 3) that follows a representative sample of children initially part of the Primary School Deworming Project randomized experiment 10 and 15 years after the intervention and study the impact of deworming on diabetes. We find that children who were enrolled in early treated schools and received two to three additional years of deworming treatment are twice more likely to declare suffering from diabetes 10 to 15 years later (n=31 for 6,390 treated individuals) than individuals in the control group (n=7 for 3,284 individuals). Our results are consistent with a protective effect of worm infection against diabetes and suggest potential adverse long-term health impacts of mass deworming administration. Given the cost of diabetes treatment in low and middle-income countries, the cost-benefit balance of mass deworming may need to be reevaluated.

Keywords : deworming ; diabetes ; health ; long-run impacts ; Kenya

*Declarations of interest: none.

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Introduction

Mass deworming has long been used in many developing countries as a cost-effective device to improve child health and education. Recent contributions (Hamory et al., 2021; Baird et al., 2016) suggest that they can also have long-term positive effect on income and employment outcomes. One key argument for promoting mass deworming, ie treating all individuals regardless of their infection status, is the very low cost of the treatment, which makes it more cost-effective than selective treatment. Another argument is that treatment at the population level may break transmission by limiting reinfection of treated individuals by non-treated ones. A vigorous academic debate however followed the publication of a meta-analysis (Taylor-Robinson et al., 2012) that put into question the benefits of mass deworming administration. Two surveys replicated Taylor-Robinson et al. (2012): Welch et al. (2017) found no or little evidence of health or education benefits for children, while Croke et al. (2016) concluded to statistically significant gains in height, weight, and mid-upper arm circumference. Croke et al. (2016) reaffirmed the cost-effectiveness of mass deworming treatments and the WHO confirmed in 2017 its support to mass deworming programs. However all contributions to this debate focus on short-term effects and a limited set of physical measurement indicators. Welch et al. (2017) includes weight, height, proportion stunted, and several cognition and education outcomes. The set of outcomes analysed in Croke et al. (2016) is restricted to weight, height, mid-upper arm circumference, and hemoglobin. Hamory et al. (2021) extends the analysis to longer-term effects of mass deworming administration and finds positive income effects for specific subgroups of treated children 10 to 20 years after the initial treatment. However, long-term health effects are out of the scope of their study. In parallel to the debate over the real benefits of mass deworming administration which was held mainly on methodological grounds, a growing literature in immunology and parasitology has highlighted the complex relationships between humans and worms. In particular, as shown by animal models, worms - or helminths - interact with the host immune system and may protect against obesity or metabolic syndrome including Type-2 diabetes characterized by insulin resistance (Guigas and Molofsky, 2015). Helminths are even investigated as a promising therapeutic strategy for treatments of inflammatory diseases (Lothstein and Gause, 2021). However, for lack of experimental data, most studies documenting the protective health impacts of helminths are limited to showing negative correlations between helminth infections and the prevalence of metabolic syndrome at the population level (Wiria et al., 2014; Tracey et al., 2016). To our knowledge only two trials directly tested the impact of anthelminthic treatments on insulin resistance. A first trial conducted in Indonesia found that after one year of deworming treatment received every 3 month, insulin resistance significantly increased in the subgroup of worm infected individuals, but not in the whole group of treated individuals (Tahapary et al., 2017). A cluster-randomized trial testing in Uganda found no significant difference in insulin resistance in groups submitted to four years of intensive and standard deworming treatment (Sanya et al., 2020). However both focused on short-term impacts (one to four years), and the second one tested the impact of treatment intensity rather than treatment itself. We add to this literature by investigating the long-term impact of anthelmintic treatments on diabetes in a randomized experimental setting using publicly available data from waves 1-3 of the Kenyan Life Panel Survey (KLPS). We exploit the original design of the mass deworming treatment program, the Primary School Deworming Project (PSPD), which was launched in 1998 in 75 schools (50 treatment schools and 25 control schools), and the follow-up KLPS surveys that are extensively documented in Miguel and Kremer (2004) and Hamory et al. (2021). We use replication files from Hamory et al. (2021) and apply their empirical model to the estimation of the long-term impact of deworming treatment on a different outcome (diabetes). Our objective is not to replicate their results, but to ensure that our results on health outcomes are comparable to their results on income and consumption and not subject to different methodological choices. As in Hamory et al. (2021), treatment is a binary variable equal to one for children enrolled in schools that started to receive the treatment in 1998 and 1999, 2 to 3 years earlier than control schools. Our health indicators are constructed using data from waves 2 and 3 of the KLPS, collected in 2007-2009 and 2011-2014, that is about 10 and 15 years after the initial experiment was launched. Hamory et al. (2021) also uses wave 4 which is not publicly available yet. Our main dependent variable is a dummy equal to one if individuals declare having suffered from diabetes in the past four weeks. Given that body mass index (BMI) is a major determinant of type-2 diabetes, we use BMI as a secondary health outcome. BMI is computed based on physical measures (height and weight) that are available only in wave 3. Although the medical literature suggests that helminths could protect against several diseases that are widespread in developing countries, such as allergic disorders (Staal et al., 2018; Wammes et al., 2014) or asthma (Wammes et al., 2014) , we choose to focus on diabetes for several reasons. First, the role of helminths on insulin resistance is more largely documented and less controversial. Second, diabetes is the only pathology that is clearly identified in the health questionnaire of the KLPS, while other health question refer to non-specific symptoms (such as cough, or skin rash) that could relate to many pathologies.

Table 1: The 10- to 15-year effect of deworming treatment on diabetes and BMI

	(1) Diabetes (LPM)	(2) Diabetes (LPM)	(3) Diabetes (LPM)	(4) Diabetes (Probit)	(5) BMI
Treatment	0.0041**	0.0040**	0.0041**	0.0029**	-0.0070
	(0.0018)	(0.0018)	(0.0018)	(0.0012)	(0.1367)
Urban residence		0.0021	0.0025		
		(0.0025)	(0.0026)		
Annual individual earnings			-0.0000		
			(0.0000)		
Control mean	0.0016	0.0016	0.0016	0.0016	22.1397
Treatment effect %	254.65	249.92	257.30	178.98	-0.03
Treatment P-value	0.028	0.028	0.026	0.014	0.959
Number observations	9674	9672	9552	7103	4375

Diabetes is a binary indicator equal to one for individuals who declare having suffered from diabetes in the past four weeks. A linear probability model is estimated in columns 1 to 3. Columns 4 reports marginal effects after the estimation of a probit model. BMI is the body mass index. Health information regarding diabetes was collected in KPLS-2 and KPLS-3. Physical measurements used to compute BMI were collected in KPLS-3. Pregnant women were excluded from the regresion sample in column 5. Treatment is a binary variable defined that comes from ref.[1] and is equal to one for children in Group 1 and Group 2 schools that were treated from 1998 and 1999 respectively. All regressions include the same set of covariates as in ref. [1], that is, controls for baseline 1998 primary school population, geographic zone of the school, survey wave and month of interview, a female indicator variable, baseline 1998 school grade fixed effects, the average school test score on the 1996 Busia District mock examinations, total primary school pupils within 6 km, and a cost-sharing school indicator). Standard errors in parentheses are clustered at the 1998 school level. * denotes significance at 10%, ** denotes significance at 5%, *** denotes significance at 1%

Results

Estimation results are reported in Table 1 below. OLS estimates reported in Column (1) show that treatment significantly increases the probability to declare suffering from diabetes. The effect is large at it amounts to a 250% increase, and significant at the 5% level. Hamory et al. (2021) finds that treatment increases in some subsamples individual earnings and sector of residence, that could also affect the probability to develop diabetes, or to have the pathology detected. For this reason, we add urban residence and individual earnings as controls in Columns (2) and (3) and find a similar impact of treatment on diabetes as in Column (1). Column (4) reports marginal effect from a probit model. A high body mass index is a major risk factor for diabetes, and if deworming treatment is associated with significant weight gains, our estimated effect of treatment on diabetes could be explained by an increase in BMI. We thus estimate the impact of treatment on BMI on the subsample of individuals surveyed in wave 3, as height and weight measurements are not available in wave 2. We additionally exclude pregnant women for which measures of BMI are inaccurate. Column (5) shows that there is no significant effect of treatment on BMI, which suggests that the impact of treatment on diabetes is unlikely to be mediated by weight gains.

Discussion

Our findings suggest that mass deworming has long-term harmful health consequences by significantly increasing the probability of diabetes. Nonetheless our study suffers from several limitations due to the type of data used and needs to be complemented by additional research. First, all children in both the treatment and control group were virtually exposed to deworming drugs (albendazole), the difference between the two groups being the approximate length of treatment: schools in the treated group are expected to have received an average 2 to 3 additional years of treatment compared to control school. The fact that we find a significant effect of treatment on diabetes suggests that the impact of deworming drugs is dose-dependent or vary with the length of treatment. However the design of the initial experiment does not allow us to compare treated individuals to individuals who never received albendazole. Second, diabetes is measured in waves 2 and 3 of the follow-up survey based on self-declaration. Self-declaration likely underestimates the true prevalence of diabetes in the population (Mohamed et al., 2018)[1], although we have no reason to believe that individuals in the treated group would be more likely to have their diabetes diagnosed. The coefficient on the treatment variable remains significant when we control for urban environment or individual income that may be correlated with a either a higher probability to develop diabetes due to different lifestyles, or to be diagnosed. Note that the prevalence of diabetes is small (=0.004) in the total sample, regardless of treatment status.[2] Measures of blood parameters and test for insulin resistance may help improve our understanding of the long-term impact of deworming drugs on diabetes, by providing continuous indicators less dependent on diagnosis. Third, our analysis is limited to the 10 to 15 year impact of treatment, as the fourth wave of the KLPS is not publicly available yet. When available, this additional dataset should be included in our analysis to cover longer-term impacts of treatment. Our results call for further investigation of the long-term health impact of mass deworming programs. If the significant and large impact of mass deworming treatments on diabetes were to be confirmed, the cost-benefit balance of mass deworming may have to be reconsidered, given the prohibitive cost of diabetes treatment in many developing countries (Seuring et al., 2015; Moucheraud et al., 2019).

[1]Based on survey data collected in 2015 among 4069 respondents, Mohamed et al. (2018) find a 52.8% proportion of undiagnosed diabetes

[2] Mohamed et al. (2018) estimate a diabetes prevalence of 2.4% in their sample of 18-69 years-old participants, but individuals in our sample are much younger.

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