Bombing Good Bacteria?
The Effect of Antibiotic Use on Child BMI

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Abstract

I explore the effect of antibiotic usage on children's body mass and propensity to obesity. I exploit variation in physicians' prescribing behavior and implement an instrumental variable approach which uses the random assignment of patients to doctors within clinics, as well as a fixed-effects methodology, and find that receiving an additional antibiotic prescription significantly increases children's BMI z-score and obesity propensity. I use data on about one million, overall healthy, children under 25 in Mexico City using a panel dataset from administrative and clinical records. I find that effects of antibiotics on body mass are considerably larger for girls and that they are stronger for children who suffer from malnutrition (wasting). Effects from antibiotic usage are cumulative, although they wear off over time.

Antibiotics are the most commonly prescribed therapy to children. While the positive health impact of antibiotics for curing bacterial diseases is well known, antibiotic usage is also associated with substancial costs, such as the rise of superbug and antimicrobial resistance (Rogawski et al. 2017). An additional concern which has received relatively less attention is antibiotics' effect on weight and body mass index (BMI), likely due to a known detrimental effect of antibiotics on the gut microbiota—the "good bacteria" present in the gastrointestinal tract—that plays a key role in digestion and metabolism (Allen et al. 2014).

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This paper studies the causal effect of antibiotic usage—measured by prescriptions issued by physicians to a patient—on weight gain and obesity propensity in children and adolescents, and analyzes how this effect varies across age and gender groups. Additionally, it explores differential effects according to patients' baseline nutritional status. I find that antibiotic usage is associated with a significant increase in BMI for children and adolescents and that it is significantly stronger for girls. I find that the effect is stronger for children with lower baseline BMI—in particular for children who are wasted (low weight-for-height)—, although it remains significant across the distribution. I find a positive effect of antibiotic prescriptions on the probability of being obese. Additionally, I analyze the effect of antibiotics on other health outcomes which are correlated with children's weight, namely glucose levels, diabetes status, and blood pressure (BP).

Antibiotics are generally prescribed when a child's health worsens, which may in turn also lead to changes in body mass or weight. As there might be an omitted variable affecting both the probability of receiving an antibiotic prescription and a child's body mass, it is necessary to address endogeneity concerns in order to properly analyze the causal effect of antibiotics on body mass. I use two empirical strategies to explore this effect. First, I use an instrumental variable approach exploiting variation in physician prescribing behavior and an institutional setting where patients are assigned randomly to a family physician at the time of their first contact with the clinic. I find that the tendency to prescribe antibiotics varies considerably across doctors (even within clinics) and that it affects the probability that a given child is treated. Given that there exists a possibility that patients change physicians, I directly address concerns regarding endogenous doctors selection by patients, and present empirical evidence showing that results are not driven by this type of self-selection.

Children that use more antibiotics are likely to be different than those that use less—they are likely to be in worse health and might also differ in body mass or weight (for example, if heavier children tend to get sick more often)—which may produce selection bias. My second strategy exploits the panel structure of the data as I implement a fixed effects methodology at the patient level, which allows me to control for time-unvarying patient characteristics. These results show how an additional antibiotic prescription affects changes in a patient's BMI. An additional advantage of this methodology is that, by exploiting the panel dimension of the data, I am able to analyze how the effect of antibiotics evolves over time, whether it is cumulative, and how it depreciates.

I analyze whether certain gender and age groups are more vulnerable to being affected by antibiotic usage, as there is evidence that the gut microbiota composition varies by sex and age (Million et al. 2013), and may be thus differentially affected. I find that the effect is significantly larger for girls than for boys, and that it is slightly larger for adolescents than

for children. I also find that antibiotics cause a greater increase in BMI for children that had lower nutrition at baseline. Finally, I explore how the effect of antibiotics varies over time, and find that the full effect is realized after about 6 months of the antibiotic being prescribed. I also find evidence of a cumulative effect of repeated rounds of antibiotics as well as evidence of the effect wearing off over time.

I use large, clinical data providing objective health measures from clinical records as well as reliable administrative data for antibiotic prescriptions. The data includes the health and prescription filling history of all patients between 5 and 25 years of age receiving healthcare from IMSS (*Instituto Mexicano del Seguro Social*, Mexico's largest public healthcare provider) in Mexico City, and provides information for over 900,000 patients over three years. There are few studies using large-scale, population-based, administrative, panel data focusing on overall healthy children.[1] These data have several advantages over survey data, which is typically used to analyze the effects on body mass. First, they rely on a large sample of patients—the universe of Mexico City children receiving healthcare from IMSS. This sample includes all children that visited a clinic (either for treatment or a routine health check-up) and is not restricted to children suffering from specific conditions which need to be treated by antibiotics, for example. Second, as they are administrative and clinical records the data are therefore not affected by the existence of recall bias, often present in survey data. Finally, they are panel data, making it possible to follow individuals and physicians over time, thus allowing the use of fixed effects strategies.

The rest of the paper is organized as follows. Section 1 presents some context on antibiotics and the microbiota, as well as the evidence on how changes in the microbiota can affect body mass. Section 2 presents the data, Section 3 discusses the empirical strategies I use to analyze the causal effect of antibiotics on body mass. Section 4 shows the empirical results of the paper. Section 5 concludes.

1 Context

1.1 Antibiotics and the microbiota

Human beings—like other species—host tens of trillions (10^{14}) of different types of microorganisms in their gastrointestinal tracts, commonly know as the microbiota, the vast majority of them being bacteria. These "good bacteria" tend to have a mutualist (win-win) relation with the host and live in a healthy dynamic equilibrium with it. In fact, the intestinal

[1] Most randomized trials analyzing the effect of antibiotics on BMI are disease specific and focus on populations that suffer from a specific condition (for example, cystic fibrosis, Million et al. (2013)), as opposed to the general population.

microbiota has been found to have important effects on the host's physiology, metabolism, nutrition, immunology, and ability to resist pathogens (Allen et al. 2014) as well as hormonal homeostasis (Cho et al. 2012); it is actually a key actor in the digestive process; they aid in the breakdown of polysaccharids—complex sugar chains—and remove toxic dietary compounds, for example. These bacteria are originally obtained from maternal gut microbiota, and these 'pioneer' bacteria colonize their microhabitats during infancy (Allen et al. 2014; Mor et al. 2015).

There exists ample evidence linking the microbiota and its general composition to weight and obesity in humans an other animals. The composition of microbiota has been found to differ across individuals, depending on their characteristics, such as sex, age, or nutritional status. While certain types of bacteria tend to be more prevalent in lean individuals (*Bacteroidetes*), others are more common in obese individuals (*Firmicutes*) (Ley et al. 2006). In fact, there is evidence that altering the microbiota can have a direct effect on body mass. For example, a study transplanting microbiota from obese mice to lean mice (while keeping diets constant) found that these started to gain weight (Million et al. 2013).

If unperturbed, gut microbiota maintain stable population levels in normal adult hosts. However, there are several factors that may influence the microbiota through changes in the host, the microbiota's environment or the bacteria themselves. Diet, prebiotics, and probiotics have been found to affect the composition of the human microbiota. Additionally, there is a large literature documenting the effects of antibiotics on the microbiota (see the review presented in Million et al. (2013)), which finds significant effects of antibiotics on the composition of the microbiota. There is evidence that certain types of antibiotics may have a larger effect on weight gain that others, such as macrolides (Million et al. 2013; Schwartz et al. 2016).

Antibiotics are medications that are used to treat bacterial diseases, as they help to eliminate the presence of disease causing microbes inside the host. However, besides affecting the bacteria causing the disease that is being treated, antibiotics have been reported to also decrease the bacterial load and its composition in the digestive tract (Million et al. 2013). Actually, antibiotic usage has been found to have an effect on humans' (and other vertebrates') microbiota by directly altering its composition. Cho et al. (2012) find that antibiotics alter the population structure of the gut microbiome of mice, as well as their metabolic capabilities by administering sub-therapeutic doses of antibiotics to some mice (but not others in a control group). Additionally, they find an increase in body fat, and increased early life growth rates, and increased body mass for *female* mice by significantly affecting gut microbiota's composition.[2] They postulate that antibiotics increased metabolic

[2]Antibiotics significantly elevated the *Firmicutes* to *Bacteroidetes* ratio, which accompanied the increases

activity, allowing mice to extract a higher proportion of calories from carbohydrates, one of the mechanisms of weight gain.

My research advances the understanding of this topic as it directly addresses endogeneity issues that arise when trying to identify the causal effect of antibiotics on weight and nutrition, as antibiotic prescriptions are likely to be affected by patient characteristics and underlying health. Although some papers try to address this issue (Mor et al. 2015; Trasande et al. 2013; Schwartz et al. 2016), the causal interpretation of their result is affected by potential endogeneity concerns, such as selection bias and omitted variable bias, which are often not properly addressed. To identify this causal effect I use two alternative strategies which yield similar results: an instrumental variables approach and a patient fixed effects methodology.

There has been a growing interest in the literature in analyzing the effect of antibiotics on weight and obesity, especially for children. Several studies provide evidence that there does appear to exist an effect of antibiotic usage on weight gain, but the interpretation of these effects is not necessarily a causal one, as endogeneity concerns are often overlooked. For example, Mor et al. (2015) find a higher prevalence of overweight and obesity for schoolchildren that had prenatal exposure to antibacterials, using medical and administrative data but it cannot rule out underlying infections during pregnancy as an omitted variable (consistent with the fetal origins hypothesis, which links the perinatal period to childhood obesity). Trasande et al. (2013) use a longitudinal study of parents and children and find that exposure to antibiotics during the first 6 months of life is associated with modest increases in body mass from 10 to 38 months, although causality cannot be directly established as the measure of antibiotic exposure is constructed from a survey administered to parents regarding their children's exposure to antibiotics, which may be affected by recall and measurement bias, in addition to the potential selection bias if heavier (or leaner) children are more likely to have taken antibiotics.

Additional studies linking antibiotic usage and weight gain that address endogeneity concerns by implementing randomized controlled trials also find a positive effect on weight. However, the generalizability of some of these studies is not straightforward. Many of these papers are disease-specific and focus on diseases that may themselves cause weight-loss, such as cystic fibrosis or infections from *Helicobacter pylori* (Million et al. (2013), Pirzada et al. (2003)), or low birthweight infants (Mansi et al. 2011). Therefore, it is not clear whether observed weight gain is due to a health improvement or caused directly by antibiotics. Additionally, the sample of patients that they focus on suffer from a specific condition and may

in adiposity. Increases in the *Firmicute* population have been observed in mice that are genetically prone to obesity.

therefore have different reactions to antibiotics than overall healthy children.

Schwartz et al. (2016) presents strong evidence of an effect of antibiotic use on BMI trajectories throughout childhood. It is one of the very few large-scale, population-based, longitudinal studies on this topic. They use electronic health record data for children 3-18 years and analyze different types of associations of antibiotics on children's BMI. In particular, they are able to differentiate reversible, persistent, and progressive associations (this is, recent, cumulative, and lagged cumulative antibiotic exposure) and present a good analysis of changes in BMI trajectories offset by increased antibiotic usage. The paper uses mixed effects linear regression models which may fail to adequately control for all time unvarying characteristics, and potentially leading to the existence of a bias arising from selection into treatment.

While Schwartz et al. (2016) analyzes the differential effects by age, it does not address differential effects which may exist by gender and may be a potentially important factor for the relationship between antibiotic usage and BMI, especially given that antibiotic usage affects hormonal processes (Cho et al. 2012). My paper complements the results in Schwartz et al. (2016) by presenting differential effects not only by gender, but also by nutritional status. Additionally, I analyze the effect of antibiotics on other relevant health measures, such as glucose, diabetes status, and BP, which may be indirectly affected by antibiotics through weight increase. Finally, I am able to present a more complete picture of the dynamic process of the effect of antibiotics on BMI by fully exploiting not only the number of antibiotics prescribed but also the timing in which they are given to patients.

1.2 Antibiotics in animal agriculture

Growth promoting antibiotics have been used in livestock since the 1940's, as their effect on body mass has been known for years. Surprisingly, however, it is until very recently that the effects of antibiotics on human weight gain have started to be documented and studied. Recent evidence suggests that there is a link between greater antibiotic use and weight, and that this effect may be stronger and persistent for children and adolescents. The channel through which antibiotics are thought to affect weight is by altering individuals' gut microbiota composition, which has been found to have a direct impact on hosts' weight and metabolism.

After the development of large-scale production during World War II, the costs of antibiotics fell dramatically, and became cheap enough to start being administered to farm animals. Shortly after, a series of reports found that some types of antibiotics enhanced the growth rate of chickens and pigs. Therefore, since the 1940's antibiotics have been used in farming

for maintaining health an improving farm productivity. Antimicrobials are generally used as dietary additives for treating sick animals (acute therapy), to prevent disease (prophylactic therapy), and improving feed efficiency (weight gain/weight of food consumed/specific time period)—a non-therapeutic purpose (Allen et al. 2014).

An important difference between animal and human antibiotic use to keep in mind is that growth-promoting antibiotic use for animals tends to include low (sub-therapeutic) doses over long periods of time, while therapeutic use for humans tend to be high, but over a short period of time. Understanding the ways in which antibiotics affect animals' weight might be useful to understand why we would expect to see effects in humans as well. While the precise mechanism through which antibiotics promote growth in animals remains unknown, it is thought that it is mediated through gut bacteria by reducing the number of growth-depressing organisms, reduction of microbes competing for host nutrients, reducing subclinical infections, or enhancing nutrition by thinning the intestine walls (Allen et al. 2014).

2 Data

I use an administrative panel dataset, which allows me to follow approximately one million patients over more than three years (January 2012 through June 2015) in Mexico City. I use (anonymized) data from all patients between 5 and 25 years of age receiving healthcare at Mexico's largest healthcare provider, IMSS, which covers more than half the Mexican population. I use administrative data which includes electronic medical records with health variables such as weight, height, body mass index (BMI), BP (both systolic and diastolic), sex, age, in addition to the appointment's date, main diagnosis (ICD-10), as well as a doctor and clinic identifiers.

I merge this data with administrative prescription filling (01/2012-12/2014) records from IMSS.[3] From this data it is possible to identify every medication prescribed to a patient as well as the physician who issued the prescription. I am able to identify the 26 antibiotics prescribed by IMSS, which are defined in its institutional clinical guidelines.[4]

Finally, I use IMSS data on doctor characteristics (for the year 2014) which includes age, gender, and wage, and complement it with the characteristics of the patient population

[3]There is a pharmacy at every IMSS clinic where patients may fill the prescriptions issued by their (IMSS) physician free of charge. IMSS doctors are salaried workers.

[4]These include Metronidazole, Amikacin, Ampicillin, Azithromycin, Benzylpenicillin, Benzylpeniline, Benzathine, Benzathine benzylpenicin, Cefotaxime, Ceftriaxone, Ciprofloxacin, Clindamycin, Chloramphenicol, Dicloxacillin, Doxycycline, Erythromycin, Streptomycin, Gentamicin, Isionazide, Neomycin, Nitrofurantoin, Rifampicin, Tetracycline, Ticarcillin, Tinidazole, Trimethoprim. These antibiotics are included in a total of 54 distinct medications (due to different doses and presentations, for example).

under 25 each doctor provides healthcare to. In particular, I am able to compute the average age and BMI of each doctor's patients.

Using these data sources, I am able to construct doctors' propensity to overprescribe antibiotics (the measure of 'overprescription'), which as discussed below, will work as an instrument for antibiotics prescribed to a patient. This measure is constructed at the physician level from pharmacy records, and is defined as the number of patients that were prescribed an antibiotic by doctor d when the patient's diagnosis (from clinical records) was a *viral* condition (referred to as *misprescription*), divided by the total number of patients that were prescribed any medication by doctor d (over the whole period). In particular, a doctor's measure of overprescription Z^d is given by:

$$Z^d = \frac{\sum_{t=0}^{T} \sum_j \mathbb{1}[misprescription_{j,d,t} = 1]}{\sum_{t=0}^{T} \sum_j \mathbb{1}[prescription_{j,d,t} = 1]}, \tag{1}$$

where $\sum_j$ is the sum over all patients seen by doctor d.

Figure 1 shows the distribution of Z^d, physician overprescription.[5] The figure shows that there is ample variation in physicians' overprescribing behavior, which is key in order to use this measure as an instrument. We can see that a significant share of doctor has a positive share of 'overprescription', and that it is not unusual for doctor's to 'misprescribe' antibiotics when they have diagnosed a viral condition.

Although the prescriptions data from IMSS presents a semi-closed pharmacy system which allows me to follow patients over time, it is also possible that patients may get antibiotics from a non-IMSS pharmacy. This concern is attenuated by the fact that IMSS fills prescriptions free of charge. However, it is possible that additional antibiotics are consumed. Additionally, I cannot observe patients' medication adherence, so it is also possible that less antibiotics are consumed than are filled. An additional limitation of the data I use is that there exists left- and right-censoring, and therefore medication and clinical histories may be truncated.

Summary statistics are presented in Table 1. Panel A shows mean characteristics for the 8,866 physicians providing healthcare services at IMSS clinics in Mexico City, by level of physician's observed 'overprescription'—defined as the share of total prescriptions that were misprescribed—i.e. *antibiotics* prescribed to an individual with a *viral* condition.[6] Summary statistics include gender, age, and wage.[7] Additionally, it includes mean characteristics of

[5]Truncated at $TotalPatients > 8$ following Heckman (1981) and Greene (2001)'s rule of thumb of eight observations per group for ability of small sample sizes to allow for meaningful estimates.

[6]I divide physicians into high and low overprescription using the median level of overprescription of all doctors.

[7]Monthly wage in current 2013 Mexican Pesos. The PPP exchange rate at the time was of around 7.88

the population that each doctor provided services to over the 2012-2015 period; namely, it presents the mean age and BMI of the patients seen by the physician, the share of prescriptions that were antibiotics, the share of patients that were diagnosed with a viral condition, and mean level of overprescription.

Panel A of Table 1 shows that doctors that tend to prescribe more or fewer antibiotics irresponsibly differ on most observable variables; younger, female doctors tend to prescribe more antibiotics, and they tend to earn lower wages, and provide healthcare to a younger population, with a relatively lower BMI. Interestingly, both sets of doctors prescribe a similar *share* of antibiotics, as about a third of patients receive an antibiotic prescription—overprescribing doctors simply tend to do it more irresponsibly (as they prescribe them to patients diagnosed with viral conditions).

Panel B of Table 1 shows mean patient characteristics at baseline for patients that received at least one antibiotic (columns 1 and 2) never and for those that never received an antibiotic prescription over the period (columns 3 and 4) at baseline (i.e. first appointment in the data). Column 5 shows the difference in means. Patient characteristics include age, gender, weight, height, BMI z-score (as well as a set of dummies for stunting, wasting, thinness, overweight, and obesity), blood pressure, diabetes diagnosis, as well as the number of visits to clinics, and mean number of medications prescribed per visit, as well as the total number of antibiotics prescribed over the whole period.

Patient summary statistics show that patients who are prescribed antibiotics are younger than those who are not, and they tend to visit the doctor more frequently and receive more prescriptions per visit (suggesting they may be in worse health). This evidence is consistent with endogeneity in antibiotic prescriptions as patients who are prescribed antibiotics are different to those who are not, making it necessary to implement an identification strategy to adequately control for selection bias which is likely to exist. However, both sets of patients do not seem to differ significantly in terms of nutrition and have in fact similar BMI z-scores at baseline (patients that never received antibiotic prescriptions are both heavier and taller most likely due to the age difference).

3 Identification Strategy

The key problem to address the question of whether antibiotics have an effect on children's nutritional status (or some other health outcome) is that whether a child actually receives an antibiotic prescription depends on the child's own health and characteristics. For example, children with lower general health are more likely to get sick and seek treatment. This may

MXN per USD (OECD Data)

happen more frequently if they are overweight or obese. Furthermore, conditional on getting sick, the probability of receiving an antibiotic prescription may depend on the severity of the infection—which again could tend to be higher for overweight patients—and infections could lead to changes in body mass. Antibiotic prescriptions are likely to be endogenous, and a simple regression analysis would lead to biased estimates of the effect of antibiotic usage and BMI. To address these concerns I use two strategies: instrumental variables and patient fixed effects.

3.1 Instrumental Variable

In my first strategy, I exploit the random assignment of doctors to patients within a clinic upon their first visit, along with the variation in physicians' prescribing behavior (with respect to antibiotics). Some doctors tend to be more aggressive prescribing antibiotics, and this will affect the probability that a given child receives an antibiotic. The idea of this strategy is that for any given patient (with a certain level of general health, symptoms, severity) the probability that she receives an antibiotic prescription is going to be higher if she sees a more 'aggressive' doctor. Since patients are assigned randomly to doctors (within clinics) we can identify the effects on BMI from using more antibiotics (i.e. from being assigned to a more aggressive doctor). This strategy allows us to control for selection bias, as well as omitted variable bias an concerns regarding reverse causality (if heavier children tend to be prescribed more antibiotics). Similar approaches have been used by to identify the effects of ADHD medication use (Dalsgaard, Nielsen and Simonsen 2014), foster care assignment (Doyle Jr 2007), antipsychotic drug prescriptions (Duggan 2005), and prison sentences (Kling 2006).

Patients at IMSS are assigned (non-randomly) to clinics according to their zip-code of residence. However, they are randomly assigned to a specific physician *within* the clinic at a patient's first visit, who will be the assigned family doctor for subsequent visits. However, if the assigned doctor is not at the clinic for a patient's following visits (depending on the time of appointment, for example), she may be treated by another doctor, also assigned randomly according to availability. I additionally address concerns regarding the possibility of patients (non-randomly) changing doctors by (i) using the prescribing behavior of the doctor who was *originally* assigned to treat the patient and (ii) analyzing effects for patients that changed doctor at some point versus those that did not.

Doctor's vary in their tendency to prescribe certain types of medication, and can be relatively more or less aggressive in doing so. I construct an instrument that captures a patient's doctor's propensity to prescribe an antibiotic. In particular, as I may observe diag-

nosis and medication prescription, for each doctor I construct a measure of 'overprescription' which measures the frequency with which a doctor prescribes an antibiotic when in theory he should not: when the main diagnosis is a viral condition.[8] As doctor assignment within a clinic is random, the instrument is likely uncorrelated to patient characteristics conditional on clinic assignment—which I can control for by including clinic fixed effects. The identifying assumption is that the doctor's antibiotic-prescribing style only affects a patient's BMI through an increase in antibiotic consumption.

The outcome of interest is the patient's BMI z-score (referred simply as BMI from here onwards).[9] In particular, I use the patient's last measured BMI, and estimate the effect of the number of antibiotics she has been prescribed (over the whole period) as explanatory variable. In order to account for non-random clinic assignment, I include clinic fixed effects in all regressions. The specific equation I estimate is of the form:

$$zBMI_{i,\{d\},t} = \beta_0 + \beta_1 \sum_{s=0}^{t-1} RxAnti_{i,\{d\},s} + \beta_2 \boldsymbol{X}_{i\{d\},t} + \delta_t + \phi_c + \varepsilon_{i,\{d\},t} \tag{2}$$

where $RxAnti_{i,d,t}$ is a dummy variable equal to 1 if patient i was prescribed an antibiotic by doctor d at time t (where $\{d\}$ indicates that all doctors seen by patient i are considered), $\boldsymbol{X}_{i,\{d\}t}$ are patient characteristics at the time of his last doctor's appointment and doctor characteristics for all the doctors who prescribed her medication, δ_t are month-year fixed-effects, and ϕ_c are clinic fixed-effects. Patient controls include age fixed-effects and sex in order to flexibly control for age, and doctor controls include total patients, patient population mean BMI and age, total antibiotics prescribed, and share of respiratory conditions' diagnosis. The coefficient of interest is β_1.

Given that antibiotic prescription suffers from endogeneity concerns, I instrument for antibiotic prescriptions $RxAnti_{i,d,s}$ using an econometric model of the form:

$$\sum_{s=0}^{t-1} RxAnti_{i,d,s} = \pi_0 + \pi_1 \sum_{s=0}^{t-1} Z^d_{i,\{d\},s} + \phi \boldsymbol{X}_{i,\{d\},t-1} + \delta_t + \phi_c + v_{i,\{d\},t-1} \tag{3}$$

where $Z^d_{i,s}$ is doctor d's propensity to overprescribe antibiotics, *excluding* patient i's own prescription history.[10]

[8] Antibiotics should not be prescribed for treating viral conditions, as they have no effect on viruses (CDC https://www.cdc.gov/getsmart/community/materials-references/print-materials/everyone/viruses-bacteria-chart.pdf). The *viral* conditions I consider are: common cold, non-bacteria respiratory conditions, and any condition with the word 'viral' in ICD-10 (viral meningitis, viral hepatitis, viral pneumonia). Among these, the common cold is by far the most frequent occurrence.

[9] z-scores are used to account for growth patterns in children and adolescents. I use tables from the WHO Child Growth Standards to compute BMI z-scores from patients height and weight.

[10] Patient i is excluded as to not mechanically affect doctor d's measure of overprescription, as this could

I additionally consider alternative specifications by adding additional controls (doctor and patient), considering mean as opposed to cumulative antibiotic overprescription, dichotomizing the antibiotic prescription variable (a variable equal to one if the patient has received *any* antibiotic prescriptions over the time period I study, and replacing the dependent variable for an 'obese' dummy.

An important concern which could invalidate the IV estimates relates to whether patients may non-randomly change doctors, which would invalidate the assumption of random doctor assignment within a clinic and could lead to endogeneity.[11]To address this, as a robustness check, I am able to construct a modified version of the instrument which fixes the prescribing behavior (overprescription) of the *first* doctor a patient sees and imputes it to every visit the patient makes (independent of the doctor she actually sees). The instrument may be rewritten as $Z^{d_0}_{i,\{d\},s}$, which indicates that the measure of overprescription that will be considered when the patient sees *any* doctor d will always be that of his original physician, d_0. With this version of the instrument, non-random doctor changes cannot bias estimates, as long as the *original* doctor assignment is random.[12]

Additionally, I address patient self-selection into doctors by running the model (with the original instrument which does not fix the original doctor's measure of overprescription) separately for patients that were always treated by the same doctor and for those who were treated by multiple doctors. Although patients who see various physicians are not necessarily self-selecting (they may be assigned to a new doctor if their regular doctor is not present on the date/time they visit the clinic, for example), comparing the magnitude of the effect of antibiotic prescriptions on child BMI allows us to verify whether the effect is driven by non-random doctor assignment.

As additional robustness checks I analyze how antibiotics affect patients that received an antibiotic prescription when they should have not (i.e. the effect of a 'misprescribed' antibiotic for a viral condition). Arguably, these patients do not receive the health benefit of receiving an antibiotic but are exposed to its effects on their microbiota. In this case, I run

lead to bias. In particular, patient i's exposure to doctor d's measure of overprescription is given by:

$$Z^d = \frac{\sum_{t=0}^{T} \sum_{j,-i} \mathbb{1}[misprescription_{j,d,t} = 1]}{\sum_{t=0}^{T} \sum_{j,-i} \mathbb{1}[prescription_{j,d,t} = 1]},$$

where $\sum_{j,-i}$ is the sum over all patients seen by doctor d excluding patient i himself.

[11]Table A.1 in the Appendix shows patient characteristics according to whether they ever changed doctor, or whether they always saw the same physician. Patients' BMI z-score for both groups is statistically equal for both groups of patients.

[12]A plausible assumption as patients are likely to lack information about attending physicians upon their first to the clinic, and are therefore unlikely to self-select into more (or less) aggressive doctors regarding antibiotic prescribing behavior.

the baseline regressions using only the antibiotic prescriptions that were given to patients when they exhibited a viral condition (the most recurrent one being a common cold).

Finally, I check whether antibiotic prescriptions have an effect on other health outcomes. Namely, I focus on patients glucose levels, diabetes status, and BP. If patients' weight, obesity propensity, and metabolism are affected, we could expect an effect on these health variables.

3.2 Patient Fixed-Effects

As children with different general health and body mass characteristics may differ in the probability with which they receive antibiotics (which may lead to selection bias), I exploit the panel structure of the data to control for patient time-unvarying characteristics. This strategy allows me to effectively identify how youths' BMI changes from receiving one additional antibiotics prescription (i.e. difference-in-difference framework). In particular, I use patient fixed effects to estimate how increases in antibiotic usage affect changes in BMI.

By using cumulative antibiotic prescriptions received by patients, I am able to identify the variation in BMI arising from increasing antibiotic prescription. The identifying assumption necessary for this model to be correctly specified is that no unobservable patient characteristic changes at the time that the antibiotic prescription is issued. The estimated models are of the form:

$$zBMI_{i,t} = \beta_0 + \beta_1 \sum_{s=0}^{t-1} RxAntibiotic_{i,s} + \alpha_i + \delta_t + \varepsilon_{i,t} \tag{4}$$

where $\sum_{s=0}^{t-1} RxAntibiotic_{i,s}$ is the (cumulative) number of antibiotics the patient received up until her last appointment, α_i are patient fixed effects and δ_t are time fixed effects (monthly).[13] The coefficient of interest is β_1, which can be interpreted as the effect of receiving one additional antibiotic prescription on a patient's BMI z-score.

3.3 Heterogeneous Effects

To further explore the effect of antibiotics on children and adolescents' weight, I analyze the differential effect across subgroups of the population. In particular, I explore whether the effect changes depending on the patient's age, gender, and original nutritional status. I define original nutritional status using the patient's first measured BMI, and define children as wasted ($zBMI < -2SD$), thin ($-2SD < zBMI < -1SD$), overweight ($+1SD <$

[13] Clinic fixed-effects are not included as they are absorbed by patient fixed effects.

$zBMI < +2SD$), or obese ($zBMI > +2SD$). The base category is normal weight for height ($-1SD < zBMI < +1SD$).[14] By adding the patient's gender, age (in the form of age fixed-effects), and nutritional status at baseline, and an interaction term with the antibiotic prescription term, I am able to analyze whether the effect of antibiotics changes across subgroups. I perform subgroup analysis using both the instrumental variable and patient fixed-effects empirical strategies I implement. For the instrumental variable approach, I explore heterogeneous effects using reduced form estimates.

3.4 Dynamic effects

Finally, I explore the dynamic effects of antibiotic prescriptions on children's weight. Analyzing how the effects of antibiotics change with time makes it possible to determine whether the effect is persistent, cumulative or wears off over time. This information may help to better understand the mechanisms through which antibiotics affect weight and give a more complete picture of the implications of higher antibiotic use for children's weight and obesity. Additionally, assuming children do not become immediately heavier after using antibiotics, looking at the effects depending on how long ago the antibiotics were prescribed will additionally give evidence to alleviate concerns of reverse causality.

In order to explore the dynamic effects of antibiotics on BMI, I exploit the panel nature of my data. In particular, I run the fixed effects regressions considering only the antibiotic prescriptions received over the previous 30, 60, 90, 180, and 360 days to construct the dependent variable. The equations I estimate are of the form:

$$zBMI_{i,t} = \beta_0 + \beta_1 \sum_{s=0}^{t-1} RxAntibiotic_{i,s} \mathbb{1}[t - s < M] + \alpha_i + \delta_t + \varepsilon_{i,t}, \tag{5}$$

where $\mathbb{1}[t - s < M]$ is an indicator function which is equal to one when the number of months that have passed since the medication was prescribed is smaller than M, for $M \in \{1, 2, 3, 6, 12\}$. The explanatory variable is therefore effectively only including the prescriptions issued in the specified timeframe (but ignoring the ones prescribed before). The magnitude of the coefficient β_1 for different values of M yields information about how long it takes for an antibiotic to have an effect on the patient's BMI, and whether it changes over time.

[14] From WHO Child Growth Standards charts

4 Results

4.1 Instrumental Variables

Table 2 presents the first stage estimates and shows that the measure of overprescription is a good predictor of physicians' antibiotic use. The first column shows the estimates from a regression without controls, while columns 2 and 3 control for individual characteristics. Patients that are treated by more aggressive doctors do in fact receive, on average, more antibiotic prescriptions, even after controlling for clinic fixed effects, suggesting that the instrument is relevant. The estimated F-statistics provide evidence that the instrument is not weak (it is equal to 290 in the preferred specification, and always larger than 100). Estimates are robust to the inclusion of both doctor and patient controls.

Table 3 presents the baseline specifications, and main results of the paper. Columns 1 through 3 show OLS estimates, while columns 4 through 6 present the instrumental variable, two-stage least squares (2SLS) specifications. Column 6 represents the preferred baseline specification, which includes patient and doctor controls. While the estimates from the OLS are positive and statistically significant, the magnitude of the estimates increases significantly when using the IV specification. This suggests there exists an omitted variable bias on the OLS estimates.

Controlling for patient and doctor characteristics decreases the magnitude of the estimates from the model with no controls, although they are still significant and larger than the OLS estimates. The results suggest that receiving an additional antibiotic prescription increases a child's BMI z-score by 0.03 (an increase of around 4%) This effect is statistically significant at the 1% level (as are all the estimates presented in Table 3).

Estimates from some alternative specifications using the IV approach are presented in Table 4. Column 1 shows the baseline estimates. Column 2 uses the *mean* overprescription tendency (i.e. mean doctor aggressiveness) that the patient was exposed to during her doctor's appointments (as opposed to the *cumulative* overprescription she was exposed to). This estimate suggests that the whole effect is not entirely explained by the *frequency* with which a patient was exposed to the measure of overprescription.[15] Column 3 includes additional controls, such as gender $\times$ age (and age squared) to control more flexibly for age-gender groups, and the total number of prescriptions she received over the whole period. Including these controls does not modify the coefficient.

Column 4 uses a dummy of whether a patient was ever prescribed antibiotics over the whole period as opposed to the cumulative number of antibiotics prescribed as the explana-

[15]The magnitude of this coefficient should be interpreted with caution as it is not directly comparable to other coefficients, given that it ignores the *number* of doctor's visits.

tory variable. Again, the IV estimate finds a positive relationship suggesting that being prescribed at least one antibiotic prescription significantly increases children's weight. Finally, column 5 uses a dummy variable indicating whether the patient is considered obese at his last appointment as the dependent variable (instead of her BMI z-score). The coefficient is positive and significant, and it suggest that antibiotic prescriptions increase the probability of becoming obese. In all models we can see that the effect for females is significantly larger.[16] Except for the regression which uses 'mean overprescription' as the dependent variable in column 2, all models yield statistically significant coefficients that suggest that exposure to antibiotics has an effect on youths' BMI.

4.2 Patient Fixed-Effects

The results of models that include patient fixed-effects show a positive effect of antibiotic prescriptions on children and adolescents' BMI. Estimates are in line with those from an IV methodology and show similar , suggesting that there exist a causal effect of antibiotics on body mass. In fact, the pointwise estimates are similar to those from the IV models, suggesting that both empirical approaches taken are successfully controlling for endogeneity issues.

Table 5 shows the baseline estimates for fixed-effects models. They show that receiving one additional antibiotics prescription is associated with an increase in BMI z-score of 0.03 (column 1). The effect appears to be increasing with age, as can be seen in the interaction term of column 2 and comparing the magnitude of estimates for patients under and over 16 years of age in columns 3 and 4 respectively. The effect is significantly larger for females (columns 5-6) with the results in the IV estimates. These differential effects are analyzed in further detail in the following subsection. Column 7 shows that the effect does not appear to be stronger for macrolide antibiotics, as suggested in Million et al. (2013); Schwartz et al. (2016); Pirzada et al. (2003).[17]

4.3 Heterogeneous Effects

4.3.1 Age and Gender

I first explore whether there are differential effects by age or gender. Table 6 shows reduced form estimates, from regressing BMI z-score directly on patients' exposure to physician over-

[16] Column 3 shows a positive coefficient in male, but when considering the interaction term between age and sex the total effect of being male is also negative (except for 5-7 years olds).

[17] Macrolide antibiotics prescribed in IMSS are clarithromycin, erythromycin, and azithromycin, and correspond to four distinct medications.

prescription. Column 4 presents the estimates corresponding to the baseline IV regression shown in column 6 from Table 3 (columns 1-3 show estimates without the full set of controls). Consistent with the IV results, the estimated coefficients are positive and statistically significant at the 1% level.

Column 5 shows that there is a positive differential effect for relatively older patients, although it is small and statistically weaker than the rest of the estimates. Column 6 shows that the effect of antibiotic prescriptions on BMI is considerably stronger for female patients (significant at 1%) and that the effect for female patients is about twice that of male (from looking at the magnitude of the interaction term between the instrument and *male* variable). This differential effect is not being driven by the fact that girls are heavier (as that is captured by the coefficient on tha *male* variable alone). Figure 2 graphically shows the results from interacting age and gender fixed-effects with the measure of overprescription. While there is no clear differential effect by age (although the effect does seem to be on average larger for patients over 16 than those under), the interaction with a dummy for being male is negative and statistically different from zero.

4.3.2 Baseline BMI z-score

Estimates across different baseline nutritional status are presented in Tables 7 and 8, which use the IV and patient fixed-effects methodologies, respectively. Table 7 presents reduced form estimates, where the measure of overprescription is used directly as the explanatory variable of interest. Column 1 presents the reduced form estimates corresponding to the baseline IV regression (column 6 from Table 3). Column 2 suggests that the effect of antibiotics on BMI is weaker for patients who were stunted at baseline (low height for age). The opposite is true for patients who were wasted at baseline (column4). From column 3, we can see that the magnitude of the effect of antibiotics on BMI tends to be lower for patients who were heavier at baseline, as the negative coefficient on baseline BMI z-score suggests. Using dummy variables for different nutritional categories according to children's baseline BMI, Columns 4-8 show that the effect is in fact lower for patients who were originally heavier (the implicit base category is children with normal BMI for their age-gender group).

Table 8 shows equivalent results using patient fixed-effects. Column 1 is the baseline fixed-effects regression (column 1, Table 5). Column 2 includes an interaction term between receiving an antibiotic prescription and being male, and—consistent with the IV estimates—implies that the effect is considerably larger for female patients. Columns 3-8 show the differential effects by baseline nutrition and again, we see the same pattern as in Table 7, where patients with lower BMI z-score at baseline tend to gain more weight after being

prescribed antibiotics. Figure 3 shows the coefficients for both tables graphically.[18]

4.4 Dynamic effects

Figure 4 shows the coefficient from fixed-effects regressions using only the *cumulative* antibiotics prescribed exclusively over the past x days as explanatory variable. The marker on the top row corresponds to the estimate from the baseline model, considering the full history of antibiotic overprescription. The figure shows that the full effect of antibiotics on BMI is not immediate—the magnitude of the effect increases systematically from 30 days to 180 days when it reaches its maximum value. However, when we consider a window of a whole year (360 days), the magnitude actually decreases with respect to 6 months, suggesting that the effect of antibiotics may fade away as time goes by. However, it is interesting to note that the effect after one year is well above that of after 30 or 60 days.

4.5 Robustness Check

The results from the models that address the concern regarding patients self-selecting into doctors with different prescribing behaviors are presented in Table 9. Column 1 shows the baseline IV estimate. Column 2 shows the estimates from using the instrument that fixes the level of overprescription from the first doctor who cared for the patient and imputes it to all other subsequent visits. Columns 3 and 4 correspond to running regressions separately for patients that always saw the same doctors and for those who ever changed doctors. The table shows that all specifications are positive and significantly different from zero, and that the effect does not appear to be driven by from patients endogenously choosing the doctor they see. In fact, we see that when we control for this potential concern the estimates of the effect of antibiotic prescriptions on BMI is actually *larger* (both in column 2 which fixed the original physician's measure of overprescription and in column 3 which focuses on patients that never changed doctor).

Results for the effect of misprescribed antibiotics are presented in Table 10. The effect from the preferred IV models (columns 4-6) show a positive, large significant effect of antibiotic use on BMI. Additionally, it is interesting to note that the estimates from the OLS estimates lose significance when we use only misprescribed antibiotics as explanatory variable and are significantly different from IV estimates, suggesting that endogeneity problems exits (in Table 3 estimates for IV and OLS were closer in magnitude).

[18]Figure A.1 in the Appendix shows that differential effects by age and baseline nutrition for girls are qualitatively and quantitatively similar for girls and for the whole population.

The effect of receiving antibiotic prescriptions on other health outcomes besides BMI are presented in Table 11. I find a significant effect of antibiotic prescriptions on diabetes status and glucose—were both variables are related to metabolic processes and associated with weight gain. It is important to note that the effect on glucose is not measured for every patient on every consultation, which could potentially induce selection bias (less than 6% of patients had their glucose level assessed during their last appointment).

5 Conclusion and Discussion

Antibiotics are among the most commonly prescribed medications in the world, and they effectively combat some of the most deadly diseases for humankind. However, their use entails a set of important costs that must be taken into account by health practitioners and patients when using antibiotics. Among these, antibiotic resistance seems like the most menacing for health worldwide. However, antibiotic resistance is an externality more than an effect directly experienced by the individual who uses antibiotics, and therefore is a cost that is often not internalized by patients or doctors.

This paper presents evidence of another unintended effect of antibiotic usage: weight gain. I find that receiving an antibiotics prescription significantly increases BMI in children and teenagers—more so in girls—and that it increases the probability of becoming obese. As opposed to the cost of antibiotic usage related to microbial resistance, weight increase is experienced by the patient using antibiotics himself, so it is therefore more likely to be taken into account by patients and healthcare providers prescribing antibiotics, which could in turn have an effect for deterring antibiotic overuse.

I find antibiotics cause an increase of around 0.027 BMI z-score (smaller, fixed effects model). A simple and conservative back-of-the-envelope calculation implies that this effect corresponds to an increase of approximately 0.15kg (from 59.74kg to 59.89kg) for an 18 year old female patient—the mean patient in the sample.[19] In terms of BMI, the gain is of approximately 0.06 kg/m^2. This increase is similar in magnitude to the 0.068 kg/m^2 increase in BMI z-score associated to girls who drank 1 serving per day of sugar added beverages found in Berkey et al. (2004).

Unlike the costs associated with antibiotic overuse related to antibiotic resistance and the rise of superbugs, the effect of antibiotic use on body mass and weight translates into a direct cost for the individual. Excess weight has been associated with increased morbidities,

[19]The mean BMI z-score for this age group is 0.77, which corresponds to a BMI of 23.9. To convert BMI to weight in kilograms, I use the average height of 18 year old female patients of 1.58m, which yields an implied weight of 59.74. Taking the increase in BMI z-score from antibiotic use of $0.77 + 0.027 = 0.797$ yields an implied weight of 59.89.

higher health costs, worse labor outcomes, and ultimately shortened life expectancy. In this sense, it is a cost that is experienced by individuals themselves, so these findings may have a further impact for antibiotic use as patients (or their parents) internalize the concerns of abusing this type of drugs.

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6 Figures and Tables

6.1 Figures

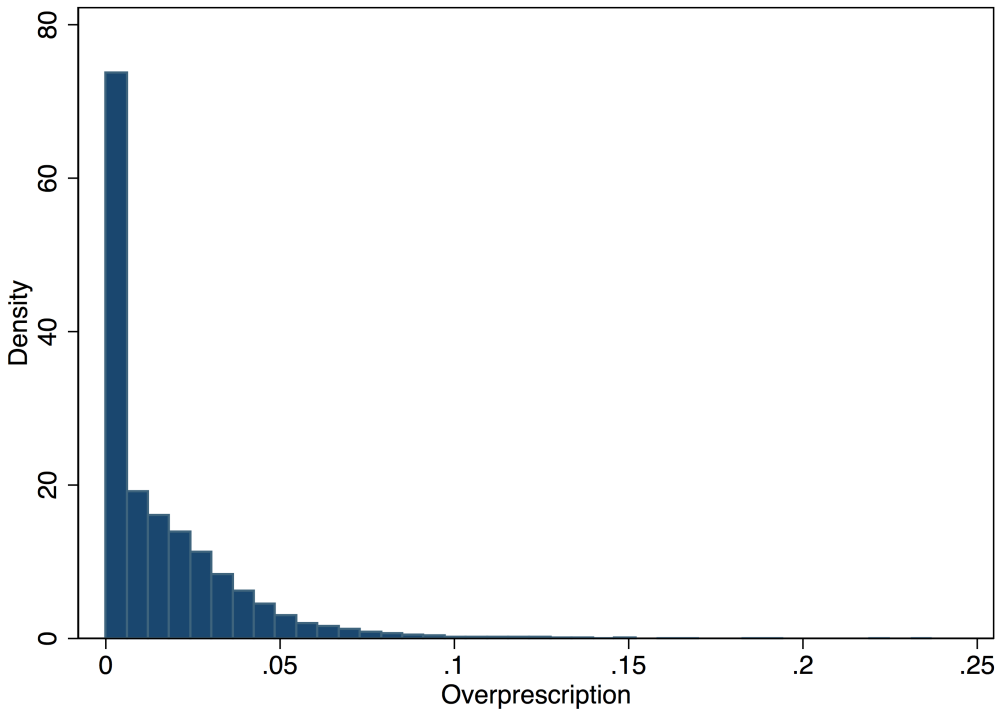


Figure 1: Physician Measure of Overprescription

Notes: Histogram of measure of overprescription at the physician level. Truncated at $TotalPatients > 8$ following Heckman (1981) and William H. Greene (2001)'s rule of thumb of eight observations per group for ability of small sample sizes to allow for meaningful estimates

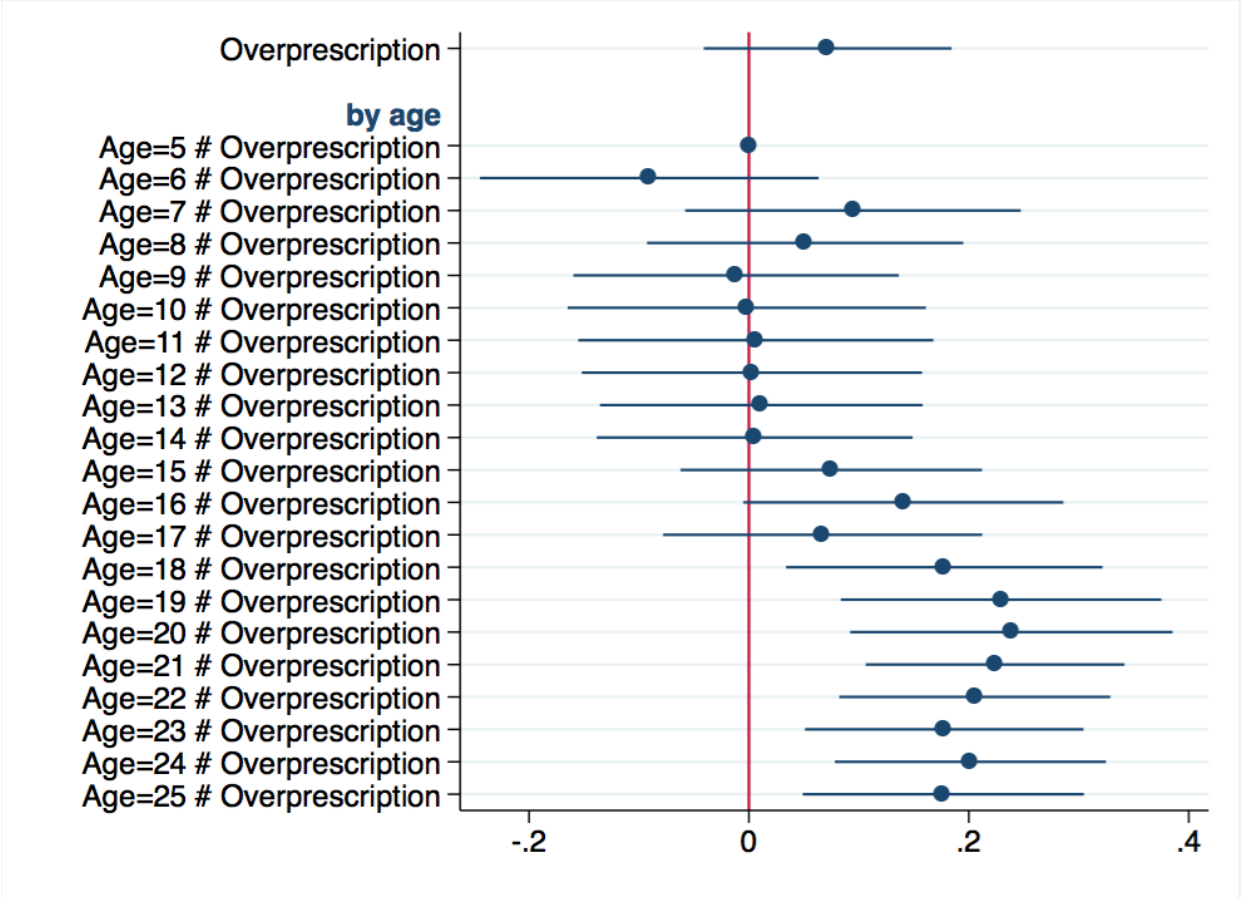
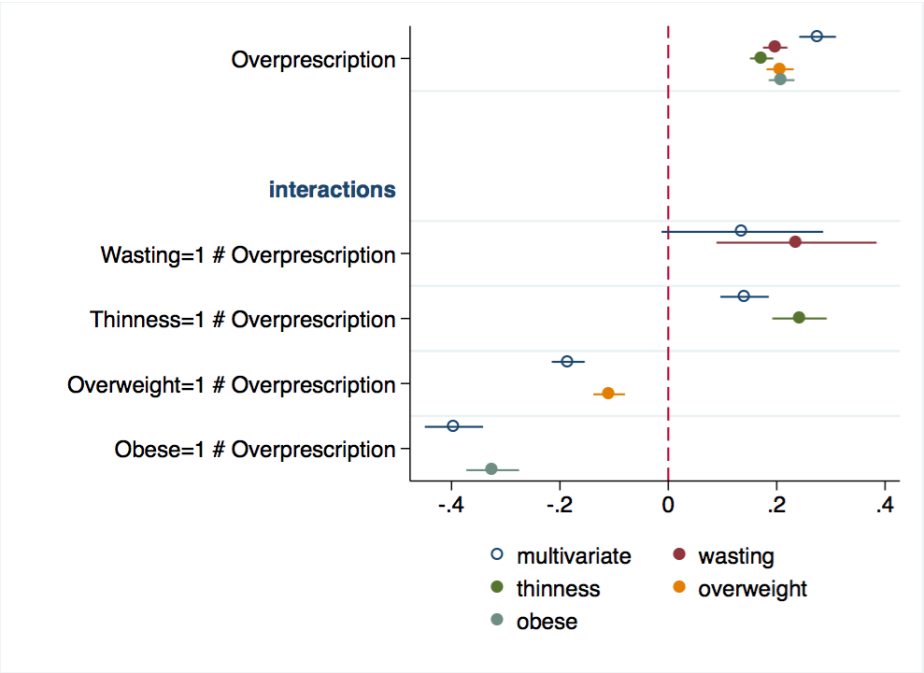


Figure 2: Effect by Age & Gender

Notes: Effects of interaction terms with patients' age and gender. Regressions include clinic and time fixed effects, as well as patient and doctor characteristics

Panel A: Instrumental Variable (Reduced Form Estimates)



Panel B: Patient Fixed-Effects

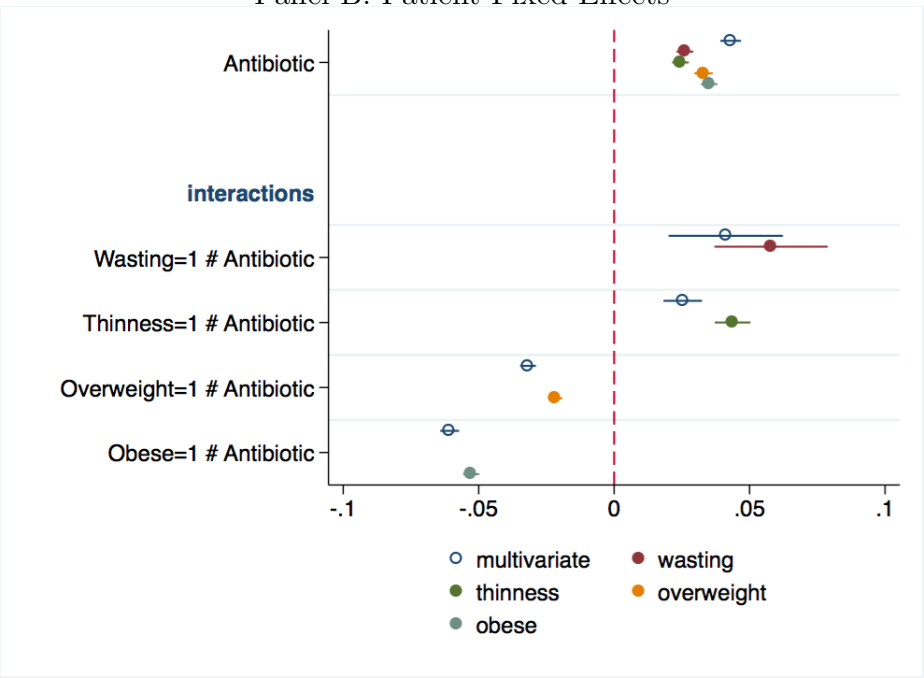


Figure 3: Effect by Original Nutritional Status

Notes: Effects of interaction terms with original nutritional status. Regressions include clinic and time fixed effects, as well as patient and doctor characteristics.

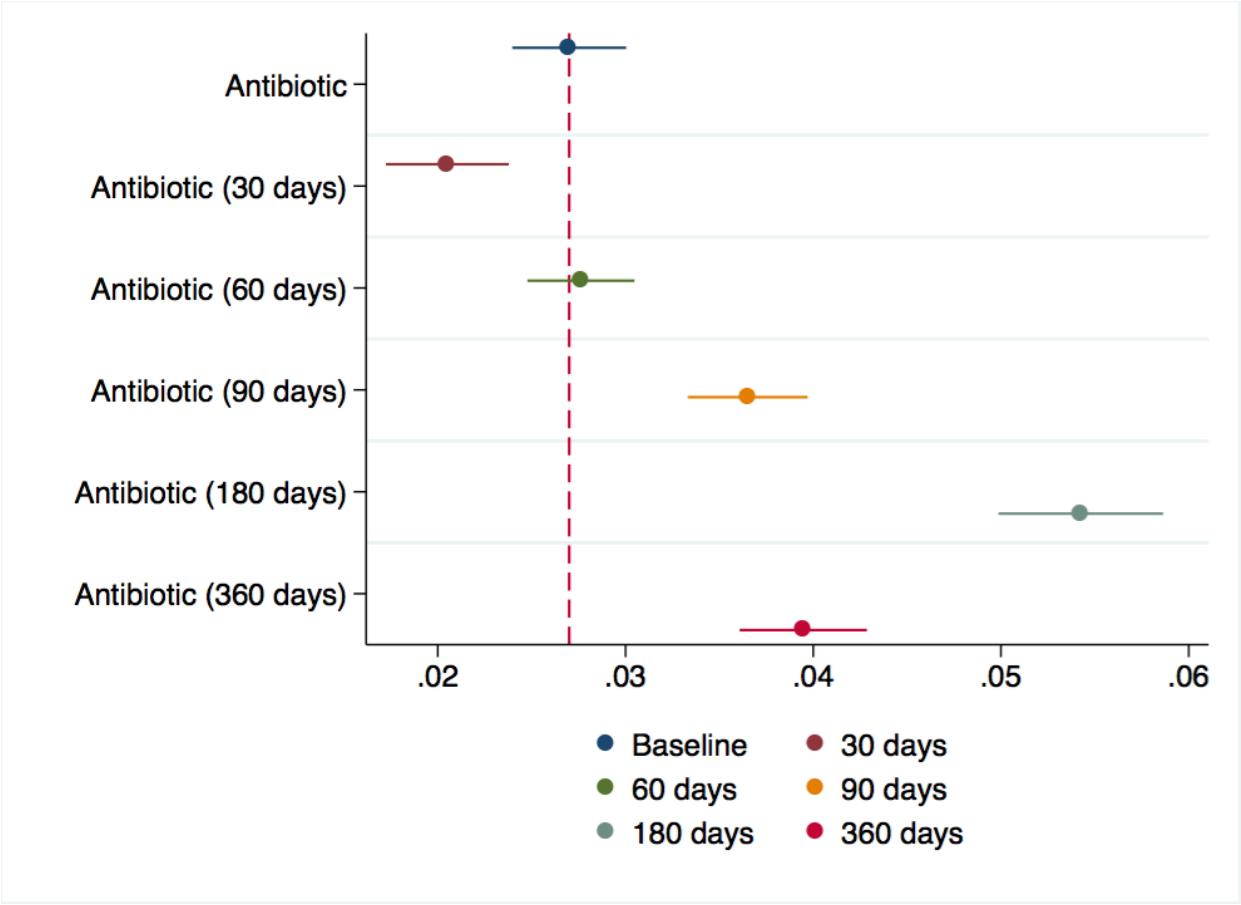


Figure 4: Fixed effects estimates: Effect of antibiotics prescribed over certain window frames

Notes: Effects of cumulative effect of antibiotic prescribed over the past x days. Regressions include clinic and time fixed effects, as well as patient fixed effects

6.2 Tables

Table 1: Summary Statistics
A. Doctor Characteristics—by level of overprescription

	high		low			
	Mean	Std. Dev.	Mean	Std. Dev.	Diff	t-test
Male (dr)	0.41	0.49	0.50	0.50	0.08***	(6.84)
Age (dr)	42.45	10.21	43.28	9.31	0.83***	(3.43)
Wage	4238.13	420.02	4346.10	470.27	107.98***	(9.84)
Pat. Age	10.45	2.07	11.56	5.35	1.11***	(12.03)
Pat. BMI	24.33	0.94	24.64	1.12	0.31***	(11.61)
Share Antibiotics	0.33	0.09	0.34	0.24	0.00	(0.21)
Share Viral Diag.	0.03	0.03	0.01	0.02	-0.02***	(-42.71)
Overprescription	0.03	0.02	0.00	0.00	-0.03***	(-90.16)
Observations	4,433		4,433		8,866	

B. Patient Characteristics—by antibiotic usage

	used antibiotics		never antibiotics			
	Mean	Std. Dev.	Mean	Std. Dev.	Diff	t-test
Age	16.80	5.55	18.70	4.43	1.89***	(180.56)
Male	0.41	0.49	0.41	0.49	-0.01***	(-5.43)
z-BMI	0.74	1.18	0.74	1.13	-0.00	(-0.62)
Stunting	0.10	0.30	0.11	0.31	0.01***	(20.05)
Wasting	0.01	0.11	0.01	0.10	-0.00***	(-7.27)
Thinness	0.06	0.23	0.05	0.23	-0.00***	(-9.50)
Overweight	0.27	0.44	0.28	0.45	0.01***	(7.43)
Obese	0.15	0.36	0.14	0.35	-0.01***	(-12.82)
Weight	56.57	18.40	61.33	15.67	4.77***	(133.91)
Height	154.53	16.24	159.21	12.17	4.69***	(155.66)
Syst. BP	108.85	11.51	109.25	10.29	0.41***	(17.90)
Diast. BP	70.43	8.09	70.65	7.41	0.22***	(13.56)
Diabetes	0.00	0.03	0.00	0.03	0.00	(1.37)
Glucose	90.65	18.11	91.14	18.67	0.49***	(2.62)
No. Visits	5.58	5.19	3.51	2.74	-2.07***	(-233.59)
No. Meds	2.02	0.93	1.07	1.00	-0.94***	(-477.73)
Antibiotic Rx	2.15	1.89	0.00	0.00	-2.15***	(-734.15)
Observations	546,290		414,562		960,852	

Notes: Doctors' (monthly) wage expressed in current 2013 Mexican Pesos. The PPP exchange rate at the time was of around 7.88 MXN per USD (OECD Data).

Table 2: Fist Stage Regressions: Overprescription is a Good Predictor of Antibiotic Use

	(1)	(2)	(3)
Overprescription	5.15***	5.12***	5.57***
	(0.157)	(0.161)	(0.169)
Mean dept. var.	1.22	1.22	1.22
No. patients	976,576	976,576	976,575
R-sq.	0.27	0.32	0.35
F-stat.	175.16	212.08	289.98
Indiv. X's	no	yes	yes
Doctor X's	no	no	yes

Notes: Dependent variable is the (cumulative) number of antibiotics received by the patient. Time and clinic fixed effects included. Standard errors clustered at the clinic level in parentheses. Patient characteristics include gender and age fixed effects. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis.
$^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 3: Antibiotic Use is Associated with a Higher BMI

	(1)	(2)	(3)	(4)	(5)	(6)
Antibiotic Rx	0.01***	0.01***	0.01***	0.05***	0.03***	0.03***
	(0.001)	(0.001)	(0.001)	(0.002)	(0.002)	(0.002)
Mean dept. var.	0.81	0.81	0.81	0.81	0.81	0.81
No. patients	960,852	960,852	960,852	960,852	960,852	960,852
Model	OLS	OLS	OLS	IV	IV	IV
Indiv. X's	no	yes	yes	no	yes	yes
Doctor X's	no	no	yes	no	no	yes

Notes: Dependent variable is patient BMI z-score at last appointment. Antibiotic Rx is the (cumulative) number of antibiotics received by the patient. Time and clinic fixed effects included. Std. errors clustered at the clinic level. Patient controls include gender and age fixed effects. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis. $^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 4: Effect on BMI. Alternative Specifications (IV)

	(1)	(2)	(3)	(4)	(5)
Antibiotic Rx	0.03***	0.10***	0.03***		0.01***
	(0.002)	(0.023)	(0.002)		(0.001)
Male	-0.14***	-0.13***	0.96***	-0.14***	-0.00**
	(0.005)	(0.006)	(0.024)	(0.005)	(0.001)
Male × Age			-0.11***		
			(0.003)		
Male × Age Sq.			0.00***		
			(0.000)		
No. Meds			-0.04***		
			(0.002)		
Ever Antib. Rx				0.23***	
				(0.011)	
Mean dept. var.	0.81	0.81	0.81	0.81	0.16
No. patients	960,852	960,852	960,852	960,852	960,852
Details	Baseline	Mean Overpres.	Additional X's	Rx Antibiotic {0,1}	y=obese

Notes: Dependent variable is patient BMI z-score at last appointment. Antibiotic Rx is the (cumulative) number of antibiotics received by the patient. Time and clinic fixed effects included. Std. errors clustered at the clinic level. All regressions include doctor controls (total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis). $^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 5: Effects on BMI: Patient Fixed Effects

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Antibiotic	0.027***	-0.013***	0.005***	0.035***	0.039***	0.003**	
	(0.002)	(0.004)	(0.002)	(0.002)	(0.002)	(0.001)	
Antib. × Age		0.002***					
		(0.000)					
Macrolide							0.010***
							(0.004)
Mean dept. var.	0.87	0.87	0.77	0.90	0.95	0.71	0.87
No. patients	970,017	970,017	294,989	675,028	570,771	399,247	970,017
N: patient - app't.	3,779,621	3,779,621	782,330	2,997,291	2,534,927	1,244,694	3,779,621
R-squared	0.91	0.91	0.91	0.90	0.89	0.92	0.90
Population	all	all	under 16	over 16	female	male	macrolides

Notes: Dependent variable is patient BMI z-score at last appointment. All regressions include patient and time fixed effects. Standard errors clustered at the clinic level in parentheses.
$^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 6: Reduced Form: Effects by Age & Gender

	(1)	(2)	(3)	(4)	(5)	(6)
Overprescription	0.23***	0.14***	0.30***	0.18***	-0.03	0.22***
	(0.015)	(0.010)	(0.016)	(0.011)	(0.033)	(0.015)
Male		-0.14***		-0.14***	-0.13***	-0.13***
		(0.005)		(0.005)	(0.005)	(0.006)
Age					-0.06***	
					(0.003)	
Overpres. × Age					0.01***	
					(0.002)	
Overpres. × Male						-0.11***
						(0.021)
Mean dept. var.	0.81	0.81	0.81	0.81	0.81	0.81
No. patients	960,852	960,852	960,852	960,852	960,852	960,852
R-squared	0.00	0.03	0.01	0.03	0.02	0.03
Indiv. X's	no	yes	no	yes	yes	yes
Doctor X's	no	no	yes	yes	yes	yes

Notes: Dependent variable is patients' BMI z-score. Time and clinic fixed effects included. Std. errors clustered at the clinic level. Patient controls include gender and age fixed effects. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis.
$^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 7: Reduced Form: Effect of Antibiotics on BMI by Baseline Nutrition

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Overprescription	0.18***	0.22***	0.30***	0.20***	0.17***	0.21***	0.21***	0.28***
	(0.011)	(0.013)	(0.016)	(0.011)	(0.011)	(0.013)	(0.012)	(0.017)
× Stunting o		-0.31***						
		(0.033)						
× z-BMI o			-0.17***					
			(0.008)					
× Wasting o				0.24***				0.14*
				(0.075)				(0.075)
× Thinness o					0.24***			0.14***
					(0.025)			(0.023)
× Overweight o						-0.11***		-0.18***
						(0.015)		(0.015)
× Obese o							-0.32***	-0.40***
							(0.025)	(0.027)
Mean dept. var.	0.81	0.81	0.81	0.81	0.81	0.81	0.81	0.81
No. patients	960,852	960,852	960,852	960,852	960,852	960,852	960,852	960,852
R-squared	0.03	0.03	0.77	0.08	0.17	0.13	0.33	0.65
Indiv. X's	yes	yes	yes	yes	yes	yes	yes	yes
Doctor X's	yes	yes	yes	yes	yes	yes	yes	yes

Notes: Dependent variable is the patients BMI z-score. Time and clinic fixed effects included. Std. errors clustered at the clinic level. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis. $^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 8: Fixed-Effects: Effects on BMI by Baseline Nutrition

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Antibiotic	0.027***	0.035***	0.028***	0.026***	0.024***	0.033***	0.035***	0.043***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
× Male		-0.025***						
		(0.001)						
× Stunting o			-0.004*					
			(0.002)					
× Wasting o				0.058***				0.041***
				(0.011)				(0.011)
× Thinness o					0.044***			0.025***
					(0.003)			(0.004)
× Overweight o						-0.022***		-0.032***
						(0.001)		(0.001)
× Obese o							-0.053***	-0.061***
							(0.002)	(0.002)
Mean dept. var.	0.87	0.87	0.87	0.87	0.87	0.87	0.87	0.87
No. patients	970,017	970,017	970,017	970,017	970,017	970,017	970,017	970,017
N: patient - app't.	3,779,621	3,779,621	3,779,621	3,779,621	3,779,621	3,779,621	3,779,621	3,779,621
R-squared	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91

Notes: All regressions include patient and time fixed effects. Standard errors clustered at the clinic level in parentheses.
$^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 9: IV: Effect on BMI controlling for changes in patients' physicians

	(1)	(2)	(3)	(4)
Antibiotic Rx	0.03***	0.05***	0.07***	0.03***
	(0.002)	(0.003)	(0.008)	(0.002)
Mean dept. var.	0.81	0.81	0.79	0.82
F	1,096	1,388	706	1,103
No. patients	960,852	960,852	243,255	717,597
Instrument		dr. at t=0		
Sample	all	all	no Δ dr	ever Δ dr

Notes: Dependent variable is patient's BMI z-score on last appointment. Antibiotic Rx is instrumented by doctor's measure of overprescription. Time and clinic fixed effects included. Std. errors clustered at the clinic level. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis. $^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

Table 10: Effect is stronger when antibiotics are misprescribed

	(1)	(2)	(3)	(4)	(5)	(6)
Antibiotic Rx (for viral)	0.01	-0.00	0.00	0.70***	0.43***	0.48***
	(0.005)	(0.004)	(0.004)	(0.056)	(0.035)	(0.033)
Mean dept. var.	0.81	0.81	0.81	0.81	0.81	0.81
No. patients	960,852	960,852	960,852	960,852	960,852	960,852
Model	OLS	OLS	OLS	IV	IV	IV
Indiv. X's	no	yes	yes	no	yes	yes
Doctor X's	no	no	yes	no	no	yes

Notes: Dependent variable is patient's BMI z-score on last appointment. Antibiotic Rx is the (cumulative) number of antibiotics received by the patient when main diagnosis was viral. Time and clinic fixed effects included. Std. errors clustered at the clinic level. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis. $^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

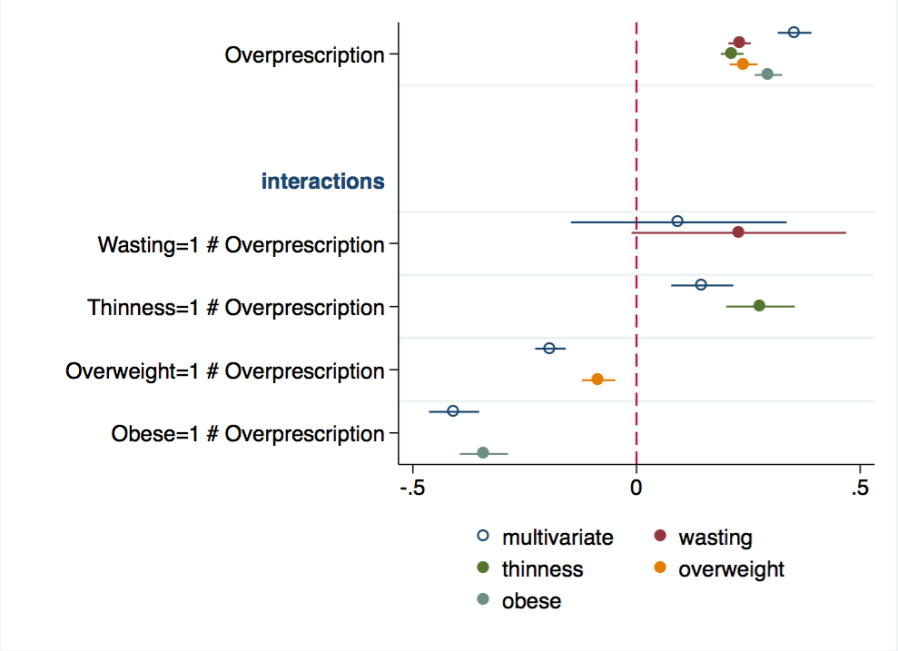
Table 11: The effect of antibiotics on other health outcomes

	(1) z-BMI	(2) Glucose	(3) Diabetes	(4) Syst. BP	(5) Diast. BP
Overprescription	0.179***	4.474***	0.004***	-0.123	-0.239
	(0.011)	(0.996)	(0.000)	(0.213)	(0.150)
Mean dept. var.	0.810	91.344	0.001	109.401	70.768
No. patients	960,852	54,623	976,575	976,575	976,575
R-squared	0.03	0.08	0.00	0.06	0.05

Notes: Dependent variables relate to patients' health outcomes on last appointment. Time and clinic fixed effects included. Std. errors clustered at the clinic level. Doctor controls include total patients, patients' BMI (mean), age (mean), share (non-bacterial) respiratory diagnosis.
$^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$

A Appendix Figures

Panel A: Effects by Baseline Nutrition—Girls



Panel B: Effects by Age—Girls

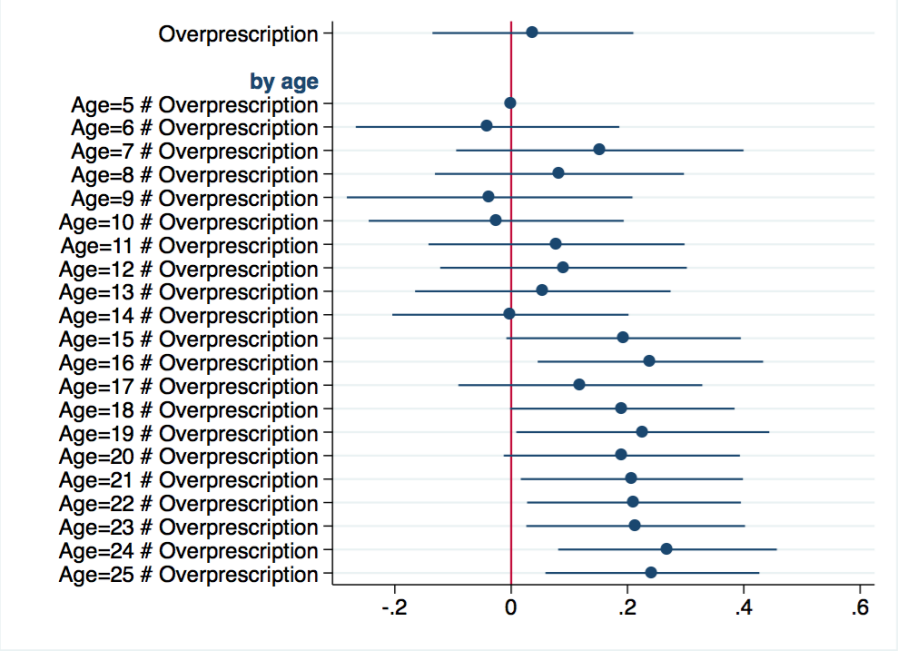


Figure A.1: Effect Nutritional Status & Age: Girls

Notes: Effects of interaction terms with original nutritional status. Regressions include clinic and time fixed effects, as well as patient and doctor characteristics. Reduced Form Estimates

B Appendix Tables

Table A.1: Patient characteristics (SAMPLE)—by distinct doctors seen

	Δ Dr.		no Δ Dr.		Diff	
	Mean	Std. Dev.	Mean	Std. Dev.	Diff	t-test
Age	17.40	5.28	18.02	5.01	0.62***	(5.10)
Male	0.39	0.49	0.44	0.50	0.05***	(4.34)
z-BMI	0.72	1.17	0.75	1.16	0.03	(1.28)
Stunting	0.11	0.32	0.09	0.29	-0.02**	(-2.38)
Wasting	0.01	0.11	0.01	0.10	-0.00	(-0.66)
Thinness	0.06	0.24	0.06	0.23	-0.01	(-1.15)
Overweight	0.28	0.45	0.28	0.45	0.00	(0.17)
Obese	0.14	0.34	0.14	0.35	0.00	(0.43)
Weight	57.74	17.71	60.08	16.76	2.34***	(5.70)
Height	155.78	15.18	158.01	14.20	2.23***	(6.36)
Syst. BP	109.02	10.80	109.30	10.86	0.28	(1.11)
Diast. BP	70.53	7.69	70.96	7.65	0.43**	(2.39)
Diabetes	0.00	0.04	0.00	0.05	0.00	(0.72)
Glucose	94.16	27.13	89.55	21.72	-4.60	(-1.50)
No. Visits	5.19	4.75	2.93	1.90	-2.26***	(-22.88)
No. Meds	1.64	1.02	1.42	1.19	-0.22***	(-8.97)
Antibiotic Rx	1.43	1.89	0.52	0.89	-0.91***	(-22.97)
Observations	7,177		2,429		9,606	

Notes: "Δ Dr." includes patients that saw more than one doctor, while "no Δ Dr." only includes patients that were always treated by the same physician. $^{*}p < 0.1,^{**}p < 0.05,^{***}p < 0.01$